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Journal of the Anatomical Society of India (ISSN: Print 0003-2778) is peer-reviewed journal. The journal is owned and run by Anatomical Society of India. The journal publishes research articles related to all aspects of Anatomy and allied medical/surgical sciences. Pre-Publication Peer Review and Post-Publication Peer Review Online Manuscript Submission System Selection of articles on the basis of MRS system Eminent academicians across the globe as the Editorial board members Electronic Table of Contents alerts Available in both online and print form. The journal is published quarterly in the months of January, April, July and October.

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continued...

Enteric Nervous System: Gastrointestinal and Neurological Disorders

Introduction

The enteric nervous system (ENS) is the largest and the most complex unit of the peripheral nervous system.

Actually, it is a web of sensory neurons, motor neurons, and interneurons embedded in the wall of the gut extending from the esophagus to the rectum. It consists of about 200–600 million neurons releasing a huge number of neurotransmitters to facilitate motor sensory, absorptive, and secretory functions of the gastrointestinal tract (GIT). It is unique in the sense that it can orchestrate and regulate gastrointestinal activities independent of the central nervous system (CNS); hence, it is called as "second brain or gut brain."[1]

Location and Function

The ENS is divided into two components:

Submucosal plexus (Meissner's plexus) and myenteric plexus (Auerbach plexus).

The Meissner's plexus is located in the submucosa, while the myenteric plexus is located between the circular and longitudinal layers of smooth muscle fibers in the gut wall.

Both these plexus are made up of sensory and motor neurons. Principally, the Meissner's plexus is responsible for glandular secretion, while the myenteric plexus is responsible for gastric motility.[2]

Development and Colonization of the Gut by Microbes

The neural network of ENS is laid down during the first trimester of pregnancy but continues to go modifications throughout the pre- and postnatal life under the influence of normal microbes of the gut.

The colonization of the gut occurs by trillions of microbiota/microorganisms, namely, bacteria, which not only affects the development but also the functionality of ENS.[3]

These microorganisms live in symbiotic relationships within the gut throughout life and are called resident microbes. They synthesize Vitamin K, thiamine, folate, and riboflavin, aid in digestion, and promote angiogenesis. They further prevent the colonization of the gut by pathogenic transient microbes.

Functions

The sensory functions of ENS involve processing a range of sensations, such as the nature of gut contents and gut distension, and integrate this information with input from the autonomic nervous system to optimize the muscular and secretory activity of the GIT.

The motor functions of ENS include: propulsion of food, nutrient handling, regulation of blood flow, and immune defense.

Gut Brain – Axis

The gut–brain axis is a network of communication between ENS and CNS. The connections between ENS and CNS occur through vagus nerves, pelvic nerves, and sympathetic pathways.

This links peripheral intestinal function with the emotional and cognitive centers of the brain.[4] This neuronal network is not only anatomical but also responsible for endocrine, humoral, metabolic, and immune routes of communication.

Disorders Caused by Enteric Nervous System

- Gastrointestinal disorders: due to involvement of ENS are well established
  These include: functional constipation, irritable bowel syndrome, gastroparesis, achalasia, functional constipation, bloating of the abdomen, and diarrhea.
- Neurological Disorders: Due to the involvement of ENS, namely, anxiety, depression, dementia, and Alzheimer's disease, have been implicated in recent research.[5]

Treatment

It is based on the following two factors:

- The presence of receptors on neurons of ENS for enteric hormones (namely, cholecystokinin, glucagon-like peptides-1 receptor, gastric inhibitory polypeptide, and gastrin) provides clues for future therapies to get rid of a broad range of GIT disorders
- Dependency of ENS on normal bacterial flora of the GIT
- The health of normal microbiota/microorganisms of GIT is dependent on the nature of the food we take.

If the food is rich in probiotics, the normal bacterial flora (resident microorganisms) flourishes, and GIT functions normally; however, if unhealthy food is taken, the functions of GIT get deranged due to the colonization of transient pathogenic microbes on the surface of GIT. This leads to various types of GIT disorders.

Furthermore, microorganisms influence the production of various chemical substances that constantly carry messages from the gut to the brain, leading to the production of dopamine and serotonin. Dopamine is responsible for feeling pleasure, satisfaction, and motivation, while

serotonin makes you feel more focused, emotionally stable, happier, and calmer. The deficiency of these hormones leads to anxiety, depression, insomnia, and mood disorders.

Thus, changing the residential gut microbes may improve or potentially treat gastrointestinal and brain disorders.

Therefore, nowadays, clinicians have started advising patients to take food rich in probiotics, namely, yogurt, or probiotic capsules.

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Original Article

Comparison of Variability in duration of Aluminum-induced Neurodegeneration and Treatment with *Ficus religiosa* Leaf Extract in Male Wistar Rats

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Abstract

Introduction: Aluminum (Al) is a known neurotoxic which is found in air, food and utensils, medicinal preparations, etc., *Ficus religiosa* (FR) is known as the peepal tree which is worshipped by people at large and has many medicinal importance. The objective of the study is to compare the Al groups of different durations and the treatment groups with FR leaf extract in male Wistar rats. **Materials and Methods:** In this study, we have taken seven groups of male albino Wistar rats, six in each. Group 1 was normal control group. Groups 2 and 3 were induced groups and Groups 4–7 are treated groups. On the last day of treatment, the brain of the animals was removed, and histology slides were prepared, and viable neurons were counted using software. For behavioral analysis, the passive avoidance test was carried out. Here, the treated Groups 4 and 5 are the groups in which the leaf extract of FR was given after treating with Al for 25 days and for Groups 6 and 7, given after treating with Al for 45 days. The comparison of different durations of the Al groups and treated groups was carried out based on neuronal count in CA3 region of hippocampus. **Results:** We have observed the neurodegeneration in all regions of hippocampus including dentate gyrus, but mainly, the neurodegeneration was observed in CA3 region of hippocampus. In both the parameters, there was no significant difference observed in terms of change of duration of Al ($P > 0.05$). The neurodegeneration observed in both Al groups was the same. The effect of treatment was observed a similar improvement in all treated groups even after in change in duration of Al ($P > 0.05$). **Conclusion:** Aluminium induced neurodegeneration in rat's brain in both higher and lower duration and in both cases Ficus religiosa treated effectively against neurotoxicity of Al.

Keywords: *Aluminum, CA-3 region, Ficus religiosa, hippocampus, neurodegeneration, neurotoxicity*

Introduction

Aluminum (Al) is a neurotoxic metal which is known to the world. The accumulation of Al in the brain mainly occurs in hippocampus which leads to neurodegeneration.[1] After accumulation of Al in brain, there is generation of free radicals which leads to memory loss and behavioral alteration.[2,3] Enas[4] demonstrated Al chloride ($AlCl_3$)-induced dementia in rats (300 mg/kg bw) when administered for a month. Al can cross blood–brain barrier by certain receptors opined by Roskams and Connor.[5] Al causes the inflammation in brain which leads to loss of memory.[6]

The traditional use of *Ficus religiosa* (FR) was reported by Vinutha *et al*. for the management of Alzheimer's disease (AD).[7] Aiyegoro and Okoh (2010) warrant a thorough research for the competency of FR against neuroinflammatory, neuropsychiatric, and cardiovascular disorders, as well as oxidative stress-related disorders.[8] The leaf extract of FR inhibited/reduced the production of pro-inflammatory cytokines in brain, as discovered by Makhija *et al*.[9]

In this study, we have induced neurodegeneration by $AlCl_3$ and compared the same dose of Al in different durations. After the treatment was given by FR leaf extract, all groups have been compared by behavioral study, histological slides, and neuronal count.

There are many studies have been done on Al neurotoxicity and on the effectiveness of FR leaf extract, but the comparative study of different doses of $AlCl_3$ in rats with treatment comparison to check the effect of it has not been observed.

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Materials and Methods

Animals

Around 3-month-old male albino *Wistar* rats, which are in-house bred and weighing 250–300 g (at the start of the study), were used. Rats were fed with water and food *ad libitum*. The rats were maintained under controlled conditions of light-dark cycle (12:12), temperature (22°C ± 3°C), humidity (approximately 50% ±10%), and pathogen-free environment. Rats were housed in polypropylene cage and for bedding paddy husk as bedding material was used for housing the rats. The institutional animal ethics committee's approval for the pilot study and for the full study was obtained before starting with the experiment. The experiment was carried out in accordance with the guidelines of the Government of India for the use of laboratory animals.[10]

Animal groups

Rats were divided into 7 groups with 6 rats ($n = 6$) in each group. All groups of rats were given Al and FR leaf extract per oral. The groups of rats were as follows:

- Group 1: Control group
- Group 2: Rats received 100 mg/kg body weight of $ALCL_3$ for 25 days
- Group 3: Rats received 100 mg/kg body weight of $ALCL_3$ for 45 days
- Group 4: Rats received 100 mg/kg body weight of $ALCL_3$ for 25 days followed by 200 mg/kg FR leaf extract for 15 days
- Group 5: Rats received 100 mg/kg body weight of $ALCL_3$ for 25 days followed by 300 mg/kg FR leaf extract for 15 days
- Group 6: Rats received 100 mg/kg body weight $ALCL_3$ for 45 days followed by 200 mg/kg of FR leaf extract for 15 days
- Group 7: Rats received 100 mg/kg body weight $ALCL_3$ for 45 days followed by 300 mg/kg FR leaf extract for 15 days.

On the last day of treatment, animals were anesthetized by sodium pentobarbital and then perfused and fixed with 10% formaldehyde.

Leaf extract of *Ficus religiosa*

"FR" leaves were initially washed with water, dried over the shad for 1 month, and made into a coarse powder form using the grinder. Then, the obtained coarse powder of leaves was placed in a Soxhlet apparatus with ethanol, which was then heated to reflux. Ethanol was used as a solvent in a ratio of 1:1 along with distilled water. The heater of Soxhlet apparatus was set at 50°C and extraction procedure was performed for 3 days with approximately 50 cycles. The silicon metallic balls were added on a daily basis to identify the increased temperature. The extract was heated with Bunsen burner to evaporate ethanol from the extract. The total dry extract was amounting to a yield of approximately 7%. This extract was kept in a refrigerator (about 4°C) for further use.

Histological study

Cresyl violet stain was used to stain the slides of hippocampus of the rat's brain as it is a reliable stain to study the morphological changes in the neurons since it highlights the structural features of the neurons. This stain is often used to count the number of nerve cells. It demonstrates chromatolysis, swelling of the perikaryon, and eccentricity of the nucleus of degenerating neurons.

Scoring

For capturing images and counting the normal neurons, two software were used. After mounting the stained slides, the slides focused using compound trinocular microscope attached with monitor and installed NIS/VUE software (NIS elements software- Nikon corporation company from Japan), (VUE software- Visual understanding environment developed by Evan You from China). The slides were screened using a light microscope at ×20 magnification. The six transverse sections from rat's hippocampus were cut using microtome and CA 3 (Cornua Ammonis) area among different areas of hippocampus was selected for counting the neurons (pyramidal cells) by using software. The cell counts were expressed as the number of cells per unit length of the cell field cells/300 μm length from CA3 region of hippocampus.

Behavioral study

In this study, passive avoidance test was chosen for behavioral study to test the memory retention in rats.[11] Passive avoidance apparatus consists of a wooden box with a larger, bright compartment and a smaller, dark compartment with grid floor, which is attached to a shock source. On the 1st day of test, rats were allowed to explore both chambers for 5 min. This was followed by three test trials of 5 min each. In each trial, fraction of time spent in each compartment was measured. In the 4th trial, as soon as rats stepped into dark compartment, a foot shock was given, and the rat was replaced to home cage. After 1 day, rats were placed in the test chamber and latency to enter the dark compartment was measured. Normal rats avoid entering the dark chamber, where they received shock on previous day, suppressing their normal behavior of exploring the dark compartment. Decreased latency to enter the dark compartment suggests poor memory retention.

Results

In this comparitive study, we have compared two Al groups (G2vsG3), two FR groups (treated with 200mg) (G4vs G6), two FR groups (treated with 300mg) (G5vs G7). For comparison of these we have used analysis of variance with Tukey's test as stastical tool.

Passive avoidance test

The result of passive avoidance test shows the latency to enter into dark chamber has deceased in Al-treated rats of both groups (G2 and G3) with different durations compared to control group, but when compared to two Al-induced groups, the result is almost same ($P > 0.05$) [Figure 1]. The treatment groups showed an improvement in retention of memory ($P < 0.001$). When treated groups G4 compared with G6 and G5 compared with G7, no significant difference was noted in latency period ($P > 0.05$).

Neuronal count

We have observed the neurodegeneration in all regions of hippocampus including dentate gyrus (DG), but mainly, the neurodegeneration was observed in CA3 region of hippocampus. The degeneration of the neurons was identified by counting viable neurons in CA3 region of hippocampus and compared with all the groups. The counting of neurons in control group and induced groups (G2 and G3) suggest degeneration of neurons in Al groups (G1vs G2 and G3) ($P<0.001$). Whereas both induced groups comparison has not shown significant result in term of neuronal damage ($P>0.05$) [Figure 2]. The treated groups have shown a significant improvement ($P < 0.001$) compared to induced groups in neuronal counting. When the neuronal count of G4 versus G6, and G5 versus G7, was compared, there was no significant difference ($P > 0.05$).

Figure 3 shows H- and E-stained slides in which Group 1 shows the normal neurons (pyramidal cells). When compared with different durations of $AlCl_3$ 25 days and 45 days, the neurodegeneration was found to be the same in quality as well as quantity. The treated groups have shown more number of and quality of neurons improved compared to Al groups [Figures 3-5].

Discussion

There have been many studies done on Al effectiveness in different dosages for inducing neurodegenerative diseases such as AD, Huntington's disorder, and Parkinson's disease (PD), but there was no study found, which compares the effectiveness of different doses of Al in rats. The different dosages of Al were used to induce neurotoxicity in rats with different durations. Al-Balawi *et al*.[12] have used Al, 100 mg/kg/b.w. in male Wistar rats for 30 days and they could observe the neuronal damage in the hippocampus. The Al was used orally 100 mg/kg/b.w. in albino Wistar rats by many authors to induce the neurodegeneration.[13-16] In the present study, we used 100 mg/kg/b.w. dose of Al in the duration of 25 days and 45 days and compared its effectiveness and also with the treatment with FR leaf extract, given in the same duration and in the same dosage. The dose of Al which was given 25 days in our previous study[17] is compared with 45 days duration here.

It has been noted that accumulation of Al in brain leads to amyloid deposition as it affects the antioxidative defense mechanism by forming the reactive oxygen species (ROS), which in turn reduces the normal antioxidant defense mechanism.[18] Al has shown both types of neuronal cell death, necrosis as well as apoptosis.[19] Liaquat *et al*. observed that Al along with D-gel produces Alzheimer-like

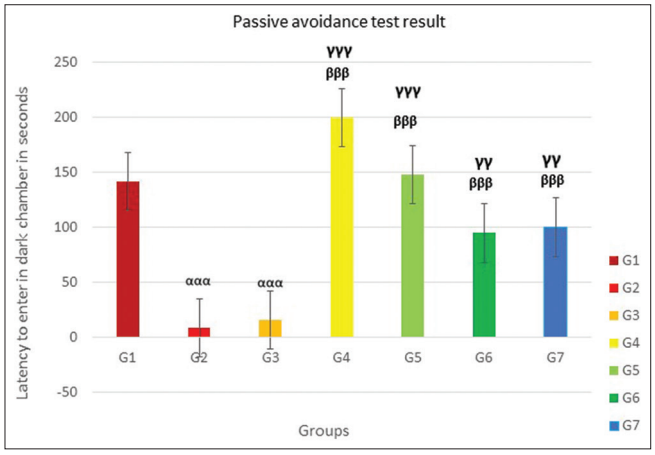

Figure 1: Comparison of passive avoidance test result in all groups. G1 versus G2 *P* < 0.001, G1 versus G3 *P* < 0.001, G2 versus G3 *P* < 0.001, G2 versus G4 *P* < 0.005, G2 versus G5 *P* < 0.001, G3 versus G6 *P* < 0.005, G4 versus G5 *P* < 0.001, G6 versus G7 *P* < 0.001. The comparison with G1 shows as "α," with G2 shows "β," G3 shows as "γ," with G4 shows as "δ." Group 1: Control group. Group 2: Induced group (aluminum [Al] for 25 days). Group 3: Induced group (Al for 45 days). Group 4: Treated group (Al for 25 days followed by *Ficus religiosa* [FR] leaf extract 200 mg/kg for 15 days). Group 5: Treated group (Al for 25 days followed by FR leaf extract 300 mg/kg for 15 days). Group 6: Treated group (Al for 45 days followed by FR leaf extract 200 mg/kg for 15 days). Group 7: Treated group (Al for 45 days followed by FR leaf extract 300 mg/kg for 15 days)

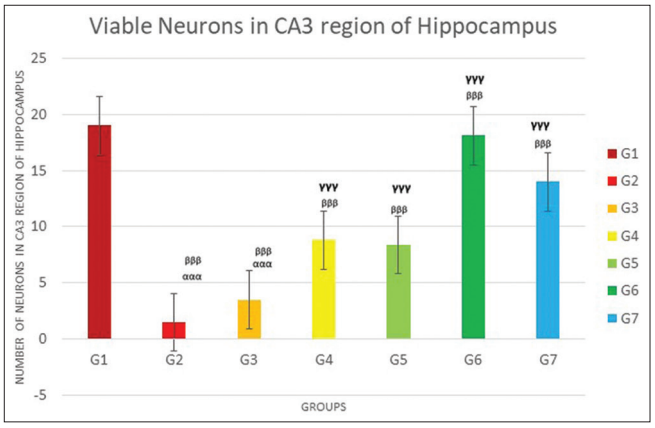

Figure 2: Comparison of neuronal count result in all groups in CA3 region of Hippocampus. G1 versus G2 *P* < 0.001, G1 versus G3 *P* < 0.001, G2 versus G3 *P* < 0.001, G2 versus G4 *P* < 0.001, G2 versus G5 *P* < 0.001, G3 versus G6 *P* < 0.001, G4 versus G5 *P* < 0.001, G6 versus G7 *P* < 0.001. The comparison with G1 shows as "α," with G2 shows "β," G3 shows as "γ," with G4 shows as "δ." Group 1: Control group. Group 2: Induced group (aluminum [Al] for 25 days). Group 3: Induced group (Al for 45 days). Group 4: Treated group (Al for 25 days followed by *Ficus religiosa* [FR] leaf extract 200 mg/kg for 15 days). Group 5: Treated group (Al for 25 days followed by FR leaf extract 300 mg/kg for 15 days). Group 6: Treated group (Al for 45 days followed by FR leaf extract 200 mg/kg for 15 days). Group 7: Treated group (Al for 45 days followed by FR leaf extract 300 mg/kg for 15 days)

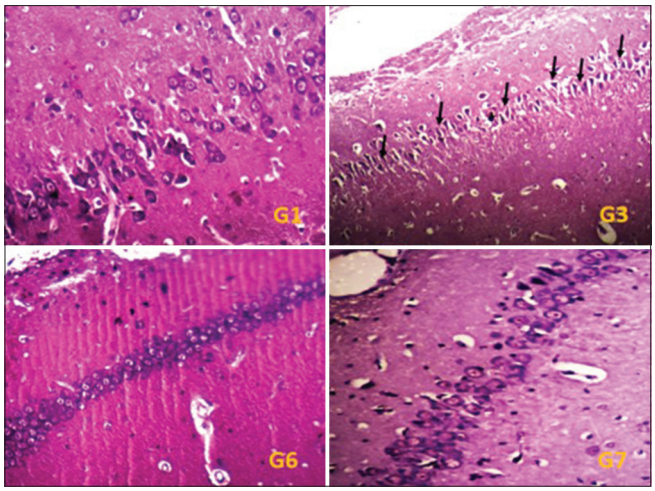

Figure 3: The hematoxylin and eosin slides (×20 magnification) of CA3 region in different groups. Black arrows showing the degenerated neurons in CA3 region. G1 = Control group, Group 3 = Aluminum given for 45 days, Group 6 = Treated group (*Ficus religiosa* [FR] leaf extract 200 mg/kg), Group 7: Treated group (FR leaf extract 300 mg/kg)

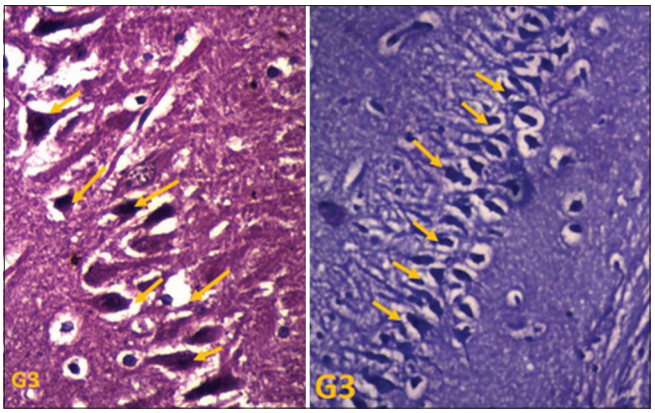

Figure 4: The H- and E-stained slide of aluminum-induced neurodegeneration (left side) and cresyl violet-stained slide (right side) (×40 magnification) of CA3 region of hippocampus in male Wistar rats. Yellow arrows showing the degenerated neurons

symptoms in the rats and can be used to induce AD in animal models, as it has increased the acetylcholinesterase and lipid peroxidase levels in the brain and altered the antioxidant activity.[20] Maya *et al*. observed that Al causes neurotoxicity by alteration of various pathways such as DNA binding, increased ROS production, and reduced antioxidants. Furthermore, Al toxicity can lead to cross-linking of DNA strands.[21] Al-induced neurotoxicity was observed in dogs and rabbits, the hind limb weakness was observed in rabbits, and convulsion was noticed in dogs.[22] Klatzo *et al*. noted convulsions, ataxia, and degeneration of neuronal fibrils, when Al was injected in the rabbits through the cisterna magna or directly into the cerebrum within 2 weeks.[23] The Al accumulation was noted in brain, when the injection was given repeatedly, and this resulted in lower eye blink reflex.[24-26] Similar behavioral changes were seen in human AD subjects.[27-29] AL can enter in our body by inhaling dust, which contains AL and welding fumes which contain Al particles and aluminium oxide.[30] As per the observation by Julka *et al*., the behavioral disorders in which specific neurotransmitters got impaired are associated with the memory loss and motor dysfunctions. In their laboratory, cholinergic dysfunction was found due to the acute and subacute exposure to the Al.[31] The brain cholinergic system was found to be involved in the mechanisms of learning and memory,[32] and the damage to them was found in neurodegenerative diseases[33] which are well known. Loss of memory is one of the first and most consistent symptoms of neurodegenerative diseases such as AD and dialysis encephalopathy.[34] The pathological changes are seen in the hippocampus, a brain region which contains the cholinergic neurons.[35]

The Al-induced neurodegeneration happens by different mechanisms. The Al promotes the formation and accumulation of insoluble β-amyloid protein in the brain. It also promotes the aggregation of hyperphosphorylated tau protein. The deficits of cortical cholinergic neurotransmission, which is associated with Alzheimer's disease, are imitated by Al. Al increases iron-induced oxidative injury. The Al toxicity to humans, animals, and plants may share the same mechanisms. The Al-induced increase in iron-induced free radical generation and disruption of calcium regulation may constitute some of the primary molecular mechanisms of Al-induced neurotoxicity.[36]

Ficus belongs to Moraceae family and is one of the largest trees in the plant kingdom. *Ficus* has two major species, namely FR and *Ficus benghalensis*, which are found abundantly in most Asian countries, including Malaysia. *Ficus* species possessed a broad range of biological properties, including the anti-inflammatory, antioxidants, antitumor, antidiabetic, anticancer, antiproliferative, antimicrobial, antimutagenic, hepatoprotective, anti-helminthic, anticoagulant, antistress, wound healing, toxicity studies, immunomodulatory activities as well as mosquitocidal effects. FR is used in the treatment of convulsion in traditional treatment.[37] Aqueous aerial root extract of FR produced a significant dose-dependent anticonvulsant activity.[38] Bhangale *et al*. have shown a promising effect of FR on Huntington's rat model.[39] The methanolic extract of figs of FR exhibited anticonvulsant activity in a dose-dependent manner against maximum electroshock and picrotoxin-induced seizures.[40] Petroleum ether extract of FR leaves exhibited a beneficial effect in animal models of PD.[41] An anti-inflammatory activity of methanolic extract of FR leaves was reported by Makhija *et al*.[9]

The aqueous aerial root of FR showed anticonvulsant effect dose dependently in maximal electroshock and pentylenetetrazole-induced seizure in mice.[38] The protective effect of FR was observed against haloperidol-induced catalepsy by Bhangale *et al*.[39] Chronic oral administration

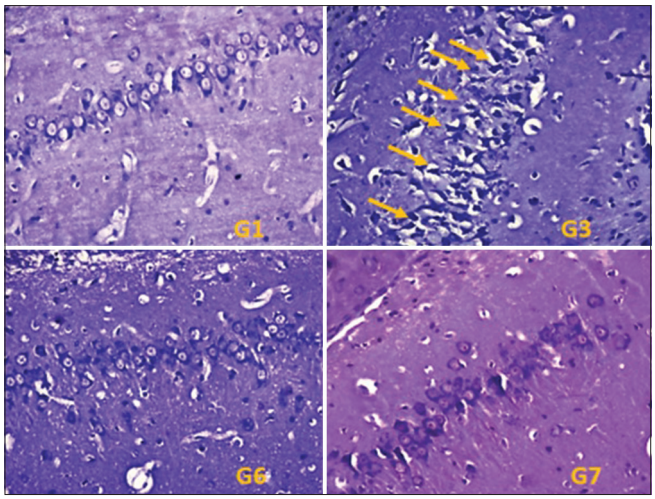

Figure 5: Cresyl violet-stained slide (×20 magnification) of CA3 region of hippocampus in male Wistar rats. Yellow arrows showing the degenerated neurons. G1 = Control group, Group 3 = Neurodegeneration induced by aluminum in 45 days, Group 6 = Treated group (*Ficus religiosa* [FR] leaf extract 200 mg/kg), Group 7 = Treated group (FR leaf extract 300 mg/kg)

of ether extract of FR leaves demonstrated significant anti-Huntington capacity.[40] Methanolic extract of FR figs improved memory in a dose-dependent manner against the scopolamine-induced anterograde and retrograde amnesia.[42]

The Hippocampus which is encoding information is a part of limbic system and play very important role in retention of short and long term memories. It plays a very important role in pathological conditions in AD, epilepsy, and intellectual disability. It is divided into DG and cornu ammonis (CA) regions. The DG has fascia dentate and hilus. The CA has CA1, CA2, and CA3-fields. The hippocampus has other areas such as presubiculum, subiculum, parasubiculum, and entorhinal cortex.[43] The hippocampus develops on the telencephalon, which is a subdivision of the neural tube of the embryo. The telencephalon gives rise to the cerebral cortex and hippocampus once it is polarized by signals from tissues from surrounding regions into the dorsal pallium.[44,45] Hippocampus has the hippocampus proper and four regions of CA, namely cornu ammonis 1, cornu ammonis 2, cornu ammonis 3, and cornu ammonis 4.[46] The neuronal layer in brain is the pyramidal cell layer, which is densely packed in CA1 region of hippocampus and less in number in the CA3 and CA2 regions. Neurons in CA3 region can be variable in size whereas in CA1 tend to be smaller and more uniform in comparison to neurons in the CA3 region. The various aspects of the neurons fill the CA subfields with a heterogeneous structure. The regions of hippocampal formation are linked unidirectionally and starting from entorhinal cortex to DG and CA3 regions through perforant pathway.[47] The hippocampus is a part of the brain, which is vulnerable for neuron degeneration due to hypoxia, ischemia, seizure, and hypoglycemia. This susceptibility of hippocampus has inspired significant research.[48]

The neurodegeneration, which occurs in the hippocampus, causes loss of memory as the hippocampus has a very important role in the constitution of memory. The memory develops due to synaptic stimulus generated by mobilization of calcium due to the activation of the N-methyl-D-aspartate (NMDA) receptor and enters the neuron through NMDA- and voltage-gated channels, as well as being released from intracellular organelles. The activation of NMDA depends on binding of glutamate with glutamate receptor in the synapse, and the glutamate is known as an excitatory neurotransmitter which is the key for normal function of memory. In neuronal degeneration, the overexcitation of glutamate leads to excess mobilization of calcium which produces protein mal-folding, oxygen radical generation, and cytoskeletal degradation leading to neuronal cell death.[49] The role of the hippocampus in neurodegenerative disorders has been investigated by many authors in AD, PD, PD dementia (PDD), and dementia with Lewy bodies (DLB).[50,51] In neurodegeneration disease, hippocampal atrophy is observed by functional magnetic resonance imaging.[52] The feature of neurodegenerative disease includes depigmentation of the substantia nigra and the neuronal accumulation of α-synuclein aggregates in the form of Lewy neurites and Lewy bodies in PD. Among neuronal degenerative diseases, synucleinopathy is observed in PD, whereas DLB and AD have common pathology.[53]

Conclusion

Here, we conclude that different durations of $AlCl_3$ (25 days and 45 days) have shown the same neurodegenerative effect in hippocampus of rat brain and treatment after that also has shown a similar result. Hence, the different durations of Al and FR with the same dose have not considered to be significant. However, this study had performed limited parameters. It will be more accurate to include the immunohistological parameters and other special stains like Congo red.

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Conflicts of interest

There are no conflicts of interest.

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Original Article

Analysis of Major Lobe Volume and Asymmetry of the Brain by Gender: A vol2Brain Study

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Abstract

Objective: In recent years, with the use of three-dimensional (3D) software tools, volumetric measurements of brain morphometry have gained importance. In this study, we aim to investigate the ratio of the volumes of the major structures of the brain (frontal, parietal, temporal, and occipital lobes) to the volume of the intracranial cavity (ICC) and the change of asymmetry according to gender, using web-based vol2Brain, which is one of the current and automatic software tools. **Materials and Methods:** 3D-T1-weighted magnetic resonance images of 80 healthy individuals (43 females and 37 males) of both genders were included in our study. The volumes of major brain lobes were calculated with the vol2Brain pipeline software tool and their ratio to ICC was compared by gender. **Results:** Males ICC volume, frontal, parietal, temporal, and occipital lobe total volume values were statistically higher than females ($P < 0.05$). Similarly, the right and left volume values of male were higher than those of female in all measurements. However, when the frontal, parietal, temporal, and occipital lobe volumes of male and female were proportion to the ICC volume, there was no statistically significant difference ($P > 0.05$). There was no statistically significant difference in the asymmetry results of these cortical structures examined in both genders ($P > 0.05$). **Conclusions:** Although the male brain is known to be large, no difference was found between the male and female brains as a result of the ratio. Considering the asymmetry values, frontal, parietal, occipital, and temporal lobe volume asymmetry values did not differ statistically in both genders.

Keywords: *Asymmetry, cortical, proportion, three-dimensional imaging, volume*

Introduction

Many studies investigate the relationship between gender and volume or morphometric measurements of neuroanatomical structures.[1-3] Some studies have reported that it does not differ according to gender.[4,5] The prognosis of many neurodegenerative and neuropsychiatric diseases related to the brain shows sexual dimorphism.[6,7] Many studies in the literature state that male brain components are greater than females.[8,9] In a large-scale meta-analysis study, it was reported that total brain volume (11%) and intracranial volume (12%) were greater in males.[10] This situation reveals the differences in structures such as cortical volume, surface area, and thickness.[11]

Many techniques have been used to measure cerebral structures.[3,12,13] First, autopsy studies are included because the actual volume and weight are measured. However, in autopsy studies, it was thought that the type of disease and the duration of removal of the brain would affect the results.[9] With the development of non-invasive imaging methods, objective information about the brain structures of living people can be obtained.[14] The human brain is examined using different methods with developing and advancing technology. Magnetic resonance imaging (MRI) is especially important in the detailed investigation of brain structure and function.[15]

In recent years, traditional data processing has been replaced by automatic/semi-automatic volume and segmentation techniques.[16-19] One of these software tools, volBrain, provides web-based, reliable, online, and time-saving volumetric analysis of three-dimensional (3D) structural MRI. Thus, MRI volumetric measurements of brain structures are important in the early diagnosis and follow-up of various diseases.[20]

Our aim in this study is to investigate the effects of the brain's major lobes on the

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intracranial cavity (ICC) volume ratio and asymmetry change according to gender using the vol2Brain software program, which is one of the volBrain segmentation tools.

Materials and Methods

Participants

MRI of eighty healthy individuals (43 females and 37 males) between the ages of 18 and 75 years was included in the study. Healthy individuals of both sexes, who did not undergo neurosurgery and did not have neurological or psychiatric diseases, were included in the study.

This study was approved by the human subjects ethics board of Kirsehir Ahi Evran University Faculty of Medicine Clinical Research Ethics Committee (Date: June 21, 2022, Approval Decision No: 2022-12/119).

Neuroimaging

MRI data were taken using a standard head coil on a 1.5 Tesla (GE SIGNA Explorer, 2020, United States) device. High-resolution, sagittal plane, T1-weighted 3D BRAVO sequence was taken. Repetition time: 7, echo time: 2.99 ms, field of view: 250 mm × 250 mm, matrix: 256 × 256, section thickness was taken as 1 mm.

The participants' 3D T1-weighted brain MRI data were exported with Picture Archiving and Communication Systems. These transferred data are uploaded to the personal computer. These data in Digital Imaging and Communications in Medicine format were anonymized with the free software MRIcron (https://www.nitrc.org/projects/mricron) and converted into the Neuroimaging Informatics Technology Initiative (NIfTI) format. In NIfTI format, these MRI data were uploaded to the vol2Brain pipeline system, volBrain's segmentation tool (v. 1.0, http://volbrain.upves). When the data processing process was finished, two reports were automatically created by the program, in the form of Portable Document Format and Comma-separated Values files, containing patient information, brain volumes, and their results in the Montreal Neurological Institute space.

The vol2Brain is a free, online, web-based data processing program that automatically segments MRI data. It provides automatic segmentation by dividing the human brain into 135 structures. The vol2Brain pipeline segments tissues, macrostructures, and lobes and provides information about cortical thickness.[15] Calculated tissue volumes are measured in absolute value (cm^3) and presented as a ratio (covering 100%) to ICC volume. It is expressed as the sum of ICC tissue, namely, white matter (WM), gray matter (GM), and cerebrospinal fluid (CSF).[20] In our study, cortical volumes will be examined using this program. The vol2Brain data were displayed in 3D with ITK-SNAP and MRIcroGL (https://www.itksnap.org and https://www.nitrc.org/projects/mricrogl) [Figures 1 and 2].

The asymmetry index (AI) provides information about the differences in the bilateral cortical structures of the brain. In our study, the AI value of the volumes of cortical structures (frontal, parietal, occipital, and temporal lobe) was calculated in the gender category. The AI value was obtained by dividing the right and left volume differences by their mean (as a percentage).[20,21] Hence, AI = (right volume-left volume)/2 (right volume + left volume) ×100. Positive values of the calculated AI results represent a right-oriented asymmetry, and negative values represent a left-oriented asymmetry. It was thought that the area showed lateralization as the AI value calculated with the volume values of the left and right regions of the cortical structures moved away from zero.

Statistical method

The data were evaluated in the Statistical Package Program of IBM SPSS Statistics Standard Concurrent User V 26 (IBM Corp., Armonk, New York, USA). Descriptive statistics were given as number of units (*n*), percentage (%), mean, standard deviation (SD), standard error (sh), median (M), minimum (min), maximum (max), and interquartile range values. The normal distribution of the data of numerical variables was evaluated with the Shapiro–Wilk normality test. The ages of the participants by gender were compared with the *t*-test in independent samples. The relations between age and asymmetry variables were evaluated with the Spearman correlation coefficient, and the relations between age and other variables were evaluated with the Pearson correlation coefficient. Asymmetry data by gender were compared with the Mann–Whitney *U*-test. One-way analysis of covariance was used to compare age-related variables by

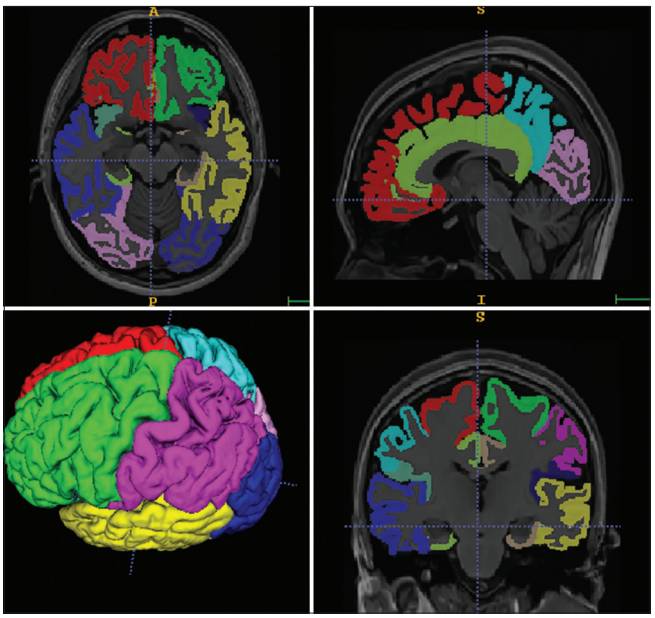

Figure 1: ITK-SNAP rendering and three-dimensional modeling of cortical structures in different planes

gender. A value of $P < 0.05$ was considered statistically significant.

Results

A total of 80 participants, 37 (46.3%) males and 43 (53.7%) females participated in the study. The participants were between 18 and 75 years old, and the mean age (±SD) was 41.5 ± 15.6. The mean age of males (±SD) was 40.9 ± 17.3 years, and the mean age of females (±SD) was 42.1 ± 14.1 years. There was no statistical difference between the ages of males and females ($t = 0.332$; $P = 0.741$).

Pearson correlation analysis revealed a negative correlation between ICC volume, total frontal volume, total temporal volume, total parietal volume, and occipital total volume variables and age values ($P < 0.05$; $r_1 = -0.291$, $r_2 = -0.593$, $r_3 = -0.544$, $r_4 = -0.637$, and $r_5 = -0.469$, respectively).

According to the results of Pearson correlation analysis, a negative correlation was found between the proportion of frontal lobe, temporal lobe, occipital lobe, and parietal lobe volumes to ICC volume separately and age values ($P < 0.001$; $r_1 = -0.684$, $r_2 = -0.599$, $r_3 = -0.447$, and $r_4 = -0.716$, respectively).

According to the results of Spearman's correlation analysis, there was no statistically significant relationship between the age of the participants and the frontal lobe, temporal lobe, parietal lobe, and occipital lobe asymmetry values ($P > 0.05$; $rho_1 = 0.122$, $rho_2 = -0.165$, $rho_3 = 0.012$, and $rho_4 = 0.029$, respectively).

In the comparisons made according to gender, the variables other than the asymmetries were adjusted for age.

Table 1 shows that male's ICC, frontal, temporal, parietal, and occipital total volume values were statistically higher than female's ($P < 0.05$).

Right and left frontal, temporal, parietal, and occipital lobe volume values of males are statistically higher than females ($P < 0.05$) [Table 2].

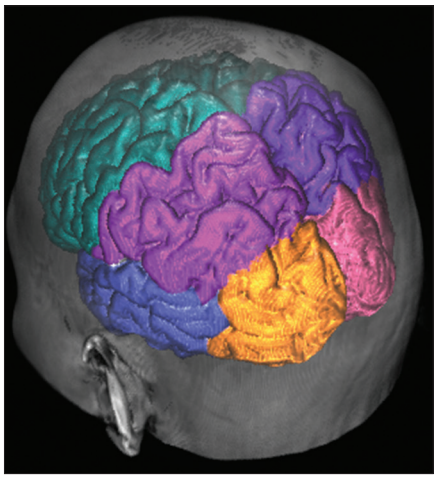

Figure 2: Three-dimensional imaging of vol2Brain data with MRIcroGL

Table 3 shows no statistically significant difference between male's and female's frontal lobe volume/ICC volume, temporal lobe volume/ICC volume, occipital lobe volume/ICC volume, and parietal lobe volume/ICC volume values ($P > 0.05$).

