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Archives of Surgical Research

Bringing Surgical Science and Art Closer

Archives of Surgical Research (ASR) is a double blind peer-reviewed quarterly ICMJE and COPE compliant journal dedicated to the local, national, and global advancement of surgical research, education and clinical practice. It aims to promote continued development in surgery through the dissemination of knowledge, ideas and good practice across surgical specialties. ASR provides readers with critically peer-reviewed, carefully selected and edited, and up-to-date publications about advancements in all surgery specialties.

Archives of Surgical Research

A Peer Reviewed Journal of Surgical Research & Education

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About Archives of Surgical Research

Archives of Surgical Research (ASR) is dedicated to the local, national, and global advancement of surgical research, education and clinical practice. It aims to promote continued development in surgery through the dissemination of knowledge, ideas and good practice across surgical specialties. ASR provides readers with critically peer-reviewed, carefully selected and edited, and up-to-date publications about advancements in all surgery specialties.

The journal aims to uphold the highest standards at the cutting-edge of research, provide a focus for evidence-based medicine through the publication of review articles and special issues, and give the findings context through the publication of editorials, commentaries and letters from the surgical community. We ensure enforcement of reporting guidelines and mandate the registration of all research involving human participants in a publicly accessible research registry.

As a journal covering all surgical specialties, ASR aims to facilitate the transfer of important ideas and thought systems between and across specialties. Hence, ASR will help prevent the trend of increasing sub-specialization which leads to 'tunnel-vision' and the unfortunate concealment of important surgical advances within specific specialties.

Editor in Chief

KMA

Editorial Team

PREFACE

Shalamar Medical & Dental College has exceptionally excelled in the field of science, education and research over the last decade and has produced quality graduates who are currently serving around the world. Quality of education and research in surgery has been instrumental in this regard under the leadership of Prof Khawaja Muhammad Azim to achieve our core objective of producing quality education. Inception of Pakistan Endocrine & Thyroid Surgeons Association (PETSA) has aligned well to my vision, institutional requirements and overall rapport of the institution.

I witnessed and supported the birth of Pakistan Endocrine & Thyroid Surgeons Association here at Shalamar Medical College three years back and during this period it has evolved into a mature tree and is bearing fruits to surgical education and training here at our institution. Legacy of its founding visionary, Late Prof Syed Zafar Haider has continued. PETSA has been conducting Annual Thyroid & Parathyroid Master Class since its inception with great reception. Currently, we are the largest endocrine surgery center in Pakistan with highest volume turnover.

Now the introduction of "Archives of Surgical Research" is another feather into our institutions' cap. This journal would not only satisfy the needs of the society but would also serve to promote culture of science, education and research within our institution. This culture advocacy remains instrumental in promoting the quality of learning process of the medical graduates within our institute and is aligned with my vision about this medical college.
In the end, I am happy to write about "Archives of Surgical Research" and its inaugural issue and wish the editorial team best of luck for their endeavors for years to come.

Prof Zahid Bashir

Principal

Shalamar Medical & Dental College, Lahore

MESSAGE FROM THE PRESIDENT

Pakistan Endocrine & Thyroid Surgeons Association (PETSA)

Prof Zafar Haider was the teachers of the teachers and a great surgeon. He was the one who made thyroid and endocrine surgery safe in Pakistan and we carry the light now with aim to improve the endocrine surgery in light of modernization in the field of the surgery.

Archives of Surgical Research aims at improving the standard of surgical research and education. It would function as official Journal of Pakistan Endocrine & Thyroid Surgeons Association (PETSA).

The journal would cover endocrine, breast and surgical oncology primarily. It would also focus on the surgical education for medical students and residents to enhance the learning process through addition of technology, blended learning and modern concepts in medical education.

Prof. Khwaja M Azim FRCS
President PETSA

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Archives of Surgical Research | Editorial

Are Surgeons Born or Trained?

Rehan Ahmed Khan

IMPORTANCE In professions that require a high level of psychomotor skill acquisition, such as surgery or flying a plane, this is an ongoing debate: are they born or made? The qualities of the surgeon are not only mechanical but are also related to mental, social-psychological, and educational elements. It is not very wise to think that all good surgeons around us are gifted with all these qualities and their practice, hard work and experience have a lesser role in the acquisition of these qualities that are required to become a good surgeon. In this editorial, I will present different views on this debate and try to reach a conclusion.