There was no statistically significant difference between the frontal lobe, temporal lobe, parietal lobe, and occipital lobe volume asymmetry values of males and females ($P > 0.05$) [Table 4].

Discussion

Brain morphometry has gained momentum with the development of neuroimaging methods.[9] In the past, manual segmentation was used with MRI volume analysis of brain structures. However, this method was limited in terms of application in neuroanatomical structures. Because it took much time, it was replaced by software tools that perform automatic brain volume analysis. Among these software tools, volBrain, which provides modern, web-based, up-to-date, unbiased, and automatic segmentation, can be used as a neuroimaging study in MRI.[20] In the current study, we aimed to investigate the ratio of the volumes of the major structures of the brain to the ICC volume and the variation of the asymmetry according to the genders using vol2Brain in a homogeneous and healthy population. This study may be one of the first studies, as we know, to analyze gender differences in healthy individuals using both the

Table 1: Comparison of volumes by gender

Region volume (cm^3)	Gender		Test statistics*	
	Male	Female	*F*	*P*
ICC volume	1408.2±20.5	1302.4±19.1	14.208	<0.001
Frontal total volume	182.9±2.9	171.8±2.7	7.634	0.007
Temporal total volume	120.9±1.7	110.4±1.6	18.997	<0.001
Parietal total volume	106.8±1.5	98.9±1.3	14.964	<0.001
Occipital total volume	77.1±1.2	69.5±1.1	21.789	<0.001

*One-way analysis of covariance. The parts determined in bold are statistically significant ($P<0.05$). Numerical data corrected for age are given as mean±SE. SE: Standard error, ICC: Intracranial cavity

Table 2: Comparison of right and left volumes by gender

Region volume (cm^3)	Gender		Test statistics*	
	Male	Female	*F*	*P*
Frontal right volume	92.22±1.49	86.38±1.38	8.337	**0.005**
Frontal left volume	90.65±1.46	85.48±1.36	6.738	**0.011**
Temporal right volume	60.80±0.92	55.33±0.86	18.709	**<0.001**
Temporal left volume	60.14±0.86	55.14±0.79	18.041	**<0.001**
Parietal right volume	53.88±0.81	49.71±0.74	14.434	**<0.001**
Parietal left volume	53.01±0.73	49.24±0.68	14.049	**<0.001**
Occipital right volume	38.67±0.60	34.97±0.55	20.207	**<0.001**
Occipital left volume	38.42±0.66	34.57±0.61	18.525	**<0.001**

*One-way analysis of covariance. The parts determined in bold are statistically significant ($P<0.05$). Numerical data corrected for age are given as mean±SE. SE: Standard error

Table 3: Comparison of lobe volume values/intracranial cavity volume proportion by gender

Parameters	Gender		Test statistics*	
	Male	Female	*F*	*P*
Frontal lobe volume/ICC volume	0.130±0.001	0.132±0.001	1.966	0.165
Temporal lobe volume/ICC volume	0.086±0.001	0.085±0.001	1.149	0.287
Occipital lobe volume/ICC volume	0.055±0.001	0.053±0.001	3.152	0.080
Parietal lobe volume/ICC volume	0.076±0.001	0.076±0.002	0.034	0.854

*One-way analysis of covariance. Numerical data corrected for age are given as mean±SE. SE: Standard error, ICC: Intracranial cavity

Table 4: Comparison of volume asymmetry values by gender

Parameters	Gender		Test statistics*	
	Male	Female	*Z*	*P*
Frontal volume asymmetry	1.44 (3.96)	0.79 (3.09)	1.134	0.257
Temporal volume asymmetry	1.13 (4.21)	0.61 (4.69)	0.767	0.443
Parietal volume asymmetry	1.61 (6.72)	0.81 (5.25)	0.883	0.377
Occipital volume asymmetry	2.04 (8.19)	1.41 (9.87)	0.005	0.996

*Mann–Whitney *U*-test. Numerical data are given as median (IQR) values. IQR: Interquartile range

vol2Brain method and the ratio of major brain structures to ICC.

The size of the human brain has been investigated for many years.[22] Many studies stated that the female brain is generally smaller than the male brain.[10,23] Filipek *et al*.[24] reported in their study that the difference between the sexes in total brain volume was 8%. It has been stated that the effect of gender on the volume difference is small, and most of the difference may be related to the ICC volume.[25] It has been reported that the ICC volume increases during childhood and adolescence and decreases after age 40.[26] Similarly, in our study, the mean age of the participants was 41.5 ± 15.6, and it was determined that the ICC volume differed according to the age variable.

Whether the brain exhibits sexual dimorphism is still debated.[27] Many studies have determined that the ICC volume measured in healthy individuals is greater in males.[9,25,28,29] Similarly, in our study, ICC volume was higher in males ($P < 0.05$). However, it was stated that the difference was almost gender independent when the brain volume was proportional to the ICC volume.[9]

Murphy *et al*. reported that males' whole brain volume was greater. In addition, it has been reported that whole brain volume and frontal and temporal lobe volumes decrease with age in males, whereas parietal lobe volume decreases more in females.[30] Similarly, in our study, all measured volumes were higher in males, and there was a negative correlation with age in both sexes.

Garcia-Falgueras *et al*.'s study, GM, WM, and CSF volumes were higher in males. However, it has been reported that there is no difference between genders when each of these structures is proportioned to the total brain volume separately and when the GM volume is proportioned to the WM volume in the same way.[31] In another study, the proportion of GM, WM, and CSF volume to ICC volume was reported to be higher in males.[9,28] Although there were methodological differences in our study, Garcia-Falgueras *et al*.[31] as in the results, there was no statistically significant difference between the genders ($P > 0.05$). It is thought that the reason for the differences in the results may be due to the sample size, differences in the measurement methods, and ethnic origin.

Carne *et al*.[32] examined the right–left volumes of the frontal, parietal, occipital, and temporal lobes in 97 healthy individuals (49 females and 48 males) aged between 15 and 69 years, according to gender. Other lobe volumes were statistically higher in males except for the left parietal lobe ($P < 0.066$). Allen *et al*.[8] the major brain lobe volumes of 46 healthy individuals aged between 22 and 49 years (23 females and 23 males) were found to be statistically higher in males in all cases. However, the occipital lobe volume is less dimorphic, and the left occipital lobe volume was not statistically significant. In our study, males' right and left lobe volumes were statistically higher than females. We think the differences in the right or left lobe volumes are due to the number of participants, age factor, and differences in measurement methods.

Cowell *et al*.[1] analyzed the frontal and temporal lobe volumes of the 18–40 (young) and 41–80 (old) age groups according to gender. It has been reported that the total frontal volume of males in the young group is 16% larger than in the elderly group, whereas there is no difference in volume between the two groups in females. Temporal lobe volume was similarly larger in males, and the right volume has been reported to be larger than the left.[1] In our study, although there were no age groups, bilateral frontal and temporal lobe volumes were statistically higher in males according to gender. Therefore, it is mentioned in the literature that dimorphisms in human neuroanatomy vary in conditions such as the person's lifestyle, sexual hormone levels, smoking, and alcohol use. However, since our study was retrospective, no comment could be made on these parameters.

Allen *et al*.[8] reported that the temporal and occipital lobe asymmetry was not statistically significant in both genders, and the frontal and parietal lobe AI was not statistically

significant only in males. In addition, only female's frontal and parietal lobe asymmetry was right oriented. Kovalev *et al*.[33] reported that the male brain is more asymmetrical than the female brain. Gurlek Celik and Tiryaki[34] examined the asymmetry differences between gender and age, in which subcortical structures were examined in detail. In this study, it was reported that SR-SL-SM asymmetry values were high only in males. In the same study, it was determined that there were no asymmetry differences in the age category.[34] Lehtola *et al*.[35] study, 68 healthy infants aged 2-5 weeks showed asymmetry towards the right in the temporal lobe and towards the left in the parietal and occipital lobes in both genders. In the same study, frontal lobe asymmetry results were not statistically significant. Cowell *et al*.[1] reported that right frontal lobe asymmetry values were higher in females aged 41–80 and right temporal lobe asymmetry values in males in the same age group. In our study, frontal, parietal, occipital, and temporal lobe asymmetry values were high in the right region in both genders. However, although the asymmetry results were high, there was no statistically significant difference between the asymmetry values of males and females ($P > 0.05$). The differences between studies are related to the anatomical structure and physiology of the human brain. Although it is thought that this structural and morphometric variability may be affected by factors related to gender, age, and dominant hand use, it is thought to be an area open to extensive research.[36]

Many studies are in the literature on the proportion of total brain volume to ICC. However, as far as we know, no studies evaluate the proportion of bilateral major brain lobes to ICC and their asymmetry according to gender. We think that such studies will be meaningful in neurodegenerative diseases.

Conclusions

In our study, the proportion and asymmetry of major brain lobes to ICC in healthy individuals between the ages of 18–75 were investigated. Our results showed that, as in many studies, the brain volume of males was larger than that of females. However, when we proportion each of the frontal, parietal, occipital, and temporal lobe volumes to ICC, it was found that there was no statistically significant difference in both genders. Therefore, although the male brain is known to be large, as a result of the proportion, no difference was found between the male and female brains. Furthermore, considering the asymmetry values, frontal, parietal, occipital, and temporal lobe volume asymmetry values did not differ statistically in both genders. Therefore, we think that the volume ratio and asymmetry measurements between the major brain structures will be important in evaluating the diseased structures from a clinical point of view and whether there is a difference between the sexes.

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Conflicts of interest

There are no conflicts of interest.

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Original Article

Diagnostic Accuracy of Plain Computed Tomography to Detect the Morphological Variations of Liver: An Update

Abstract

Introduction: The prevalence of accessory fissures (AFs) in the liver ranges from 6% to 56%, as reported by cadaveric studies, which is much higher than the prevalence of 25% on computed tomography (CT) scans. Despite reporting many morphological variations in the liver by various cadaveric studies worldwide, the imaging studies are very few. Radiological imaging of patients undergoing liver surgery is a routine preoperative investigation. Despite there are several occasions where liver variations occur as a surprise during surgery which reflects on the diagnostic capacity of CT. **Materials and Methods:** Sixty cadaveric livers removed and stored in 10% Formalin were studied for all morphological abnormalities. The same livers were analyzed separately by anatomists by gross examination and radiologists by plain CT imaging. The radiologists were blinded from the gross examination findings. The data obtained by both methods were compared and the diagnostic accuracy of CT was estimated. **Results:** The common surface morphological variations detected were AFs, accessory lobes (ALs), pons hepatis (PH), and multilobed caudate and quadrate lobes (QLs). Out of the total 89 AFs identified by gross examination, only 73 could be detected by CT scan, thus the sensitivity of CT scan in detecting AFs is 82%. Similarly, the sensitivity of CT scan in detecting ALs, PH, and multilobed caudate, and QL was 64% (low), 81%, and 19% (very low), respectively. Thus, plain CT has variable sensitivity depending on the morphological variation. **Conclusions:** This study has highlighted some of the diagnostic inaccuracies that may arise during plain CT examination of the liver in a person posted for liver surgery or a person with abdominal trauma. Contrast-enhanced CT scans can circumvent many of these problems. Lack of awareness of these issues may affect the normal course of treatment and prognosis in such patients.

Keywords: *Accessory fissure, accessory lobe, caudate lobe, liver variations, pons hepatis, quadrate lobe*

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Introduction

The liver, the largest organ is divided into four anatomical lobes which are the right, left, quadrate, and caudate lobe (CL). There are 3 major and 3 minor fissures on the liver. Morphological variations of the liver are commonly seen during surgeries and routine dissection. The common morphological variations of the liver include accessory fissures (AFs) and accessory lobes (ALs). Morphological variations in liver such as AF and AL are thought to occur mostly due to diaphragmatic indentation during growth and development. AF is most common in the superior surface of the right hepatic lobe. Their frequency and depth increase with age. Some pathologic fissures occur secondary to traumatic or iatrogenic causes. Many of these variations are important as they may act as a guide for surgeons during segmental hepatectomy, cholecystectomy, and repair of liver trauma due to their association with branches of veins.[1] Radiological imaging by computed tomography (CT) is a mandatory preoperative investigation that helps the surgeon in the accurate diagnosis and proper planning of treatment. Hence, the surgical outcome depends to a large extent on the accuracy of radiological findings.[2]

The prevalence of morphological variations of liver is found to be variable during gross examination (autopsy, dissection, laparoscopy, or laparotomy) and radiological imaging (ultrasonography, CT, or magnetic resonance imaging). The prevalence of AF in liver is around 56% as reported by cadaveric studies[3] which is much higher as compared to the prevalence of 25% on CT scans.[4] The low prevalence of variations during radiological

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investigations shows that many of them are not visualized. The reason for this is that an AF that gets filled with blood or inflammatory exudate may be confused with liver cyst, laceration, hematoma, or abscess.[5] Multiple AF or AL may masquerade pathological liver nodules such as metastasis or macronodular cirrhosis. Hence, on several occasions, the surgeon will experience these variations as a surprise during surgery. which can increase the chances of surgical trauma and complications. Awareness of such morphological variations of the liver would aid the surgeons and radiologists to avoid misdiagnosis and complications during surgery.

Despite the reporting of a large number of morphological variations in liver by various cadaveric studies across the world, the imaging studies on liver morphological variations are very few. A few studies have compared the prevalence of morphological variations in cadaveric livers by gross examination with CT images of living persons.[2,4,6] This does not predict the diagnostic accuracy of the CT as the study samples are different. There is a paucity of literature on the diagnotic accuracy of radiological investigations to detect morphological variations of the liver. With the advent of newer techniques for both radiology and surgery it is important to have an update in this regard. Thus, the present study aims at assessing the diagnostic accuracy of plain CT in detecting morphological variations in cadaveric livers in comparison with gross examination – the gold standard.

Materials and Methods

After obtaining the institute research committee and ethics committee approval (IEC: RC/19/51), 60 livers that were removed during routine dissection and stored in 10% Formalin were studied. All the livers were apparently normal in weight and had very minimal damage. All the dimensions and abnormalities of normal and AFs, ALs, CL, quadrate lobe (QL), and gall bladder were measured using a probe, thread, measuring tape and digital Vernier calipers. The variations were photographed. These livers were subjected to plain CT imaging with the specimens being kept in near anatomical positions inside a transparent Perspex container filled with water. Water was chosen as a medium after a pilot study. The system used was the 128-slice, multiphasic, Philips CT scan machine. All CT images were acquired with 120 kV and 200 mAs, and 5 mm slice thickness raw data was taken and reconstructed into multiplanar (axial, sagittal, and coronal orientation) 1 mm slice thickness images. For identification of all possible surface morphological variations of the liver, the images were independently reviewed by 2 experienced radiologists – with an experience of 8 years and 30 years, respectively. Their readings were compared, and any disagreements were resolved by reviewing the images together until a consensus was reached. Radiologists reporting the CT findings were blinded from the gross anatomical observations.

The prevalence of variations obtained by gross examination and CT imaging were compared. The images of each liver obtained by both the methods were compared to estimate diagnostic accuracy. Similar variations detected in gross examination and CT imaging were considered as true positives. The total number of livers with the absence of variations on gross examination and CT imaging were considered as true negatives. Any variation that was detected on gross examination but not in CT was considered as false negatives, and that was detected on CT and not on gross examination was considered as false positives. As there are several surface variations on liver, the ability of CT to detect each of them was analyzed separately. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and Likelihood ratio (LR) were calculated for each surface variation using the standard formulae [Table 1]. Post-test probability was calculated using Fagan's nomogram.

Results

Of the 60 livers that were examined, 3 were excluded because of inadequate visualization or insufficient information or due to grossly variant morphology. The findings in the remaining 57 livers were analyzed. The prevalence of various abnormalities by both methods is given in Figure 1. The common surface morphological variations identified by gross examination and CT were AFs, ALs, lobulated CL and QLs, and pons hepatis (PH) [Figures 2 and 3]. The most frequent abnormality detected was lobulated caudate and QLs by gross examination and AFs by CT. The frequencies of various variations are summarized in Tables 2-5.

The diagnostic accuracy of CT (Sensitivity, specificity, PPV, NPV, LR) for anatomical variations is tabulated [Table 6]. Post-test probability using Fagan's Nomogram for AF, AL, and PH is given in Figure 4. LR and hence Post-test probability could not be calculated for lobulated CL and QL due to 100% specificity.

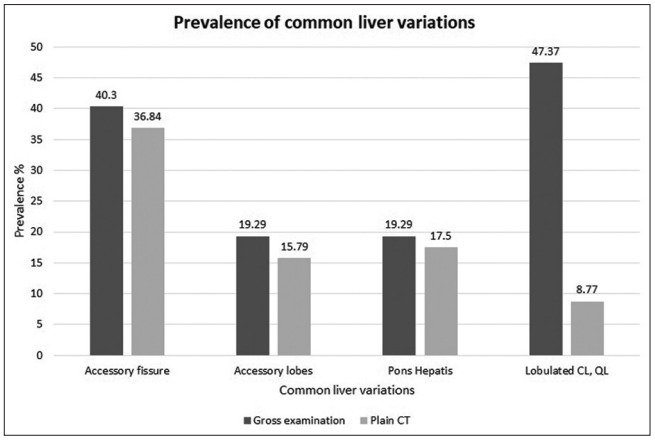

Figure 1: Prevalence of common surface morphological variations by gross anatomy and Plain computed tomography. CL: Caudate lobe, QL: Quadrate lobe

Discussion

The present study aimed at estimating the diagnostic accuracy of plain CT scan in detecting surface morphological variations of livers in comparison with gross anatomical examination by using cadaveric livers. The prevalence of common variations by both the methods was also determined. In the current study, we used the same cadaveric livers that were removed and stored in 10% formalin for gross examination as well as CT scan. Common and clinically relevant surface morphological variations as detected during gross anatomical examination were compared with the CT findings. These were AFs, ALs, PH, lobulated caudate, and QLs. Sensitivity, specificity, PPV, NPV, and LR is estimated for all common variations. Our findings revealed that CT scan has variable diagnostic accuracy in detecting various surface morphological variations in liver.

A higher sensitivity of CT in detecting AF will help the surgeon to plan segmentectomy based on these fissures and will also reduce surprises during surgery. Higher specificity will reduce unwanted operative intervention in cases of blunt trauma of the abdomen. This should be kept in mind when a person with abdominal trauma with hemoperitoneum or a person with ascites posted for a hepatobiliary surgery undergoes a screening CT scan where the blood and peritoneal fluid will affect the visualisation of AF or traumatic fissure.[4] The radiological appearance of a traumatic fissure and an anatomical fissure (normal or accessory) of the liver is not the same. Usually, when there is a natural hepatic fissure – normal or accessory, the peritoneum invaginates into it and may contain a variable amount of fat. The presence of fat is responsible for the radiolucent appearance of the fissure.[2] Thus, the fat that fills the fissure will help in easy detection. The lesser the amount of fat in the fissure, the less is the chance of visualization on CT. This explains why narrow and shallow AFs (<0.5 cm) get unnoticed on CT scan. A normal fissure and true AF will have smooth contours due to the peritoneum dipping into the fissure. However,

Table 1: Parameters and formulae used

Parameter	Formula
Sensitivity	TP/TP + FN
Specificity	TN/TN + FP
PPV	TP/TP + FP
NPV	TN/TN + FN
Positive LR	Sensitivity/1−specificity
Negative LR	1−sensitivity/specificity

NPV: Negative predictive value, PPV: Positive predictive value, LR: Likelihood ratio, TP: True positives, FP: False positives, FN: False negatives, TN: True negatives

Table 2: Accessory fissures

		Gross anatomical examination		
	AF	**Present**	**Absent**	**Total**
CT liver	Present	73 (TP)	14 (FP)	87
	Absent	16 (FN)	10 (TN)	26
	Total	89	24	113

TP: True positives, FP: False positives, FN: False negatives, TN: True negatives, CT: Computed tomography, AF: Accessory fissures

Table 3: Accessory lobes

		Gross anatomical examination		
	AL	**Present**	**Absent**	**Total**
CT liver	Present	7 (TP)	2 (FP)	9
	Absent	4 (FN)	44 (TN)	48
	Total	11	46	57

TP: True positives, FP: False positives, FN: False negatives, TN: True negatives, CT: Computed tomography, AL: Accessory lobes

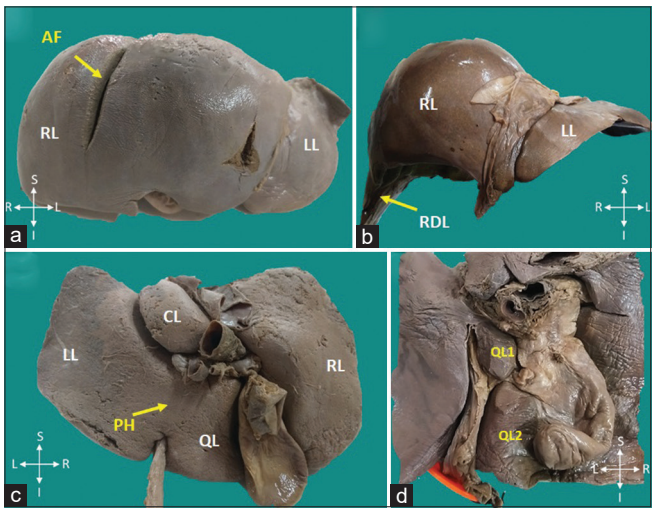

Figure 2: Gross Anatomical appearance of cadaveric livers showing common surface morphological variations. (a) Accessory fissure (b) Accessory lobe (c) Pons hepatis (d) Lobulated quadrate lobe. AF: Accessory fissure, RDL: Riedel's lobe PH Pons hepatis QL1 and QL2 Bilobed quadrate lobe, RL: Right lobe, LL: Left lobe, CL: Caudate lobe, QL: Quadrate lobe

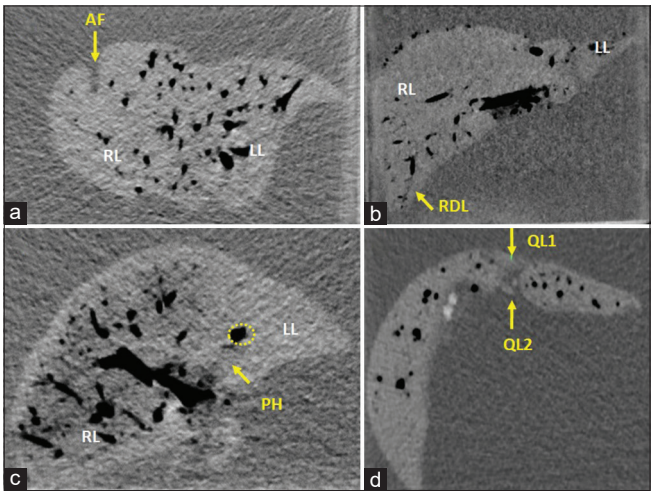

Figure 3: Plain computed tomography images of cadaveric livers showing common surface morphological variations. (a) Accessory fissure (b) Accessory lobe (c) Pons hepatis (d) Lobulated quadrate lobe. AF: Accessory fissure, RDL: Riedel's lobe PH Pons hepatis QL1 and QL2 Bilobed quadrate lobe, RL: Right lobe, LL: Left lobe, Dashed encircled area - Ligamentum teres hepatis/Round ligament of liver

in a traumatic or iatrogenic fissure, there will be peritoneal discontinuity and no fat will be seen in the fissure and the margins of the fissure will not be smooth. The most common site of AF is the superior surface of the right lobe of liver. As the major reason for the development of AF is diaphragmatic indentation during development, the presence of muscle fibers in the fissures will act as a guide for natural fissures *in vivo*.[1] Hence, anomalies of the diaphragm such as eventration and hernia may also affect the appearance of liver. Associated pathologies of pleura and base of the lung will also alter the appearance of diaphragm and liver. Moreover, AF in many cases is associated with radicles of the portal vein or hepatic artery in the depth of the fissures and can act as a guide during surgery.[7] Whereas a traumatic fissure will not have such an association.

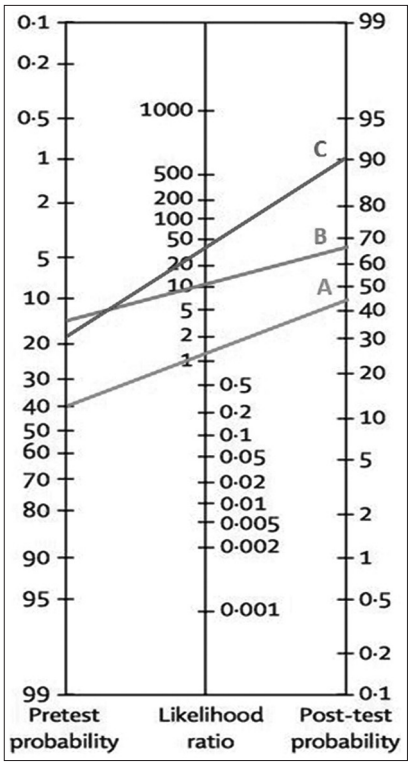

Figure 4: Fagan's Nomogram showing posttest probability of common surface morphological variations. (A) Accessory fissures (blue) (B) accessory lobes (green) (C) pons hepatis (red)

Table 4: Pons hepatis

		Gross anatomical examination		
	PH	**Present**	**Absent**	**Total**
CT liver	Present	9 (TP)	1 (FP)	10
	Absent	2 (FN)	45 (TN)	47
	Total	11	46	57

TP: True positives, FP: False positives, FN: False negatives, TN: True negatives, CT: Computed tomography, PH: Pons hepatis

In the current study, the blood vessels in the liver had collapsed post-mortem. The intensity of liver tissue was slightly lesser than in a living person due to lack of blood. Trapping of water and air bubbles in small fissures would have hindered the visualisation of normal contour, fat content and peritoneal covering of the fissure. Due to the above reasons, the diagnostic accuracy of plain CT may be low despite using cadaveric livers that had minimal trauma. Our findings are similar to the findings by Schramek *et al*. who found that the presence of gas artifacts, perimortal changes, and fixation artifacts made precise detection of details of organs difficult resulting in a low prevalence of variations by CT.[2] Contrast-enhanced CT can overcome many of these drawbacks.

The discrepancy between cadaveric and CT observations has been noted in other previous studies also.[4,6] However, these studies used cadaveric livers for gross examination and compared the prevalence and distribution of AF in CT scans of patients undergoing CT for other abdominal conditions.

The sensitivity and specificity of CT to detect AL such as Riedel's lobe, Beaver's lobe, and others were found to be 63.63% and 95.65%, respectively. Bilobed, trilobed, and multilobed caudate and QLs were seen in 27 livers during gross examination. But CT could detect only 5 and thus an extremely low sensitivity (18.52%) was detected. The reason for low sensitivity in lobar anomalies could be attributed to slight changes in the orientation of the organ and post-processing effects. The images that are taken as 5 mm slices are later reconstructed into 1 mm slices. In this process, small variations get smoothened and may appear as undulations of the surface or border which are not detected as variations and thus results in a low sensitivity. The radiologists should keep these possibilities in mind, as such findings may be missed and will pose surprises during surgeries. A pathology arising from an AL may thus get undiagnosed. A proper diagnosis of a supernumerary lobe is also necessary for follow-up as a pedunculated AL may undergo torsion.[8]

Table 5: Lobulated caudate and quadrate lobes

		Gross anatomical examination		
	Lobulated CL and QL	**Present**	**Absent**	**Total**
CT liver	Present	5 (TP)	0 (FP)	5
	Absent	22 (FN)	30 (TN)	52
	Total	27	30	57

TP: True positives, FP: False positives, FN: False negatives, TN: True negatives, CT: Computed tomography, QL: Quadrate lobes, CL: Caudate lobes

Table 6: Performance of computed tomography in comparison with gross anatomical examination to detect common surface variations – accessory fissures, accessory lobes, pons hepatis, lobulated caudate and quadrate lobes

Parameter	AF (%)	AL (%)	PH (%)	Lobulated caudate and QL (%)
Sensitivity	82.02	63.63*	81.81	18.52*
Specificity	41.67*	95.65	97.82	100
PPV	83.9	77.78	90	100
NPV	38.46*	91.67	95.74	57.69*
Positive LR	1.41	12.6	40.5	-

*Low value. AL: Accessory lobes, AF: Accessory fissures, PPV: Positive predictive value, NPV: Negative predictive value, LR: Likelihood ratio, PH: Pons hepatis, QL: Quadrate lobe

With a sensitivity and specificity of more than 80% to detect PH, plain CT is a good investigation to detect this condition both in groove for Inferior vena cava (IVC) or Fissure for ligamentum teres (FLT) which were the two sites where PH was detected in our study. Posttest probability was also found to be high for detecting PH.

Conclusions

The current study showed that Plain CT has a variable diagnostic accuracy depending on the surface variation of the liver; most accurate for PH and least accurate for lobar anomalies though these could be attributed to the post-processing effects and perimortal changes. But, radiologists and surgeons should be aware of all possible anatomical variations and their appearances especially lobar anomalies that are least detected by plain CT, to prevent misdiagnosis and mismanagement. The study also highlights the high frequency of liver variations which are probably overlooked by anatomists also. The increased awareness of these findings would reduce surgical trauma and thus aid good prognosis among patients undergoing abdominal surgeries.

Ethical approval

The study was approved by the Institute research committee and Institute ethics committee of Pondicherry Institute of Medical Sciences (RC/19/51).

Authors' contributions

Conception of Idea: A M; Conducted the research experiment: A M, S R and G N; Data curation and analysis: A M and G N; Manuscript writing: S R, A M and G N; Critical reviewing and overall supervision: N N, R D, D P.

Availability of data and materials

Data can be shared upon request from the author.

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Conflicts of interest

There are no conflicts of interest.

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Original Article

Insulin Resistance through High-sugar Diets and its Effects on the Endometrium in Swiss Albino Mice: An Experimental Study to Elicit the Beneficial Effects of Coconut Sugar

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Abstract

Introduction: Insulin resistance (IR) has an insidious onset and is mainly due to the consumption of high-energy diets. Refined sugars contain high fructose which predisposes to IR and affects the endometrium since endometrium exhibits high-affinity insulin receptors, and the natural unrefined sugars such as coconut sugar are proved to be beneficial, but scientific studies are scarce to validate the findings. **Subjects and Methods:** A cross-sectional study was carried out, in which 36 female Swiss albino mice were divided into control and high-fructose and high-coconut sugar diet groups. The respective diets were prepared daily and fed for a period of 12 weeks, and the animals were sacrificed by the administration of ether. Biochemical parameters were assessed, and the uterus was removed and processed for histopathological analysis. **Results:** Glucose, insulin, and homeostasis model assessment-IR were assessed, in which there was an increase in the levels in the high-fructose group than the control and coconut sugar groups. The values were statistically significant in the Kruskal–Wallis analysis ($P < 0.001$) and *post hoc* test showed a significant difference between the control and fructose diet groups. Hormonal assay showed elevated testosterone levels in the fructose group (Kruskal–Wallis test, $P < 0.001$), which showed significance in *post hoc* test when compared with the control group ($P < 0.030$). Histopathological examination revealed complex hyperplasia with nuclear atypia in the fructose group, whereas the findings were normal in the coconut sugar and control groups. **Discussion:** The present study proved coconut sugar to be beneficial, and there is a strong correlation of high-energy diets on the endometrium due to IR. **Conclusion:** The present study concludes that the intake of natural sugars does not cause damage to the endometrium which is sensitive to insulin resistance.

Keywords: *Endometrial morphology, high-sugar diets, hyperinsulinemia, metabolic syndrome, unrefined natural sugar*

Introduction

Insulin resistance (IR) is a subclinical condition which is precipitated by various factors including the intake of high-energy diets rich in refined sugars. Hyperinsulinemia in the context of IR affects the female reproductive system, especially the endometrium because it possesses high-affinity insulin receptors. It has been nearly 100 years since the association between diabetes (Type II) and cancer was established.[1] It is due to the mitotic potential of insulin, which plays a key role in the cancer pathogenesis in the endometrium. Three mechanisms cause cancer pathogenesis in women, namely, activation of insulin pathway, activation of insulin-like growth factors (IGFs), and endogenous sex hormones. Insulin-like peptides (ILPs), especially IGF-1 in addition to insulin, are the key factor that leads to the development and progression of cancers in the body, because IGF-1 is more mitogenic than insulin.[2]

IR develops due to excess accumulation of free fatty acid released from the adipose tissue. The increase in free fatty acid in the plasma causes an increase in the uptake and oxidation of free fatty acid in the liver and muscles, which eventually leads to metabolic changes that prevent these tissues to uptake glucose for energy metabolism.[3] With regard to intake of sugars, fructose is observed to be more lipogenic than other forms of sugars and implicated in IR, steatosis, and metabolic syndrome.[4] In the earlier days, fructose was considered an ideal sweetener for

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diabetic patients due to its lower glycemic index (GI), and fructose does not stimulate insulin secretion or fructose metabolism is not under the regulatory control of insulin.[5] However, recent studies prove a strong link between fructose and the development of IR. This is because of the lipogenic nature of the sugar, which increases the deposition of triglycerides in adipose tissue and ectopic tissues such as liver and muscles, resulting in impaired insulin signaling and resistance. Furthermore, fructose bypasses a major rate-controlling step in glycolysis and is converted into fatty acids in the liver faster than other forms of sugars.[6]

The fructose content present in sugar-sweetened beverages (SSB) is very high and predisposes to the early onset of IR and affects endometrium in women. The World Cancer Research Fund/American Institute for Cancer Research (2013) categorized intake of SSB as an established risk factor for endometrial cancer. Various prospective cohort studies strongly implicate the role of SSBs in the development of endometrial carcinoma.[7-10] In this regard, the beneficial effect of consuming natural sugars cannot be overlooked. Coconut sugar or coconut sap sugar is a whole natural sugar obtained by cutting the flower of the coconut palm, and the sap is collected in the containers. The collected sap is placed under heat until the water content in the sap gets evaporated completely. The resulting hard sugar is the coconut sugar. In this method of natural production of coconut sugar, it retains minerals such as iron, zinc, calcium, and potassium mainly with some short-chain fatty acids, polyphenols, and antioxidants. Coconut sugar has low glycemic index (GI) of 35 than other refined sugars which is 60 GI/serving because coconut sugar contains a fibre called inulin which slows down the absorption of glucose into the blood stream.[11] Hence, in the present study, an attempt has been made to correlate the development of endometrial carcinoma due to IR and to elicit the beneficial effects of coconut sugar in the development of IR in Swiss albino mice.

Table 1: Composition of diets (g/100 g)

Ingredients	High-fructose diet (g)	High-coconut sugar diet (g)
Experimental ingredients	D - fructose: 60	Coconut sugar: 60
Casein (fat free)	20	20
Methionine	0.7	0.7
Groundnut oil	5	5
Wheat bran	10.6	10.6
Salt mixture	3.5	3.5
Vitamin mixture	0.2	0.2

Subjects and Methods

A cross-sectional study was carried out in 21-day-old female Swiss albino mice for the duration of 12 weeks. A total of 36 animals were divided randomly into control and high-fructose and high-coconut sugar groups with 12 animals in each group, respectively. The atmospheric control of the animal facility was maintained throughout the study period with relative humidity (55%) in a 12 h light/dark cycle at 25°C ± 2°C. The animals were kept in polypropylene cages (47 cm × 34 cm × 18 cm) in sterile paddy husk bedding, which was renewed daily.

Ethical consideration

The experiment was carried out in the Centre for Toxicology and Developmental Research and Department of Anatomy with the approval of the Institutional Animal Ethics Committee (IAEC) (Approval No.: IAEC/XLVII/SRU/476/2016). The study was done in strict conformity with the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals, Government of India.

Experimental diets

Normal pellet diet was fed to the control group animals, whereas the diets for fructose and coconut sugar group animals were prepared according to the American Institute of Nutrition-93G for standard diets in Rodents [Table 1].[12] Analytical grade fructose was procured from Nice Chemicals Pvt. Ltd., Kochi, and coconut sugar from *I*^{2}Cook Organic Foods, Bengaluru. The animals were maintained in the respective diets soon after the weaning period which is normally between the 3rd and 4th week after birth in mice. All the diets were prepared fresh every day and fed to the animals.

Sample collection

After the study period, all the surviving animals were sacrificed by the administration of ether, and blood samples were collected from retro-orbital sinus for biochemical analysis. The samples were centrifuged at 4000 RPM, and the serum samples were stored at −20°C for further evaluation. Basal IR parameters such as fasting glucose, insulin, and homeostasis model assessment (HOMA–IR) levels were assessed. Hormonal assay was done to elicit the changes due to IR.

Tissue processing and staining

After the sacrifice, the uterus of the animals was fixed in neutral-buffered formalin. The tissues were later dehydrated in ascending grades of alcohol, cleared in

Table 2: Kruskal-Wallis test for glucose parameters

Parameters	Control group	High-fructose diet group	High-coconut sugar diet group	*P*
Glucose (mg/dL)	139.20±10.82	218.83±18.09	141.62±6.09	<0.001***
Insulin (mU/L)	1.488±0.25	4.085±0.26	1.521±0.08	<0.001***
HOMA-IR	0.52±0.13	2.217±0.24	0.61±0.70	<0.001***

***Statistically highly significant. HOMA - IR: Homoeostasis model assessment-insulin resistance

xylene, and embedded with paraffin. The sections were cut with the thickness of 5 µ in rotary microtome (LEICA RM2125RT) and were affixed in glass slides for further staining with eosin and hematoxylin and Masson's trichrome.

Statistical analysis

The data were represented in mean ± standard deviation. Statistical analysis was performed using SPSS software (version 23.0. IBM, Chicago, Illinois, United States of America). Analysis was done using the Kruskal–Wallis test and *post hoc* test. Statistical significance was set when $P < 0.05$.

Results

Biochemical analysis

The plasma glucose, insulin, and HOMA-IR values of the high-fructose group were higher than the control and high-coconut sugar diet groups. The values were statistically significant [Table 2]. *Post hoc* analysis showed a significant difference between the high-fructose and control groups [Table 3]. The testosterone and estradiol levels were higher in the high-fructose group, whereas the levels were similar between the control and high-coconut sugar diet groups. The data of hormonal analysis are shown in Tables 4 and 5.

Histopathological observation

The control group and coconut sugar group exhibited a normal appearance of the uterus. High-fructose diet group exhibited complex atypical hyperplasia with papillary infoldings. Glands were numerous and crowded. Focal stratification of epithelium and elongated and spindled out nuclei were seen [Figures 1 and 2].

Discussion

There is a direct correlation between IR and endometrial carcinoma. Insulin as a hormone is very crucial for the normal cellular proliferation in the endometrium. Even the growth hormone that helps in the somatic growth requires insulin to exert its action in the endometrium. The hyperandrogenic state in the present study is due to the increase in the insulin levels because various *in vitro* studies proved that insulin and ILPs, especially IGF-1, enhance the synthesis of androgens by the gonads and adrenal glands.[13] Such androgenic state would lead to anovulatory cycles, in which deficiency of progesterone indirectly increases the activity of estrogen and causes tissue damage. The development of IR due to high-sugar intake follows a certain pattern. A large cohort study involving 23,039 postmenopausal women in the United States population showed that fruit juice intake is not associated with the risk of Type I endometrial cancer, whereas fruit juice added with SSBs (fructose content) increases the risk of endometrial cancer for up to 38% or higher.[6] Similarly, in the present study, animals fed with a

Table 3: *Post Hoc* analysis of glucose parameters

Parameter	Group	Mean±SD	*P*
Glucose	Control group	139.20±10.82	0.003***
	High-fructose diet group	218.83±18.09	
	Control group	139.20±10.82	0.865
	High-coconut sugar diet group	141.62±6.09	
Insulin	Control group	1.488±0.251	0.001***
	High-fructose diet group	4.085±0.260	
	Control group	1.488±0.251	0.829
	High-coconut sugar diet group	1.521±0.083	
HOMA - IR	Control group	0.52±0.130	0.001***
	High-fructose diet group	2.217±0.248	
	Control group	0.52±0.130	0.823
	High-coconut sugar diet group	0.61±0.707	

SD: Standard deviation, HOMA - IR: Homoeostasis model assessment-insulin resistance

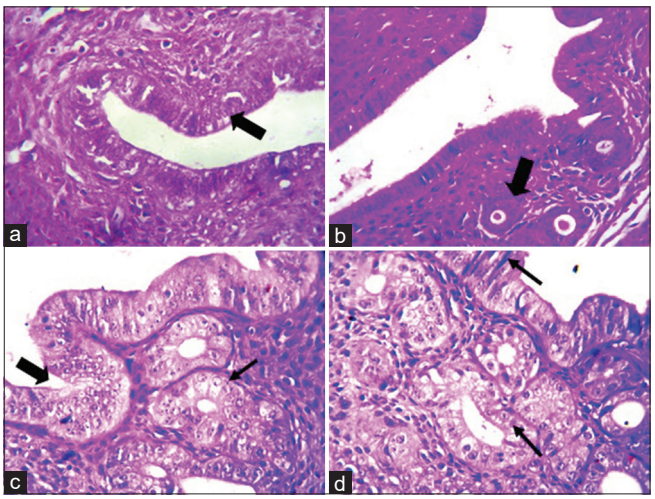

Figure 1: Endometrium stained with eosin and hematoxylin at ×400. (a) (Control) and (b) (high-coconut sugar group) – Endometrium appears normal (thick arrows). (c and d) (High-fructose group) – Focal stratification of epithelium (thick arrows), complex glandular hyperplasia with crowding (thin arrows), nuclear atypia – thin arrow in (d)

Table 4: Kruskal-Wallis test for hormonal parameters

Parameters	Control group	High-fructose diet group	High-coconut sugar diet group	*P*
FSH (mIU/mL)	0.12±0.02	0.16±0.04	0.12±0.02	0.441
LH (mIU/mL)	0.12±0.02	0.11±0.01	0.12±0.02	0.968
Testosterone (ng/mL)	0.025±0.002	0.073±0.004	0.028±0.003	<0.001***
Progesterone (ng/mL)	0.744±0.06	0.755±0.04	0.75±0.03	0.725
Estradiol (pg/mL)	5.5±0.45	9.63±0.47	5.32±0.44	<0.001***

***Statistically highly significant. FSH: Follicle-stimulating hormone, LH: Luteinizing hormone

Table 5: *Post hoc* analysis of hormonal parameters

Parameter	Group	Mean±SD	*P*
Testosterone	Control group	0.025±0.002	0.030**
	High-fructose diet group	0.073±0.004	
	Control group	0.025±0.002	1.000
	High-coconut sugar diet group	0.028±0.003	
Estradiol	Control group	5.5±0.45	0.006***
	High-fructose diet group	9.63±0.47	
	Control group	5.5±0.45	0.924
	High-coconut sugar diet group	5.32±0.44	

**Statistically significant. SD: Standard deviation

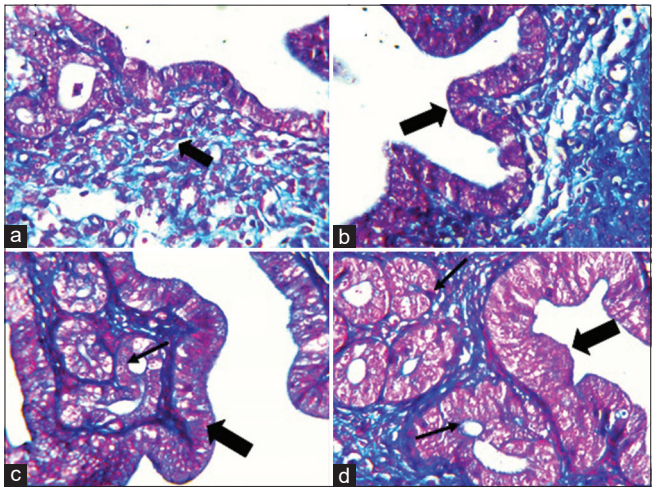

Figure 2: Histopathological observation of endometrium stained with Masson's Trichrome at 400X. (a) (Control) and (b) (High coconut sugar group) – Endometrium with simple columnar epithelium, connective tissue stroma appears normal (Thick arrows). (c) and (d) (High fructose group) – Endometrial epithelium shows Focal stratification (Thick arrows), glandular hyperplasia with crowding (Thin arrows) and increased glands: stroma ratio

high-fructose diet showed endometrial hyperplasia and other premalignant lesions due to IR.

There is a biological cross-talk potential of insulin with obesity-related inflammatory mechanisms; increased adipokine can affect the insulin signal transduction, leading to IR.[14] In this context, adipocytokines such as leptin and adiponectin are implicated in IR.[15] Insulin directly promotes cell proliferation through P13/Akt and Ras/MAPK pathways and indirectly changes the levels of sex hormones and causes increased estrogen level.[16] Therefore, the understanding of insulin as a carcinogen stems from various biochemical events mediated by insulin which promotes carcinogenesis.

Thus, the assessment of IR is important to understand the degree of hyperinsulinemia. Early diagnosis of IR will be helpful for prompt treatment and prevention of this metabolic syndrome. The need to quantify the IR is therefore obligatory, and there is no single gold-standard method for its precise estimation. In the present study, HOMA-IR has been used. It is a mathematical assessment developed by Matthews *et al*. in 1985. It is derived from the product of fasting glucose and fasting insulin divided by a constant. The product of fasting insulin and fasting glucose is the index of hepatic IR. Thus, HOMA-IR = (glucose × insulin)/22.5.[17] In the present study, fructose group animals exhibited HOMA-IR of more than 2 which suggests the development of IR.

In contrast to the elevated biochemical levels in the high-fructose diet group animals, the administration of high coconut sugar in the animals did not show an increase in glucose and insulin levels, and there was no development of IR or increase in the hormone levels in mice. The endometrium of coconut sugar animals is similar to the control group animals in the histopathological evaluation. This is probably due to the increased metabolism of natural unrefined sugars than the refined sugars. The coconut sugar being an organic sweetener proved to be beneficial in the present study.

Conclusion

In the present study, the development of IR is triggered by high-fructose intake, and the endometrium showed marked pathological changes including complex glandular hyperplasia with nuclear atypia. The findings reveal the complex relationship of insulin and endometrial lesions and support the hypothesis of insulin as a serious cancer-inducing agent through its mitotic potential. The coconut sugar though fed every day in high concentrations similar to fructose did not develop IR. This could be due to the rapid metabolism of natural unrefined coconut sugar. The present study concludes that the intake of natural sugars not only prevents the development of IR but also beneficial to the reproductive health of women.

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Conflicts of interest

There are no conflicts of interest.

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Original Article

Correlation Analysis of the Anatomical Structures Related to Maxillary Sinus Augmentation

Abstract

Aims: Preoperative evaluation of maxillary sinus anatomy is crucial to minimize procedural complications. The aim of this study was to assess the anatomical structures associated with sinus augmentation and investigate the correlation between these structures. **Materials and Methods:** This retrospective study included cone-beam computed tomography scans of patients referred for the reconstruction of the posterior maxilla with dental implants. The intraosseous anastomosis (PIA) and septa were evaluated on the images. Lateral wall thickness (LWT), the diameter of the PIA (DIA), the vertical distance of the PIA to the sinus floor (DSF), and sinus floor angle (SFA) were also measured. **Results:** A total of 250 sinuses were examined. PIA was detected in 46.8% of the sinuses. The mean SFA value was 77.11° ±11.11° (range 48.25°–112.33°). The LWT ranged from 0.63 to 10.23 mm with a mean value of 1.35 ± 0.79 mm. Of 250 sinuses, 82 (32.8%) showed septa. A strong negative correlation was found between SFA and PIA detection (r = 0.98, P = 0.008), SFA and DSF (r = 0.99, P = 0.000), and SFA and septa (r = 0.98, P = 0.000). LWT showed a positive correlation with DIA (r = 0.72, P = 0.082), although not statistically significant. **Conclusions:** The relationships highlight the combined effect of the structures on membrane perforation. As this makes the lateral window approach more problematic, the surgeon may seek minimally invasive approaches. Moreover, the strong correlation of SFA-PIA-DSF may significantly affect graft vascularization and needs to be evaluated with clinical studies.

Keywords: *Anatomy, cone-beam computed tomography, dental implant, maxillary sinus augmentation, posterior superior alveolar artery, sinus floor angle*

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Introduction

Maxillary sinus floor elevation by lateral window approach is a predictable method for increasing posterior maxillary alveolar bone height.[1] However, clinicians should be aware of the intra- and postoperative complications when performing this procedure. Procedural complications such as Schneiderian membrane perforation and bleeding may occur during lateral window preparation and membrane elevation.

Membrane perforation, the most common intraoperative complication associated with this procedure, has been reported to occur in 11%–56%.[2] Several factors such as irregularities in the sinus floor, lateral wall thickness (LWT), angulation of the sinus walls, sinus septa, and intraoperative bleeding may pose a risk for membrane perforation.[3] The disruption of membrane integrity increases the risk of graft contamination and sinus infection, compromising treatment outcomes.[4]

According to Cho *et al*.,[5] the angle between the buccal and palatal alveolar walls was associated with membrane perforation (37.5% in sinuses angled ≤30 and 0% in sinuses angled ≥61). The angle is related to the mediolateral width of the sinus, so it also plays a role in graft maturation. A larger mediolateral width negatively affects vital bone formation after sinus augmentation through the lateral window technique.[6] In addition, a higher resorption rate of the graft may be anticipated with the larger mediolateral width.[7]

Vascular supply to the grafted area in the maxillary sinuses occurs through three arteries: the posterior superior alveolar artery (PSAA), the infraorbital artery (IOA), and the posterior lateral nasal artery (PLNA).[8] While PLNA provides vascularization to the medial wall of the sinus, PSAA and IOA vascularize the lateral wall and Schneiderian membrane. PSAA and IOA have extra- and

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intraosseous branches that form anastomoses in the lateral wall. The intraosseous anastomosis of posterior superior alveolar artery and infraorbital artery (PIA) may be severed during lateral window preparation, resulting in bleeding, the second-most common intraoperative complication.[3] As a result of bleeding, the vision of the surgical field may deteriorate, and membrane perforation may occur. In addition, graft neoangiogenesis is adversely affected due to the compromised vascular supply.

Preoperative imaging with cone-beam computed tomography (CBCT) provides accurate measurements for assessing the maxillary sinus anatomy, which may be helpful in terms of procedural modifications to minimize the complications and maximize augmentation outcomes. This retrospective study aimed to assess the anatomical structures associated with sinus augmentation on CBCT images and investigate the correlation between these structures.

Materials and Methods

The study protocol was prepared according to the Declaration of Helsinki,[9,10] and it was approved by the Ethics Committee of Kutahya Health Sciences University (Decision Number: 2019 / 03). This retrospective study included CBCT scans of patients referred to the Department of Periodontology, Faculty of Dentistry, Kutahya Health Sciences University, to reconstruct the posterior maxilla with dental implants between October 2018 and December 2019.

High-quality images with a sufficient field of view (covering the maxillary sinus regions) were included in the study. CBCT evaluation was performed in the presence of at least one edentulous space in both the right and left posterior maxillary regions. CBCT images of grafted maxillary sinuses, tumor pathologies or traumatic lesions, and rehabilitated posterior maxilla with implants were excluded from the study.

Radiographic measurements

CBCT scans were performed with the OP300 CBCT device (Instrumentarium, Tuusula, Finland). The images were obtained at 90 kV, 3.2 mA with an exposure time of 8.14 s and volume size of 80 mm ×150 mm. The scans were saved in DICOM format, and the images were analyzed using OnDemand3D Dental (Cybermed, Seul, South Korea). The measurements were made to the nearest 0.01 mm or degree with a digital caliper on cross-sectional images.

All measurements were carried out by one calibrated investigator (EG). Intraobserver reliability was assessed with 78 randomly selected scans measured for a second time, 2 months after the first measurement. The following measurements were performed on the images. Linear (LWT, the diameter of the PIA [DIA], the vertical distance of the PIA to the sinus floor [DSF]), and angular measurements (sinus floor angle [SFA]) are illustrated in Figure 1.

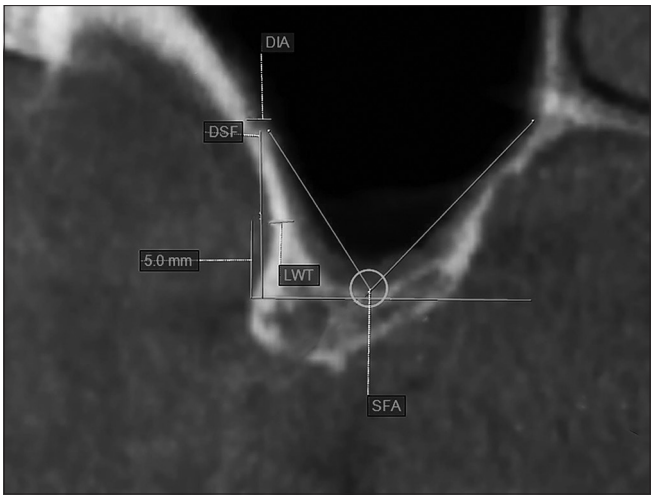

Figure 1: Representative image of linear and angular measurements made on cross-sectional images

Lateral wall thickness

LWT was measured at a distance of 5 mm from the maxillary sinus floor, taking into account the inferior border of the lateral window.[11] The average of all measurements taken from the mesial, midbuccal, and distal of the corresponding edentulous space was obtained. The mean of all the edentulous spaces was recorded as the final value.

Diameter of the PIA

The greatest value between the apparent anterior and posterior position of the anastomosis was measured. DIA was classified into three groups: (a) <1 mm, (b) 1–2 mm, and (c) >2 mm.[12]

Distance of the PIA to the sinus floor

The lower border of the anastomosis was considered in measurements. The mean of all measurements taken from the mesial, midbuccal, and distal of the corresponding edentulous space was obtained. According to the final average value, DSF was classified into the following groups: (a) <5 mm, (b) 5–10 mm, (c) >10 mm. The inferior and superior borders of the window from the sinus floor were considered in this classification.[11]

Sinus floor angle

The angle between the lateral and medial walls at 10 mm from the sinus floor was measured [Figure 2].[13] The mean of all measurements taken from the mesial, midbuccal, and distal of the corresponding edentulous spaces was obtained.

Septa

The detection of septa was evaluated dichotomously.

The health status of the Schneiderian membrane was assessed by the thickness of the membrane. Membrane thickness (MT) >3 mm was considered pathologic.[14]

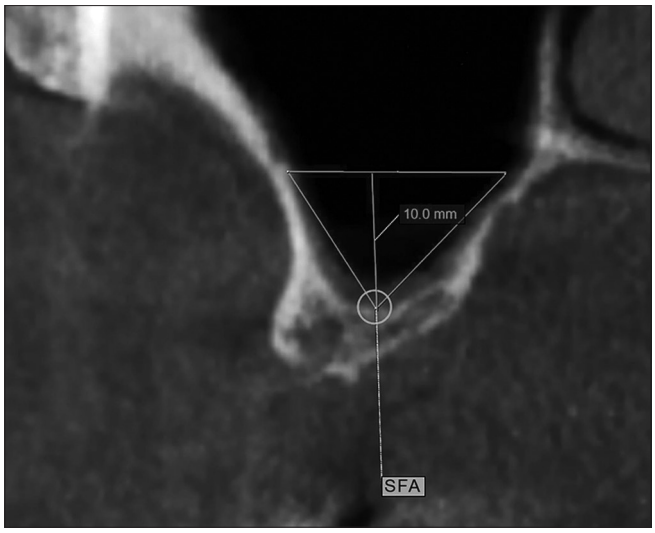

Figure 2: Representative image of sinus floor angle measurement

Statistical analysis

The data obtained in the study were evaluated using SPSS statistical software (SPSS for Windows, version 20, IBM Corp, Armonk, NY, USA) program for statistical analysis. Descriptive statistics such as mean, standard deviation, and largest–smallest value were used for quantitative data in the data evaluation. Frequency tables with frequency and percentage values were used for qualitative data. 2 × 2 or larger cross tables and Chi-square tests were used to examine the relationship between variables. Pearson correlation, Phi, Cramer V, contingency coefficient, Eta, and gamma correlation coefficients were used to calculate the degree and direction of the relationship between the variables. Independent-samples *t*-test and one-way analysis of variance were used to examine the difference between groups. The results were evaluated at 0.01 alpha level.

Results

Statistical analysis showed high intraobserver reliability for all measurements (ranging from 0.81 to 0.97).

The inclusion process of the study is summarized in the flowchart [Figure 3]. Of the 125 patients, 61 were men and 64 were women. The mean age of the patients was 48.71 ± 12.02 years (ranging from 20 to 74 years). A total of 250 maxillary sinuses were examined. PIA was detected in 46.8% of the sinuses. The mean DIA was 1.24 ± 0.51 mm (range 0.51 mm–2.94 mm). According to the DIA classification, 43.6% of the anastomosis was <1 mm, 45.3% was 1–2 mm, and 11.1% was >2 mm. The DSF ranged from 1.96 mm to 19.83 mm (mean distance 7.58 ± 3.06 mm). When DSF was classified, 14.5% of the anastomosis was <5 mm from the sinus floor, 67.5% was between 5 and 10 mm from the sinus floor, and 18% was more than 10 mm.

The LWT ranged from 0.63 to 10.23 mm with a mean value of 1.35 ± 0.79 mm. Of 250 sinuses, 82 (32.8%) showed septa, and 146 (58.4%) showed MT >3 mm. The mean SFA value was 77.11 ± 11.11° (range 48.2°–112.3°).

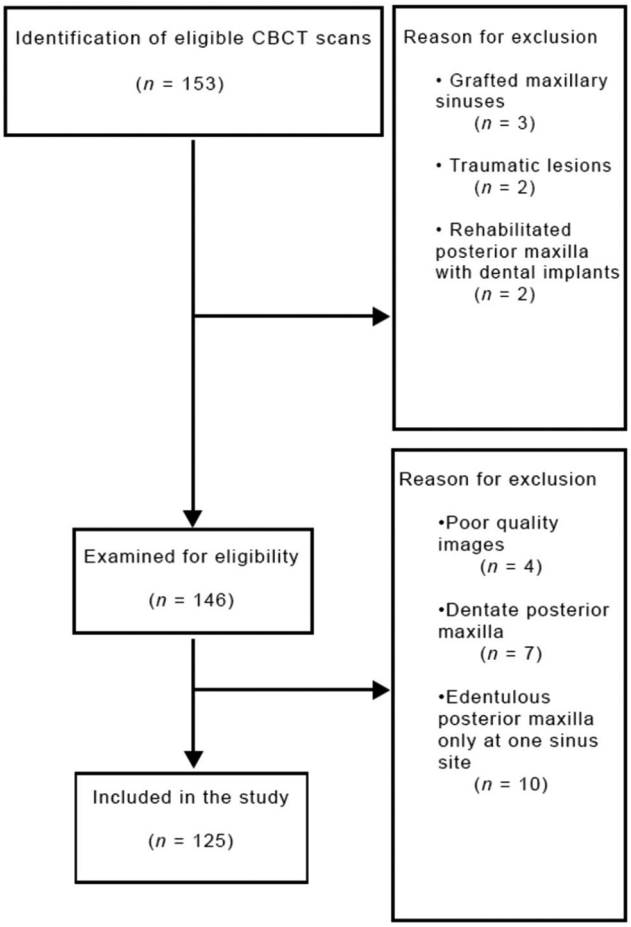

Figure 3: Flowchart depicting the inclusion process

Statistical analysis revealed correlations between study parameters. A strong negative correlation was observed between SFA and PIA detection [$r = 0.98$, $P = 0.008$; Table 1]. Although not statistically significant, a strong positive correlation was found between the angle and DIA ($r = 0.98$, $P = 0{,}056$). While the angle value was 74.3° in the <1 mm diameter class, it was 75.7° and 76.2° in the 1–2 mm and >2 mm class, respectively. The categorical analysis of correlation after stratification of DSF revealed that SFA and DSF displayed a quite strong correlation [$r = 0.99$, $P = 0.000$; Table 2].

There was no significant relation between MT and SFA ($P = 0.786$). However, a strong negative correlation was observed between SFA and septa [$r = 0.98$, $P = 0.000$; Table 3]. LWT showed a positive correlation with DIA, but this association was not statistically significant ($r = 0.72$, $P = 0.082$). There was no significant correlation between LWT and DSF and MT ($P = 0.201$, $P = 0.561$, respectively).

Discussion

A maxillary sinus augmentation is a simple procedure for an experienced surgeon; however, the procedure

Table 1: Descriptive statistics of sinus floor angle with anastomosis detection and analysis of the correlation between sinus floor angle and intraosseous anastomosis of posterior superior alveolar artery and infraorbital artery

	SFA				*r*	*P*
	n	Mean±SD	Minimum	Maximum		
PIA (−)	133	78.85±11.81	49.82	112.33	0.98	0.008*
PIA (+)	117	75.14±9.93	48.25	105.71		
Total	250	77.11±11.11	48.25	112.33		

*Correlation is significant at the 0.01 level. SFA: Sinus floor angle, PIA: Intraosseous anastomosis of posterior superior alveolar artery and infraorbital artery, SD: Standard deviation

Table 2: Descriptive statistics of sinus floor angle based on the DSF classification and correlation analysis between these parameters

	SFA				*r*	*P*
	n	Mean±SD	Minimum	Maximum		
<5 mm	17	80.59±11.76	58.92	105.71	0.99	0.000*
5–10 mm	79	75.91±8.97	54.87	96.80		
>10 mm	21	67.8±7.97	48.25	78.85		

*Correlation is significant at the 0.01 level. SFA: Sinus floor angle, DSF: Vertical distance of the intraosseous anastomosis of posterior superior alveolar artery and infraorbital artery to the sinus floor, SD: Standard deviation

Table 3: Correlation analysis of angle and septa

	SFA				*r*	*P*
	n	Mean±SD	Minimum	Maximum		
Septa (+)	82	73.48±10.04	48.25	103.67	0.98	0.000*
Septa (−)	168	78.88±11.20	54.87	112.33		
Total	250	77.11±11.11	48.25	112.33		

*Correlation is significant at the 0.01 level. SFA: Sinus floor angle, SD: Standard deviation

may become complicated if the sinus anatomy is not adequately evaluated. For this reason, it is very important for the surgeon to examine the relevant structures in three dimensions, namely with CBCT, and to modify the surgical approach before the procedure.

This study evaluated the anatomical structures associated with sinus augmentation. As a result, intraosseous anastomosis was detected in 46.8% of the sinuses. The detection rate of anastomosis varies in the literature. The findings of Güncü *et al*.[15] (64.5%), Velasco-Torres *et al*.[16] (84.5%), and Şimşek Kaya *et al*.[17] (87.7%) were found to be higher than that of the current study. However, Jung *et al*.[18] (52.8%) and Lozano-Carrascal *et al*.[13] (48.6%) reported rates closer to this study. This discrepancy might be due to the anatomical variations, the difference in the CBCT device, and the plane where the measurement was performed. The measurements were made on cross-sectional images in this study. Only one of the studies reported above used cross-sectional images similar to this study.[18] The others reported that measurements were performed on coronal (Velasco-Torres *et al*.,[16] Şimşek Kaya *et al*.[17]), sagittal (Lozano-Carrascal *et al*.[13]), and axial (Güncü *et al*.[15]) sections. In addition, the difference in detection rate can be attributed to the intrasinusal location, which renders the anastomosis radiographically undetectable.[19]

According to the results of this study, SFA showed strong correlations with parameters related to anastomosis. To our knowledge, this is the first study to examine the relationship between sinus angle and artery. One of the strong correlations in this study was between SFA and DSF. The distance of the anastomosis to the sinus floor decreased as the angle value increased. Velasco-Torres *et al*.[16] found similar results when examining the sinus dimensions with respect to the artery and concluded that the mediolateral dimension of the sinus increases as the distance of the artery to the sinus floor decreases. Accordingly, the lower border of the lateral window should be prepared more cranially so as not to damage the anastomosis and thus to provide vascularization to the grafted area in larger sinus areas. In addition, according to the correlation analysis of the current study, the diameter of the anastomosis being higher in the larger angle values underlines the importance of the preparation level in wider sinuses. Nevertheless, more cranial preparation of the lower border makes membrane elevation more difficult. Therefore, in the presence of both an anastomosis and a wider sinus, a transcrestal approach using minimally invasive techniques may be an option.[20,21] Thus, the bone wall and blood supply necessary for the remodeling of the graft can be preserved.

Although not statistically significant, LWT showed a positive correlation with the diameter of the anastomosis. A study examining the anatomical structures of the maxillary sinus emphasized that the risk of bleeding increases in the presence of a thick lateral wall.[22] Therefore, in the presence of a thick lateral wall, it should be anticipated that the risk of perforation may increase due to bleeding caused by a large-diameter artery.

More than half of the CBCT images (58.4%) displayed MT >3 mm. This rate is consistent with the findings of Lana *et al*.[14] (62.6%), Rege *et al*.[23] (66%), and Brüllmann *et al*.[24] (50%). According to the correlation analysis, there was no significant association between LWT and MT. The thickness of the lateral wall is assumed to be affected by the inflammatory conditions of the sinus.[25] However, a recent cadaveric study observed no correlation between the thickness of the membrane and the lateral wall.[26] Considering that the thickest value of the membrane was 0.50 ± 0.19 mm in the cadaveric study, the relationship between these parameters needs to be evaluated with further studies.

The present study defined sinus septa as cortical bone partitions more than 3 mm height and found a detection rate of 32.8%. The studies that used the same definition

criteria found similar rates (Şimşek Kaya *et al*.[17] [32.9%], Park *et al*.[27] [27.7%]). A strong association was found between sinus septa and angle. This finding highlights the difficulty of the lateral window approach and the possibility of perforation in the presence of a narrow sinus.

This study has several limitations. First, residual crest height was not evaluated, and the correlation between the parameters was analyzed irrespective of the crest height. After tooth loss, the alveolar ridge resorbs as a result of the loss of mechanical stimulus and bundle bone.[28] According to the findings of Velasco-Torres *et al*.,[28] the dimensional changes of the sinus largely depend on tooth loss. Therefore, crestal change triggered by the resorptive process may have an impact on the relationships found in this study. Second, the sinus floor was accepted as the reference for LWT and DSF measurements, with the expectation that the change in the sinus floor position after tooth loss would be lower than the residual crest change. Third, edentulous spaces, including the premolar and molar regions, were evaluated in this study. However, the premolar region, especially the first premolar, rarely requires sinus augmentation with a lateral window approach because of adequate bone height.

Conclusions

This radiographic study revealed important relationships between sinus augmentation-related anatomical structures. Relationships (SFA-DSF, SFA-Septa) highlight the combined effect of the structures on membrane perforation. As this makes the lateral window approach more problematic, the surgeon may seek minimally invasive approaches.

The results are not only related to procedural complications but also graft healing. In particular, the strong correlations observed between the angle and the artery may significantly affect graft vascularization. Therefore, the assumptions need to be evaluated by clinical studies.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Original Article

Surgical Significance of Variant Anatomy of Inferior Mesenteric Artery and Left Colic Artery: A Computed Tomography Angiographic Study

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Abstract

Introduction: A variation in vessel morphology determines flow dynamics and vascular disease pathogenesis. Definite information on the distinctive anatomical variations of the mesenteric vessels is extremely important for laparoscopic surgical procedures and interventional radiological procedures in the abdominal region. Three-dimensional-computed tomography angiography (3D-CTA) is a less invasive method to evaluate vascular anatomy using a visual tracking method on high-definition images, contrast-enhanced inferior mesenteric artery (IMA) can be traced to its terminal branches beside the colon wall. **Subjects and Methods:** Abdominal contrast-enhanced computed tomography scan data from 180 patients was retrospectively collected, reconstructed, and analyzed. The origin, length of IMA from origin to the first branch, branching patterns of IMA, and tracking patterns of the ascending branch of left colic artery (LCA), were examined, and their associations with clinical features were analyzed. **Results:** IMA displayed variations in the level of origin ranging from upper 1/3 of L3 to upper 1/3 of L4, mean length from origin to the first branch was 27.4 ± 7.8 mm. Observed branching patterns of IMA were grouped according to Yada classification: Type 1 (52.2%), Type 2 (15.5%), Type 3 (14.4%), and Type 4 (17.7%). Tracking of the ascending branch of LCA before anastomosis with marginal artery revealed four patterns: Type A LCA pattern in 43.9%; Type B LCA anatomy pattern was (19.4%); Type C LCA anatomy pattern was (20.0%); and Type D LCA anatomy pattern was observed (16.7%). **Conclusion:** Preoperative understanding of the vascular variations of IMA and LCA can be obtained by 3D-CTA. This may be helpful to surgeons in planning preoperative strategies to prevent iatrogenic injuries.

Keywords: *Cancer, computed tomography angiography, inferior mesenteric artery, left colic artery, vascular*

Introduction

The inferior mesenteric artery (IMA) is the last incongruous branch of the abdominal aorta arising at L3–L4 vertebral level. It supplies the distal part of the intestine, including left 1/3 of the transverse colon, descending colon, and upper segment of the sigmoid colon and rectum. The branches of IMA from proximal to distal are left colic artery (LCA) which lies behind the peritoneum supplying descending colon, the sigmoid artery (SA) which supplies the sigmoid colon, and the superior rectal artery (SRA) supplying the rectum and upper anal canal.[1]

The LCA shows a variable and short course and divides into ascending and descending branches. The ascending branch runs superiorly, anterior to the left kidney before it supplies the transverse mesocolon. Around the splenic flexure of the colon, a collateral is formed among the ascending branch of LCA and a branch arising from the left of the middle colic artery called the Arc of Riolan. This anastomosis plays a significant role during stenosis and occlusion by providing collateral blood flow.[2] The anatomical characteristics of these IMA branches are particularly important in colorectal surgery and directly affect the choice of IMA treatment.[1] The IMA ligation is preferred during surgery for colonic cancer yet, studied by few surgeons while planning a surgical approach.[3] Patients' postoperative quality of life and mortality time are directly impacted by how the IMA is managed during surgery. In order to conduct safe ligation of the artery and lymph node dissection, surgeons should have an idea about the mesenteric vasculature. To develop preoperative strategies for surgical procedures, the accurate knowledge of anatomical

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variations, branching pattern, and IMA root value are of great significance.[4]

Diagnostic contrast-enhanced computed tomography (CT) is one of the important and commonly used preoperative tools for patients' workups. It helps to confirm the clinical diagnosis and distant metastasis and to define the vessel anatomy. In their daily practice, vascular anatomy of colon is not routinely described by reporting by radiologist. The preoperative assessment of vessels should be incorporated by surgeons for identifying and evaluating the IMA branching pattern to perform anatomy-oriented segmental resections. This preoperative step is necessary to plan an approach to IMA skeletonization if selective branch ligation is supposed.[3]

Subjects and Methods

The study was conducted in the Department of Anatomy in collaboration with the Department of Radiodiagnosis at King George's Medical University, Lucknow, U.P. The present study was conducted on CT data belonging to 180 patients (79 males and 101 females), visiting the Department of Radiodiagnosis for CT angiography (CTA) of abdominal vessels for any medical or surgical indication.

Approval of the study was obtained from the Institutional Ethical Committee, Office of Research Cell, KGMU, U.P, Lucknow, Registration NO.ECR/262/Inst/UP/2013/RR-19, Ref code Approval letter no. 96/ANAT/21.

Inclusion criteria

CT scan data belonging to subjects who visited the radiodiagnosis department for CTA of abdominal vessels for various medical and surgical indications, including elective and emergency medical conditions were included in the study.

Exclusion criteria

1. History of previous upper abdominal surgery or organ transplantation
2. Any condition that could modify normal arterial blood flow or which is associated with abnormal collateral vessels, such as stenosis or occlusion, dissection, vasculitis, or suprarenal aortic aneurysm
3. Arterial atherosclerosis
4. Incomplete data or images where arterial anatomy could not be observed clearly.

Methodology

Computed tomography angiography scanning protocol

Examination was carried out using Philips Brilliance-64 Slice. Careful attention was given to the technique for accurate and detailed imaging of mesenteric vessels.

The examination included the region between Dome of diaphragm to the pubic symphysis.

IMA was localized using specific landmarks in three dimensional (3D) volume-rendered images and vessel morphology was observed with special reference to:

1. Vertebral level of origin: It was observed in reformatted coronal view by manual tracing. Vertebrae were counted from the sacral to lumbar region, for specific localization of origin the body of the vertebra was divided into upper 1/3, middle 1/3 and lower 1/3 [Figure 1]
2. The length of IMA from its origin to its first branch was measured in a 3D volume-rendered image as the distance from the IMA root to the origin of first branch [Figure 2]
3. IMA's branching pattern, also called IMA typing, and four classical types of IMA branching were identified according to the Yada classification
   - Type 1 LCA independent origin from IMA [Figure 3]
   - Type 2 LCA and SA origin from a common trunk [Figure 4a]
   - Type 3 LCA, SA, and SRA origin at same point [Figure 4b]
   - Type 4 LCA absent [Figure 5].
4. Tracking pattern of the course of ascending branch of LCA on 3D volume rendered image by 3D vessel tracing:
   - Type A: ascending branch of LCA runs straight upward, medially to the inner border of the left kidney [Figure 6]
   - Type B: ascending branch of LCA runs superolateral towards the left kidney and diagonally crosses the middle of the left kidney [Figure 7]
   - Type C: ascending branch of LCA traveled inferolateral below the lower border of the left kidney [Figure 8]
   - Type D: LCA was absent.

Statistical analysis

The SPSS (Statistical Package for the Social Sciences) version 21.0 Statistical Analysis Software was used

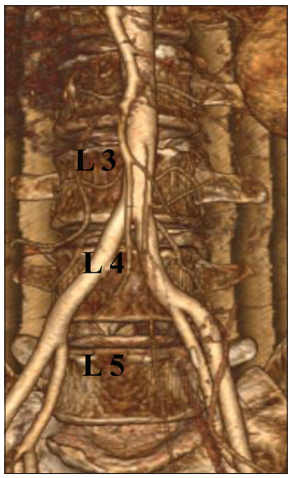


Figure 1: Three-dimensional volume-rendered image; red arrow showing inferior mesenteric artery vertebral level l3 upper 1/3

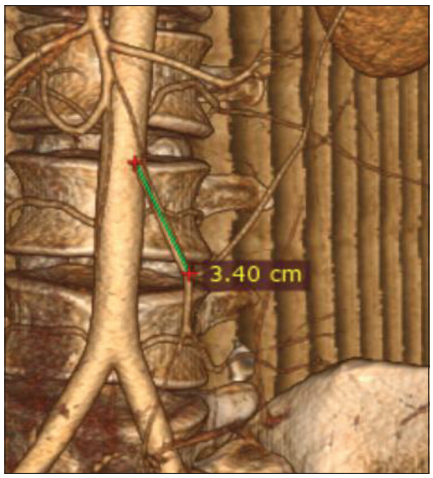


Figure 2: 3D – Volume-rendered image; inferior mesenteric artery distance from the origin to the first branch

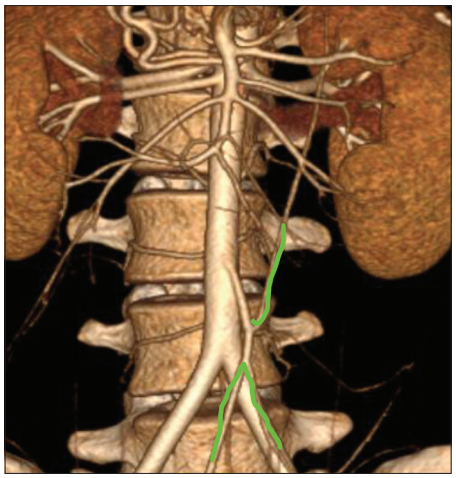


Figure 3: 3D – Volume-rendered image; branching pattern of inferior mesenteric artery TYPE 1

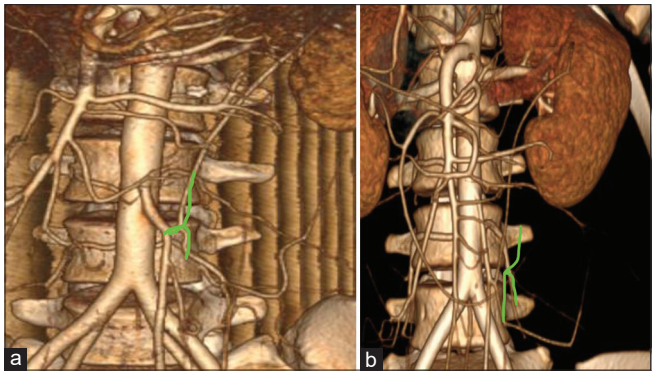


Figure 4: (a) 3D – Volume-rendered image; branching pattern of inferior mesenteric artery Type 2 (b) 3D volume-rendered image; branching pattern of inferior mesenteric artery Type 3

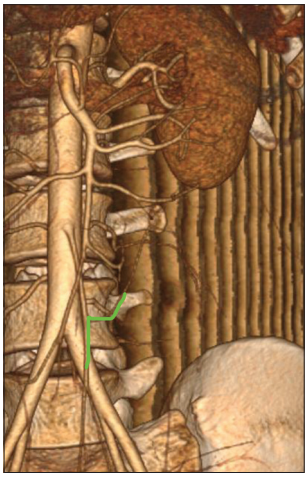


Figure 5: 3D – Volume-rendered image; branching pattern of inferior mesenteric artery Type 4

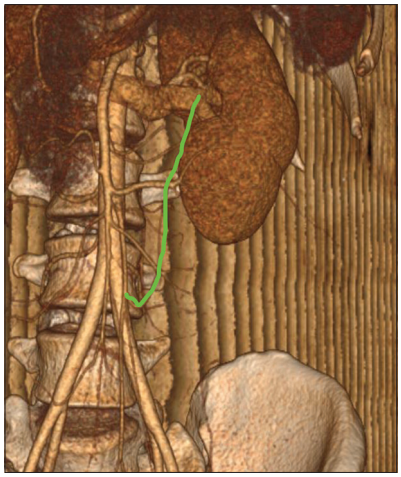


Figure 6: 3D – Volume-rendered image; left colic artery course TYPE A

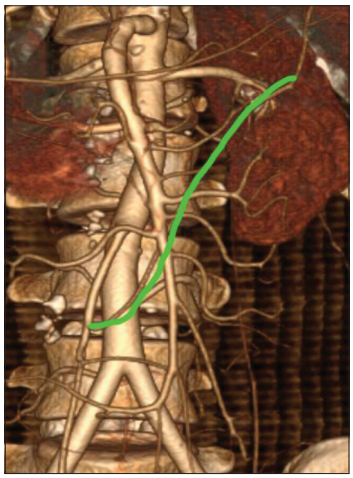


Figure 7: 3D – Volume-rendered image; left colic artery course TYPE B

to conduct the statistical analysis. Number (%) and mean ± standard deviation were used to display the values.

Results

In the present study, IMA originated from abdominal aorta in all 180 cases. No variation in the source artery was observed in the study sample 79 male cases (43.9%) and 101 female cases (56.1%). This was consistent with how the textbooks normally describe the origin of IMA.