KEYWORDS Qualities of surgeon; surgical skills; surgical talent

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Editorial

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In the field of surgery, when a surgical trainee starts the training, we would hear comments such as "s/he is a born surgeon", "s/he is a natural surgeon" etc. On the other hand, we may also hear other comments such as "s/he cannot become a surgeon", "s/he does not have what it takes to become a surgeon"," etc. If we dig deep into the source of these perceptions; the reason why these perceptions are developed about the surgical trainees or surgeons in practice, we will find that these are based mainly on the observations of near peers and supervisors. The list of these observations is exhaustive, but the major ones would entail skills that the surgeon demonstrates like making an incision, handling, and dissecting the soft tissues, knotting, and suturing, identifying the surgical anatomy, and handling the bleeding during operations. If the surgeon demonstrates these skills with accuracy and speed, s/he gets a label of 'born to be surgeon'. On the other hand, if the surgeon struggles to demonstrate these competencies, s/he may be labeled a 'poor surgeon'.

However, some people have a pragmatist view on this topic. They support both the arguments that surgeons are born but they are made as well. So, surgeons with inherent skills can easily learn the art and craft of surgery with little effort in comparison with others, however others without the inherent skills can become equally good or better surgeons with hard work and practice.

But is being a surgeon all about cutting? The answer is 'No'. In this regard the famous saying that a good surgeon knows how to operate, a better surgeon knows when to operate and the best surgeon knows when not to operate stands true. Because as soon as the surgeon gives an incision, how precise it is, if not required, the harm has been done[1,2]. Being a surgeon is about making decisions, managing a patient pre and post-operatively. It's about being ethical, professional, and empathetic with the patient. It is about being a good communicator, having high emotional intelligence, and having good leadership skills. Are we born with all these skills cumulatively, or do we learn them through education and experience?

If we consider good surgeon and inherent skills as two variables in which we would like to establish a co-relation, we should not forget that it will only establish an association and not cause and effect phenomenon. And even this association of being born with surgical skills and becoming a good surgeon would be hard to establish. This is because there are many moderating variables that we ignore when we establish the inherent skills as the only cause of becoming a good surgeon. To list a few of them, these variables are hard work, practice, leadership, communication, and emotional intelligence as mentioned earlier.

Also, to reach a conclusion or make an opinion regarding this debate, we need to understand how a good surgeon is made. And even before that, what is a good surgeon? This in fact is not an easy answer; however, a literature search suggests that a good surgeon is an amalgam of good manual dexterity, sound theoretical knowledge, and is well versed in non-technical skills[3, 4]. The journey of becoming a surgeon is also reflective of resilience, passion, and hard

work. The qualities of the surgeon, hence, are not only mechanical but are also related to mental, social-psychological, and educational elements. It is not very wise to think that all good surgeons around us are gifted with all these qualities and their practice, hard work and experience have a lesser role in the acquisition of these qualities that are required to become a good surgeon. It may be true that an individual has some of these qualities that may make the journey of becoming a good surgeon easy but someone lacking these qualities by default can also acquire them with hard work, resilience, and passion. Hence, we can say that surgeons are not in fact born but are fashioned by steady coaching, much practice, and experience.

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Archives of Surgical Research | Original Research Communication

Ghrelin Impedes Oxidative Stress Induced Intestinal Epithelial Cell Apoptosis through Varying Signaling Pathways

Talha Asad, Usman Arshad, Saleem Arif

IMPORTANCE Ghrelin, a gut brain peptide, has been primarily studied in the regulation of body weight homeostasis. Recent studies indicate, however, that it has potent anti-apoptotic effects in various cell types and exogenous ghrelin prevents gastric mucosa from ethanol-induced ulcer formation. Given ghrelin is cytoprotective, here we hypothesized ghrelin's anti-apoptotic effect in intestinal epithelial cells when exposed to severe oxidative stress, which plays a key role in the pathogenesis of various intestinal disorders.

MATERIALS & METHODS Intestinal epithelial cells, FHs74Int, IEC-6 and Caco-2 were used to assess anti-apoptotic effects of ghrelin following H2O2 treatment by TUNEL technique and flowcytometric analyses. In addition, mechanisms responsible for these effects were explored in relation to relevant signaling pathways including PI3K/Akt pathway and cytochrome 'c' dependent caspase-3 activation. PI3K/Akt and mitochondrial cytochrome 'c' release was assessed by western analysis and caspase-3 activity was determined by ELISA and Immunoflorescence.