IMA displayed origin spanning varying vertebral levels ranging from upper 1/3 of L3 to upper 1/3 of L4. More common IMA vertebral level of origin was lower 1/3rd of L3 (38.9%) and upper 1/3rd of L4 (38.3%). Least common vertebral level was upper 1/3rd of L3 (6.7%).

Origin of IMA was at higher levels in females as compared to male subjects. Origin of IMA was at middle 1/3 of L3 and lower 1/3 of L3 in higher proportion in females and lower 1/3 of L3 and upper 1/3 of L4 level of origin was proportionately higher among males; the difference in level of origin was found to be significant statistically (P = 0.016).

The mean length of IMA from the origin to the first branch was 27.4 ± 7.8 mm ranged 12.9–49.6 mm. The overall mean length of IMA from origin to the first branch was more in males (27.7 ± 8 mm) as compared to females (27.2 ± 7.7 mm).

Branching pattern of the IMA was observed and categorized as per the Yada classification[5] and various patterns were observed Table 1. Type 1 branching pattern was most common at all the vertebral levels of origin Graph 1.

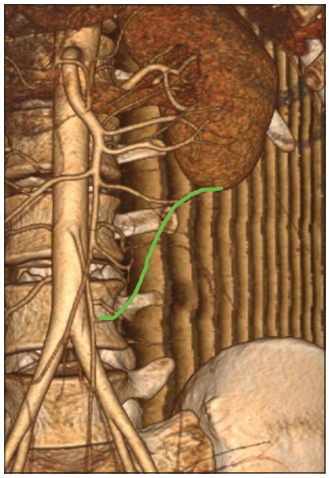
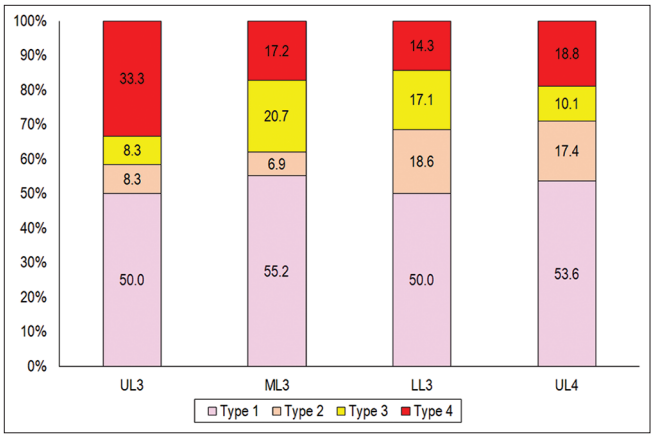


Figure 8: 3D – Volume-rendered image; left colic artery course TYPE C

Tracking pattern of the course of the ascending branch by 3D vessel tracing revealed four patterns. The comparison was done at different vertebral levels [Table 2]. Overall Type A LCA anatomy pattern was most common (n = 79; 43.9%). Although different vertebral levels of origin displayed different proportions of patterns of origin the difference were significant statistically [Graph 2], we studied the relationship between the branching pattern of IMA and length and it was observed that the maximum length of IMA was associated with Type C (2.97 ± 1.07 cm) and the minimum length with Type A (2.61 ± 0.63 cm) pattern [Table 3].

Discussion

Colorectal cancers are accountable for about 10% of all cancers worldwide and about 9.2% of all cancer-related deaths are caused by colorectal cancer. Surgery remains the most radical treatment method for colorectal cancer.[6] Laparoscopic surgery is becoming more popular as a minimally invasive treatment for colorectal cancer as patients undergoing laparoscopic colorectal cancer resection experience better post-surgical outcomes with a considerably minimal hospital stay due to fast



Graph 1: Comparison of branching pattern of different vertebral levels

Table 1: Comparison of branching pattern of different vertebral levels

Branching pattern	Total (n=180)	UL3 (n=12), n (%)	ML3 (n=29), n (%)	LL3 (n=70), n (%)	UL4 (n=69), n (%)
Type 1	94	6 (50.0)	16 (55.2)	35 (50.0)	37 (53.6)
Type 2	28	1 (8.3)	2 (6.9)	13 (18.6)	12 (17.4)
Type 3	26	1 (8.3)	6 (20.7)	12 (17.1)	7 (10.1)
Type 4	32	4 (33.3)	5 (17.2)	10 (14.3)	13 (18.8)

χ^2=7.002 (df=9), P=0.637

Table 2: Comparison of left colic artery anatomy pattern of different vertebral levels

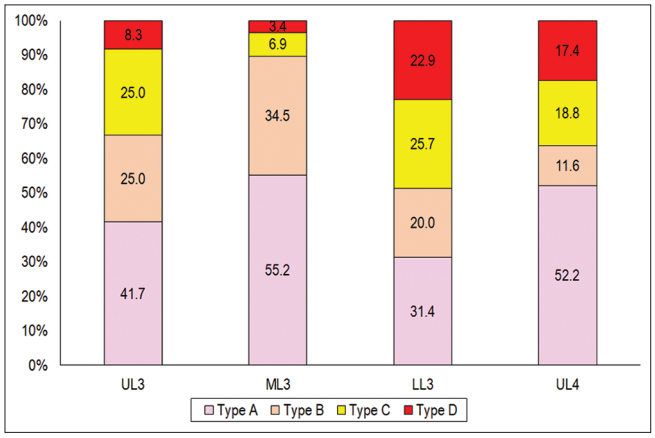
LCA anatomy pattern	Total (n=180)	UL3 (n=12), n (%)	ML3 (n=29), n (%)	LL3 (n=70), n (%)	UL4 (n=69), n (%)
Type A	79	5 (41.7)	16 (55.2)	22 (31.4)	36 (52.2)
Type B	35	3 (25.0)	10 (34.5)	14 (20.0)	8 (11.6)
Type C	36	3 (25.0)	2 (6.9)	18 (25.7)	13 (18.8)
Type D	30	1 (8.3)	1 (3.4)	16 (22.9)	12 (17.4)

χ^2=19.172 (df=9), P=0.024. LCA: Left colic artery

recovery.[7] The surgeon should have detailed information of the colorectal vascular anatomy and associated variations to prevent postoperative morbidity and favorable long-term results.[6] One of the most serious complications of colorectal cancer surgery is anastomotic leakage; there are various factors that affect anastomotic leakage, but insufficient blood supply is the key factor.[6]

This research aimed to examine the structural variances of IMA in humans, as well as any potential clinical and surgical implications. The key findings of our study were as follows:

IMA originated from the abdominal aorta in all 180 cases and the most common IMA vertebral level was lower 1/3rd of L3 (38.9%) and upper 1/3rd of L4 (38.3%). which was comparable to a CT angiographic study in an Indian population of 300 subjects that reported that the level of origin was upper 1/3 of L3 (29.33%); middle 1/3 of L3 (25.33%); lower 1/3 of L3 (14%); and upper 1/3 of L4 (6%).[8] The differences seen were due to more cases in their study. A CT angiographic study on 227 Jordanian subjects also reported the level of origin as L2 (n = 10; 4.4%), L2/L3 (n = 58; 25.6%), L3 (n = 122; 53.7%), L3/L4 (n = 32; 14.1%), and L4 (n = 5; 2.2%).[9]



Graph 2: Comparison of left colic artery anatomy pattern of different vertebral levels

In the present study, the mean length from the origin to the first branch was 27.4 ± 7.8 mm (range was 12.9–49.6 mm). On comparing with other previous studies conducted, the differences were observed [Table 4]. The differences in the result observed were mainly due to the different ethnicity of the study group in the study population.

The overall mean length of IMA from origin to the first branch was more in males (27.7 ± 8.0 mm) as compared to females (27.2 ± 7.7 mm), but no statistical significance was found (P = 0.718). The findings were concordant with previous studies.[4] who reported that the mean length in male subjects was 37.45 ± 9.02 mm, but no statistical significance was observed among gender.

D3 approach surgical management of colorectal cancer involves dissection of the pericolic/perirectal, intermediate, and main lymph nodes for surgical management of cancer colon and rectum. Lymph nodes extending along the IMA from its origin to the origin of LCA are known as inferior mesenteric root nodes (No. 253 lymph nodes).[13] Surgical resection of IMA is preferred at 1.0–1.5 cm distal to its origin, following dissection of lymph nodes, and exposure of aorta avoided to minimize the chances of autonomic nerve injury.[13] Greater length of IMA translates into increase surgery time for lymph node dissection. Preoperative awareness of IMA length can avoid unnecessary intraoperative IMA exposure.[14]

We followed the Yada classification accepted by most researchers to observe the branching pattern of the IMA[5] and found that the Type 1 branching pattern was the most common (n = 94; 52.2%). We compared our data with other studies [Table 5].

Table 3: Relation between the length of inferior mesenteric artery (length from origin to first branch) and branching pattern of inferior mesenteric artery

LCA pattern	*n*	Minimum	Maximum	Mean±SD	95% CI lower bound	95% CI upper bound
Type 1	94	1.31	4.05	2.61±0.63	2.48	2.74
Type 2	28	1.44	4.60	2.71±0.86	2.37	3.04
Type 3	26	1.29	4.96	2.97±1.07	2.53	3.40
Type 4	32	1.74	4.53	2.95±0.77	2.67	3.23
Total	180	1.29	4.96	2.74±0.78	2.62	2.85

P=0.0382. SD: Standard deviation, CI: Confidence interval, LCA: Left colic artery

Table 4: Inferior mesenteric artery mean length comparison in different studies

Author	Population group	Type of study	Mean length (mm)
Zhou *et al*., 2022[4]	212, Chinese	CT angiographic	39.77±10.98
Zuo *et al*., 2020[10]	249, Chinese	CT angiographic	38.5±10.7
Ke *et al*., 2017[11]	188, Chinese	CT angiographic	41.1±10.5
Sinkeet *et al*., 2013[12]	55, Black African	Cadaveric	35.6±10.3
Present study, 2022	180, Indian	CT angiographic	27.7±7.8

CT: Computed tomography

Table 5: Statistics of inferior mesenteric artery branching type in different studies

Authors	Year	Study type	Population group	Subjects	Type 1 (%)	Type 2 (%)	Type 3 (%)	Type 4 (%)
Zhou *et al*.[4]	2022	CT imaging	Chinese	212	53.8	23.1	20.7	4.8
Cai *et al*.[15]	2017	CT imaging	Chinese	123	49.6	28.5	19.5	2.4
Zuo *et al*.[10]	2020	CT imaging	Chinese	249	44.6	22.5	31.3	1.6
Balcerzak *et al*.[16]	2021	Cadaveric	Polish	40	57.5	25	5	5
Wang *et al*.[17]	2018	CT imaging	Chinese	110	46.4	23.6	30	-
Ke *et al*.[11]	2017	CT imaging	Chinese	188	47.3	27.1	20.7	4.8
Murono *et al*.[14]	2015	CT imaging	Japanese	471	41.2	44.7	-	5.1
Present study	2022	CT imaging	Indian	180	52.2	15.5	14.4	17.7

CT: Computed tomography

On studying the relationship between the branching pattern of IMA and length, it was observed that the maximum length of IMA was associated with Type C (2.97 ± 1.07 cm) and the minimum length with Type A (2.61 ± 0.63 cm) pattern. Knowledge of the IMA branching type helps to guide lymph node dissection and LCA preservation as required peroperatively.[10]

Two types of techniques are included in colorectal surgery high tie and low tie ligation. In high-tie procedure, IMA is ligated 2 cm from its origin and in low tie the ligation is done after the origin of LCA or 5 cm from the origin of IMA.[18] The ligation techniques have remained debatable; high ligation is less commonly done as compared to low ligation, each has its own *pros and cons*, but the decision should be individualized on the basis of findings of vascular anatomy.[6] As per their study, high ligation is compulsory when there is a common trunk between LCA and the SA which is a type 2 branching pattern in our study. Preoperative knowledge of root level, length of IMA, and branching pattern help in proper planning and accurate vascular ligation and prevention of autonomic nervous damage and anastomotic leakage.

Tracking pattern of the course of the ascending branch of LCA was done on 3D volume rendering by 3D vessel tracing. Three patterns were visualized and Type A LCA anatomy pattern was the most common (n = 79; 43.9%). while in a previous study Type, A pattern was commonly followed by Type B.[11] Other author has also conducted a similar CT angiographic study on 123 Chinese subjects but has considered only two patterns. In Type A (57.7% n = 71) patients, LCA ascended medial to the lateral border of the left kidney, while in Type B (13.0% n = 16) patients, LCA was arranged below the inferior border of the left kidney.[15]

The anatomy of the IMA and its branches has a significant role in the surgeon's choice of whether to ligate the IMA in a high or low location. Knowledge of these variables is relevant in this context since their study and investigation are important and valid, particularly for surgeons and professionals who operate in this area, avoiding difficulties and iatrogenic circumstances.

Conclusion

IMA anatomy is prone to frequent variations; if lymph node resection along with vasculature preservation is needed, and then preoperative information is helpful to avoid poor outcomes. This knowledge of variant anatomy will help to resolve anatomical ambiguity that could affect the result of surgery for rectal cancer. Variations in IMA bifurcation patterns may complicate surgical procedures making them difficult and time-consuming; hence, presurgical awareness regarding these variations may help to facilitate the surgery. Prior knowledge of the vessel anatomy helps the surgeon in better preoperative planning and avoiding iatrogenic errors.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Original Article

Recent Advances in Research on Acupuncture Treatment for Knee Osteoarthritis

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Abstract

Background and Objective: Knee osteoarthritis (KOA) is one of the leading causes of disability worldwide. In recent years, the incidence of KOA has been gradually increasing due to population aging and lifestyle changes. As a result, there has been a growing body of research and clinical applications related to acupuncture treatment for KOA. The aim of this study is to analyze and summarize the clinical research progress of acupuncture treatment for KOA in the past 5 years. It seeks to understand the current developments and trends in this field and lay the foundation for future research. **Methods:** Conducted a systematic review and analysis of clinical research literature on acupuncture treatment for KOA published in the last 5 years, both domestically and internationally. **Results:** Acupuncture treatment for KOA has shown diverse and effective methods. However, the quality of research literature varies, leading to differences in reported treatment outcomes and a lack of high-quality research findings. **Conclusions:** It was recommended that future research should develop comprehensive and well-designed study protocols, conduct research with scientific rigor, and improve the overall quality of scientific investigations. In addition, it is advisable to include a few horizontal comparative studies to provide more evidence for the clinical application of acupuncture in treating KOA.

Keywords: *Acupuncture treatment, knee osteoarthritis, literature, research progress, review*

Introduction

Knee osteoarthritis (KOA) is characterized by degenerative changes in articular cartilage and chronic inflammation involving the joint structures. It leads to limited cartilage destruction and bone fragment formation.[1,2] Clinical manifestations include knee pain, swelling, stiffness, and functional impairment.[3,4] KOA prevalence and incidence increase with age, more common in women. In middle-aged and elderly over 40 years, the prevalence ranges from 6.5% to 36.4%, reaching 50% in those over 60% and 65% in those over 75 years.[5-8] Age, obesity, joint trauma, inflammation, and genetics contribute to KOA development.[9]

The literature on acupuncture for treating KOA is extensive. Acupuncture techniques have evolved alongside modern technology and clinical practices. As KOA incidence rises due to aging and lifestyle changes, acupuncture research and clinical applications have grown, and its efficacy and safety gain increasing interest. Reviewing recent clinical studies on acupuncture for KOA within the last 5 years is crucial for a comprehensive and systematic summary of the latest research findings and advancements in this field. By ensuring scientific validity and credibility and avoiding outdated or unreliable literature, this approach enhances the review's validity and lay the foundation for future studies and research in this area.

Acupuncture treatment

Acupuncture treatment primarily includes traditional acupuncture (TA), warm needle acupuncture (WNA), fire needle (FN), electro-acupuncture (EA), knife-needle (KN) therapy, blood-letting therapy through channel puncture, balance acupuncture (BA) therapy, catgut embedding therapy, and comprehensive therapy.

Traditional acupuncture therapy

TA is a common and essential treatment for KOA using acupuncture.[10] Studies[11,12] show that TA reduces local knee joint inflammation, promotes chondrocyte proliferation, inhibits chondrocyte apoptosis, and decreases expression of inflammatory

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factors such as tumor necrosis factor (TNF)-α and interleukin (IL)-1β. These effects improve clinical symptoms and enhance KOA patients' quality of life.

Tu *et al*.[13] conducted a study to evaluate acupuncture's clinical efficacy in treating KOA. They randomly assigned 42 patients into two groups: The acupuncture group (21 cases) received conventional acupuncture treatment and the sham acupuncture group (21 cases) received superficial nonacupoint needling. The acupuncture group received treatment at 5–6 local acupoints and 3–4 distal acupoints for 8 weeks, three times per week. Results showed that the acupuncture group exhibited significantly higher pain and daily activity scores compared to the sham acupuncture group after treatment and during follow-up ($P < 0.05$). Acupuncture demonstrated more substantial improvements in pain and daily activity function of the affected joints than sham acupuncture, indicating its effectiveness in alleviating pain symptoms and enhancing daily activity capacity in KOA patients. Chen[14] conducted a study with 54 KOA patients treated using TA or oral Celecoxib capsules. Acupoints like Yanglingquan, Yinlingquan, and two additional acupoints (A'shi points) near the knee joint, or Neixiyan, Dubi, were selected for acupuncture. Both groups showed reductions in Visual Analog Scale (VAS) and WOMAC scores after 2 weeks. The acupuncture group exhibited significant decreases in serum C-reactive protein (CRP) and IL-6 levels ($P < 0.05$). In contrast, the celecoxib group showed less pronounced changes in serum IL-6 and CRP levels compared to acupuncture. The changes in serum CRP levels in the acupuncture group were positively correlated with the changes in VAS scores ($r = 0.576$, $P < 0.05$). Results indicate that both methods alleviate knee joint pain and improve function, but acupuncture demonstrates superior efficacy and significantly influences serum inflammatory factors in KOA patients. A meta-analysis by Vickers *et al*.[15] demonstrated acupuncture's effectiveness in treating osteoarthritis pain. Compared to sham acupuncture, it significantly alleviates pain and improves knee joint function in KOA patients. Therapeutic effects persisted over time, suggesting benefits beyond placebo effects. For patients with chronic pain, referral for acupuncture is a reasonable choice, aligning with American College of Rheumatology guidelines,[16] recommending acupuncture when pharmacological treatments are ineffective.

Warm needle acupuncture therapy

WNA combines acupuncture's needling effects, regulating Qi and blood, promoting blood circulation, and moxibustion's benefits of warming meridians, dispelling cold, and alleviating pain. By utilizing both approaches, it aims to relieve knee joint swelling and pain, effectively treating the disease.[17]

In a study by Li *et al*.,[18] WNA added to conventional therapy (control group) for KOA led to better reductions in IL-1β, matrix metalloproteinase-1 (MMP-1), MMP-3, and transforming growth factor-β1 levels in knee joint synovial fluid of the knee joint. It significantly improved VAS, WOMAC, and LKSS scores, with a higher total effective rate of 90.91% compared to the control group's 75.00%. WNA effectively improved functional activities, alleviating pain and regulating the expression of various cytokines in the knee joint, reducing cartilage damage and exerting a therapeutic effect on KOA. In a study by Sun *et al*.,[19] WNA added to the control group (using flurbiprofen gel patch) resulted in a higher total effective rate of 87.0% compared to 60.0% in the control group. WNA effectively reduced IL-1β, IL-6, and TNF-α levels in synovial fluid and significantly downregulated TLR4, MyD88, and NF-κB mRNA expression in the synovial fluid. It also effectively reduced VAS, WOMAC, HAQ, and SF-36 scores. The results show that WNA can alleviate clinical symptoms, help restore joint function, and improve the quality of life in KOA patients, demonstrating good clinical efficacy. WNA appears to inhibit the release of inflammatory factors and reduce damage to articular cartilage, leading to relatively positive therapeutic effects. Research by Lin *et al*.[20] showed that WNA increased serum OPG, BGP, and FGF-2 levels, while reducing MMP-3, VEGF, and Ang-1 levels in KOA patients. These findings suggested that WNA can improve free radical metabolism in KOA patients, reduce inflammatory factors, inhibit osteoclast proliferation, enhance bone metabolism, and promote cartilage repair. WNA reduced inflammation, joint effusion, synovial thickening, and improved clinical symptoms in KOA patients. This study provided insights into WNA's potential mechanisms in treating KOA.

Fire-needle therapy

FN is a specialized acupuncture technique where a flame-heated needle is swiftly inserted into affected areas or specific acupoints for treatment. The therapy aims to warm channels, dispel cold and dampness, eliminate stasis and nodules, relieve Bi syndrome by stimulating the body's meridian, nerves, and immune system.[21,22]

In a study by Gao,[23] KOA patients were treated with FN Therapy (33 cases) or ordinary acupuncture (33 cases). The FN group showed a total effective rate of 72.4%, higher than the ordinary acupuncture group's 58.1%. FN therapy improved knee joint function, pain, overall symptoms, and overall health more effectively. It may also be superior in improving psychological health and social function of KOA patients. FN therapy's mechanism of action is attributed to the high temperature of the FN, dispelling cold pathogens, stimulating Qi flow in meridians, and promoting circulation. It is commonly used for pain and stiffness caused by cold pathogens. Ding and Ma[24] allocated 120 KOA patients into two groups: The FN group and the sodium diclofenac group. The FN group showed significantly lower expression of IL-1 and IL-6 in serum compared to the

sodium diclofenac group. WOMAC scores and total scores significantly decreased more in the FN group, indicating significant clinical efficacy in treating KOA and reducing IL-1 and IL-6 expression levels in serum.

Electro-acupuncture therapy

EA combines modern technology with TA, applying pulsed electric currents on specific acupoints. It has advantages such as fast onset, good efficacy, and minimal adverse reactions, showing significant benefits in treating knee joint disorders.[25,26]

In Liu and Wu study,[27] 90 KOA patients were allocated into three groups: Medication group (oral Celecoxib), TA group, and EA group (acupoints: ST34, SP10, ST35, EX-LE4, GB34, EX-LE2, SP6). The EA group had significantly lower VAS and WOMAC scores, and serum IL-1 β and TNF-α levels compared to the TA and medication groups. The EA group also showed a higher total effective rate (86.67%) than the acupuncture (73.33%) and medication groups (70.00%). EA, TA, and Celecoxib alleviated clinical symptoms of KOA and reduced the serum levels of relevant inflammatory factors. However, EA exhibited greater advantages, suggesting its potential for clinical application. Han and Sun[28] treated KOA with EA and TA, showing EA had significant advantages in improving walking speed and stability, effectively enhancing walking ability and functional limitations of KOA patients and their activity levels. In Shi *et al*.'s study,[29] it was found that both EA and TA could effectively reduce inflammatory cytokine levels such as TNF-α, IL-1 β, and IL-13, treating mild to moderate KOA, but EA had demonstrated a more significant reduction in these inflammatory factors compared to TA. Jiao *et al*.'s study[30] was found that EA could increase serum IL-10 levels and reduce TNF-α levels ($P < 0.05$), significantly improve Emotional Scale, present pain intensity scores and knee joint mobility in KOA patients. This suggested that EA may improve clinical symptoms of KOA by upregulating the anti-inflammatory cytokine IL-10 and downregulating the pro-inflammatory cytokine TNF-α levels.

Knife-needle therapy

KN is a unique technique that combines Western surgical knives with acupuncture needles, striking a balance between acupuncture and surgical incisions. It aims to adjust joint mechanical balance, promote blood circulation, release adhesions, dredge collaterals, and alleviate pain, thereby improving KOA symptoms.[31,32]

Zhou *et al*.[33] conducted a systematic review and meta-analysis, finding that KN therapy significantly improved the overall effective rate, LKSS, and reduced VAS, WOMAC, and TNF-α levels. It showed advantages in improving KOA symptoms, protecting knee joint cartilage, and restoring joint function. Wang *et al*.[34] treated 65 KOA patients with KN therapy (treatment group) and TA (control group). After treatment, KN group exhibited a more significant reduction in VAS scores ($P < 0.05$), improving HSS knee joint scores and steps per minute ($P < 0.05$), outperforming the TA group in overall efficacy. KN therapy is more effective than TA in alleviating KOA pain, restoring knee joint structure by adjusting the balance of soft tissues, and improving joint function and activity levels. Shi and Liu[35] used small KN therapy (observation group) and intra-articular sodium hyaluronate injection (control group) to treat KOA. The results showed the observation group showed a higher total effective rate (90.91%) than 77.78% in the control group ($P < 0.05$). Both groups showed improvements in WOMAC and VAS scores ($P < 0.05$), but the improvement was more significant in the observation group ($P < 0.05$). Regarding antioxidant capacity (SOD, NO, MDA), the KN therapy group exhibited better regulatory effects than the control group ($P < 0.05$). These findings indicated that KN therapy can enhance antioxidant capacity, effectively improve symptoms such as pain, joint stiffness and dysfunction, and demonstrate significant therapeutic efficacy.

Bloodletting therapy via channel puncture

Bloodletting Therapy via Channel Puncture (BLCP) is a method that involves puncturing superficial veins with triangular needles to release stagnant blood and treat diseases. It is rooted in TCM's meridian and Qi-blood theories, dredging meridians, promoting Qi and blood flow, and alleviating pain. BLCP has shown therapeutic effects for Bi syndrome.[36,37]

Hu and Guo[38] treated KOA with warm needling, BLCP, and cupping alongside oral Western medicine (control group). The observation group showed lower Lequesne, WOMAC, and McGill scores compared to the control group ($P < 0.05$). 3 months after treatment, the observation group demonstrated significantly lower inflammatory markers (IL-1, TNF-α, and MMP-2) in the joint fluid ($P < 0.05$), indicating that acupuncture combined with BLCP improved symptoms and reduced inflammation. These studies support the efficacy of BLCP in treating KOA and suggest its potential as a valuable treatment option, either alone or in combination with other therapies.

Balance acupuncture therapy

BA is a novel acupuncture method based on the principle of "Harmony of Yin and Yang, Essence Governs Spirit" from the Yellow Emperor's Inner Canon. It aims to restore balance in the body through peripheral nerve stimulation, regulated by the central nervous system. BA therapy has been recognized for its rapid effectiveness and immediate pain relief in treating various diseases.[39,40]

In Zhang *et al*.'s study,[41] 70 KOA patients were treated with BA therapy (treatment group) and conventional acupuncture (control group). The treatment group showed a more significant decrease in VAS scores ($P < 0.05$),

along with increased step length, walking speed, and decreased EKAM peak value compared to the control group ($P < 0.05$). These results suggested that BA therapy improved pain symptoms in KOA patients by relieving central inhibition caused by pain and activating muscles around the knee joint, leading to increased knee joint stability.

Catgut embedment in acupoint therapy

Catgut embedment in acupoint therapy (CGE) is an emerging long-lasting acupuncture treatment method. It involves inserting protein or medication threads into acupoints, providing continuous and long-term stimulation. CGE effectively regulates meridians, harmonizes Qi and blood, and restores the balance of Yin and Yang due to its gradual degradation within the body.[42-44] This long-lasting stimulation reduces the need for frequent acupuncture, enhancing patient compliance.[45]

In Pan *et al*.'s study,[46] 70 KOA patients received either acupuncture with CGE Therapy or TA. Both groups experienced significant improvements in VAS scores and Knee Injury and Osteoarthritis Outcome Score (KOOS) total scores after treatment ($P < 0.05$), with no significant difference in VAS and KOOS between the two methods ($P > 0.05$). Huang[47] treated 40 KOA patients using acupuncture with CGE therapy (treatment group) and intra-articular injection of sodium hyaluronate (control group). The treatment group showed a higher total effective rate (88.00%) than 80.77% in the control group ($P < 0.05$), along with significantly reduced WOMAC score and IL-1, TNF-α levels in the synovial fluid compared to the control group ($P < 0.05$). In Dong *et al*.'s study,[48] KOA patients received acupuncture with CGE therapy (treatment group) and sham acupuncture (control group) in addition to basic treatment. The treatment group demonstrated a higher total effective rate (100%) than 26.67% in the control group, and a more significant decrease in TCM syndrome and WOMAC scores compared to the control group ($P < 0.05$). This indicates that both methods can improve the clinical symptoms of KOA patients, but acupuncture with CGE therapy has a better therapeutic effect compared to sham acupuncture.

Comprehensive therapy

Comprehensive therapy, also known as combination therapy, involves using two or more different treatment methods to treat KOA, rather than a single approach. It leverages the advantages of various TCM treatments, such as acupuncture, massage, topical and oral herbal medicine, to achieve better therapeutic efficacy compared to using a single treatment method.[49]

In Hu An'hua's study,[50] 100 KOA patients treated with EA (control group) and EA combined with Zhu's Yi Zhi Chan Pushing Method (experimental group). Experimental group, with total effective rate 75%, showed better results in improving knee joint stiffness and pain symptoms, as well as restoring knee joint mobility, compared to using EA alone. Combination therapy maximizes the advantages of both methods and demonstrates superior clinical efficacy compared to a single-treatment approach. Wang *et al*.[51] treated 80 KOA patients with methods glucosamine hydrochloride capsules + tonifying kidney and activating blood formula (Bu Shen Huo Xue Fang) (control group) and glucosamine hydrochloride capsules + tonifying kidney and activating blood formula (Bu Shen Huo Xue Fang) + WNA Therapy (study group). After 1 month of treatment, the total effective rate in the study group was 95.00%, was higher than the control group (80.00%). After treatment, WOMAC scores, serum levels of IL-1, TNF-α, serum N-telopeptide of type-I collagen and cartilage oligomeric matrix protein all significant decreases ($P < 0.05$); the study group showed significantly lower levels than the control group during the same period ($P < 0.05$). This indicated that the combination treatment effectively improved symptoms and knee joint function, protected the articular cartilage from damage, reduced the levels of inflammatory factors and bone-cartilage markers.

Discussion and Comparative Analysis of the Acupuncture Methods

Through reviewing reports and literature on KOA treatment and conducting research on various acupuncture methods mentioned above, it is evident that different acupuncture therapies effectively alleviate symptoms and yield therapeutic benefits. Each approach has distinct mechanisms, characteristics, advantages, and disadvantages, necessitating a comparative analysis.

WNA therapy, FN therapy, and EA therapy all integrate additional stimulation techniques with TA to treat diseases. They share a common principle: Stimulating acupoints to regulate Qi, blood, and meridians, achieving therapeutic outcomes. However, subtle differences exist among these methods:

a. Different stimulation methods: WNA Therapy uses moxibustion for heat stimulation, FN therapy utilizes fire for stimulation, and EA therapy employs electrical currents
b. Varied intensity of stimulation: WNA provides mild stimulation, FN involves more intense stimulation, and EA allows for adjustable stimulation intensity
c. Slightly different indications: WNA therapy is suitable for conditions with poor blood circulation and Qi and blood deficiency; FN therapy benefits rheumatism, cold-induced paralysis, and muscle strain; EA therapy is applicable to nervous system disorders, muscle spasms, paralysis, and pain-related conditions.

In WNA therapy, close supervision is required to prevent burns or scalds due to improper operation. FN therapy can cause mild burns and infection if not performed correctly,

while also being more painful and challenging for patients to accept.[52] FN therapy requires good control over the force applied during needling, the depth of insertion, and the accuracy of needle insertion points, which imposes stricter requirements on the practitioner.[53] KN therapy has disadvantages such as greater trauma, intense pain, and scar repair limitations, poor compliance. Improper manipulation can easily lead to damage to blood vessels, nerves, tendons and other structures of the body, which demands higher anatomical knowledge and a sterile environment to avoid infections. BLCP can quickly address blood stasis and pathogenic factors, but improper execution may lead to complications such as subcutaneous hematoma, bleeding, and infections. Patients may experience discomfort and pain during the procedure. BLCP is not suitable for certain groups, including the elderly, those with weakened physical conditions, and pregnant women. BA therapy is commonly used for neck, shoulder, back, and leg pains, but its clinical efficacy varies in different studies, and its mechanisms of action require further research. CGE therapy has developed gradually with advancements in materials science, but its global dissemination is limited due to strict requirements on aseptic operations, risk of infections, and potential damage to nerves and blood vessels. Patients may experience discomfort and allergic reactions to the thread material, which can lead to fear and apprehension toward the treatment. Reports[47] indicate that CGE therapy is less commonly used in the treatment of KOA.

EA therapy offers advantages in replacing manual acupuncture techniques such as manual lifting, thrusting and twisting, and expanding the scope of acupuncture treatment with the combined application of electrical current stimulation. It is widely accepted in clinical practice for its safety, simplicity, and good controllability, and continuously propelling TA toward new directions and developments.[25] However, it is not suitable for patients with implanted cardiac pacemakers.

Summary and Conclusion

Acupuncture treatment for knee osteoarthritis shows good clinical efficacy

In recent years, the prevalence of KOA has been on the rise due to an aging population. There has been an increased emphasis on TCM, including acupuncture, by the government, particularly after the COVID-19 pandemic. As a result, acupuncture has gained clinical widespread recognition and acceptance. TCM is also advancing its research and modernization, leading to diverse and expanding applications of acupuncture. Acupuncture has shown unique therapeutic effects in treating bone and joint diseases and functional disorders, making it a common KOA treatment.

Acupuncture treatment methods, regardless of their specific approach, share the fundamental therapeutic effects of acupuncture. They work by dredging meridians and collaterals, harmonizing Yin and Yang, regulating Qi and blood circulation, achieving therapeutic benefits such as promoting blood flow, removing blood stasis, activating meridians and collaterals, reducing inflammation and swelling, relieving pain, improving joint mobility, and alleviating symptoms of KOA.[54] Recent literature reports on acupuncture treatment for KOA consistently show positive clinical outcomes, whether used alone or in combination with other therapies. These findings highlight the potential of acupuncture as an effective and beneficial treatment option for KOA.

Gradual improvement in research quality

Based on the recent clinical research publications on KOA, majority of clinical studies on acupuncture treatment for KOA have adopted randomized controlled methods, indicating a gradual improvement in research quality. With the implementation of large-scale studies and epidemiological investigations at the national level, along with the development, updates, and release of guidelines related to KOA, the diagnostic criteria and inclusion standards for research participants have gradually become more stable, standardized, and unified.

Existing challenges

Current acupuncture clinical research on KOA still faces the following challenges:

Most studies focus on clinical efficacy observation

Apart from some doctoral and master's research theses, many published journal articles primarily focus on the short-term clinical efficacy of acupuncture treatment for KOA, while long-term observation and follow-up studies are limited. Clinical efficacy evaluation often relies on subjective rating scales such as WOMAC and VAS, which can be influenced by various factors, leading to potential research biases and reduced credibility of study results. In addition, there are significant differences in reported clinical efficacy, with some studies claiming a 100% efficacy rate.[55] Further research is needed to address these limitations and provide more comprehensive and reliable evidence for the efficacy of acupuncture treatment for KOA.

Limited research has been conducted to explore the underlying mechanisms of acupuncture treatment for knee osteoarthritis

Despite extensive research on factors contributing to the onset and progression of KOA, the mechanisms behind acupuncture treatment for KOA remain incompletely understood. Journal articles often lack comprehensive and in-depth investigations into the underlying mechanisms of acupuncture treatment for KOA, leading to reduced scientific rigor in relevant research.

Many studies lack adequate consideration of sample size calculation and fail to conduct multicenter, large sample randomized controlled trials

Evidence-based medicine emphasizes the importance of sufficient sample sizes to ensure robust statistical power in experiments.[56] However, in previously published literature on acupuncture treatment for KOA, many studies reported treatment efficacy without clear indications of rigorous sample size estimation. Furthermore, there is a dearth of large-sample, multicenter randomized controlled trials. Some studies included only around 20 cases, undermining the credibility of reported results and treatment efficacy to a certain extent.

Most clinical studies predominantly employ comprehensive therapy and emphasize longitudinal comparisons

In clinical studies of acupuncture treatment for KOA, longitudinal comparison involves evaluating the efficacy and safety of a treatment method on the same group of subjects or patients at different time points. However, in studies with Comprehensive Therapy involving multiple combined methods, the selection of reference groups can vary, leading to uncertainty in determining the main therapeutic effect. For instance, some studies compare acupuncture with FN therapy + WNA therapy to Western medication treatment in the control group. This ambiguity can hinder a clear interpretation of the treatment's effectiveness: The main clinical effect is produced by WNA therapy, FN therapy, or comprehensive therapy?

Prospects in future

The future prospects of acupuncture therapy in KOA treatment are as follows:

a. Clinical efficacy evaluation indicators should be standardized, incorporating objective quantitative measures that reflect research changes. Therapeutic evaluations should use a combination of subjective and objective indicators to comprehensively assess treatments and minimize errors from subjectivity. Patient follow-ups should be conducted whenever possible to observe long-term therapeutic efficacy
b. Advancements in scientific technology, particularly in cellular and molecular biology, offer promising opportunities for in-depth exploration of the mechanisms underlying acupuncture treatment for KOA. Standardized and improved detection techniques for signaling pathway transductions and gene expression differences enable systematic studies. This can provide scientific evidence to enhance acupuncture's clinical application and enrich its theory[57]
c. When designing research protocols, careful consideration of sample size and dropout rate is crucial to calculate the minimum required for clinical studies. In addition, when conditions permit, collaborating with other hospitals or institutions can facilitate multi-center and large-sample size studies, ensuring scientific, reliable, and credible data and results
d. Before initiating clinical research, it is imperative to design comprehensive, rigorous, and logically sound research protocols. These protocols should address the innovativeness, scientific validity, and feasibility of the study. Selecting appropriate reference groups or control groups is crucial for the reliability of the research findings. Furthermore, conducting horizontal comparisons among different treatment methods within comprehensive therapy is essential to evaluate and compare their therapeutic effects and safety. Such comparisons can aid researchers in identifying the most effective treatment approach and ensuring better patient outcomes.

Conclusions

In conclusion, while acupuncture shows promise in treating KOA, there is still much research needed to identify the most effective, safe, and patient-friendly treatment methods. Scientific and reliable research evidence is essential to support its use and understanding the underlying mechanisms of acupuncture in treating KOA is crucial. By focusing on these areas, we can advance and innovate acupuncture therapy, furthering our understanding of acupuncture theory. Future clinical research should prioritize these directions to improve KOA treatment and enhance patient outcomes.

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Conflicts of interest

There are no conflicts of interest.

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Original Article

Thoracolumbar Burst Fracture Treatment Using Posterior Pedicle Screw Fixation and Autogenous Bulk Iliac Bone Graft Fusion

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Abstract

Background: Thoracolumbar vertebral fracture is the most common type of thoracolumbar vertebral fracture. For the patients with severe thoracolumbar vertebral burst fracture and neurological impairment, surgical decompression and reconstruction of spinal stability is an important intervention method, however, there is still controversy on the way of postoperative stability reconstruction. **Objective:** This study was to investigate the efffcacy of posterior open reduction, pedicle screw ffxation, and autogenous iliac bone graft fusion in the treatment of thoracolumbar burst fractures with neurological impairment. **Methods:** The clinical data of 43 patients with thoracolumbar single vertebral burst fracture with neurological function injury treated in our department from January 2016 to December 2020 were retrospectively analyzed. The Visual Analog Scale (VAS) score of lumbothoracic pain, the occupying rate of spinal canal, the ratio of the anterior height of the injured vertebral body to the normal height, Cobb angle, and the American Spinal Injury Association (ASIA) classiffcation of neurological function were compared before and after operation. All patients completed the procedure successfully. **Results:** Bone graft fusion was achieved in all patients, and no screw or rod was broken. The VAS score of thoracolumbar pain, the ratio of the anterior height of the injured vertebral body to the normal height, and the Cobb angle were signiffcantly lower than those before operation at 1 and 12 months after operation ($P < 0.001$). There was no signiffcant difference in the VAS score of thoracolumbar pain, the ratio of the anterior height of the injured vertebral body to the normal height, and the Cobb angle between 1 and 12 months after operation. The occupying rate of spinal canal 6 months after operation was lower than that before operation (12.02% ±7.35% vs. 46.98% ±9.26%), and the difference was statistically signiffcant ($t = 20.066$, $P < 0.05$). There was a signiffcant difference in ASIA classiffcation of neurological function between 12 months after operation and before operation ($Z = -5.372$, $P < 0.001$). The neurological function was signiffcantly improved 12 months after operation. **Conclusion:** Reconstruction of vertebral lamina with iliac bone graft is an effective method for the treatment of thoracolumbar burst fractures, which can reduce the loss of vertebral height and recurrent kyphosis and avoid the neurological impairment caused by secondary spinal stenosis.

Keywords: *Iliac bone, lamina reconstruction, neurologic impairment, thoracolumbar burst fracture*

Introduction

In the thoracolumbar fracture injury, the incidence of thoracolumbar vertebral fracture is the highest, and 15%–20% of patients have neurological impairment.[1] For patients with neurological impairment, especially those with neurological insufficiency, surgery can effectively restore spinal stability, relieve pain, and create favorable conditions for the recovery of neurological function.[2] The main purpose of surgical treatment is to decompress the spinal canal and nerve root, reconstruct the stability of the spine, correct and prevent kyphosis after trauma, provide long-term stability for the injured vertebra, and provide conditions for patients to exercise early and resume normal work and life as soon as possible. Surgical decompression and restoration of spinal stability[3] are indicated for patients with severe thoracolumbar burst fractures and spinal cord compression with neurologic impairment. However, laminectomy decompression further reduces the stability of the spine, and the pedicle screws bear greater stress, which is prone to complications such as broken screws and rods, loss of vertebral reduction height, and aggravation of kyphosis deformity and may lead to scar hyperplasia and adhesion of soft tissue behind the spinal canal to

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compress the dura mater, leading to recurrent stenosis of the spinal canal. This study was to investigate the efficacy of posterior laminectomy decompression, pedicle screw fixation, and iliac bone reconstruction in the treatment of thoracolumbar burst fractures with neurological impairment.

Materials and Methods

Object of study

The patients with thoracolumbar burst fracture and neurological impairment were collected from January 2016 to December 2020 in the Orthopaedics Department of Xinjiang Military General Hospital. The inclusion criteria of this study were as follows: single-segment thoracolumbar burst fracture, neurological impairment, age 16–60 years, and high-energy injury (falling injury, traffic accident injury, and heavy injury). The exclusion criteria of this study were as follows: patients with no neurological impairment, osteoporotic vertebral fracture, traumatic spondylolisthesis, severe medical diseases that cannot tolerate surgery, and incomplete postoperative follow-up data. A total of 43 patients were enrolled, including 29 males and 14 females, aged from 16 to 58 years, with an average of 37.86 ± 10.75 years. The injured segments were T11 in 7 cases, T12 in 19 cases, L1 in 10 cases, and L2 in 7 cases. The causes of injury included falling injury in 27 cases, traffic accident injury in 12 cases, and heavy object injury in 4 cases. According to the American Spinal Injury Association (ASIA) classification, there were 3 patients in Grade A, 4 in Grade B, 10 in Grade C, and 26 in Grade D. The preoperative Visual Analog Scale for pain score of thoracolumbar pain ranged from 1 to 9, with an average of 5.86 ± 1.86. All patients underwent X-ray, computed tomography (CT), and magnetic resonance imaging examination before operation and underwent posterior laminectomy decompression + pedicle screw fixation + iliac bone reconstruction laminectomy and bone graft fusion. The operation time was 2–16 days after injury, with an average of 6.44 ± 3.22 days.

Surgical treatment

After tracheal intubation and general anesthesia, the patient was placed in the prone position. C-arm X-ray machine was used to locate the injured vertebra, with the injured vertebra as the center, and the posterior median approach was used to cut and expose the vertebra layer by layer. The conventional method is to insert pedicle screws into the pedicles of the injured vertebra and the upper and lower normal vertebrae, connect the prebent connecting rods with the screws at both ends, and then moderately open them to correct kyphosis deformity. The degree of opening should be based on intraoperative fluoroscopy. The lamina of the injured vertebra was resected with rongeur or drill, and the spinal canal was decompressed. After decompression, under the protection of the nerve dissector, the front of the spinal canal was explored. If there was a bone block protruding to the spinal canal, an L-shaped hammer was slowly placed in front of the dural sac, and the bone block was carefully repositioned by hammering to completely relieve the compression on the dural sac. The reduction of the bone block and the tightness of the dural sac and nerve root were explored, and the position of the instrument and the reduction of the bone block were confirmed by fluoroscopy. If the dural sac is found to be damaged during the operation, it should be repaired. A piece of iliac bone of appropriate size was cut from the posterior superior iliac spine and trimmed into the shape of the lamina. The cortical bone of the vertebral lamina adjacent to the vertebral body of the injured vertebra was resected to form a bone graft bed, in which the trimmed iliac bone block was implanted, and the decompressed bone block was implanted around the reconstructed vertebral lamina, and the transverse connection was placed after bone grafting. Antibiotics and dehydrant were routinely given for 5 days after operation. Stitches were removed 10–12 days after operation, and thoracolumbar braces were worn for training. The internal fixation was removed 12–18 months after operation.

Follow-up and evaluation index

All patients were followed up regularly in an outpatient clinic after operation and were examined by X-ray and CT. The VAS score of lumbothoracic pain, the ratio of the anterior height of the injured vertebral body to the normal height, the Cobb angle, and the occupying rate of the spinal canal were recorded before operation and 1 and 12 months after operation. Internal fixation failure, bone graft fusion, and neurological function were observed 12 months after operation. The median sagittal diameter of the spinal canal was measured according to the axial CT images. The occupying rate of the spinal canal = 1 −median sagittal diameter of the vertebral canal of the injured vertebra/([median sagittal diameter of upper vertebral canal + median sagittal diameter of lower vertebral canal]/2).[4] The ratio of the height of the front edge of the injured vertebral body to the normal height = the height of the front edge of the injured vertebral body/([height of front edge of upper vertebral body + height of front edges of lower vertebral body]/2). The Cobb angle was measured by the method proposed by Kuklo *et al*.,[5] that is, the vertical angle between the upper endplate of the upper vertebral body of the injured vertebra and the lower endplate of the lower vertebral body of the injured vertebra.

Statistical analysis

SPSS (IBM SPSS 19.0 software in New York State, USA) statistical software was used for statistical analysis. The VAS score of lumbothoracic pain, the occupying rate of vertebral canal, the ratio of the anterior height of the injured vertebral body to the normal height, and the Cobb angle were statistically analyzed to be in line with normal distribution, expressed as X ± s. One-way analysis of

variance was used to compare the VAS score of lumbar and thoracic pain, the ratio of the anterior height of the injured vertebral body to the normal height, and the Cobb angle before operation, 1 month after operation, and 12 months after operation, and least significant difference *t*-test was used to further compare the two groups. Paired samples *t*-test was used to compare the difference of spinal canal occupying rate between preoperative and postoperative 6 months. Mann–Whitney *U*-test was used to compare the differences of ASIA classification of neurological function between preoperative and postoperative 12 months. The difference was statistically significant when $P < 0.05$.

Results

General information of the patient's operation

The operation time was 85–150 min, with an average of 117.49 ± 19.15 min, and the intraoperative blood loss was 50–300 ml, with an average of 130.47 ± 57.53 ml. All bone grafts were fused at 6-month follow-up.

Improvement of thoracolumbar pain and spinal canal occupying rate after operation

VAS scores of thoracolumbar pain at 1 and 12 months after operation were lower than those before operation, and the difference was statistically significant. There was no significant difference in VAS score of thoracolumbar pain between 1 and 12 months after operation [Table 1]. The occupying rate of spinal canal 6 months after operation was lower than that before operation (12.02% ±7.35% vs. 46.98% ±9.26%), and the difference was statistically significant (t = 20. 066, $P < 0.05$). The imaging data of typical cases are shown in Figure 1.

Improvement of the ratio of the height of the anterior edge of the injured vertebral body to the normal height and the Cobb angle after operation

At 1 and 12 months after operation, the ratio of the height of the anterior edge of the injured vertebral body to the normal height and the Cobb angle were smaller than those before operation, and the differences were statistically significant. However, there was no significant difference in the ratio of anterior vertebral body height to normal height and Cobb angle between 1 and 12 months after operation [Table 1].

Postoperative improvement of neurological function

There was a significant difference in ASIA classification of neurological function between 12 months after operation and before operation [Table 2]. Twelve months after the operation, the neurological function of the patients was significantly improved [Table 3], the original neurological symptoms were not aggravated, and no new neurological symptoms occurred in any patient.

Complications of patients after operation

All patients were followed up for 12–25 months, with an average of 16.95 ± 4.03 months. There was no internal fixation loosening or breakage in all patients during the follow-up period. No patient had recurrent spinal stenosis; two patients had pain in the iliac bone harvesting area, and the symptoms were relieved after symptomatic treatment; one patient had lateral femoral cutaneous nerve injury, and the symptoms were improved after neurotrophic treatment.

Discussion

The thoracolumbar segment is located at the junction of the thoracic spine with little mobility and the lumbar spine with good mobility, and its stress is the largest. At the same time, the thoracolumbar segment is located at the intersection of the two physiological curvatures of thoracic kyphosis and lumbar lordosis, which is a turning point of spinal biomechanics, so the incidence of thoracolumbar fracture is high, about 50% of thoracic and lumbar fractures occur here,[6] and 15%–20% of fracture patients have neurological impairment. Surgical intervention[7] is often required for patients with severe deformities or neurological impairment. Current surgical approaches for thoracolumbar vertebral fractures include posterior, anterior, and combined anterior and posterior approaches.[8,9]

The implementation of decompression surgery depends on the patient's own choice and the experience of the surgeon. Anterior surgery can decompress under direct vision, decompress thoroughly, and achieve good reconstruction and fixation of the vertebral body, with reliable decompression effect. However, the anterior approach is traumatic and difficult to operate, and may damage internal organs and large blood vessels, resulting in serious adverse consequences.[10,11] Posterior decompression with pedicle screw fixation was

Table 1: Comparison of thoracolumbar pain, ratio of anterior vertebral body height to normal height, and Cobb angle before and after operation (X±s)

Time	Number of cases	VAS score	Ratio of height of anterior border of injured vertebral body to normal height	Cobb angle
Preoperative	43	5.9±1.9	52.2±15.9	22.5±5.5
1 month postoperatively	43	1.3±0.9[a]	97.7±3.5[a]	6.9±3.0[a]
12 months postoperatively	43	0.8±0.7[a]	97.2±3.7[a]	7.8±3.1[a]
F		210.909	317.093	203.538
P		<0.001	<0.001	<0.001

[a]Compared with preoperative, the difference was statistically significant (P<0.001). VAS: Visual Analog Scale

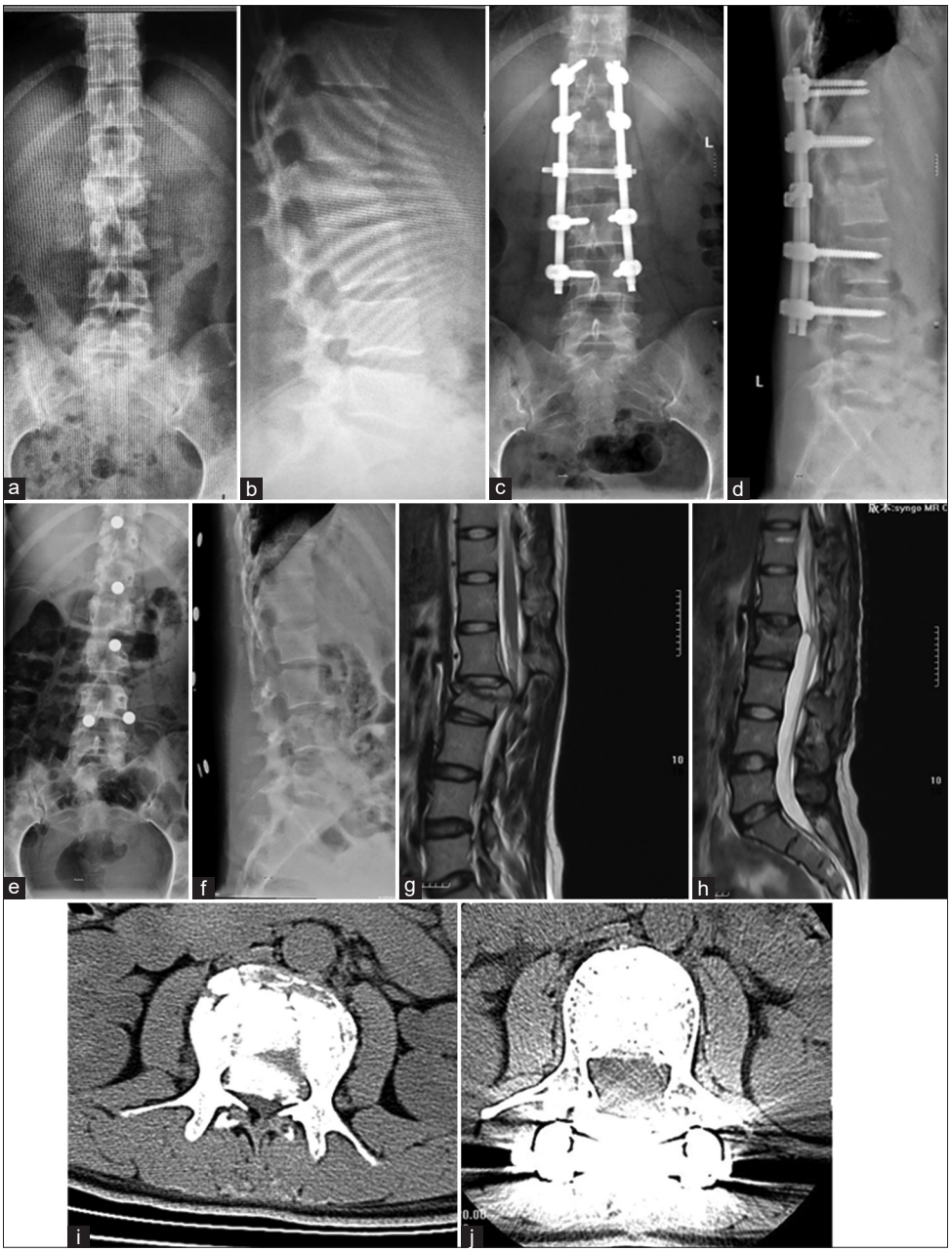

Figure 1: A 20-year-old female patient was injured by falling from a high place, with L2 vertebral fracture and incomplete paralysis. (a and b) Preoperative X-ray showed fracture of L2 vertebral body and kyphosis deformity, (c and d) Postoperative X-ray showed that the height of L2 vertebral body was well reduced without kyphosis, (e and f) The internal fixation was removed 1 year after operation, and the X-ray showed that the height of L2 vertebral body was good and there was no kyphosis, (g) Preoperative magnetic resonance imaging (MRI) showed compression fracture of L2 vertebral body, protruding to the spinal canal and compressing the spinal cord, (h) One year after the operation, the internal fixation was removed and the MRI showed that the height of L2 vertebral body was acceptable and the spinal canal was not narrowed, (i) Preoperative computed tomography (CT) showed burst fracture of L2 vertebral body. The fracture fragment protruded to the spinal canal and compressed the spinal cord. The degree of spinal canal stenosis was 80%, (j) Six months after operation, CT showed that the fusion of the reconstructed iliac lamina was good and the spinal canal was not narrowed

found to be as effective as the anterior approach but with shorter operative time, less bleeding, and similar functional outcomes.[12-14] However, the possibility of internal fixation failure or loss of vertebral reduction height[15] will occur in 9%–54% of vertebral fractures treated with posterior pedicle screw fixation without vertebral reconstruction. Because the vertebral body is cancellous bone, it takes a long time to restore the bone strength after reduction. Because the lamina of posterior decompression is resected, the supporting and stabilizing function of the posterior column is obviously weakened. After the patient's activity, the reduction of the vertebral body is gradually lost, resulting in the aggravation of kyphosis deformity and back pain. In severe cases, complications such as aggravation of spinal cord injury, screw breakage, epidural adhesion, and spinal stenosis may occur.[16-18] In order to avoid iatrogenic instability and maintain the stability of the spine after laminectomy, different methods of bone graft fusion are often used during the operation.

Table 2: Comparison of the American Spinal Injury Association classification of neurological function of patients before and after operation (cases)

ASIA classification of neurological function	Number of cases	Level A	Level B	Level C	Level D	Level E
Preoperative	43	3	4	10	26	0
12 months postoperatively	43	1	1	3	13	25
Z				−5.372		
P				<0.001		

ASIA: American Spinal Injury Association

Table 3: Improvement of neurological function in patients 12 months after operation (cases)

ASIA classification of preoperative neurological function	Number of cases	ASIA classification of neurological function 12 months after operation				
		Level A	Level B	Level C	Level D	Level E
Level A	3	1	1	0	1	0
Level B	4	0	0	1	2	1
Level C	10	0	0	2	3	5
Level D	26	0	0	0	7	19

ASIA: American Spinal Injury Association

Posterior pedicle screw fixation combined with posterolateral bone graft fusion has been considered to be the first choice for the treatment of burst fractures. Posterior surgery can effectively avoid the complications related to anterior decompression, but posterolateral bone graft needs to expose the transverse process and articular process joints, resulting in posterolateral soft-tissue injury and accessory structure injury, which results in longer operation time and more blood loss.[19] Posterior interlaminar fusion was found to have a similar outcome to posterolateral fusion but with less impact on facet joints and paraspinal muscles, shorter operative time, less blood loss, and possibly lower rate of fixation failure.[20]

In this study, we retrospectively analyzed the data of 43 patients with thoracolumbar burst fractures combined with neurological impairment who underwent surgical treatment in the Department of Orthopaedics of the General Hospital of Xinjiang Military Area Command. It was found that the main injury factors were falling from high places and traffic accident trauma, and the main vertebral bodies involved were T12 and L1, which were similar to those reported in previous studies.[21] The pain symptoms, spinal canal area, height of injured vertebra, Cobb angle, and neurological function were significantly improved in all 43 patients after surgical treatment. Bone graft fusion was achieved in all patients, and no screw or rod was broken in all patients. The height of the injured vertebra and Cobb angle were not decreased at 12 months after operation compared with 1 month after operation, and the differences were not statistically significant. Autologous iliac bone reconstruction of vertebral lamina to restore the integrity of the spinal canal, after the reconstruction of vertebral lamina fusion, can effectively maintain the stability of the posterior column of the spine, so that the fracture vertebral body and the upper and lower vertebral bodies can be fused into a whole to bear the weight-bearing function of the spine, thereby reducing the occurrence of complications such as pedicle screw breakage, internal fixation loosening, loss of vertebral reduction, aggravation of kyphosis deformity, and recurrent stenosis of the spinal canal.

Our research group believes that iliac bone reconstruction of vertebral lamina has the following advantages: (1) the three motion units of the injured vertebra and the upper and lower vertebral bodies are fused into one motion unit using posterior vertebral lamina reconstruction. By reconstructing the posterior column, the stress of the injured vertebra is effectively conducted, the stress of the injured vertebral body is reduced, the reduction effect of the vertebral body is maintained, and the compression and deformation of the anterior and middle columns and the reduction vertebral body are avoided, as well as kyphosis and spinal cord compression. (2) The amount and area of iliac bone supply are large, and the lamina can be reconstructed by decompressing the multi-segmental vertebral body. (3) The ilium is an autogenous bone, which can avoid rejection of allograft and artificial bone, and has a high fusion rate. (4) Reconstruction of spinal canal can effectively prevent re-compression injury of spinal cord and avoid secondary spinal stenosis and spinal cord injury.

However, reconstruction of vertebral lamina with iliac bone graft also has some disadvantages, such as prolonged operation time, increased intraoperative bleeding, lateral femoral cutaneous nerve injury, and postoperative pain in the donor site. In this group, 43 patients were treated with reconstruction of vertebral lamina with iliac bone, no patient had complications such as iliac hematoma and lateral femoral cutaneous nerve injury, 2 patients had pain in the donor area, and the symptoms were relieved after symptomatic treatment. One patient had lateral femoral

cutaneous nerve injury, and his symptoms were improved after neurotrophic therapy.

To sum up, reconstruction of vertebral lamina with iliac bone graft can effectively improve the pain symptoms and the degree of spinal stenosis, create favorable conditions for the recovery of neurological function, reduce the loss of vertebral height and recurrent kyphosis after operation, and avoid neurological damage caused by secondary spinal stenosis compressing the spinal cord, which is an effective method for the treatment of thoracolumbar vertebral fracture.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Original Article

Lateralization of the Fine Motor Skills in Right - and Left-handed Men and Women

Abstract

Introduction: Motor performance is an important feature that can be measured to observe the development of the central and peripheral nervous system. Fine motor skill assessed by Morische-Leistungs-Serie (MLS) was studied in normal male and female right-handers and left-handers considering familial sinistrality and writing hand. Evaluations were conducted by measuring fine motor performance through the use of a modern computerized model. **Materials and Methods:** Hand preference was assessed by the Edinburgh Handedness Inventory Geschwind score (GS). Fine motor skills were measured by the MLS in the computerized Vienna Test System. **Results:** Left-handed volunteers had a significantly higher fine motor skills in both dominant and nondominant hands compared to right-handed volunteers. **Conclusions:** These results suggest that the contributions of the right and left cerebral hemispheres to the motor output of the brain depend on sex and more importantly, hand preference. It was determined that left handed subjects were more skillfull than right-handed subjects when dominant hands or weak hands were compared.

Keywords: *Fine motor skills, hand preference, handedness, lateralization, manual asymmetry, MLS*

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Introduction

Studying brain structures and functions have been a crucial issue in neurosciences for decades.[1] The first observation on brain asymmetry (cerebral asymmetry) was made by Broca the research by Broca, Wernice, Geschwind (2014) and have proved to be key to our understanding of the functional differences between brain hemisphere.[2-5,19] Handedness, or hand lateralization, is considered to be the among the most important markers of the functional specialization of brain hemispheres.[6] The relationship between cerebral asymmetry and hand preference has been an inspiration to many studies since the founding of neurophysiology.[7] Hemispheric specialization for the control of fine motor performance may be an important factor in the diagnosis, treatment, and outcome of motor cortex injury, hand injury, hemiplegia etc., and therefore, studies investigating this aspect of motor function could influence the design and implementation of rehabilitation methods.[8]

Motor skills come to fruition as a series of stimuli constituted in the brain that are almost simultaneously translated into motion or a sequence of movements. The proprioceptive, visual, and auditory inputs supervise the initiated movements and their precision.[9] The complex and fine motor skills are controlled by the dominant cerebral hemisphere; whereas other brain functions, such as linguistic skills, spatial intelligence, and logic are associated with specific brain regions.[6] The acquisition of new motion sequences and motor skills take place in the primary motor cortex (M1). The M1 contains dopaminergic terminals that are involved in the conversion of postsynaptic potential long term potentiation (LTP) in motor synapses which lead to motor skill learning (Hosp *et al*. 2011).[10] Motor movements have been the subject of many physiological and clinical studies. The measurement of hand skills were first performed by what was known as the pegboard test which was initially utilized by Annett then modified later by Tan (Annett 1992).[11,12] Since then, several methods have been developed to precisely measure coordinated movements of the arms, hands and fingers, including the Valpar system, the box and block test, and the Purdue pegboard test.[13]

The data obtained from sensitive neuropsychological tests that determine

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high brain functions are widely used in fundamental studies and also in other fields, especially in health, industry, technology, and innovation studies. Neuropsychological tests provide quantitative measurement of cognitive and motor functions, thereby describing the complex information processing and making it possible to use the statistical analysis on the data.[14]

The Vienna Test System, a standardized computerized system developed by Schuhfried GmbH, enables the measurement of basic mental functions, such as attention, memory, motor skills, and executive functions, in a validated and reliable way. The specific tests in the Vienna Test System include the MLS which is a fine motor skill test that evaluates hand skills.[15] A study using the Reaaktiongerat test in the Vienna Test System found that the dominant hand is better at responding to visual-auditory stimulus, regardless of sex.[16] In another study on adults with advanced age (>70 years), the MLS revealed functional asymmetry in all of the four motor tests applied.[17]

In the present work, the fine motor skill assessed by MLS test to hand skill was studied in male and female right-handers and left-handers. An attempt was made to elucidate the relative contributions of the right and left cerebral hemispheres to the brain's motor output.

Materials and Methods

Subjects

The subjects comprised about 36 left-handed and 64 right-handed 48 males 52 females who ranged in age from 18 to 35 years (students in the faculties of nursery and medicine). All were healthy, devoid of neurological or psychiatric signs and symptoms. They did not object to participation in the study, i.e. a volunteer bias was avoided. The subjects originated from different cities, constituting a random sample.

Hand preference

To assess their hand preference, all subjects received a Turkish adaptation of Oldfield's questionnaire[18] modified by Geschwind and Behan.[19] The questions pertained to which hand was used by the subject for writing, throwing, scissors, toothbrush, knife (without fork), spoon, holding the handle for a shovel, striking a match, and twisting off the lid of a jar. The columns "always right," "usually right," "either hand,' "always left," "usually left" were scored as +10, +5, 0, −10, and −5, respectively. Following Geschwind's suggestion (personal communication), the laterality score was taken as the sum of all these scores, and no quotient was calculated. In memory of Norman Geschwind, this laterality score was called the "Geschwind score." A score of −100 indicated that the subject responded "always left" on all items, and a score of +100 indicated "always right" on all items.

Assessment of fine motor skill

In order to measure motor skills and to obtain objective data in accordance with international norms, tests were carried out on the computerized Vienna Test System in a standardized isolated test room. We used the MLS which is a test battery developed by Shoppe based on Fleishman's work on motor skill factor analysis [Figure 1].[15] The MLS test includes a work panel of 300 mm × 300 mm × 15 mm size that has holes, grooves, and various contact surfaces. Two pencils are attached to the panel, one on the right and one on the left. The computer measures fine motor performance by testing Arm-hand Steadiness (STE), Hand-Eye Coordination, Hand-Arm Sensitivity, and Wrist-Finger Speed with respect to the following sub-tests: STE: Hand-Arm Stability, Line tracking (LINE): Arm Sensitivity, Aiming (AIM): Hand-Eye Coordination, long pins insertion (L.IP): Hand-Finger Skill, Tapping (TAP): Wrist-Finger Speed. The mean duration of the test is 17 min. The sub-tests were consecutively applied to the dominant hand, followed by the nondominant hand, and all analyses were recorded continuously.

Steadiness

In this subtest, the volunteer is asked to hold the pen and keep their hand steady for 32 s. The pen that he/she holds must be placed vertically inside the center of the smallest borehole (diameter: 4. 8 mm) on the test panel. Any contact between the pen and work panel was counted as an error.

Line tracking test

The volunteer is asked to track the line in the test board without causing any contact to the boundaries of the line with the pen. Any contact between the pen and the panel was counted as an error.

Aiming test

Each circular contact surface (20 small targets, 2 bigger circles indicating the "start" and "stop" positions) had to be hit with the pen as fast and accurately as possible from the start (right) to the stop (left). The hits made outside the circular surfaces were recorded as the number of errors.

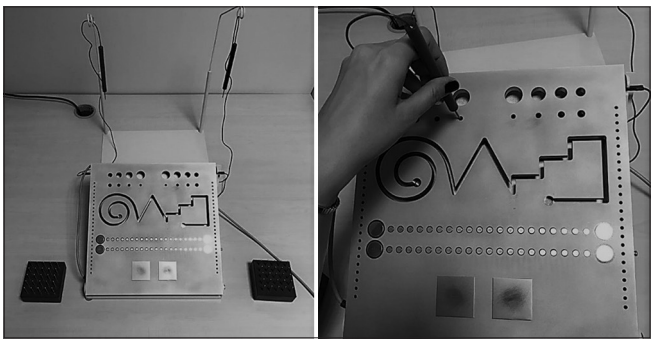

Figure 1: The working panel for the motor performance test (MLS)

Long pins insertion test

The pins are placed 30 cm away from the test board, the volunteer is asked to place them in small holes within the test board one by one and as quickly as possible. The computer automatically records the time between the first and the last pin placement.

Tapping test

in this sub-test, the volunteers are asked to tap on the square-shaped area within the test board as quickly as they can, for 32 s. The number of all hits is recorded.

All the results of the sub-tests are directly recorded by the computer, and the obtained data are assessed and analyzed statistically.

Statistical analysis

We used the independent samples *t*-test to analyze hand preference (right or left) in sex-based groups. Group-wise comparisons (right female, left female, right male, and left male) were performed by the one-way ANOVA test. Any $P = 0.05$ or lower was considered to demonstrate statistical significance. All statistical analyses were conducted using the SPSS version 15.0 software (SPSS Inc, IBM, Chicago IL, USA).

Results

The mean and standard deviation values of analyzed parameters and the *P* values of statistical comparisons between dominant and nondominant hands and sex-based groups in terms of the five different motor skill tests are shown in the below charts and graphs.

As shown in Table 1, there were differences in the motor skills of left handers and right handers; left handers were more skilled in using their dominant hands than right handers. Statistically significant differences were observed in the hand-arm STE, hand-eye coordination (Aiming), wrist-finger speed (Tapping), and LIP tests ($P < 0.001$ and $P < 0.05$). The nondominant hands of left handers were more skilled than the nondominant hands of right handers; yet, only the tapping and line-tracking skill tests demonstrated statistical significance ($P < 0.01$).

Table 1: Hand skills in right-handed and left-handed subjects

Tests	Hand preference	Mean±SD		*P*
		Left handed (*n*=36)	Right handed (*n*=64)	
STE (number of error)	Dominant	2.94±2.63	6.67±8.01	0.001*
	Nondominant	7.86±7.94	11.33±11.37	0.078
LINE (number of error)	Dominant	21.17±7.88	23.98±9.12	0.123
	Nondominant	30.81±11.53	37.92±12.33	0.006*
AIM (number of error)	Dominant	0.36±0.64	0.86±1.34	0.014*
	Nondominant	1.50±1.95	2.25±2.62	0.138
TAP (number of hits)	Dominant	213.78±19.85	204.88±20.87	0.040*
	Nondominant	190.61±24.44	177.58±22.79	0.009*
L.IP (s)	Dominant	42.96±3.85	47.25±5.69	0.000*
	Nondominant	50.05±5.40	50.86±6.51	0.527

**P* values were calculed using the independent *t*-test. STE: Steadiness, LINE: Line tracking, AIM: Aiming, TAP: Tapping, SD: Standard deviation, L.IP: Long pins insertion

Table 2: Hand skills in right-left handed male and right-left handed female subjects

Tests	Hand preference	Mean±SD				*P*
		Left handed male (*n*=17)	Right handed male (*n*=31)	Left handed female (*n*=19)	Right handed female (*n*=33)	
STE (error)	Dominant	3.41±3.04	5.32±4.85[a]	2.53±2.20[a,b]	7.94±10.05[b]	0.005*
	Nondominant	8.88±8.82	12.45±10.52	6.95±7.18	10.27±12.18	0.312
LINE (error)	Dominant	21.00±6.87	25.68±10.00	21.31±8.88	22.39±8.04	0.201
	Nondominant	31.00±7.82[a]	41.48±14.79[a]	30.63±14.28	34.58±8.38	0.017*
AIM (error)	Dominant	0.24±0.56[a]	1.16±1.63[a]	0.47±0.70	0.58±0.94	0.044*
	Nondominant	1.41±2.29	2.41±2.47	1.58±1.64	2.09±2.79	0.472
TAP (hits)	Dominant	214.71±18.24	209.71±25.43	213±21.66	200±14.40	0.055
	Nondominant	193.88±23.44	179.13±26.85	188±25.58	176±18.50	0.053
L.IP (s)	Dominant	43.43±3.60[a,c]	47.01±4.72[b,c]	42.53±4.10[b]	47.48±7.04[a]	0.001*
	Nondominant	49.88±4.77	51.72±6.61	50.20±6.04	50.05±6.40	0.662

**P* values were calculed using the one-way ANOVA, [a,b,c]Values were calculed using the *post hoc* multiple comparisons, [a,b,c]The top icons show differences between the groups. There are differences between the same icons ($P<0.05$). STE: Steadiness, LINE: Line tracking, AIM: Aiming, TAP: Tapping, SD: Standard deviation, L.IP: Long pins insertion

As shown in Table 2, the dominant hand of left-handed women displayed higher performance in the STE test compared to right-handed men and women. The nondominant hand performance of left-handed men was superior to the nondominant hand performance of right-handed men in the line-tracking test ($P < 0.05$).

As shown in Table 3, there was no statistically significant difference in motor skills according to sex ($P > 0.05$).

As shown in Figure 2, there were differences in the motor skills of left handers and right handers; left handers were more skilled in using their dominant hands than right handers.

As shown in Figure 3, the nondominant hands of left handers were more skilled than the nondominant hands of right handers ($P < 0.01$). The nondominant hand performance of left-handed men was superior to the nondominant hand performance of right-handed men in the line-tracking test ($P < 0.05$).

Table 3: Hand skills in male and female subjects

Tests	Hand preference	Mean±SD		*P**
		Male (*n*=48)	Female (*n*=52)	
STE (error)	Dominant	4.65±4.36	5.96±8.49	0.338
	Nondominant	11.19±10.00	9.06±10.68	0.307
LINE (error)	Dominant	24.02±9.22	22.00±8.28	0.251
	Nondominant	37.77±13.64	33.13±10.94	0.063
AIM (error)	Dominant	0.83±1.42	0.54±0.85	0.207
	Nondominant	2.06±2.44	1.90±2.43	0.745
TAP (hits)	Dominant	211.48±23.06	204.94±18.26	0.118
	Nondominant	184.35±26.42	180.35±21.85	0.409
L.IP (s)	Dominant	45.75±4.66	45.67±6.54	0.949
	Nondominant	51.06±6.03	50.11±6.21	0.436

**P* values were calculed using the independent *t*-test.
STE: Steadiness, LINE: Line tracking, AIM: Aiming,
TAP: Tapping, SD: Standard deviation, L.IP: Long pins insertion

As shown in Figure 4, there were differences in the motor skills of left handers and right handers; left handers were more skilled in using their dominant hands than right handers. The dominant-hand performance of left-handed men was superior to only the dominant hand performance of right-handed men in the hand-eye coordination (Aiming) test ($P < 0.05$).

As shown in Figure 5, there were differences in the motor skills of left handers and right handers; left handers were more skilled in using their dominant hands than right handers. The nondominant hands of left handers were more skilled than the nondominant hands of right handers ($P < 0.01$).

As shown in Figure 6, there were differences in the motor skills of left handers and right handers; left handers were more skilled in using their dominant hands than right handers. The dominant hand of left-handed males displayed better performance compared to right-handed men and women in the LIP test; furthermore, left-handed women showed better performance than right-handed men in the same test ($P < 0.05$).

Discussion

We studied fine motor skills with respect to sex and hand preference in healthy people. The fine motor skills of both the dominant and nondominant hands of left handers were superior to the corresponding hands of right-handed individuals. The arm-hand stability of left-handed females and the finger skills of left-handed males and females were found to be superior compared to right-handed individuals. Motor skills have been tested with many different devices, but the majority of tests measure a single motor movement based on performance time. The MLS test provides the assessment of multiple motor skills with a single device and records quantitative data on a computer [Figure 1]. In clinical practice, it is important to obtain reliable results in

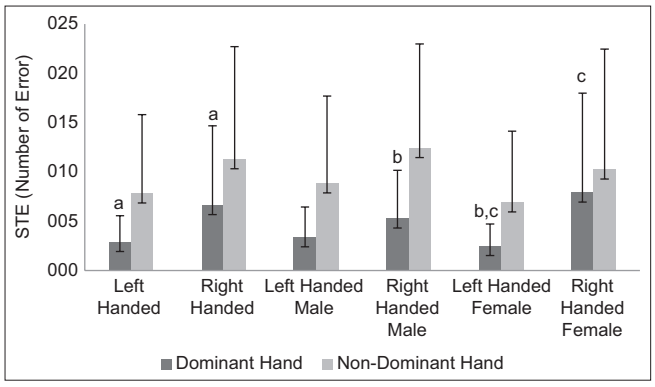

Figure 2: Comparison of mean and standard deviation values of dominant/nondominant hand STE (number of error) in left-right handed, left-right handed male/female. [a]*P* values were calculed using the independent *t*-test. [b, c]*P* values were calculed using the one-way ANOVA. [b, c]Values were calculed using the *post hoc* multiple comparisons. [a, b, c]The top icons show significance differences between the groups. Those indicated with the same icon are statistically significant (*P* < 0.05)

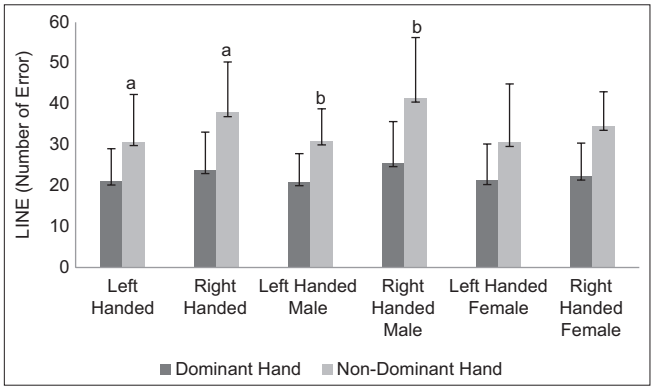

Figure 3: Comparison of mean, standard deviation values of dominant/nondominant hand lıne (number of error) in left-right handed, left-right handed male/female. [a]*P* values were calculated using the independent *t*-test. [b]*P* values were calculed using the one-way ANOVA. [b]Value were calculated using the *post hoc* multiple comparisons. [a, b]The top icons show significance differences between the groups. Those indicated with the same icon are statistically significant (*P* < 0.05)

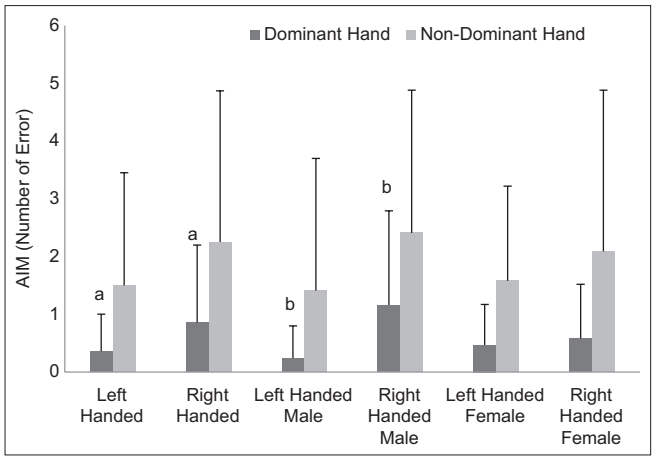

Figure 4: Comparison of mean and standard deviation values of dominant/nondominant hand AIM (number of error) in left-right handed, left-right handed male/female. [a]*P* values were calculated using the independent *t*-test. [b]*P* values were calculed using the one way ANOVA. [b]Values were calculated using the *post hoc* multiple comparisons. [a, b]The top icons show significance differences between the groups. Those indicated with the same icon are statistically significant (*P* < 0.05)

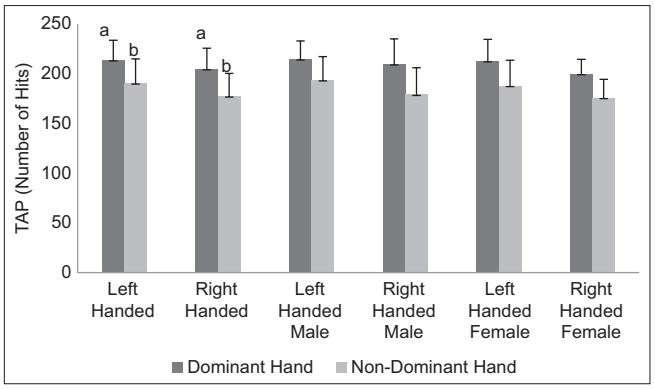

Figure 5: Comparison of mean, standard deviation values of dominant/nondominant hand TAP (number of hits) in left-right handed, left-right handed male/female. [a, b]*P* values were calculed using the independent *t*-test. [a, b]The top icons show significance differences between the groups. Those indicated with the same icon are statistically significant (*P* < 0.05)

an efficient manner, and therefore, the MLS test may be a suitable option in this context.