RESULTS H2O2 potently increases the intestinal epithelial apoptosis and necrosis. Ghrelin inhibits intestinal epithelial cell apoptosis through growth hormone secretagogue receptors (GHS-Rs). Further, ghrelin's anti-apoptotic effect against H2O2 –induced apoptosis is associated with activation of PI3K/Akt, inhibition of mitochondrial cytochrome-c release and likewise inhibition of caspase-3 activation.

CONCLUSION In aggregate, our findings suggest that ghrelin inhibits oxidative stress-induced apoptosis in intestinal epithelial cells and hence might serve as a therapeutic strategy in states associated with intestinal mucosal injury, where oxidative stress plays a central role.

KEYWORDS Ghrelin, Intestinal apoptosis, signaling pathways, Intestinal epithelial cells, Intestinal tract

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Original Research Communication

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Ghrelin is a recently characterized short gastrointestinal peptide, which has been implicated in the physiological regulation of body-weight homeostasis [1-3]. It is mainly produced by gastrointestinal tract and is subsequently released into systemic circulation to perform numerous functions during set of physiological and pathological states[1-3]. The systemically available ghrelin binds to diversely expressed, known as growth hormone secretagogue receptors (GHS-Rs) to perform its molecular activities[4]. One of the relatively newer functions attributed to ghrelin is its role in cytoprotection and mitogenesis [5-15]. Few previous reports suggest that ghrelin has potent cytoprotective effects on various cell types when exposed to pro-apoptotic agents [5-15]. Baldanzi et al were the first to demonstrate ghrlein's anti-apoptotic effects on endothelial cells and cardiomyocytes when exposed to doxourubicin, a well-known anti-cancer drug that has potent pro-apoptotic effects [14]. Later Choi et al complemented this finding by revealing that ghrelin protects adipocytes from iso-proterenol-induced cell death [15]. Preliminary evidences indicate that ghrelin promotes cytoprotection by activating intracellular cell survival proteins such as PI3K/Akt and MAPK [21]. Sibilia et al have extended this information to in vivo models of gastric mucosal injury[8]. They have demonstrated that ghrelin prevents ethanol-induced ulcer formation in rats, however the mechanism of this cytoprotective effects remains largely uncharacterized.

Reactive oxygen species (ROS) -induced intestinal epithelial cell apoptosis contributes to intestinal mucosal barrier dysfunction in various intestinal states including ischemia-reperfusion injury, inflammatory bowel disease and

necrotizing enterocolitis [16-25]. The mechanism of ROS-mediated cellular injury is not completely understood however it is known that ROS alter the mitochondrial structure and function of the cell to promote the pro-apoptotic effects [16]. The reactive oxygen species alter the permeability of the mitochondrial membrane and release the mitochondrial cytochrome 'c' into the cytosolic compartment. In the cytosolic compartment, cytochrome 'c' binds to the Apaf-1 (apoptosis initiating factor-1) and initiates its ATP-dependent oligomerization prior to caspase-9 activation. Caspase-9 then further stimulates the activation of various other caspases to ultimately converge at caspase-3, which serves as an endpoint of caspase-dependent apoptosis [16-25].

We hypothesized ghrelin's cytoprotective role in intestinal epithelial cells on two previously published reasons. First, ghrelin has cytoprotective effects in variety of in vitro cell systems and second, ghrelin protects the gastric mucosa from ethanol-induced ulcer formation [8, 16-25]. Therefore we sought ghrelin's cytoprotective effect in ROS-mediated apoptosis in intestinal epithelial cells. In current set of experiments, we have demonstrated ghrelin's anti-apoptotic effect in the presence of H_2O_2, and subsequently have explored mechanisms in relation to PI3K/Akt pathway, mitochondrial cytochrome 'c' release and caspase cascade.