In a study consisting of 353 males and females (age range, 3.5–50 years), it was found that, in almost all age groups, males were faster in the pin insertion test with their left hands.[20] However, motor skills were measured manually in this study, and thus, results may not be reliable. On the contrary, in our study there was no difference in fine motor skills between males and females [Table 3].

Researchers evaluating hand performance claim that the use of multiple measures to determine hand performance is a stronger predictor for evaluating hand dominance than relying on a unilateral measure.[21] In our study used modern methods that enabled more precise measurements for the evaluation of five different motor skills, supporting the researchers. In a study using Annett's pegboard test on 41 right-handed students, females were found to have performed better than males, and interestingly, a negative correlation was observed between score and finger length.[22] In our study, we found similar results with respect to left-handed females, who were more successful than their male counterparts in most motor skill measures [Table 2]. The LIP test of the MLS performs a similar assessment with the Annett's pegboard test, but the pegboard test is based on manual measurement. Unlike the peg-board test, in the MLS test, the time to place the pins during the test is recorded by the computer. In addition, the MLS test panel [Figure 1] is more useful in that it can measure many motor skills in a short time. In another study using the Annett's pegboard test, 52 right-handed and 48 left-handed subjects were assessed. While the two groups had superior performance in their dominant hands (as expected), it was also demonstrated that the nondominant hand performance of left-handers was better than that of right-handed individuals.[23] This result is consistent with our study [Table 1], and these findings may be associated with social and environmental factors that compel left-handed individuals to use their right hands more frequently, thus increasing their motor skills. In another study, 73 right-handed and 7 left-handed men and women aged between 19 and 87 years were subjected to the MLS test. The authors reported that the dominant hands of subjects were more successful in the line tracking, aiming and LIP tests; and similar to our study, the nondominant hand of left-handed individuals demonstrated relatively greater success when compared to right-handed subjects. It was also noted that no difference was found between the sexes in any test.[24]

In another study, the pegboard test was applied to 22 right-and 22 left-handed individuals. Similarly, it was found that the nondominant hands of left-handed individuals had better performance when compared to the nondominant hands of right-handed individuals.[25] Our computerized method provided results that were in agreement with the mentioned studies; the dominant and nondominant hand skills of left-handed individuals were better compared to right-handed individuals, and left-handed females and left-handed males were also more successful than right-handed individuals in terms of various motor skill sub-tests [Tables 1 and 2]. A study evaluating cross-lateral and congruent hand and foot dominance patterns in 60 healthy participants, the Vienna Test System was utilized to measure the response to sensory stimuli. The authors found that performance was similar in right-handed and left-handed individuals, and their data suggested that hand and foot lateralization was associated with the central nervous system characteristics rather than other features.[16] In a study using Annett's wooden bar test in 85 right-and 17 left-handed subjects, the hand skill speed time of right-handed subjects was found to be better when compared to left-handed subjects (Gundogan *et al*., 2007).[26] Our study reports findings that are contrary

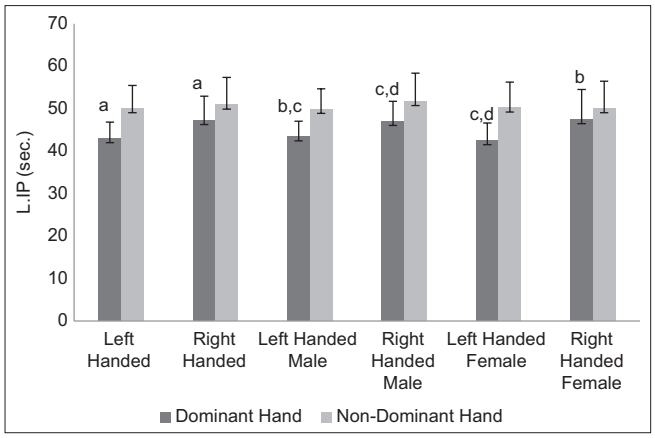

Figure 6: Comparison of mean, standard deviation values of dominant/nondominant hand L.IP (sec.) in left-right handed, left-right handed male/female. [a]*P* values were calculed using the independent *t*-test. [b, c, d]*P* values were calculed using the one-way ANOVA. [b, c, d]Values were calculated using the *post hoc* multiple comparisons. [a, b, c, d]The top icons show significance differences between the groups. Those indicated with the same icon are statistically significant (*P* < 0.05)

to this finding. We found that the dominant hand and nondominant hand performances of left-handed individuals were superior than the corresponding hands of right-handed individuals. The reason for this may be the fact that we included a comparable number of left-handed individuals in our study (n = 34); whereas the number of left-handed individuals was relatively low in the mentioned study, which would limit the accuracy of results and comparisons. In another study examining the effects of dominant and nondominant hands on motor skills in 10 right- and 10 left-handed individuals, it was shown that the dominant hand of right-handed individuals demonstrated greater skill improvement compared to their nondominant hand, whereas, interestingly, motor skill improvements were similar for the dominant and nondominant hands of left-handed subjects.[27] When this result is taken together with our findings showing superior motor skills in both the dominant and nondominant hands of left-handed individuals, it appears that fine motor skills may be accrued more quickly among individuals with left-hand dominance, possibly in relation with the fact that social, educational and cultural characteristics often compel left-handed individuals to use their nondominant hands more frequently. Such differences in dexterity and fine motor skills could have implications for rehabilitation practices in subjects with function-limiting injuries and indicate the need for patient-based approaches in this context. In a study using the MLS test in elderly subjects (age >70), functional asymmetry linked to age was observed in all tests.[17] In our study, functional asymmetry linked to hand preference was observed in all sub-tests of the MLS. However, these features were only assessed among right-handed and left-handed young individuals in the current research. Furthermore, although these results may indicate the need for patient-specific alterations in rehabilitation practices, we did not analyze patients with functional limitations. Thus, future studies would benefit from longitudinal assessments of patients that are treated for functional limitations to determine whether the re-establishment of function demonstrates the differences with respect to hand preference since, as mentioned before, previous studies have suggested left-handed individuals may be superior in terms of acquiring motor skills. It should also be noted that a more comprehensive study can be conducted if other factors affecting hand function, such as age-related asymmetry, are included in the analyses.

Limitations

The present study has certain limitations. The first potential limitation is the number of left-handed and right-handed included in the study. Increasing the number of left-handed people, performing comparisons with equal numbers of left-handed and right-handed people, and including ambidextrous subjects in the study could be important in terms of creating reliable normative data. Furthermore, the evaluation of motor skills with the MLS device during hand therapy in patients with hand injuries may provide a new methodological approach to hand therapy and rehabilitation.

Conclusions

In our study, we found significant differences in hand-arm stability, hand-arm sensitivity, wrist-finger speed, hand-eye coordination, and hand-finger skill in the comparison of right-and left-handed individuals. Depending on the relationship between hand preference and fine motor performance, it was concluded that motor performance may be asymmetric controlled in the brain. Understanding the extent of manual performance asymmetry and its control in the brain is important for clinical evaluations as well as physiological characteristics. Precise and reliable measurement is required for the diagnosis and treatment of motor functions. The fact that the motor skills of both hands were found to be superior among left-handers (compared to the corresponding hands of right-handers) suggests that left-handed people may demonstrate better improvement in hand function after possible hand or nerve injury. In addition, in the event of a permanent loss of dominant hand function, the motor skill advantage in the nondominant hand of left-handers can facilitate easier transfer of hand dominance compared to right-handed individuals. We conclude that using the MLS can be advantageous due to swift and detailed assessment of motor skills, and therefore, MLS follow-up may be valuable in the rehabilitation programs of patients who suffer from functional loss in their dominant hand. In future, we believe that it will be important to assess motor skills in patient populations including a higher number of left-handed subjects. Our study can provide the basis of a new methodological approach and the data herein may be utilized as normative data for these future studies.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Original Article

A Cross-sectional Study to Determine Pregnancy Outcomes in Transabdominal Ultrasound-guided Embryo Transfer

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Abstract

Introduction: The success of any *in vitro* fertilization (IVF) program depends upon a number of factors, including the ovarian stimulation protocol, quality and quantity of gametes obtained, and the embryo transfer (ET) procedure itself. ET procedure is a crucial step in the success of any IVF or intracytoplasmic sperm injection cycle and has to be mastered and meticulously performed. Ultrasound, being a noninvasive procedure, is used extensively in assisted reproduction and has an important role in ET procedure. Hormonal stimulation of the ovaries causes their enlargement, thereby resulting in variation of the uterine position. There is a paucity of literature documenting this change in uterine position, especially in the Indian population. Therefore, this study was undertaken to find any variation in the uterine position and its impact on pregnancy rates. **Methadology:** In vitro fertilization was done after ovarian stimulation and ET was done on day 3 at 8 cell stage. Biochemical Pregnancy Rates and clinical pregnancy rates were determined for all the ET procedures. **Results:** The anteverted uterus was present in 102 cases, amounting to 77.2%, whereas the remaining 30 cases had retroverted uterus, amounting to 22.8%. The ET procedure in anteverted cases was performed with ease in the majority of the cases. However, three cases had difficult ET. In comparison, the six difficult ETs were reported out of a total of 30 retroverted uterus, amounting to 20% of cases. **Conclusion:** The superiority of ultrasound-guided ET has been proved beyond any doubt as compared to the clinical touch method and it remains the mainstay of ET procedure.

Keywords: *Embryo transfer, in vitro fertilization, transabdominal ultrasound*

Introduction

Infertility is a global health problem affecting millions of couples worldwide. *In vitro* fertilization and embryo transfer procedure (IVF-ET) is done to help infertile couples achieve parenthood. The success of any IVF program is dependent on multiple factors, mainly involving the ovarian stimulation protocol, quality and quantity of gametes obtained, and the embryo transfer (ET) procedure. ET procedure is a crucial step in the success of any IVF or intracytoplasmic sperm injection cycle and has to be mastered and meticulously performed. Ultrasound, being a noninvasive procedure, is used extensively in assisted reproduction and has an important role in ET procedures.

Strickler *et al*. first described the use of ultrasound as an aid to ET.[1] The pregnancy outcomes in assisted reproduction depend upon a number of factors, including endometrium thickness, quality of embryos transferred, and, more importantly, the ET procedure itself.[2] Two types of methods are commonly employed by clinicians for better pregnancy outcomes in ET procedures in assisted reproduction. These methods include the clinical touch method and the use of ultrasound guidance. Although three-dimensional ultrasound-guided ET has been reported, two-dimensional transabdominal ultrasound-guided ET is popular in clinical practice.[3]

Hormonal stimulation of the ovaries causes their enlargement, thereby resulting in variation of the uterine position. This variation of uterine position can impact the ET procedure, leading to diminished pregnancy outcomes. There is a paucity of literature documenting this change in uterine position, especially in the Indian population. Therefore, this study was undertaken to find any variation in the uterine position, the use of transabdominal ultrasound in ET, and its impact on pregnancy outcomes.

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Aims and objectives

Aim

The aim of the study was to study the role of transabdominal ultrasound on the outcome of the IVF-ET procedure.

Objectives

1. To find out the uterine position on the day of ET procedure
2. To estimate the biochemical pregnancy rates (BPRs) in the anteverted and retroverted uterus
3. To estimate the clinical pregnancy rates in the anteverted and retroverted uterus.

Materials and Methods

The study was a clinical cross-sectional study done over 1 year on infertile females. Written informed consent was taken from all the patients undergoing ultrasound-guided ET in an assisted reproductive technology center of a tertiary care university teaching hospital. The ethical clearance was taken from the hospital's ethical committee.

In vitro fertilization was done after ovarian stimulation and ET was done on day 3 at 8 cell stage. A soft double-lumen catheter was used (Cook, Bloomington, Indiana, USA) [Figure 1].

ET was performed as a daycare procedure on day 3 of embryo culture at the eight-cell stage. The ET procedure involved the following steps:

1. The patients were instructed to have a full bladder for better visualization of the uterus and cervix during the ultrasound-guided ET
2. The position of the patient is lithotomy position. Initial preparation of the patient includes use of normal saline for cleaning the cervix and vagina. Povidone iodine cleaning is avoided because of its proven toxicity for the gametes and the embryos
3. Use of vulsellum is mandatory but excessive manipulation is avoided. No sedation is required for ET procedure
4. Ultrasound jelly is placed on the abdomen and the transabdominal probe is adjusted to obtain a clear visualization of the uterus and cervix. An attempt is made to obtain a midsagittal view of the uterus and cervix
5. The clinician negotiates the cervix and advances the ET catheter (Outer) through the cervical canal into the uterine cavity
6. The embryologist loads 2–3 embryos in minimal embryo culture medium into the inner catheter and hands it over to the clinician
7. The embryos are placed 1–2 cm below the fundus of the uterus. This is indicated by a hyperechogenic spot in the uterus
8. The catheter is returned back to the embryologist who checks for the presence of retained embryos, if any
9. The procedure is complete after confirmation of no retained embryos is made by the embryologist. The patient is shown the hyper echogenic spot on the ultrasound screen which indicates the position of the embryos.

Transabdominal ultrasound-guided ET in the anteverted uterus after the full bladder is depicted in Figure 2.

BPRs and clinical pregnancy rates were determined for all the ET procedures. However, multiple pregnancy rates, miscarriage rates, and ectopic pregnancy rates were not calculated.

Results

A total number of 132 IVF cycles were included in this study. The outcome measures observed were BPRs and the clinical pregnancy rates. Serum beta-human chorionic gonadotropin (HCG) value of more than or equal to 50 mIU/mL was taken as a positive test. The presence of a single gestational sac with a heartbeat on a transvaginal ultrasound scan was taken as a positive clinical pregnancy.

The angle of anteversion was noted in all the cases. An attempt was made to obtain a midline longitudinal section for better visualization of the long axis of the uterus and cervix. Data were entered in MS Excel worksheets and the use of descriptive statistics was made for generating bar charts and graphs in Microsoft PowerPoint in Windows 8 version.

The anteverted uterus was present in 102 cases, amounting to 77.2%, whereas the remaining 30 cases had retroverted uterus, amounting to 22.8% [Graph 1].

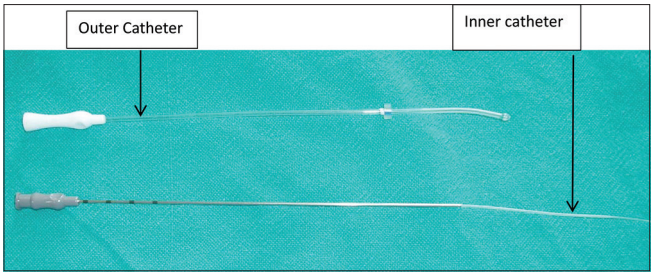


Figure 1: Embryo transfer catheter (Cook)

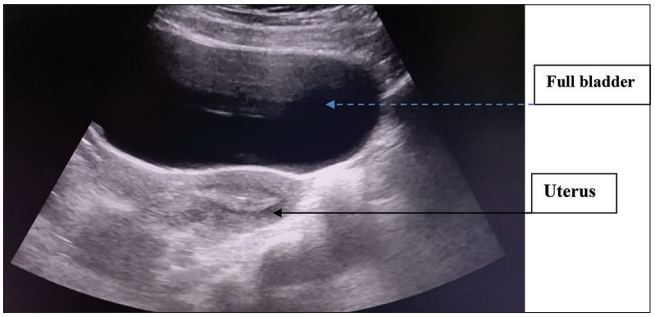


Figure 2: Embryo transfer in the anteverted uterus under transabdominal ultrasound guidance

The ET procedure in anteverted cases was performed with ease in the majority of the cases. However, three cases had difficult ET. In comparison, the six difficult ETs were reported out of a total of 30 retroverted uterus, amounting to 20% of total cases. The results of the study in the form of pregnancy outcomes are summarized in Graph 2 and Table 1. The same pregnancy outcome was also reported in Graph 2.

Discussion

BPR was taken as positive if the value of serum beta-hCG was equal to or more than 50 mIU/mL. Clinical pregnancy rate, defined as the presence of fetal cardiac activity on transvaginal ultrasound at 5 weeks gestation, was estimated. Out of a total of 102 anteverted cases studied, 46 showed biochemical pregnancy (45.0%) and 43 had the presence of fetal cardiac activity amounting to CPR of 42.1%. In the retroverted group, eight cases showed biochemical and clinical pregnancy, amounting to 26.6% of cases.

ET technique is crucial for the success of any IVF program. Smooth ET involves depositing the embryos 1–2 cm below the fundus of the uterus traumatically and without undue delay. Difficult ET is due to the distorted anatomy of the uterus, which may be retroverted or anteverted. Another common anatomical reason for difficult transfer is cervical stenosis.[4] A significant decrease in the pregnancy rates was reported in difficult ETs.[5,6] The mainstay of management of such difficult cases remains the prior dilatation of cervical stenosis followed by 1–3 weeks of ET.[7] These difficulties in the ET procedure can be detected and managed by the use of ultrasound in the ET procedure. Systematic reviews and meta-analyses of randomized controlled trials showed the advantage of transabdominal ultrasound-guided ETs compared to the clinical touch method.[8,9]

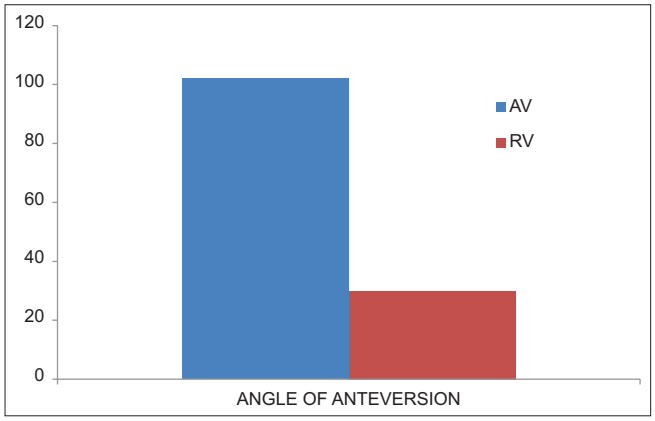
Systematic reviews and meta-analyses also showed higher clinical pregnancy rates with ultrasound guidance, but there was no statistically significant change in live birth rates. Moreover, the multiple pregnancy rates, miscarriage rates, and ectopic pregnancy rates were similar in both the ultrasound-guided and clinical touch methods of ET in some centers.[10-12] Transabdominal ultrasound allows actual visualization of the cervical canal and uterine cavity, thereby helping in exact localization of the position of embryo discharge. American Society of Reproductive Medicine (ASRM) has come up with guidelines for the optimal ET.[13] ASRM has also developed a standard ET protocol template on the principles of evidence-based medicine which strongly recommends the use of transabdominal ultrasound guidance for successful ET. Other significant recommendations of the ASRM include the removal of cervical mucus before ET and the use of a soft catheter. Moreover, it also recommends placing of embryos in the uterine cavity approximately 1 cm from the fundus.

The use of ultrasound helps to clearly visualize utero cervical axis, which helps in the proper and accurate positioning of embryos during the ET procedure. Our findings of optimal clinical pregnancy rates associated with the use of transabdominal ultrasound in ET corroborate with the recommendations of the ASRM, which strongly recommends the use of ultrasound guidance in ET. In a study comparing the use of transabdominal and transvaginal ultrasound in ET, transvaginal ultrasound-guided ET was found to facilitate ET in difficult cases. Accurate visualization of the cervical canal and deposition of embryos in the midcavity were responsible for better pregnancy outcomes.[14] Recent studies point to a superior role of transvaginal ultrasound in ET procedures.[15,16] The limitations of the transvaginal ultrasound-guided ET remain the difficulty in mastering the procedure and the discomfort to the patient. Due to these limitations of the transvaginal method, the transabdominal ultrasound-guided ET is in use in clinical practice.

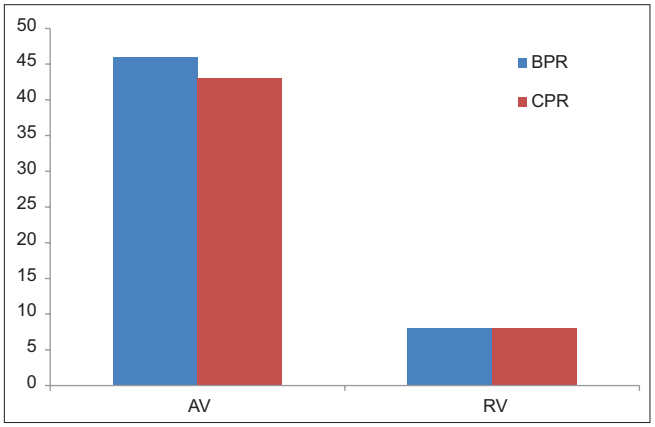
Table 1: Pregnancy outcomes in transabdominal ultrasound-guided embryo transfer

Sample size (*n*=132)	BPR, *n* (%)	CPR, *n* (%)
AV 102	46 (45.9)	43 (42.1)
RV 30	8 (26.6)	8 (26.6)

CPR: Clinical pregnancy rate, BPR: Biochemical pregnancy rate, AV: Anteverted, RV: Retroverted



Graph 1: Angle of anteversion. AV: Anteverted, RV: Retroverted



Graph 2: Pregnancy outcomes in the anteverted and retroverted groups. CPR: Clinical pregnancy rate, BPR: Biochemical pregnancy rate

Conclusion

Ultrasound-guided ET gives better pregnancy outcomes in assisted reproduction, but its exact mechanism remains unclear. The superiority of ultrasound-guided ET has been proved beyond any doubt as compared to the clinical touch method and it remains the mainstay of ET procedure. The findings of this study support the use of transabdominal ultrasound guidance for successful ET in Indian women undergoing IVF.

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Conflicts of interest

There are no conflicts of interest.

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Review Article

Decoding the Mysteries of the Obturator Nerve

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Abstract

The purpose of this systematic review is to examine the obturator nerve in detail, elucidating its intricate anatomical course and complex branching patterns. Through a comprehensive analysis of existing scholarly sources, this study aims to unravel the complexities of the obturator nerve and provide nuanced insights for professionals in the fields of morphology and clinical practice. This investigation makes a valuable contribution to the body of knowledge on the neuroanatomical intricacies of the obturator nerve, thereby enriching the understanding of anatomists, morphologists, and physicians.

Keywords: *Anatomical Quality Assurance criteria, gross anatomy, lumbar plexus, systematic review*

Introduction

The obturator nerve (n. obturatorius) is a single intrapelvic nerve that originates from the anterior branches of the L2–L4 lumbar spinal nerves.[1] Its trajectory includes proximal lumbar, pelvic, and distal canal segments. Within the obturator canal, the nerve divides into two terminal branches: anterior and posterior. These branches play a crucial role in innervating structures such as thigh muscles, the skin of the medial thigh region, and the hip and knee joints.[2]

Notably, the obturator nerve displays a significant variability in its origin, course, and branching patterns. This diversity has important implications for professionals, including surgeons, traumatologists, and neurologists, particularly in procedures involving pain management in innervated joints,[3] local surgery and pain block,[4] or addressing paralysis in innervated muscles.[5] A thorough understanding of obturator nerve morphology can greatly enhance the effectiveness of locally administered medical interventions.

The objective of this study is to systematically review the literature in order to organize knowledge regarding the variation in the course and pattern of branches of the obturator nerve for both morphologists and practitioners.

Methodology

A multi-stage literature search was conducted using available electronic databases, including Google Scholar, Scopus, Ebsco, and PubMed, to identify scientific publications suitable for analysis. Several separate review sessions were conducted using keywords such as "obturator nerve variations," "obturator nerve anatomy," "accessory obturator nerve," "lumbar plexus obturator variations," "obturator nerve branching pattern," "innervation of the hip joint by the obturator nerve," "innervation of the knee joint by the obturator nerve," and "obturator nerve branches."

The large number of search sessions was due to the small number of records associated with a single keyword. Publications in any language and time period were accepted, and the resulting list of records was sorted according to the best matches. All forms of publication were included except those that met the exclusion criteria.

To increase the reliability of the literature review, the Anatomical Quality Assurance criteria[6,7] were applied throughout the search process, as shown in Figure 1. The scientific team had experience applying these criteria[8] and designing review papers.[9,10] Exclusion criteria included papers conducted on animal material, microscopic, and histological papers and genetic papers that did not contain information on the anatomical structure of the nerve. Books (scientific monographs) were not emphasized due to the difficulty

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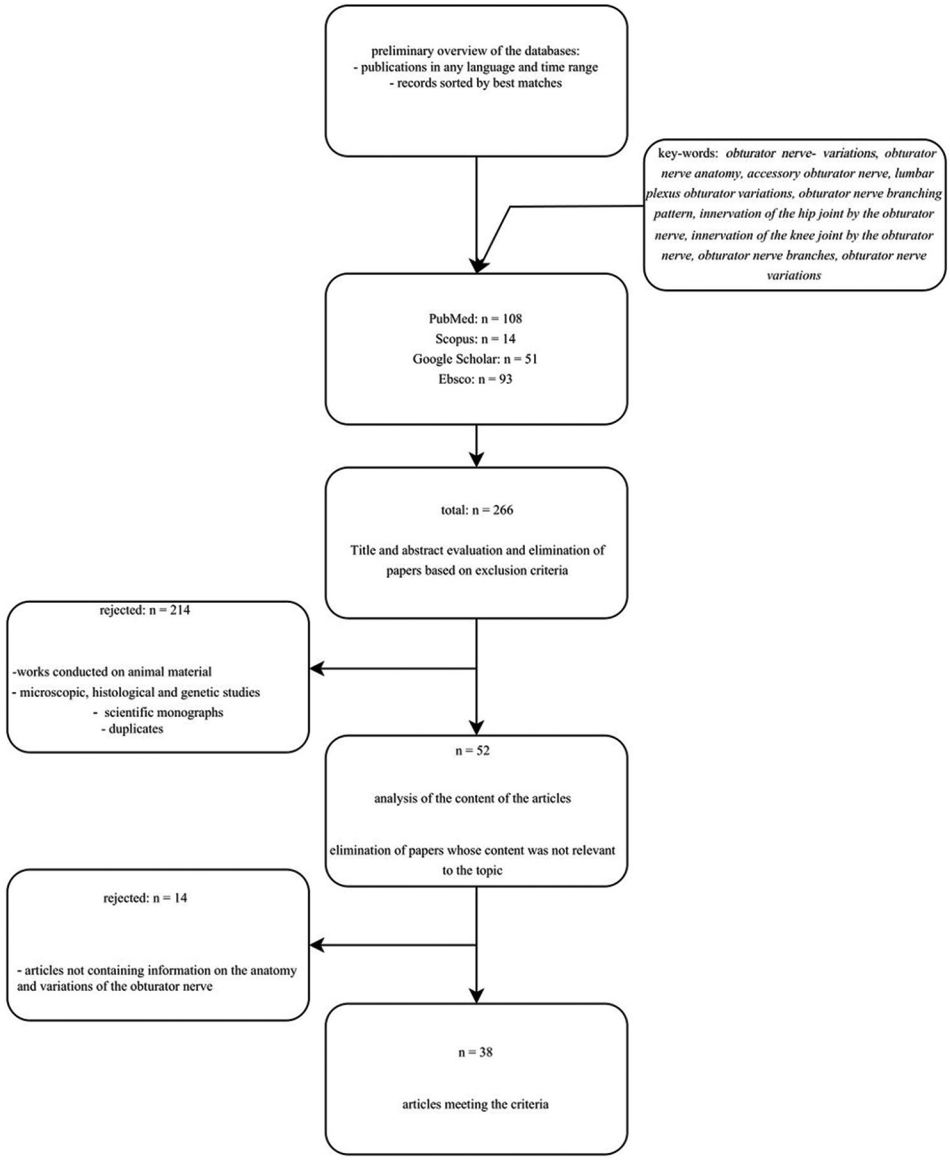

Figure 1: Systematic search process graph – a flowchart of the selection of articles and their compilation

of assessing their eligibility and their low probability of being useful for the objectives of this paper.

Any difficulties in assessing study eligibility were resolved unanimously by all authors. The results from the databases were sorted and summarized to avoid repetition. Initially, 266 articles were selected from all databases. Based on a preliminary review of titles and abstracts, 214 articles were rejected, leaving 52 articles to be analyzed for content. Articles that were not relevant to the topic of the study, i.e. did not contain information on the anatomy and variations of the obturator nerve, were rejected, resulting in 38 articles that met the criteria.

Nerve Trunk

An analysis of the available literature using systematic review techniques revealed a high variability in the origin of the obturator nerve. For example, Tshabalala *et al*.[11] demonstrated in a group of 181 cases that the predominant onset of the nerve is the L2–L4 variant, occurring in 80% of cases, while the L3–L4 variant occurs in 20%.

Anandhi *et al*.,[12] in a group of 50 cases, reported that the L1–L3 variant is present in only 2% of cases, with the L2–L4 variant still being predominant. Miura *et al*.[13] described the presence of the L1–L4 variant in a group of 100, which is relatively infrequently mentioned in the literature (11% of cases), with other variants being L2–L4 in 76%, L2–L5 in 5%, L3–L4 in 4%, and L3-5 in 4%. In contrast, Tshabalala *et al*.[11] reported that in 1.7% of cases, the fusion of L3 and L4 fibers occurs as late as the pelvic segment of the nerve (n = 181). A summary of the data obtained from the systematic review is presented in Table 1.

Table 1: Anatomical variations of the obturator nerve trunk (based on a systematic review)

Variation	Percentage range	Average percentage	Number of variation samples	Number of analyzed samples
L2–L4 root	76–98	82	231	270
L3–L4 root	4–20	13	40	281
L1–L3 root	2	-	1	50
L1–L4 root	11	-	11	100
L2–L5 root	5	-	5	100
L3–L5 root	4	-	4	100
L3–L4 connection in the pelvis	1.7	-	3	181
Division of the nerve in the pelvis	2–100	31	148	483
Division of the nerve in the canal	23.22–93	61	234	383
Division of the nerve on the thigh	5–51.78	26	100	383
Presence of accessory obturator nerve	12.1	-	16	132

Table 2: Anatomical variations of the anterior branch of the obturator nerve

Descriptive variability	Percentage range	Percentage average	Number of variation cases	Number of specimens
Two muscular branches	9–28.6	23	54	235
Three muscular branches	65.7–66.7	66.34	156	235
Four muscular branches	4.76–25.4	10.64	25	235
Piercing the external obturator muscle	52	-	13	25
Crossing over the upper margin of the external obturator muscle	48	-	12	25
Branch to gracilis muscle	85.7	-	12	14
Branch to pectineus muscle	1–10	5.9	13	220
The innervation of the additional heads of the adductor longus (2 or 3 heads) by the anterior branch	-	-	2	2 (CR)
The fibers of the accessory obturator nerve unite with the anterior branch near the obturator foramen	5	-	2	40
Cutaneous branch (presence)	43–48	45.45	25	55
Cutaneous branch to medial malleolus	-	-	2	2 (CR)
Cutaneous branch to scrotum	-	-	1	1 (CR)
Branch to hip joint	11.9–42.9	15.26	38	249
Two branches to hip joint	3.6	-	6	168
Branch to knee joint	7.1	-	1	14
Communicating branch to saphenous nerve	-	-	1	1 (CR)

CR: Case report

Another variable section of the obturator nerve is its division into terminal branches – the anterior branch and the posterior branch. This typically occurs within the obturator canal, but many authors report that division may occur earlier, either within the pelvis or after the nerve has exited the canal. Tshabalala *et al*.[11] reported that premature division of the nerve (within the pelvis) occurs in 3% of cases on the left side and 1% on the right side, while division after exiting the canal occurs on both sides in 5% of cases. The most common intracanal division occurs in 92% of cases on the left side and 94% on the right (n = 201). Other studies, such as one conducted by Iwanaga *et al*.[14] (n = 14) showed a higher percentage of nerve division within the pelvis (14.3%) and after exiting the canal (21.4%), with a more typical location of division in 64.3% of the cases; however, one limitation of this study is the sample size. On the other hand, Anagnostopoulou *et al*.[15] (n = 168) reported that division of the nerve most commonly occurs after it exits the canal (51.78%), less commonly within the pelvis (25% of cases), and rarely within the canal (23.22% of cases).

Miura *et al*.[13] also described division within the pelvis (n = 100). In addition, there have been reports of anatomical variations in the obturator canal, such as a case of a triple bony obturator canal.[16] The question remains as to whether the nerve caused adaptive changes in the skeleton or vice versa.

The presence of an accessory obturator nerve has also been described. Katritsis *et al*.[17] estimated its prevalence at 13.2% of cases. They also reported that in 12.1% of cases, it branches off from the obturator nerve trunk, making it difficult to define it as an accessory obturator nerve.

Several branches can be identified within the course of the obturator nerve trunk; Kumka[18] mentions periosteal

branches, a branch to the obturator artery, and a branch to the external obturator muscle.

Anterior Branch

In their research, Miura *et al*.[13] (n = 25) reported that the anterior branch of the obturator nerve divided the trunk and exited through the obturator orifice. In 52% of the cases, the nerve pierced the external obturator muscle, while in 48% of the cases, it passed along the upper edge of the muscle. According to Anagnostopoulou *et al*.,[15,17] the nerve then descended to the thigh and entered between the external obturator muscle and the pectinate muscle. From there, it ran between the superficially located adductor longus muscle and the more deeply lying adductor brevis muscle, where it distributed muscle branches and a nonpermanent cutaneous branch to the medial surface of the distal thigh.

The anterior branch typically gave off three muscular branches: one to the adductor longus muscle, one to the adductor brevis muscle, and one to the gracilis muscle. However, there have also been reports of innervation of the pectineus muscle or the complete lack of branches to the adductor brevis muscle.[17,19-21]

Anagnostopoulou *et al*.[15] found that the anterior branch gave off three branches (to the adductor longus, adductor brevis, and gracilis muscles) in 66.66% of cases (n = 168), two branches (to the adductor longus and gracilis muscles) in 28.57%, and four branches (to the adductor longus, adductor brevis, gracilis, and pectineus muscles) in 4.77%. In contrast, Berhanu *et al*.[19] stated that in a group of 67 individuals, the anterior branch gave rise to two branches in 9% of cases, three branches in 65.7%, and four branches in 25.3%.

The frequency of innervation of the pectineus muscle was found to be 1% by Tshabalala *et al*.[11] (n = 99), 9.5% by Takizawa *et al*.[21] (n = 21), and 10% by Kim *et al*.[20] (n = 100). Tuluy *et al*.[22] showed that the branch to the gracilis muscle appeared in 85.7% of cases (n = 14). When additional heads of the adductor longus muscle were present, they were all innervated by the anterior branch of the obturator nerve.[23]

Some studies[24-26] have demonstrated that the anterior branch of the obturator nerve can be reached by fibers of the accessory obturator nerve. Turgut *et al*.[25] reported an occurrence rate of 5% (n = 40). The cutaneous branch of the obturator nerve was found to be present intermittently; Orduña Valls *et al*.[27] reported that it occurred in 48% of cases (n = 25), while Bouaziz *et al*.[28] reported a frequency of 43% (n = 30). After puncturing the broad fascia, posterior to the saphenous vein, the dermal branch innervates a variable area of skin in the distal part of the thigh and the medial skin surface of the knee, making local anesthesia of the knee joint area more difficult.

Staples *et al*.[29] described two cases where a cutaneous branch of the obturator nerve descended below the knee posteriorly from the saphenous vein, reaching the distal part of the calf and giving end branches posteriorly from the medial ankle. Nayak and Vasudeva[30] described a branch diverging from the anterior branch of the obturator nerve, innervating the anterior portion of the scrotum.

In addition, one or two articular branches to the hip joint may also diverge from the anterior branch, with a highly variable incidence. Anagnostopoulou *et al*.[15] reported that innervation of the hip joint by a single articular branch diverging from the anterior branch of the obturator nerve occurred in 11.9% of cases (n = 168), while two articular branches were found in 3.57% of cases (n = 168). Other authors have reported a 42.9% (n = 14) incidence of the anterior branch giving off the articular branch to the hip joint,[31] while Berhanu *et al*.[19] reported a lower incidence of 17.9% (n = 67). Sakamoto *et al*.[31] also found that the articular branch to the knee joint diverged from the anterior branch in 7.1% of cases (n = 14).

Mazurek *et al*.[2] described an articular branch to the knee joint that diverged from the anterior branch with a common trunk and connected to one branch of the saphenous nerve and another branch that innervated the medial side of the knee joint.

Posterior Branch

The posterior branch of the obturator nerve descends and goes backward after leaving its main trunk. It usually goes through the external obturator muscle, providing motor branches to it. In 21.7% of cases, it passes along the upper edge of the muscle (n = 23).[27] Once it enters the thigh, it lies between the external obturator and pectineus muscles. Then, it travels between the adductor brevis and adductor magnus muscles. The nerve continuously supplies the adductor magnus and external obturator.

In a subset of the population, the posterior surface of the adductor brevis muscle is also innervated by the obturator nerve, along with its innervation by the anterior branch. However, different sources report varying data on the prevalence of this system, ranging from 60.11% (n = 168)[15] to 23% (n = 100)[13] on the left side and 10% (n = 97) and 11% (n = 98) on the right side.[11] In this instance, the branches from the anterior and posterior branches of the obturator nerve do not merge within the muscle.[13]

The posterior branch may also provide innervation to the adductor longus muscle in 7.14% of cases (n = 168).[17] One of the branches that enter the adductor magnus muscle goes through it and continues to the popliteal fossa, where it helps innervate the posterior surface of the articular capsule.[32] The fibers then spread further into the cruciate ligaments and synovial membrane of the joint.[18] Furthermore, the posterior branch of the obturator nerve is involved in the innervation of the hip joint, with sensory branches reaching the anterior or anteromedial surface of the articular capsule.[31,33]

Summary

Our comprehensive review has revealed a significant amount of variation, particularly in the anterior branch, of the obturator nerve in terms of its course and the projection of its branches [Table 2]. The main objective of our investigation was to systematically compile and analyze all documented variations of the obturator nerve. This extensive information has practical implications for both clinical and educational contexts. The complex variations in the branches and trajectory of the nerve are highly relevant in orthopedic applications, specifically in the management of hip pain,[33] knee pain,[31] and inguinal pain.[34] The variability of the obturator nerve is also important in anesthesia practices, such as during obturator nerve blocks for knee joint anesthesia[11] and for addressing spasticity in thigh muscles innervated by the obturator nerve in neurology.[5]

It should be noted that the observed variability may have clinical implications for anesthesia during arthroscopy. As anesthetics are routinely administered in the femoral and sciatic nerve regions,[35,36] the demonstrated variable innervation of the knee joint may contribute to incomplete anesthesia during these procedures.

The diverse courses and branches of the obturator nerve play a crucial role in surgical interventions, particularly in femoral nerve reconstruction using the obturator nerve.[37] Our argument is that the varying patterns of innervation of the obturator nerve, as illustrated in our study, deserve attention and consideration from all medical professionals specializing in the obturator nerve and its branches in their clinical practice.

Conclusion

The obturator nerve is highly variable anatomically, which poses a risk for complications when conducting medical procedures involving the nerve. This variability can occur in branching patterns, greatly impacting the success of a procedure. Therefore, it is crucial to consider this variability when planning an intervention on the obturator nerve and take all necessary measures to minimize the risk of complications.

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Conflicts of interest

There are no conflicts of interest.

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Systematic Review

Investigating the Integration of Anatomical Variabilities into Medical Education as a Potential Strategy for Mitigating Surgical Errors

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Abstract

Introduction: Surgical errors burden health-care systems globally, with anatomical variations being a significant contributor. This review examined the role of these variations and offers valuable insights for medical practitioners, educators, and policymakers to develop strategies to address and mitigate challenges posed by these variations. **Materials and Methods:** They keywords were generated from the title and online databases were searched with the help of a search string of keywords and Boolean operators. **Results:** A total of 13 articles were included in the present review. Thematic data analysis identified seven key themes highlighting the significance of anatomical variations in medical education. These include incorporating variations, determining optimal introduction and contact levels, identifying significant variations, teaching methods, visualization techniques, and challenges in integrating them. This systematic review has shown that earlier literature underscores the importance of anatomical variations in the context of medical education. However, there is evidence that students and trainees lack the necessary skills to effectively understand the concepts of anatomical variability and their application in the clinical setting. The final theme discusses potential solutions to enhance students' understanding of human anatomy. **Conclusion:** Medical education aims to produce qualified physicians who provide competent and safe patient care. However, students and trainees often lack the skills to understand anatomical variations, leading to misdiagnoses and health-care malpractice. Active medical education professionals should ensure familiarization with anatomical variations to clear misconceptions about the human body, provide valuable knowledge about patient uniqueness, and spark interest in physicians.

Keywords: *Anatomy curriculum, clinical malpractice, difficult anatomy, educational strategies, visualization techniques*

Introduction

Variation in anatomy rarely requires intervention; however, such occurrences can potentially affect patient's life indirectly by making diagnosis or treatment more difficult and often mimics malignancies. With the growing utilization of radiology in daily clinical practice, accurate identification of anatomical variations has become easier.[1] Nowadays, the number of computerized tomography (CT) scans performed annually has increased exponentially. In 2022, approximately 84 million CTs were done in the United States alone, resulting in more frequent detection of anatomical variations, which usually go unnoticed.[2] However, physicians lacking a full understanding of anatomical variability can be misled by these accidentally discovered variants, leading to unnecessary investigations and medical procedures that drain resources and jeopardize patient care. Surgical outcomes can be adversely affected by anatomical variability, and a significant proportion of preventable deaths can be attributed to inadequate anatomical knowledge.[3] Research examining medical malpractice claims originating from American insurance firms revealed that approximately a quarter (25%) of these claims were associated with anatomic variabilities. However, it was observed that complications arising from anatomical factors in surgical procedures tended to be insufficiently documented in the reported cases. The inability to identify atypical anatomical structures during surgical interventions places patient well-being in peril and gives rise to substantial legal actions and claims of professional negligence.[1] A concerning deficiency in attention toward anatomical variations is evident within the realm of medical

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education, a responsibility shared in equal measure by both anatomists and medical practitioners. Notwithstanding the regular exposure to anatomical variations during dissection exercises and in real-world clinical settings, minimal endeavors have been directed toward rectifying the neglect of anatomical variations within the framework of medical education.[4] Contemporary medical educational frameworks exhibit a proclivity toward prioritizing salient subjects acquired from condensed references, consequently sidelining the discourse surrounding anatomical variability and its pertinent clinical ramifications. Furthermore, the widespread utilization of pedagogical aids such as synthetic models, predominantly portraying conventional or prototypical anatomical structures, serves to perpetuate the paradigm of an idealized, unvaried anatomical norm.[5] This situation is further aggravated when instructors omit elucidating the extensive range encompassed within the domain of normal anatomical diversity. It is disconcerting that the significance attributed to anatomical variations remains conspicuously absent within contemporary medical pedagogy. It is plausible that educators might not have duly recognized that forthcoming medical practitioners will encounter a considerably augmented array of anatomical deviations compared to preceding cohorts, primarily owing to the heightened utilization of advancing imaging modalities.[6,7] Presently, a noticeable void exists within the academic discourse concerning the incorporation of anatomical variations into medical pedagogy. The primary objective of this systematic review is to comprehensively assess the representation of anatomical variations within the body of medical education literature, subsequently pinpointing pertinent challenges associated with their integration and instructional methodologies. It is anticipated that the discernments derived from this review will exert an impact on pedagogical approaches, facilitate the scrutiny of prevailing anatomy curricula, and rectify the insufficient consideration accorded to anatomical variations within the sphere of medical instruction.

Materials and Methods

To identify relevant studies on anatomical variation related to medical education, a systematic search approach using different search terms was employed. The selection of these terminologies was grounded in a recent review that underscored the prevailing lexicon frequently employed to delineate anatomical variations.

The keywords or MeSH search terms included were "anatomy," "anatomical," "variation," "variations," "variant," "variants," "variability," "variabilities," "difficult anatomy," "medical education," "anatomy education," "anatomical education," "anatomy learning," "simulation of variants" "difference," "different," "aberrant," "abnormal," "anomalous," "anomaly," "atypical," "malpractice," "surgical," "error," "surgical misdiagnosis," "clinical misdiagnosis," "surgical difficulty," "surgical difficulties," "clinical difficulty" and "clinical difficulties."

The search was conducted across multiple databases, including Education Research Complete, Educational Resource Information Centre, PubMed/MEDLINE, Excerpta Medica Database, and Science Direct. The search strategy was completed on June 16, 2023. Furthermore, open-access repositories such as Google Scholar, Open Grey, and ProQuest were systematically scrutinized to locate both published and unpublished materials germane to the focal inquiry of the review. To ensure an all-encompassing scope, a meticulous manual exploration was also conducted within the reference lists and citations of the studies encompassed in the analysis. This methodological strategy was employed with the intent of identifying any supplementary pertinent studies that could have eluded detection through the electronic search process.

Inclusion criteria

1. Original article on anatomy education dealt with perception, feedback, and knowledge acquisition
2. Participants in studies must be medical students or resident trainees
3. The study is required to specifically examine anatomical variations within the context of educational endeavors and their implications for the promotion of safe and effective clinical practices.

Exclusion criteria

1. Case Report
2. Commentary
3. Letter to Editor
4. Review Articles
5. Veterinarian Manuscript
6. Participants in the study: Nursing, physiotherapy, and other allied health professional students or trainees.

Study selection and data extraction

To ensure a methodically rigorous approach, the process of study selection and data extraction unfolded in the following manner: Initially, any duplicate studies identified during the preliminary search were eliminated to avert redundancy in data. Subsequently, one reviewer (SN) meticulously evaluated the titles and abstracts of all studies vis-à-vis the stipulated eligibility criteria. This procedural step aimed at identifying studies that potentially aligned with the inclusion criteria. The complete texts of these studies deemed to have potential eligibility were procured and subjected to independent scrutiny by two reviewers (AA and AP). This comprehensive assessment facilitated a thorough evaluation of each study's pertinence to the core research question and adherence to the defined eligibility benchmarks. In addition, scrutiny of the reference lists and citations of the included manuscripts was utilized to identify any supplementary studies that

might fulfill the eligibility prerequisites. These studies, thus identified as potentially eligible, were subsequently subjected to a detailed and independent evaluation by the same two reviewers (AA and AP) to ascertain their ultimate eligibility for incorporation into the review.

Following a comprehensive examination of the complete texts, the studies deemed suitable were chosen for integration into the review. In cases where disparities or differences emerged between the two reviewers, deliberations were undertaken to reach a consensus, and if necessary, a third reviewer (SN) was consulted for further resolution. A thorough screening was performed for the included studies to extract relevant data. This included information on study characteristics such as study design and type of publication as well as information on the study population and participants. In addition, data were extracted on the objectives of the study, the study methods used, the results obtained, and any limitations identified.

Quality appraisal

The methodological precisions of the studies included in the analysis were evaluated employing the Medical Education Research Study Quality Instrument (MERSQI).[8] This tool was specifically formulated to appraise the methodological precision of both full-text articles and conference abstracts within the realm of medical education. The MERSQI Scale encompasses six distinct facets: Study design, sample composition, data type, substantiation of validity pertaining to assessment tools' evaluations, data analysis, and outcomes. Each domain is allotted a maximum attainable score of 3. Among these, five domains carry a minimum score threshold of 1, while the sample composition domain possesses a minimum score of 0.5. Consequently, the cumulative score for each individual study spans a range from 4.5 to 18. A MERSQI score surpassing 12 is indicative of research characterized by high quality. Conversely, a score below 10 signifies a dearth of quality, whereas a range between 10 and 12 suggests a state of moderate quality.

Data synthesis

Content analysis and thematic analysis of texts on anatomical variations, surgical errors, and good clinical practice were collected from the above search strategy. Before starting the analysis, all the selected texts were read thoroughly several times to familiarize us with the content. Prenotes were made to capture first impressions and understand the overall context. The unit of analysis for this study was the paragraph level, treating each paragraph as a separate unit of coding and analysis with the help of KH Coder v3 (language processing tool or text mining tool).[9] To facilitate analysis, a coding framework based on predefined categories related to anatomical variation, surgical error, and good clinical practice was developed. These categories were identified through an extensive literature review and expert consultations. The data were coded manually and each paragraph was labeled according to the relevant categories in the coding framework. To increase the validity of the analysis, the intercoder reliability was determined. Two independent coders coded a subset of the data and compared their results to measure agreement. Any points of contention were resolved through thorough deliberation and the attainment of a collective consensus. Once coded, the data were analyzed to identify patterns and themes within each category. The focus was on identifying recurring ideas, concepts, and information related to anatomical variations, surgical errors, and good clinical practice. From the analysis, themes emerge as overarching concepts that connect multiple coded paragraphs. The themes were identified based on their relevance, frequency, and importance in the context of the research goals.

Results

Initial exploration of academic resources in online databases resulted in a collection of 275 titles and abstracts. These materials underwent initial abstracts, screening that led to the selection of 53 full-texts for the next step screening. A cumulative count of 13 studies were selected and incorporated into the analytical framework.[10-22] A graphical representation illustrating the trajectory of the search strategy and the subsequent process of study selection is visually depicted in Figure 1. The evaluation of study quality is documented in Table 1, as appraised through the utilization of the MERSQI. In order to present an all-encompassing and descriptive amalgamation of the acquired data, the outcomes of the incorporated studies have been succinctly summarized in narrative format. This methodological approach has been instrumental in facilitating a comprehensive exploration and deliberation of salient issues and findings emanating from the reviewed studies. The data extracted from the encompassed studies have been systematically compiled and concisely elaborated within [Table 1]. Predominantly, the majority of these studies were conducted within the United States (n = 5). The remaining eight were distributed across varying geographic locations: Australia (3), UK (2), Canada (1), Jordan (1), and India (1). Ten of the scrutinized studies were centered around medical students, while the remaining fraction pertained to faculty members. As for the study designs, a majority of ten studies assumed the form of cross-sectional investigations, while one study each encompassed a randomized controlled design, a nonrandomized controlled approach, and a prospective observational framework. This array of diverse study designs has effectively provided a multifaceted range of perspectives and insights into the subject matter at hand. Eighteen codes were collected from the content analysis and they were represented as word cloud according to frequencies of terms in Figure 2.

The process of thematic data analysis revealed the emergence of seven pivotal themes that underscore the

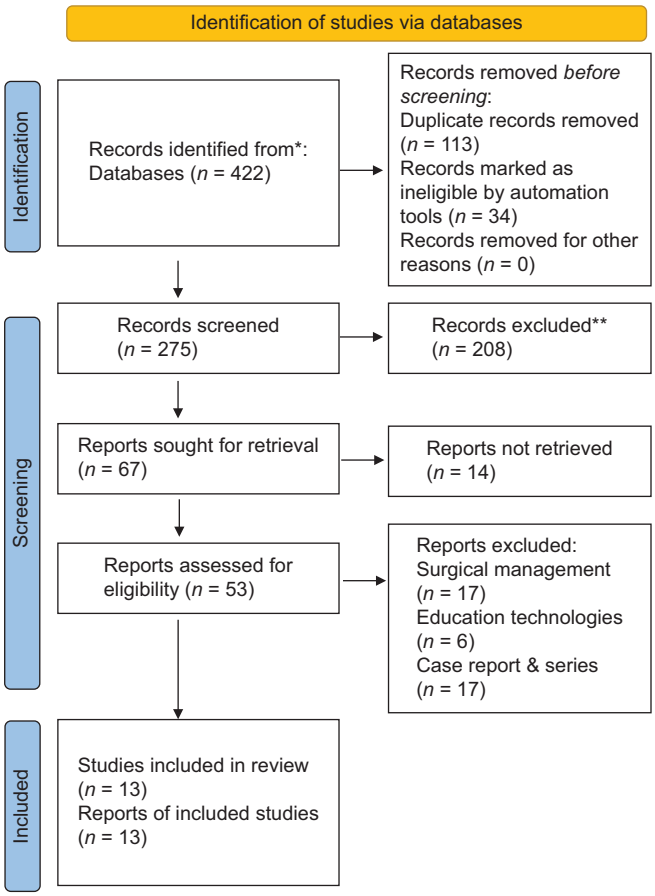

Figure 1: PRISMA flow-diagram for study selection

significance of anatomical variation within the realm of medical education as represented in Figure 3. These themes include the importance of incorporating anatomical variations, determining the optimal levels of introduction and period of contact, identifying significant anatomical variations, teaching methods, visualization techniques, assessment methods, and challenges in integrating anatomical variations into medical education. The last theme discusses potential solutions to overcome these obstacles and improve students' understanding of human anatomy.

Discussion

Through the above thematic analysis, seven key themes shed light on the vital role of anatomical variation in medical education. These themes encompass a comprehensive understanding of the subject, starting with the importance of anatomical variations to integration into the curriculum. These themes endeavor to explore potential solutions to overcome these obstacles and improve students' overall understanding of human anatomy, fostering a generation of skilled and knowledgeable medical professionals. The pros and cons of each theme are discussed as follows.

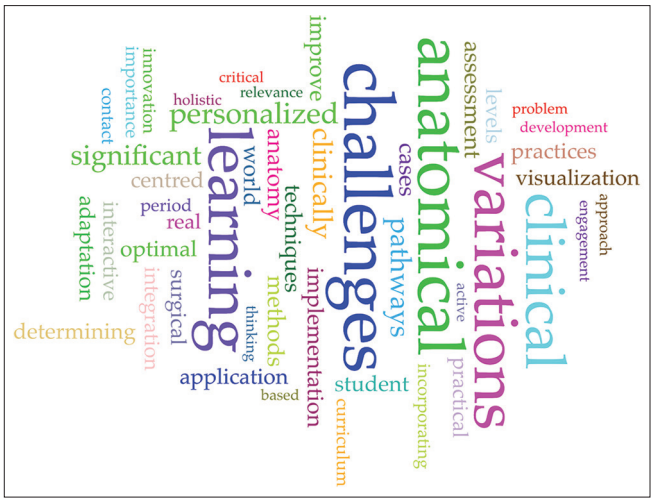

Figure 2: Word cloud representation of frequencies of codes marked in the manuscripts of included studies. Smaller size has lower frequencies

Crucial anatomical variations to incorporate within medical education

As already mentioned, there are differences in every anatomical structure. Therefore, it is impractical and of no clinical importance to seek instruction in all recognized anatomical variations. The impact of anatomical variations on various facets of clinical practice can be classified into a propensity to illness, manifestations, clinical assessments, and care for patients, encompassing surgery, for example, assessment of Calot's triangle and familiarity with biliary tract variations are crucial in laparoscopic cholecystectomy, as these differences can lead to complications and require open surgery conversion.[23] The dominance of the left coronary artery is associated with greater in-hospital mortality and myocardial reinfarction when compared to the right coronary artery.[24] The presence of variable appendix positions has the potential to lead to diagnostic errors and give rise to significant complications, such as perforation and sepsis.[25] Large body habitus may create low-quality clinical pictures, decreasing interpretation accuracy.[26] Chest radiographs show rare lung deformities like the azygos lobe, which has a prevalence of 0.30%.[27] The high division of the brachial artery may affect blood pressure measurement. Accurate diagnosis of arterial variations reduces limb problems and sepsis and so on due to vascular insufficiency.[28] This infers that the significance of an anatomical variation can be ascertained through the adverse outcomes that ensue from its misidentification or lack of identification within the clinical context. Goldberg and Royer emphasize the importance of understanding anatomical structures' relationships, particularly the femoral triangle and brachial plexus. Insufficient understanding can lead to complex surgical procedures, iatrogenic vascular injuries, and femoral nerve block complications.[14] Imparting instruction regarding the prevalence of anatomical variations in the brachial plexus, circulatory system, and various organ systems is of paramount importance due to

Table 1: Summarized result of included manuscript and study charcteristics

Author-year/design	Participant	Research question and method	Result	Quality score (MERSQI)
Al-Mnayyis *et al*., 2020[10] (Jordan): Cross-sectional study (full-text article)	227 physicians (173 interns, 28 radiology residents and 26 surgery residents) (response rate=59.9%)	Residents were tested on right azygos lobe identification. They received a lung anatomy figure and axial CT scan	No intern or surgical resident accurately recognized the anatomical variance in the picture and CT imaging. However, 57.1% of radiology residents correctly recognized the anatomical variance in the figure and CT picture	10
Buongiorno *et al*., 2020[11] (USA): Cross-sectional study	44 anatomy teaching faculty from allopathic medical schools (response rate=31.7%)	To examine how US allopathic medical schools incorporate anatomical variances into their curricula To demonstrate anatomy faculty views toward clinical training with anatomical variances	Medical students must recognize anatomic variability (mean score: 4.64±0.57), according to respondents Anatomical changes significantly enhanced clinical reasoning (mean score: 4.25±0.74) Important anatomical variations included all groups. Clinical training prioritized circulatory and organ system variances above neurological and MSK variations	9
Hong *et al*., 2018[12] (USA): Nonrandomized controlled study	125 medical students participated	Two classes were formed. The "no AR" group learned about ARSA using just text, photos, and a 3D SketchFab model. The AR group employed AR holograms and conventional resources. The "animation only" and "text only" groups studied ARSA embryology Pre- and posttest quizzes and a survey assessed resource effectiveness	To assess AR for anatomical learning. ARSA's embryological origins were shown in an AR model and animation. Both groups scored equally on the pretest quiz. Both group's posttest scores increased, but the "animation alone" group outperformed the "text alone" group (82.2% vs. 76.7%; *P*>0.05). "With AR" outscored "No AR" (83.2% vs. 76.3%, *P*>0.05). 90% of embryology students preferred animation over text. The 3D model helped students understand ARSA (4.4/5) Students assessed material's efficacy. Best to worst: AR (best) > animation >3D model > text (worst) (*P*=0.01)	12
Piromchai *et al*., 2017[13] (Australia): Randomized controlled study (full-text article)	11 otolaryngology residents	The study assessed the significance of exposing surgical residents to anatomical differences. Two groups were divided into SM and MM groups, and each underwent four training sessions. They performed cochlear implant procedures on temporal bones, with each group operating on two different models. The completed operations were evaluated using a global rating scale and task-based checklist	The MM group used the otological drill better on difficult bones, performed better in protecting facial nerves, perceiving the circular window niche, and producing less incus and facial nerve damage. They were more likely to reach the round window membrane	12
Goldberg and Royer, 2016[14] (USA): Cross-sectional study	29 anatomy teaching faculty from allopathic medical schools (response rate=24.4%)	A survey was conducted to assess the inclusion of anatomical variations in medical education and training. The survey included Likert Scale questions, forced-choice questions, Likert Scale questions, and forced-choice and open-ended questions to evaluate faculty perceptions, teaching methods, and demographics	Anatomical variances are crucial for understanding and addressing various health issues. Dissection is the primary method for introducing pupils to these variations, with relational variations being the most important. Femoral triangle arrangement and brachial plexus composition are the most relevant relationship changes. Only 52% of respondents had received official examinations of anatomical differences.	8.5

Contd...

Table 1: Contd...

Author-year/design	Participant	Research question and method	Result	Quality score (MERSQI)
			Medical school is considered the superior period for learning about variances compared to residency or clinical experience	
Raikos and Smith, 2015[15] (Australia): Cross-sectional study	31 physicians (response rate=25.4%)	A survey was conducted among physicians in Canada and Australia to examine anatomical variances in surgical and radiological training programs. The survey included 41 questions on general information, anatomy training, anatomic evaluation, training for anatomical variations, evaluation, and thoughts on anatomical differences	45.2% and 32.3% of respondents believe understanding anatomical differences is essential and extremely important in their specialization. Training curricula often examine common variations, but 85.7% are unclear about learning goals. Dissection classes are the best way to understand anatomical variances, while consultants, supervising doctors, and specialist literature are the most used sources. Over 75% of respondents believe trainees would benefit most from anatomical variety instruction in years 3 and 4. Arterial, venous, and organ system variations are taught most, while skeletal, muscular, and neurological variations are least common	9
Chapman *et al*. 2013[16] (United Kingdom): Cross-sectional study	170 students (response rate=70.8%)	To assess student opinions of instructional approaches and their capacity to meet learning goals	Dissection and prosections were substantially favored for recognizing anatomical changes (median score of 5) Lectures, software, and LA/RA scored a median 3 (P<0.05) for appreciating anatomical variances. With a median score of 2 (P<0.05), students rated models the worst resource for anatomical variations	9.5
Kerby *et al*., 2011[17] (United Kingdom): Cross-sectional study	302 students (response rate=52.1%)	Student opinions on instructional approaches for anatomy course goals were tested using six methods, evaluating their fit with course objectives and understanding anatomical/ biological variations	The students rated the instructional techniques in order to appreciate variances. Best to worst: Dissection, prosection and demonstration, LA/RA, technology, didactic training solely, models. Variations could not be taught well. Dissection, prosection, and LA/ RA were beneficial for recognizing variances, according to anatomists and students. The anatomists and students thought CAL and LA/RA were reasonable for appreciating variances. Students and anatomists agreed that models were bad for comprehending variances, and anatomists also disliked didactic learning	11
Brown *et al*., 2012[18] (USA): Prospective observational study	Three gross anatomy-integrated ultrasound didactics comprised Phase I. 1st-year medical students answered a questionnaire in Phase II	To evaluate medical student's impressions of ultrasound usage to teach gross anatomy alongside conventional techniques and their ability to recognize sonographic anatomy following concentrated didactic sessions. 96% (95% CI: 92%–99%) of 109 participants believed that ultrasound-based	Ultrasound-based instruction boosts invasive procedure confidence for 92% (95% CI: 87%–97%). 91% (95% CI: 85%–96%) said ultrasonography could be included to anatomy. Medical students correctly recognized neck ultrasonography vascular structures 98% (95% CI: 95%–100%) of the time. Interpreting visuals was 7.4 (95% CI:	13

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Table 1: Contd...

Author-year/design	Participant	Research question and method	Result	Quality score (MERSQI)
		instruction improved anatomy knowledge. Future methods	7.1–7.7) on a scale of 1–10. 94% (95% CI: 91%–99%) completed ultrasound and sonographic anatomy questions correctly	
McBride and Drake, 2018[19] (USA): Cross-sectional study	108 gross anatomy, 108 embryology, 105 microscopic, and 106 neuroanatomy course directors/ leaders	Course directors/discipline leaders at allopathic medical schools in the US were surveyed about how these changes are affecting and being implemented in gross anatomy, microscopic anatomy, neuroanatomy/neuroscience, and embryology courses. Course hours, student experiences in the classroom and laboratory, faculty engagement, peer teaching, student evaluation techniques, and best practices were discussed with research participants	A number of differences were discovered when comparing data from a comparable poll conducted in 2014: (1) Classroom hours in gross anatomy increased by 24% and by 29% in neuroanatomy/ neuroscience; (2) Laboratory hours in gross anatomy decreased by 16%, 33% in microscopic anatomy, and 38% in neuroanatomy/neuroscience; (4) The number of respondents reporting their discipline as part of a partially or fully integrated curriculum increased by>100% for all four disciplines	10
Kalthur *et al*., 2022[20] (India): Cross-sectional study	145 medical undergraduate during their 1st year (2018–2019)	To ask students on the dissection module's relevance in current teaching-learning Students who dissected anatomy were surveyed. Students identified three topics. Student's themes-related views were considered	Dissection lessons included pros, cons, and comparisons to other anatomy study materials. Dissection increases comprehension (91.8%) and gives a three-dimensional view of structures (92.4%), according to pupils. Dissection was time-consuming (57%), while prosection (64.6%) helped pupils learn faster. 86% of students opposed eliminating dissection from the curriculum. 74% of students said instructional tools should encourage dissection	9
Peeler *et al*., 2018[21]: Cross-sectional study (Canada)	108-1st year and 115-2nd year students were organized into two groups: A prosection group that consisted of medical students who were taught using primarily cadaveric prosection-based TLAs; and a dissection group that consisted of medical	Medical students were divided into two groups: A prosection group that used cadaveric prosection-based TLAs and a dissection group that did not. To retrospectively analyze how various teaching–learning activities affected student learning and MSK anatomy test performance Comparing preclerkship medical school pupils. One group did 15 h of dissection-based lab instruction, whereas the other did 15 h of prosection. The curriculum were identical else. A standardized survey compared six TLAs on eight learning goals to assess student attitudes. Comparing exam results	Overall, both groups had relatively high response rates (dissection group=34%; prosection group=50%). The data showed a significant difference (P=0.05) in response rates across groups (a much higher percentage of pupils in the prosection group replied)	10
Jeyakumar *et al*., 2020[22] (Australia): Cross-sectional study	174 medical students	After completing cadaveric dissections, 174 medical students completed a paper-based questionnaire. Data were examined quantitatively as well as qualitatively. To investigate	Students were convinced that cadaver-based learning is vital in anatomy education and that current teaching methods just supplement it. Furthermore, the majority of students indicated that dissection offered an	11

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Table 1: Contd...

Author-year/design	Participant	Research question and method	Result	Quality score (MERSQI)
		student impressions of the usefulness of a dissection program for learning MSK anatomy, as well as potential changes for suitable dissection inclusion in the current medical curriculum	extra, immersive learning experience that aided in active learning and the development of manual abilities Cadaveric dissection is an important part of medical anatomy teaching. However, time constraints and a greater emphasis on therapeutic importance need careful adjustments of established dissection techniques	

MSK: Musculoskeletal, CI: Confidence interval, CAL: Computer-assisted learning, ARSA: Aberrant right subclavian artery, AR: Augmented reality, 3D: Three-dimensional, CT: Computerized tomography, MERSQI: Medical education research study quality instrument, LA: Living anatomy, RA: Radiolgoical anatomy, TLAs:Teaching and learning activities, SM: Single model group, MM: Multiple model group

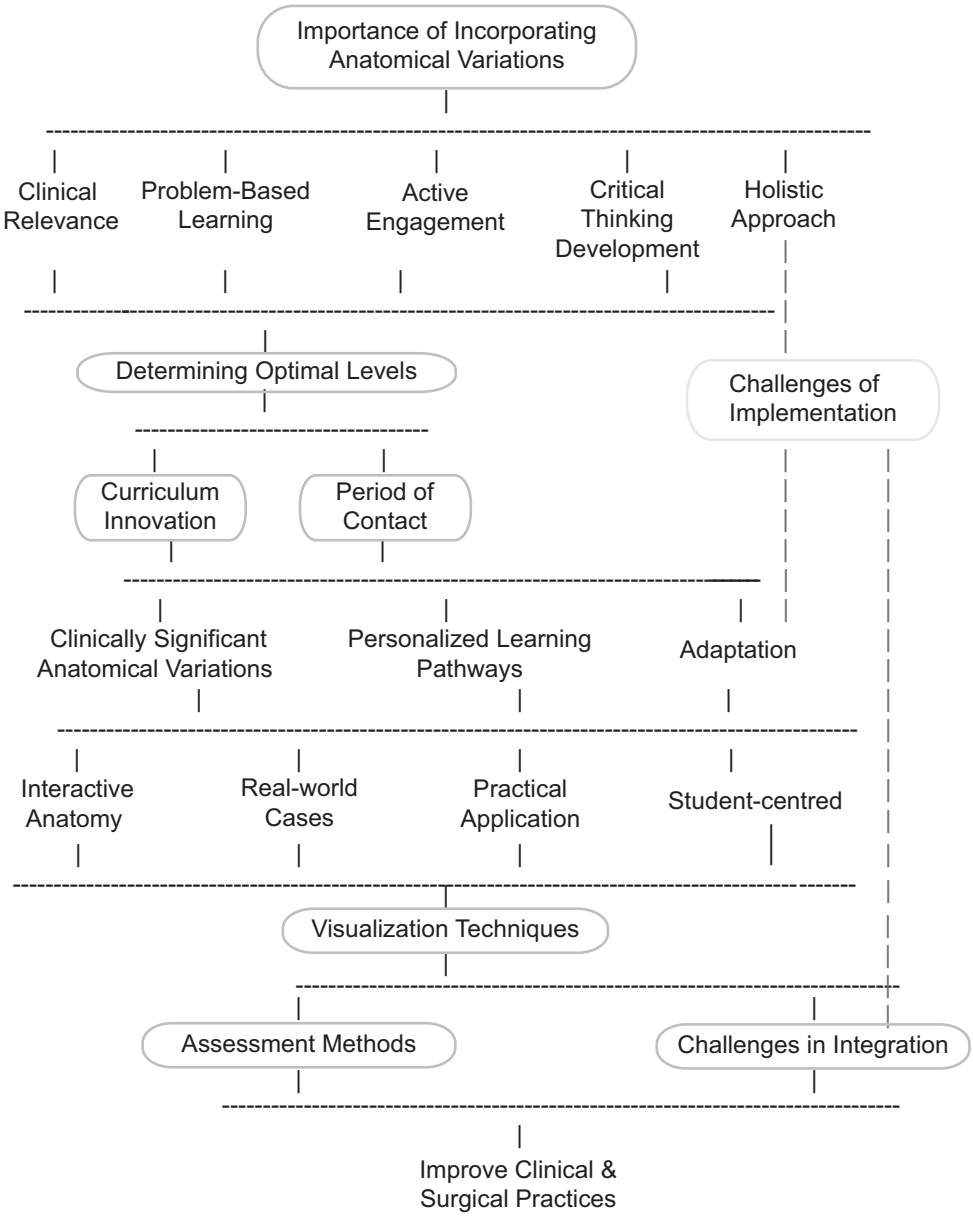

Figure 3: Map of thematic analysis developed from included studies. Themes are shaded in green color box and codes are unshaded. Limitations shaded in yellow color box

the elevated frequency of encountering such variations. Furthermore, investigations conducted by Raikos and Smith unveiled that variations within the circulatory and organ systems constituted the predominant focus within postgraduate training programs in surgery and radiology.[15] Thus, it is crucial to prioritize the inclusion of anatomical variations that are both highly prevalent and clinically significant in medical education. In addition to vascular considerations, pancreatoduodenectomies may present challenges due to other abnormalities in anatomical structure.[15] Pancreatic anastomoses may be influenced by variations in the morphology of the main pancreatic duct with the spleen being a significant organ with anatomical variations, surgeons must be aware of accessory spleen presence in 15% of the population.[1] Surgeons also face challenges with the recurrent laryngeal nerve, including additional branches, distorted branches, and nonrecurrent branches.[1] Proper attention, intraoperative detection, and familiarity with thyroid gland anatomical deviations can reduce iatrogenic injuries during surgical procedures.

Determining the optimal levels of introduction and period of contact

The current study delved into the viewpoints encompassing the most suitable timeframe for integrating anatomical variation within the medical education curriculum. Notably, one of these investigations accentuated that the opportune juncture for introducing these concepts aligns with the preclinical years.[11] Conversely, a study executed by investigators demonstrated that the introduction of anatomical variation during the intermediate phase of postgraduate medical training yielded more pronounced advantages.[15] Royer reiterated the challenge faced by medical educators in discerning the most appropriate timing for the incorporation of anatomical variations.[5] During the early clinical phase, medical students are given the opportunity to observe and participate in neonatal health care, obstetrics, and radiodiagnosis; through these encounters, students are subjected to a wide range of anatomical variations and associated symptomatology that occur in the above situations. While the outcomes exhibited variability within the context of this review, a predominant inclination within the literature favored the early integration of anatomical variations into educational curricula, with a specific emphasis on the preclinical phase of the medical curriculum.[11,14] The categorization of medical education into distinct undergraduate and postgraduate programs could potentially exert an influence on this perspective. Due to the specific nature of postgraduate education programs, the standardization of the curriculum is becoming increasingly difficult, particularly due to the tailored educational approach that trainees receive according to their particular areas of expertise. The adoption of a standardized curriculum in medical schools, as observed in the United States, is making the incorporation of anatomical variations an integral part of medical education.[29] The preclinical years will generally be favored due to the traditional incorporation of anatomy education, typically during the clinical years.[30] In addition, including anatomical variations during the time students acquire knowledge of pathophysiology would improve the process of assimilation and understanding of its clinical significance.[31]

Different strategies for teaching anatomical variation

The most efficient method for disseminating information about anatomical variability is teaching cadaver specimens, particularly by autopsy. This method is supported by reviews, as clinically meaningful changes are visible in the anatomy laboratory, especially during dissections.[32] Eizenberg and Singh *et al.* argued that actual dissection is preferable to virtual dissection for confirming theoretically taught anatomical variants, as it is faster and more resource-intensive. However, they acknowledge that they have frequently encountered more than 30 anomalies in a fully dissected cadaver.[30,33] Hence, dissection has continued to be the focal point of anatomical variation instruction, which is to be expected, but teaching strategies need to change to improve learning.[30] Zucconi *et al*. have updated standard dissection courses to enhance students' understanding of anatomical variation. They advocate for a systematic investigation into the realms of anatomy, embryology, and the clinical manifestations of variant anatomical structures identified postdissection. This active learning methodology aids students in retaining their comprehension. Moreover, a strategy that involves rotating students across different cadavers within a specific time frame ensures their exposure to multiple anatomical specimens by the conclusion of the module. Such an approach fosters an enhanced recognition of anatomical diversity and individual patient distinctions, facilitating a transition from a limited perspective to a more robust cognitive representation of diverse anatomical specimens.[34]

Imparting instruction on anatomical variability necessitates the utilization of prosections or preprepared cadaveric specimens, as these resources contribute to the preservation of variability and mandate the involvement of specialized experts. Current atlas studies often ignore these differences, and students studying about prosection may face greater variability. Cadaver specimens provide a wide range of anatomical changes but require time, faculty expertise, and facility resources.[35]

Virtual reality and simulation transforming conceptualization of anatomical variation

Virtual reality (VR) and simulation have brought about a ground breaking transformation in the conceptualization of anatomical variation.[36] By immersing learners in realistic virtual environments and providing interactive simulations, these technologies have revolutionized the way we understand and visualize anatomical complexities.

Technology-enhanced learning (TEL) has gained popularity due to the evolution of medical imaging techniques and qualities of CT, magnetic resonance imaging and ultrasound information.[37] The role of static images and diagrams is diminished; now, students can explore dynamic three-dimensional (3D) models of anatomical structures, gaining a deeper comprehension of individual variations and the interplay of different body systems. This immersive approach enhances engagement, retention, and comprehension, as learners can manipulate virtual objects, dissect virtual specimens, and witness anatomical variations first-hand. As a result, VR and simulation have emerged as indispensable tools in modern medical and anatomical education, fostering a deeper appreciation and understanding of the human body's intricacies.[38]

Augmented reality (AR), a new technique that uses 3D modeling, integrates virtual reality components to enhance the user's perception of reality. AR is particularly helpful when viewing complex anatomy, such as vascular changes. While TEL may eliminate some disadvantages of cadaver dissection, it is inconclusive that it is superior to cadaver dissection for imparting anatomical diversity.[38] The research highlights the use of different strategies and tools to teach anatomical variation. Plastic models, often created with flawless anatomy, are considered the worst method for understanding anatomical diversity. These models maintain a superficial orientation of the body without considering anatomical heterogeneity, which can be deceptive and potentially detrimental to therapeutic treatment. Plastinated specimens are a better option as they minimize deterioration caused by improper handling and prolonged use while preserving inherent anatomical diversity; also more widely available and can be used outside of the dissection hall.[36,38] The efficacy and engagement of lecture-based instruction have been subject to criticism, often characterized as lacking in productivity and failing to captivate student interest. However, lectures are more likely to be poorly graded due to a lack of depiction or exploration of anatomical changes. The claim that lectures are unsuccessful in teaching anatomical diversity should be refuted since it is the responsibility of the lecturer to include or remove material from lectures.[4]

Evaluating understanding of anatomical variation

Similar to education, assessments in medical schools do not adequately account for anatomical variabilities.[39] The investigation conducted by Goldberg and Royer revealed that approximately 50% of the surveyed anatomy institutions implemented structured assessments as a means to evaluate anatomical variabilities among their medical student cohorts.[14] Conversely, a postgraduate education study conducted by researchers indicated that program directors commonly evaluated their trainees by assessing their competence in identifying anatomical variations. This observation is in line with expectations, as assessments typically align with the constructive congruence of teaching and learning objectives. The assessment protocol plays a crucial role in facilitating and shaping the learning experience. It is imperative to prioritize the assessment of various anatomical variations, particularly those that have clear clinical significance, in preclinical assessments and regulatory reviews.[40]

This review comprehensively examines diverse methodologies available for effectively evaluating the comprehension of anatomical variations within the frameworks of both undergraduate and postgraduate medical education. The assessment modalities encompassed within this category encompass traditional paper-based evaluations, computer-based assessments, and surgical simulations.[13] In their study, Asghar *et al*. identified that the utilization of 3D models for depicting anatomical variations holds substantial advantages within the realm of research. These models effectively facilitate the assessment of both a person's understanding of anatomical variations and their ability to understand spatial relationships. This is particularly beneficial for institutions that face cadaver resource limitations, making the implementation of alternative assessment methods, such as traditional spotter testing, impractical.[38]

Limiting factors for the adoption of anatomical variation within medical curricula

Buongiorno *et al*. emphasized the challenges associated with integrating anatomical variations into the medical school curriculum; however, they did not offer a specific rationale to substantiate this assertion.[11] Nevertheless, three potential obstacles are identified in this review.

1. The debatable nature of the importance of anatomical variations in patient care
2. The students and trainees could be overwhelmed by presenting excessive amounts of information
3. A deterioration in the accessibility of anatomical resources.