MATERIALS AND METHODS

Cell lines: Non-transformed human derived from normal human small bowel (FHs74Int), rat small intestinal crypt cell line (non-transformed, IEC-6) and transformed Caco-2 cell line derived from human colon cancer cells were obtained from ATCC (Rockville, MD). FHs74Int and IEC-6 cells were maintained in Dulbecco's Minimal Essential Medium (DMEM) containing 10% fetal bovine serum (FBS) without or with insulin respectively. Eagle's Minimal Essential Medium (EMEM) containing 20% FBS in a humidified (37°C, 5% CO_2) incubator was used to maintain Caco-2 cell line. These cell lines were then sub-cultured before confluence and were seeded at a density of $5x10^4$ cells/ml to ensure harmony among cell lineage.

Preparation of total cell lysates and cytosolic fractions of cell lysates: The lineage cells were rinsed two times with phosphate buffered saline (PBS) with a pH 7.4. The cells were gently scrapped, suspended in PBS and were paletted with centrifugation at 3200 rpm. Cell lineage extracts were lysed with lysis buffer containing 20mM Tris, pH 7.5, 0.1% Triton X, 0.5% deoxycholate, 1mM phenylmethylsulfonyl fluoride, 10µg/ml aprotinin and 10µg/ml leupeptin. They were finally cleared by centrifugation at 12000g at 4°C. For obtaining cytosolic fractions of the total cell lysates for assessment of cytochrome c release, cells were lysed by three cycles of freeze-thawing in a lysis buffer containing 20 mM HEPES/KOH (pH 7.5), 1.5 mM MgCl2, 10 mM KCl, 1 mM NaEDTA, 1 mM EGTA, 1 mM DTT, 0.1 nM PMSF, and 250 mM sucrose. Cells were then spun at 100,000 x g (45,000 rpm) at 4°C for 30 min. The supernatant was collected and were subjected to western analysis.

Western blot analysis: BCA assay kit (Sigma, St Louis, MO) with bovine serum albumin as a standard was used to measure total protein concentration, according to the manufacturer's instructions. Cell extracts containing 30µg total proteins were subjected to 10% SDS/PAGE. The resolved proteins were transferred electrophoretically to PVDF membranes (Invitrogen, Carlsbad, CA). Membranes were incubated with primary antibodies in PBS containing 0.1% Tween 20 overnight at 4°C after blocking with PBS containing 0.2% casein for 1 hour at room temperature. Following secondary antibody incubation the Vecstain™ ABC kit and DAB liquid substrate were utilized for chromogenic detection. Equal protein loading was confirmed by probing with 3µg/ml anti-actin monoclonal antibody (Lab Vision, Freemont, CA). The primary antibodies used were rabbit pAkt 1/2/3 (473), rabbit Akt and rabbit cytochrome 'c' (Santa Cruz Biotechnologies, Santa Cruz, CA). The detailed protocols are described in legends of the data figure.

Assessment of Apoptosis by TUNEL staining: Cell Apoptosis was assessed by the Cell Death kit (Roche). The cells were grown in 96- well plates and at 80% confluency were subjected to overnight serum starvation and were treated with ghrelin with or without [D-lys-3]-GHRP-6. Apoptosis was induced by H_2O_2 and the anti-apoptotic effects of ghrelin were analyzed by TUNEL technique. Briefly, the cells were washed with PBS with maximum care to avoid the cell layer damage and were TUNEL-stained according to the manufacturer's instructions. The cells were counter-stained with DAPI to count the total number of the cells. The apoptotic cells were counted under the light and fluorescence microscope per field and were expressed in percentage of the total cell count.

Assessment of Apoptosis by FACS® following Annexin V and Propidium Iodide Staining: Flowcytometry was employed to analyze earlier even events of apoptosis and to confirm TUNEL assay findings; Briefly, Caco-2 cells were plated in 6 well plates to 90% confluency, subjected to H_2O_2 treatment or prolonged starvation in the presence or absence of ghrelin and were stained by Annexin V and

Propidium Iodide according to manufacturer's instructions (Vybrant™ Anexin V staining kit #3, Molecular Probes, Eugene, OR). The samples were run in FACS® (Becton-Dickinson, San Jose, CA) and the data was analyzed by using software CellQuest™ (BD Biosciences, San Jose, CA).