Incorporating anatomical variations into medical education remains challenging unless their importance is widely recognized. Raikos and Smith argued that a significant proportion of medical teachers were skeptical regarding the advantages of teaching anatomical variations; this underscores the ongoing debate within disciplines that prioritize anatomy.[15] Numerous educators hold the perspective that anatomical variations, while intriguing, pertain to a smaller demographic subset and are not fundamentally indispensable for acquisition. Bergman's initial work on anatomical variations was initially regarded as possessing restricted utility, intended primarily for discerning medical residents. However, medical education must furnish students and trainees with the requisite competencies to proficiently address diverse clinical scenarios. This is due to the fact that anatomical disparities might appear inconsequential to one clinician but carry paramount significance for another.[41]

Within the realm of medical disciplines, particularly anatomy, the theory of cognitive load is frequently employed to enhance the efficacy of students' cognitive endeavors. The capacity of working memory is influenced by cognitive load, and adeptly managing this load is integral to the process of learning. Examining anatomical variations in the absence of a clinical framework might be construed as abstract and lacking in engagement. Medical educators posit that the integration of anatomical variation theory has the potential to heighten cognitive load, compelling students to navigate uncharted information and comprehend abstract concepts.[38] Cheung *et al*. observed that the study of anatomy posed challenges due to its extensive content and abstract characteristics, rendering the assimilation of abstract information a formidable task.[42]

Anatomy teaching methods are a topic of debate in medical education. While some argue that there is no empirical evidence to support this claim, others express concern about the declining quality of anatomy education, which poses risks to clinical practice. The decrease in the use of dissection in medical schools is mainly due to the limited accessibility of cadavers. The lack of cadavers and lack of alternative resources make it difficult for medical instructors to introduce students and trainees to the anatomical variations.[38]

Faculty members encounter the formidable task of instructing anatomy within a constrained timeframe, necessitated by the inclusion of other components within the medical curriculum. In the context of the United Kingdom, the average duration of anatomy classes is approximately 149 h, thereby requiring an emphasis on the most clinically pertinent anatomical aspects. This approach subsequently leads to the necessity of content reduction to maximize time efficiency, resulting in the omission of anatomical variations from the educational agenda. Conversely, the feasibility of implementing such content is more viable in India, where the instruction of anatomy spans a significantly extensive duration of over 650 h.[38,43]

Study limitations

The diverse nature of the studies deemed eligible for inclusion in this review posed challenges in conducting meta-analysis and establishing credibility. The incorporation of studies with lower methodological quality and uneven geographical representation raised apprehensions regarding the applicability of findings to broader contexts. The employment of survey methods also brought attention to the potential for response bias. While the addition of gray literature extended the review's scope, the absence of consistent scientific rigor and standardized access to these materials introduces a potential impact on the robustness of the results' validity.

Conclusion

The primary aim of medical education lies in cultivating highly skilled physicians able to deliver competent and secure patient care, a goal that merits profound consideration within the curriculum. The current systematic review highlights the significance of anatomical variations within the landscape of medical tutoring. Nonetheless, there exists evidence indicating deficiencies among students and trainees in effectively grasping the notions of anatomical variability and their practical implications in clinical contexts. This inadequacy has the potential to lead to misdiagnoses of ailments and lapses in health-care practices. Stakeholders actively engaged in medical education bear the responsibility of ensuring that students and trainees acquire a robust understanding of anatomical variations. The integration of anatomical variations into the medical core curriculum stands to dispel misperceptions surrounding the normative human anatomy while furnishing indispensable insights crucial for comprehending patient distinctiveness. Moreover, it possesses the potential to kindle the enthusiasm and inquisitiveness of physicians, transforming encounters with anatomical variations into opportunities for valuable learning rather than mere extraneous details to be memorized.

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Conflicts of interest

There are no conflicts of interest.

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Case Report

Bilateral Psoas Minor: A Case Report with Clinical, Embryological, and Evolutionary Insights

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Abstract

A 57-year-old female cadaver donated for research contained an accidental bilateral presence of the psoas minor (PMn) muscle. Bilateral PMn is a rare finding but it may be associated with other anatomical variations or abnormalities in the abdomen or pelvis. In some cases, the muscle may be involved in the development of certain medical conditions or may compress nearby structures, leading to symptoms such as pain or discomfort. Overall, bilateral PMn is a relatively uncommon anatomical variation that may be of interest to anatomists or medical professionals. A thorough understanding of this muscle is essential, particularly when making a clinical diagnosis and carrying out procedures in the iliac area. In this case report, we tried to discuss the clinical, embryological, and evolutionary significance of PMn muscle.

Keywords: *Embryological, evolutionary, posterior abdominal wall, psoas minor, psoas minor syndrome*

Introduction

The anatomy of the posterior abdominal wall is intricate. The lumbar vertebrae, pelvic girdle, iliacus, quadratus lumborum, their corresponding fascia, and the three-psoas group of muscles – psoas major (PMj), minor, and tertius – all contribute to its formation. PMj is a long fusiform muscle found in almost every human being. It originates from the anterior surfaces of transverse processes of the L1–L4 vertebrae, the sides of the last thoracic and upper four lumbar intervertebral discs, and the tendinous arches that connect these margins and is innervated by the ventral rami of L2, 3, and 4.[1]

Psoas minor (PMn) is the best illustration of a vestigial muscle and has the highest likelihood of congenitally being absent (56%).[2] Although some of its functions include stabilizing the hip joint and bending the lumber spine, these functions are quite restricted, and the lack of muscle has no effect whatsoever on them. The muscle could be present unilaterally or bilaterally. When present, it often usually emerges with a short, fleshy belly from the bodies of the first lumbar and twelfth thoracic vertebrae and the disc between them. It terminates in a long, flat tendon that enters the iliac fascia, iliopubic eminence, and pecten pubis. The first lumbar spinal nerve typically innervates the PMn, which is located on the ventral side of the PMj muscle.[2] Due to its rarity in humans, the psoas tertius is the psoas group of muscles that has received the least amount of attention. The muscle's origins are quite varied, and there have been multiple instances of highly varying morphology, some with a clinical manifestation due to the muscle penetrating and splitting the femoral nerve.[3]

There is a dearth of clear information in the literature about human PMn variants. The muscle has been observed to have different sites of origin and insertion, as well as sexual and racial dimorphisms, when present. It is essential to do an extensive study into this little, insignificant, yet clinically crucial muscle. For the radiological and clinical interpretations, a thorough investigation of the changes in the PMn is essential. Before performing surgery in the designated location, the surgeons must have a clear understanding of the potential irregularities to better grasp the therapeutic uses of these variations.[4]

Case Report

During undergraduate and postgraduate practical sessions on the posterior abdominal

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wall of a donated 57-year-old female cadaver, an incidental bilateral presence of PMn muscle was observed. Steps for dissection were followed as per Cunningham's Manual.[5] After the removal of all the organs of the abdominal cavity, the posterior abdominal wall muscles were dissected. Incidentally, we noted the presence of a thin tendon of PMn on the anterior surface of the PMj muscle bilaterally. PMn was then cleaned properly from its origin till insertion on both sides. Photographs were taken for both sides. Proximal one-third of the muscle was found fleshy and distal two-thirds was tendinous. The origin of PMn on both sides was from the side of the bodies of the T12 and L1 vertebrae lying on the PMj muscle. The muscle fibers were found running downward, forward, and medially crossing the PMj muscle obliquely from the lateral to the medial side to be inserted on the iliopubic eminence in the form of a flattened tendon [Figure 1]. The length and width of the fleshy and tendinous part were measured with the measuring tape bilaterally. Bilaterally, the length of the muscle was 20.5 cm. The maximum width of the muscle belly on the left side was 1.7 cm [Figures 1 and 2] and on the right side was 2.1 cm [Figures 3 and 4]. The schematic representation of the cadaveric findings is given in Figure 5.

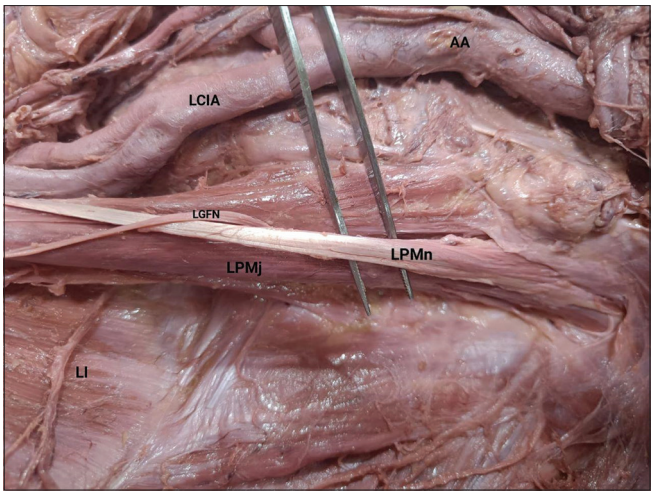

Figure 1: The origin of the left psoas minor with the left psoas major, LPMn: Left psoas minor, LPMj: Left psoas major, AA: Abdominal aorta, LCIA: Left common iliac artery, LI: Left iliacus, LGFN: Left genitofemoral nerve

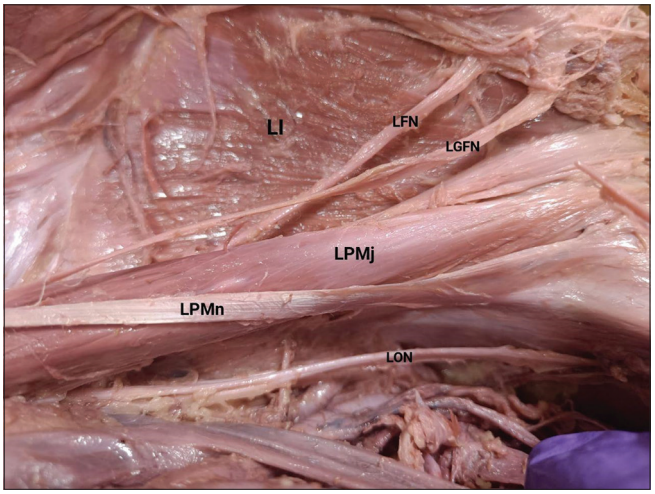

Figure 2: The insertion of the left psoas minor lateral to the left psoas major. LPMn: Left psoas minor, LPMj: Left psoas major, FN: Femoral nerve, LGFN: Left genitofemoral nerve, LI: Left iliacus, LON: Left obturator nerve

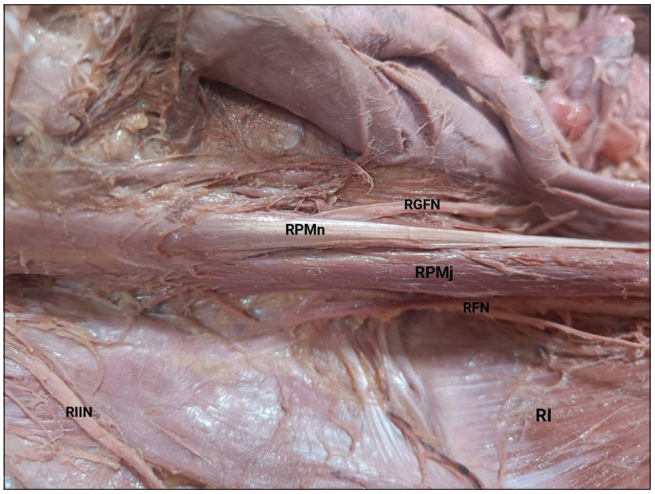

Figure 3: The origin of the right psoas minor. RPMn: Right psoas minor, RGFN: Right genitofemoral nerve, RPMj: Right psoas major, RFN: Right femoral nerve, RI: Right iliacus, RIIN: Right ilioinguinal nerve

Discussion

One of the five muscles most frequently lost to evolution is the PMn, along with the plantaris, palmaris longus, peroneus tertius, and pyramidalis.[6] The muscle has been observed to have different sites of origin and insertion, different dimensions, as well as sexual and racial dimorphisms, when present. The most commonly reported site of the origin of PMn in the literature is from the side of the bodies of the T12 and L1 vertebrae and the intervening intervertebral disc, which is consistent with our findings in the present case report. Previous studies have reported the unusual origin of PMn from only L1 to L2,[7] from the sub-diaphragmatic fascia and medial arcuate ligament, and the crus of the diaphragm.[8] Protas *et al*. reported an unusual origin of double-headed PMn with a lateral head arising from the body of the L1 vertebra and the medial head from the L4 vertebra.[9] The insertion of PMn is not very certain. In the present case, the tendon of PMn was getting inserted into the iliopubic eminence. Guerra *et al*. reported variation in the insertions of PMn, the tendon getting inserted into the pectineal line of the femur, neck of the femur, lesser trochanter with the iliopsoas, the arched line, the iliac fascia, the inguinal ligament, or the pectineal ligament.[10]

In the present study, the length of the muscle is 20.5 cm and the maximum width of the muscle belly on the right side is 2.1 cm and on the left side is 1.7 cm. In the study conducted by Joshi *et al*., 30% of the Indian population had the PMn, which had a mean length of 23.75 cm and a mean width of 1.32 cm.[11] Another Indian study reported the incidence of PMn in 4.5% of the cases with

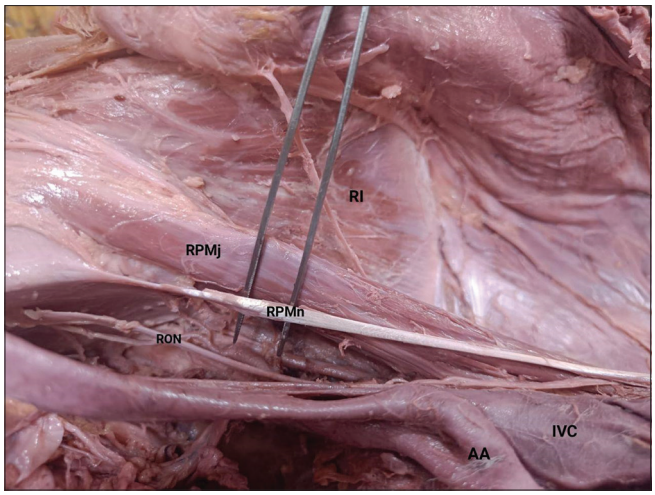

Figure 4: The insertion of the right psoas minor. RPMn: Right psoas minor, RPMj: Right psoas major, RON: Right obturator nerve, IVC: Inferior vena cava, AA: Abdominal aorta, RI: Right iliacus

the average length of the muscle being 19.66 cm and the average width being 1.73 cm.[12] According to Farias *et al*., 59% of the population in Brazil has the muscle, which has a mean length of 23.93 cm and a mean width of 1.71 cm.[13]

Embryological basis

Clarkson and Rainy described muscle fibers from the tendon of PMn merging with the PMj and fascia iliaca.[6] This suggests the incomplete separation of PMn and PMj, during embryogenesis. In the early stages of embryonic development, the PMn muscle begins as a separate muscle mass from the larger PMj muscle. As development proceeds, the PMn muscle gradually fuses with the PMj muscle, becoming functionally integrated with it.[14]

Evolutionary basis

The evolutionary basis of the PMn muscle is not entirely clear. It is believed that this muscle may have had a more significant role in the movement and stabilization of the hip joint in our evolutionary ancestors, who had a different anatomy and way of life than modern humans. In humans, the PMn muscle is considered a vestigial muscle, which means that it has lost much of its original function and importance over time. Vestigial structures are remnants of ancestral traits that have lost their original function due to evolutionary changes in the organism's anatomy or behavior. In other mammals such as some primates and carnivores, the PMn muscle is more prominent and has a more significant role in the movement and stability of the hip joint. This suggests that the PMn muscle may have been more important in the evolutionary past of our mammalian ancestors. In humans, PMn plays a minor role in lumbar spine flexion and its absence does not show any reduction of biomechanical or dynamic function, and its significance has likely decreased over time as our anatomy and way of life have evolved.[15]

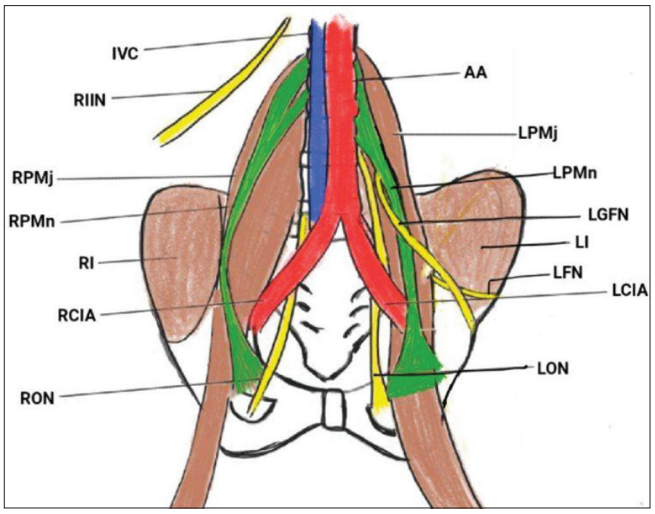

Figure 5: Schematic diagram of the cadaveric findings depicted in Figures 1-4. The inferior vena cava and abdominal aorta bifurcating into the left common iliac artery and right common iliac artery; the left psoas minor showing relations with the left iliacus, left psoas major, left obturator nerve, left femoral nerve, and left genitofemoral nerve; the right psoas minor showing relations with the right iliacus, right psoas major, right obturator nerve, and right ilioinguinal nerve. IVC: Inferior vena cava, AA: Abdominal aorta, LCIA: Left common iliac artery, RCIA: Right common iliac artery, LPMn: Left psoas minor, LI: Left iliacus, LPMj: Left psoas major, LON: Left obturator nerve, LFN: Left femoral nerve, LGFN: Left genitofemoral nerve, LPMn: Right psoas minor, RI: Right iliacus, RPMj: Right psoas major, RON: Right obturator nerve, RIIN: Right ilioinguinal nerve

Clinical implications

PMn muscle if present and strained can be a cause of PMn syndrome. PMn syndrome manifests as iliac fossa pain due to increased PMn tone. Exercises, especially leaping, will be challenging for those with PMn syndrome. Pain is aggravated by palpation of this taut tendon in lean individuals. Here, it may be mistaken for appendicitis or diverticulitis. If variations are the reason or if some variants make patients more likely to get PMn syndrome, has to be further studied.[9] The muscle may be susceptible to overstretching if it inserts low in the femur. In such cases, hip joint flexion may be reduced by 50% as a result of muscular strain. The patient can complain of persistent back discomfort, iliac fossa pain, or trouble standing up straight.[16] PMn muscle strain can occur when playing sports like football or golf with feet off the ground. This can cause inguinal discomfort that radiates to the abdominal wall and testicles, making it difficult to run or leap.[17]

Conclusion

While the PMn muscle has lost much of its original function and importance over time, it continues to be an interesting anatomical structure with developmental and evolutionary significance. Although PMn is inconstant, radiologists, physiotherapists, and orthopedic surgeons cannot ignore its clinical significance. A thorough understanding of this muscle is essential, particularly when making a clinical diagnosis and carrying out procedures in the iliac area.

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Conflicts of interest

There are no conflicts of interest.

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Case Report

An Unusual Presentation of Heterotaxy Syndrome

Abstract

Heterotaxy is a pattern of anatomical organization of the thoracoabdominal organs in a manner, which is not the usual or normal arrangement. It is classically subdivided into the subsets of asplenia and polysplenia syndrome. Here, we present our findings in a female cadaver which do not conform to the usual subset of asplenia or polysplenia, and in fact, showed hyposplenia with a subhepatic cecum and bilateral bilobed lungs. Polysplenia has traditionally been thought to be associated with anomalies of intestinal rotation. The incidence is not known, but they are collectively termed malrotation and include nonrotation, incomplete, or the rare reversed rotation. Asplenia is also documented with a high degree of abdominal heterotaxy. This particular case does not conform to the traditional classification of asplenia or polysplenia. Features suggestive of polysplenia, in this case, are bilateral bilobed lungs and situs ambiguous. In concordance with asplenia, it has a spleen of reduced size and a large liver with extra lobation, which shows that it does not confine to a single subset. It is suggested that a separate entity of hyposplenia may also be considered, that warrants further research.

Keywords: *Abdomen, heterotaxy syndrome, isomerism, situs inversus*

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Introduction

Heteros means other than and taxis means arrangement.[1] Any arrangement of organs along the left–right body axis that differs from complete situs solitus or complete situs inversus is included in this category.[2] In situs ambiguous, the thoracic and abdominal organs are positioned in such a way with respect to each other as to be not clearly lateralized and thus have neither the usual "normal" or mirror-imaged arrangement. They are usually classified into two major syndromes: polysplenia and asplenia.[3] Polysplenia is typically seen in females with duplication of left-sided structures with bilateral bilobed lungs and multiple spleens.[4] Asplenia is associated with bilateral trilobed lungs with a short bronchus and the absence of spleen. There is also more association with severe congenital heart disease as compared to polysplenia.[5]

Case Report

During routine dissection for undergraduate teaching purposes in an elderly female cadaver (no evidence of any external injury or incision), it was observed that the cecum was placed in the subhepatic region with a very small ascending colon (approximately length 1.7 cm). It was ampullary in shape with the vermiform appendix in retrocecal position and the right iliac fossa was empty [Figures 1 and 2]. The spleen was very small in size (6 cm × 2 cm × 2 cm) and triangular in shape with a notched superior border [Figure 3]. The capsule of the spleen was intact and it was positioned normally with the tail of the pancreas present at the hilum. Further, exploration of the abdomen failed to demonstrate the presence of any accessory splenic tissue. Lungs were found to be bilaterally bilobed [Figure 4] but extensive exploration of the heart failed to reveal any structural abnormality. The left side of the liver showed extra lobes which were completely septate on the inferior surface [Figures 5 and 6]. The anterior surface of the left lobe showed an accessory fissure.

Discussion

The failure to establish a normal left-to-right asymmetry results in heterotaxy. It manifests as abnormal symmetry, malposition of thoracoabdominal organs and vessels, and complex congenital heart disease, and the spleen is almost always affected. There is a syndromic clustering of malformation corresponding to the

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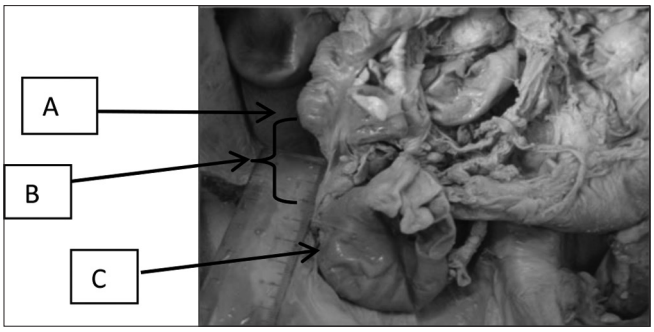

Figure 1: Subhepatic caecum with a negligible ascending colon. (A-Visceral surface of liver, B-Ascending colon, C-subhepatic caecum)

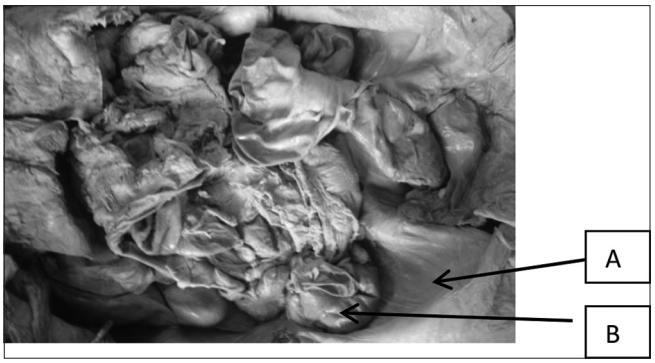

Figure 2: Subhepatic caecum with empty right iliac fossa. (A-Empty right iliac fossa, B-subhepatic caecum)

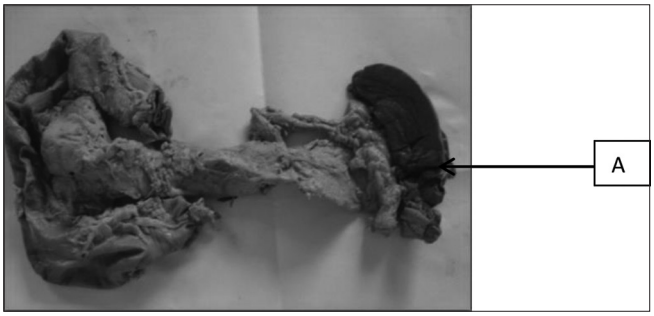

Figure 3: Small sized spleen. (A-spleen measuring 6*2*2 cm)

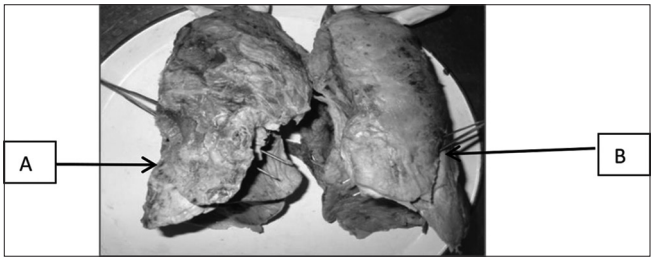

Figure 4: Bilateral bilobed lungs. (A,B- only oblique fissure in both left and right lung respectively)

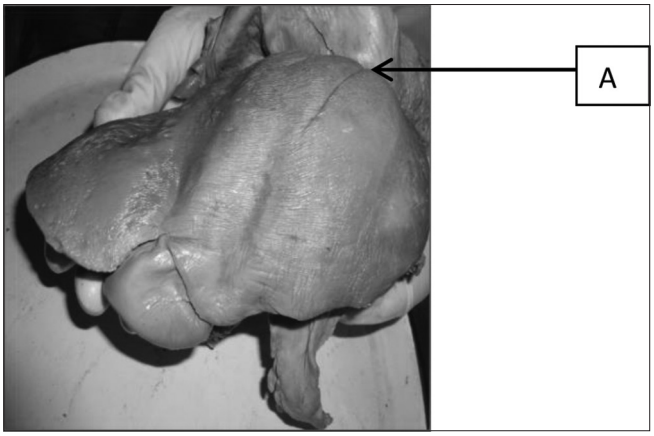

Figure 5: Large left lobe with accessory fissure. (A- accessory fissure on anterior surface of left lobe of liver)

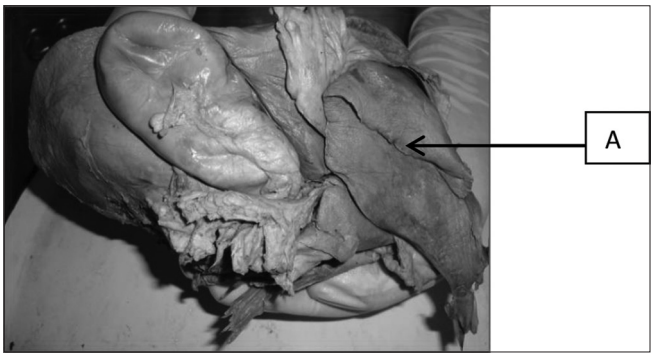

Figure 6: Left lobe of liver showing accessory lobation. (A- accessory lobation on inferior surface of left liver lobe)

type of splenic abnormality present. Polysplenia has been described as bilateral left-sidedness (left isomerism) because of duplication of structures normally found on the left side of the body only, with the absence of normal right-sided structures. The liver is abnormally symmetrical. There is a high frequency of bilateral bilobed lungs.[6,7] It is associated with malrotation or nonrotation of the gut, with the small bowel lying entirely on the right of the spine and the colon on the left. Asplenia is bilateral right-sidedness, because of the bilateral presence of organs and structures normally found on the right side with the absence of those present on the left. There is also high degree of abdominal heterotaxy indicating retention of the undifferentiated early embryonic state. The first suggestion that asplenia constitutes a clinical syndrome was made by Polhemus and Sehafer and the cause was thought to be an unknown teratogenic insult between the 31st and 40th day of gestation. The genetic pathway responsible for left–right asymmetry in animal models has been studied and recent studies have identified several gene mutations in patients with heterotaxy syndromes including CXCL2, SHROOM3, and others.[8] A study by Hutchins *et al*. suggests that the malformations in asplenia and polysplenia can be explained by minor alterations in the sequence of development of embryonic body curvature relative to the time of organ maturation.[9] A study by Rose *et al*. documented that 27 out of 28 cases of asplenia had symmetrically trilobed lungs, 12 had visceral heterotaxy, abdominal situs solitus was seen in 5 cases, situs inversus in 4, and partial situs inversus in 6 of the cases.[10] This

case in particular does not conform to the traditional classification of polysplenia and asplenia. Conforming to the usual features of polysplenia, it showed bilateral bilobed lungs and undescended cecum, with a very small ascending colon and no notable cardiac defect. As shown in asplenia, it showed a large and bilaterally symmetrical liver with extra lobation and small-sized spleen. Our case shows a single left-sided spleen but small in size as compared to average dimensions (9–14 L,6–8 W, 3–5 cm B). The presence of unusual lobes or fissures may lead to wrong radiographic diagnosis.[11,12] The accessory lobes of the liver may get herniated into the thorax through the diaphragm and cause serious complications.[13] A reevaluation of the spectrum of anomalies seen with heterotaxy is important because the altered anatomy may result in confusing imaging findings when seen in relation to acquired diseases.

Conclusion

A review of the literature indicates that a predictable pattern of malformations exists in cases with either absent spleen or polysplenia, which would permit one to regard these conditions from a clinical standpoint as separate clinical syndromes. In contrast, with our case, we would like to highlight the fact that the variations are in a broad spectrum and should also include insight into a category with small-sized spleen apart from asplenia and polysplenia.

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Conflicts of interest

There are no conflicts of interest.

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Case Report

Bilateral Olecranon Spur: A Rare Anatomical Case Report

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Abstract

Olecranon spurs are enthesophytes, observed in the posterior part of the proximal olecranon surface. They can be symptomatic in isolation but are frequently mentioned with inflammatory conditions such as triceps tendonitis or olecranon bursitis and gout. Its surgical management entails anatomical information. Olecranon spur has rarely been reported in anatomical studies. We present a case of bilateral olecranon spur in the ulnae of a 62-year-old male skeleton. To the best of our knowledge, this report is the first anatomical report on biletral olecranon spur. The size of the spur was noticed carefully. Thorough anatomical knowledge of the olecranon spur can provide clinicians, radiologists, and forensic experts with better clinical judgment and may add insight to the surgical planning by orthopedic surgeons. Olecranon spur should also be considered in the differential diagnosis of pain at the posterior elbow, which may develop spontaneously, after a traumatic event, or in association with different sports.

Keywords: *Anatomical, bilateral, olecranon process, olecranon spur, osteophyte*

Introduction

Olecranon spurs are pathology and the first case report of them in the scientific literature was published by Cimmino in 1969.[1] The author allegedly missed the fracture of an olecranon spur and a malpractice lawsuit was instituted against him. He stated that "the trained radiologist is attentive to the presence of a narrow band of radiolucency at the base of the spur." The olecranon spur is more common in males, who do heavy machine operations and sawmill workers.[1,2]

In the literature, terms olecranon "spur" and "osteophyte" have been used interchangeably. Although both are enthesophytes, they differ in their locality, symptoms, diagnosis, treatment, and possibly in their etiology. Olecranon spur forms within the superficial portion of the central triceps tendon insertion and protrudes posteriorly, with a slight upward curve.[3,4] The olecranon osteophytes are located on the posterolateral or posteromedial articular border of the olecranon.[2]

In the present case, we report the bilateral olecranon spur in the ulnae of the 62-year-old male skeleton and this is the first anatomical report on bilateral olecranon spur to the best of our knowledge. The information about this atypical anatomical structure will be important for orthopedic surgeons, radiologists, and forensic experts with better clinical judgment.

Case Report

During routine examination of the dry and processed skeleton of 62-year-old male, housed in the osteology section of the Department of Anatomy, Postgraduate Institute of Medical Education and Research, Chandigarh, bilateral olecranon spur from the posterior part of the proximal surface of the olecranon process of the ulna was noticed. No medical or professional history for the body was available. The bones were thoroughly examined and photographed [Figure 1a-c]. The maximum length of the ulna, excluding the olecranon spur, was 234 mm bilaterally. A beak-like olecranon spur was noticed on the left side. The maximum length (from apex to base), width, and thickness of the left olecranon spur were 10.5 mm, 7.02 mm, and 5.58 mm, respectively [Figure 1]. On the right side, in our case, the base of the spur was clearly visible, but its apical part was broken, so the maximum length on this side could not be measured. The maximum width and thickness of the olecranon spur were 7.38 mm and

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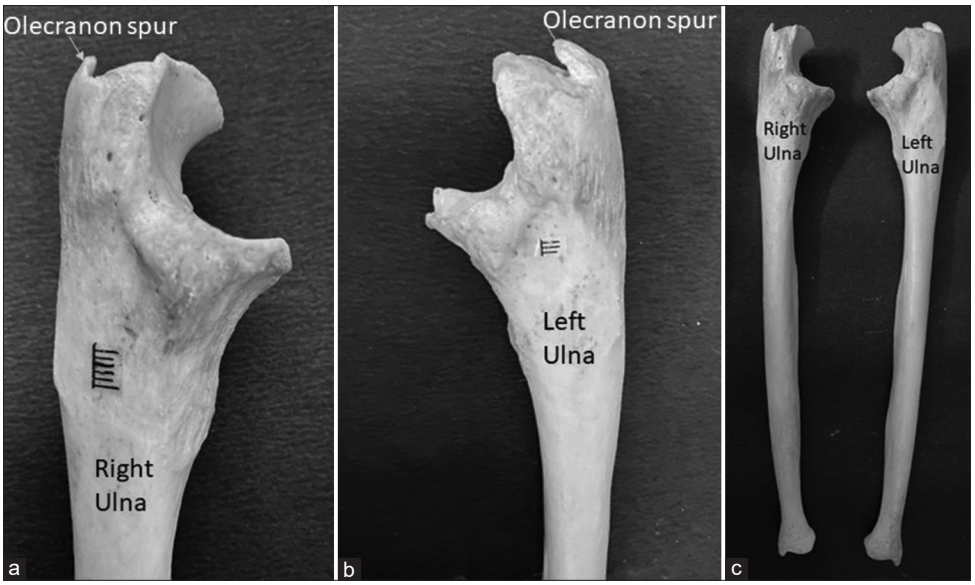

Figure 1: (a) Upper end of the right ulna showing olecranon spur, (b) Upper end of the left ulna showing olecranon spur, (c) Bilateral complete ulnae with olecranon spur

3.95 mm, respectively, on this side. The measurements were made using a digital Vernier caliper (Mitutoyo, Japan, 0.02 mm). A radiograph of the ulnae was also taken using a Philips Eleva X-ray machine [Figure 2]. The bones procured from the same cadaver were inspected thoroughly, and no spur was noticed in any other bone.

Figure 2: Plain radiograph of the ulnae showing olecranon spur

Discussion

The olecranon spurs are supposed to be traction spurs, which are formed in response to repetitive mechanical loading and microtrauma.[2,4,5] These spurs are observed in patients involved in jobs or activities demanding repetitive forceful elbow extension or patients with olecranon bursitis, triceps tendonitis, or a history of accident or injury.[1-4,6]

A microscopic study on cadaveric enthesis reveals that spurs are formed through a combination of endochondral, intramembranous, or chondroid ossification. A probable series of events leads to spur formation: pathologic thickening of calcified fibrocartilage leads to the formation of small bony nodules, which then fuse to form macroscopic spurs.[5] Although the mechanism of the olecranon spur formation has not been established, it likely to be similar to that of the spur at another enthesis.[2] The olecranon spurs seem to develop over a time scale of months to years, not days to weeks.[2]

Clinical presentation

Olecranon spurs can be symptomatic in isolation but are commonly mentioned with inflammatory conditions such as triceps tendonitis or olecranon bursitis and gout.[2,3] In olecranon bursitis, irritation of the olecranon enthesophyte on the triceps tendon is much like a pebble in your shoe.[7] Symptomatic olecranon spur presents with posterior midline elbow pain typically elicited on resisted terminal elbow extension, mainly from a beginning point of end arc flexion toward terminal extension over a range of nearly 130°–100°. However, if the spur is fractured, pain is felt in all arcs of motion. The presence of olecranon spur on physical examination hints at a prominent olecranon and point tenderness, with or without edema.[2] The diagnosis may be confirmed by plain radiography, ultrasound, or computed tomography/magnetic resonance imaging scans, especially if the patient presents with associated pathologies such as bursitis or tendonitis.[8]

The possibility of an olecranon spur in teenagers should not be overlooked, especially if the patient is presenting with elbow discomfort, and there is decreased extension without any history of injury or trauma.[9] Surgical reduction of an olecranon spur is suggested in such cases to ease the discomfort associated with elbow movement and may also result in some increase in movement.[9]

The recurrence of spur has also been reported. There are still different experiences regarding the removal of normal olecranon along with spur to avoid recurrence.[2,4] The fracture of the spur was reported to be a rare occurrence and supposed to be associated with triceps avulsion;[1,2,6] however, Jafarnia *et al*. reported that 50% of patients had a fracture of the spur during spur excision surgery as a treatment for chronic triceps tendonitis.[3] An unknown fracture can go on to become a painful nonunion, and associated soft-tissue edema can lead to a mass effect that contributes to posterior elbow pain.[2] Familiarity with olecranon spur is also important during the management of olecranon fractures, which form nearly 10% of upper-extremity fractures.[10]

Conclusion

The knowledge about the presence and possible size of the olecranon spur can provide clinicians, radiologists, and forensic experts with better clinical judgment and may add insight to the surgical planning by orthopedic surgeons. Olecranon spur should be considered in the differential diagnosis of pain at the posterior elbow, which may develop spontaneously or may be associated with trauma or sports activity. More studies on different ethnic groups may help to say if such spurs are resultant of a particular activity, profession, or geographic area.

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Conflicts of interest

There are no conflicts of interest.

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Short Anatomy Posting for Radiology Postgraduate Residents - Viewpoint on the Need of the Present Times

Dear Editor,

Radiodiagnosis or radiology is a broad specialty in India, as per the postgraduate (PG) Medical Education Board, National Medical Commission (NMC), India.

It is of 3 years duration for a degree course (MD) and 2 years for a Diploma after MBBS. It is a competency-based PG training program where NMC has stressed self-directed learning and teaching with retention of cognitive, affective, and psychomotor domains of learning.

The proposed schedule for rotation as per NMC in this training includes 2 months of elective posting. The exact nature of posting is not specified in the NMC guidelines. Anatomy is one important part of the radiology syllabus, which includes gross and cross-sectional anatomy of all the body systems. Theory paper in MD radiology includes basic sciences related to radiology (consists of anatomy, pathology, basic and radiation physics, imaging techniques, and film processing).

To reiterate, foreign exam such as the first part of the Fellowship of the Royal College of Radiologists (FRCR) examination (known as part 1 FRCR with anatomy and physics module) tests candidates' knowledge in anatomy as a separate module. The anatomy examination comprises 100 images and associated questions. A candidate has to pass separately in each module to be declared successful in clearing part 1 FRCR.

The radiodiagnosis PGs face difficulties in recalling the human anatomy knowledge they did acquire during their 1st year UG curriculum. The factual knowledge of anatomy being volatile becomes difficult to retain after completing 5.5 years of MBBS, which is immediately required for a 1st-year resident in radiology.

Good anatomical knowledge will help in understanding radiological anatomy (based on X-ray, computed tomography, magnetic resonance imaging, and ultrasound). To our dismay, there is no dedicated anatomy posting for 1st-year residents.

There are many studies reporting the perceived gap in the anatomical knowledge of PGs. Prince *et al*., 2005 collected feedback from medical trainees highlighting the shared concern regarding the level of anatomical understanding among them.[1] Fillmore *et al*., 2015 reported the observation of different program directors across specialties mentioning the struggle that recent PGs face while identifying basic anatomical features.[2] Brunk *et al*. in 2016 observed a decline in the level of knowledge regarding anatomy content and its clinical application among more recent medical graduates when compared to their predecessors.[3] Darras *et al*. in 2018 presented the fresh radiology resident reports mentioning the lack of radiological anatomy-focused teaching received by them during their undergraduate which was manifesting as the difficulty in current training, which they could curb to some limit after undertaking a self-directed radiologic anatomy course.[4] On the latter concept, Shah *et al*. in 2019 observed that resident-led small-group teaching sessions during anatomy laboratory benefits both medical students and the radiology residents themselves.[5]

Therefore, the authors would suggest a 2-week posting in the anatomy department, where 1st-year radiology residents will benefit a lot by sharpening their foundational knowledge of anatomy. It will also positively impact 1st-year MBBS students in several ways. First, it can help increase their confidence in radiologic anatomy skills as they receive guidance and explanations from residents. Second, it can enhance the perceived importance of radiology for medical training by showcasing its relevance in understanding anatomical structures and pathologies. Third, it promotes familiarity with the field of radiology, potentially sparking interest among students to explore it further as a future specialty.

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Conflicts of interest

There are no conflicts of interest.

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