Caspase-3 Profiling: Caspase-3 is an important endpoint of caspase-dependent cellular apoptosis. Caspase-3 activity was assessed by the TiterZyme Caspase-3 EIA kit (Assay Designs, Ann Arbor, Michigan) according to the manufacturer's instructions. Briefly, the Caco-2 cells were seeded and at 90% confluency were subjected to starvation in the presence or absence of various chemicals and peptides. Cell lysates were prepared as described in the western blot section and were analyzed for the caspase-3 activity according to the manufacturer's instructions.

Florescence Immunocytochemistry for Caspase-3 & 7: The role of ghrelin in modulation of caspase 3 & 7 was also confirmed by Magic RedTM detection kit (Immunochemistry Technologies, Bloomington, MN), which utilizes the fluorphore, cresyl violet coupled with MR-$(DEVD)_2$. This MR-Caspase photostable fluorogenic substrate easily penetrates the cell membrane and membrane of the internal organelles. In the presence of Caspase 3 and 7 within the cell, the caspase sequences are cleaved to yield a red fluorescent product visible under fluorescence microscope. Briefly the Caco-2 cells were grown in chamber slides and were subjected to H_2O_2 treatment for 24 hours. The cells were treated with MR-$(DEVD)_2$ for an hour and were counter stained by Hoechst 33342 for 10 minutes. The slides were analyzed by the Fluorescence microscopy using UV filter (excitation at 365 nm and emission at 480 nm) and green filter (excitation at 550 with a long pass >610nm emission/barrier filter pairing) respectively for the Hoechst staining and MR-$(DEVD)_2$.

Statistical Analysis: All of the data was expressed in terms of the means ± S.E for a series of 'n' number of the experiments. To assess the significant difference between the groups Non-parametric Mann-Whitney U t-test was employed to compare the groups. A p value < 0.05 was considered to be statistically significant. All of the statistics were performed using the program Statistica (StatSoft Inc. Tulsa, OK).

RESULTS

Ghrelin inhibits the H_2O_2 –induced apoptosis and necrosis in intestinal epithelial cells: Various reactive oxygen species (ROS) are produced on the inner mitochondrial membrane during physiological states. Hydrogen peroxide (H_2O_2) is one of the oxidants, which is known to be produced by the mitochondrial respiratory chain and induces apoptosis dose dependently in various cell types including intestinal epithelial cells [16,25]. Consistent with the previous findings, here we demonstrate that at concentrations consistent with the pathologic states like intestinal inflammation, ischemia or infection, H_2O_2 significantly induces the apoptosis in FHs74Int, IEC-6 and Caco-2 intestinal epithelial cells (*$p<0.05$ vs. untreated controls) (Fig.1 A&B). Our TUNEL analyses data suggest that ghrelin pretreatment inhibits H_2O_2-induced apoptosis in FHs74Int, IEC-6 and Caco-2 intestinal epithelial cells significantly compared to H_2O_2 treated cells in a dose dependent fashion (**$p<0.05$ vs. H_2O_2 treatment). We have previously shown that GHS-Rs are expressed in intestinal epithelial cells [26,27]. To address whether ghrelin mediates its anti-apoptotic effects specifically through GHS-Rs, we antagonized the GHS-R with a receptor specific antagonist (D[lys-3]-GHRP-6) and analyzed the apoptosis. Antagonism of GHS-Rs through a competitive antagonist (D[lys-3]-GHRP-6) leads to loss of ghrelin-mediated anti-apoptotic effect (Fig.1 A&B). In the next step, we confirmed our TUNEL assay findings with flowcytometric analysis following Annexin V and PI staining (Fig. 2 A&B). The flowcytometric experiments not only support the previous findings but also provide the assessment of oxidative stress-induced intestinal epithelial cell necrosis. Ghrelin not only inhibits the apoptosis (**$p<0.05$ vs. H_2O_2 treatment) but also significantly reduces the necrotic cell death in Caco-2 intestinal epithelial cells (¥, $p<0.05$ vs. H_2O_2 treatment) as compared to H_2O_2 treatment.

Ghrelin's anti-apoptotic effect in the presence of H_2O_2 is associated with activation of PI3K/Akt complex: In second set of experiments, we analyzed the signaling events associated with ghrelin's anti-apoptotic effects in the presence of H_2O_2. Phosphatidyl-inositol 3-kinase (PI3K) /Akt complex is an important intracellular moiety, which plays key role in cytoprotection during stress [27,29]. We analyzed the status of Akt phosphorylation in the presence of H_2O_2 and ghrelin.

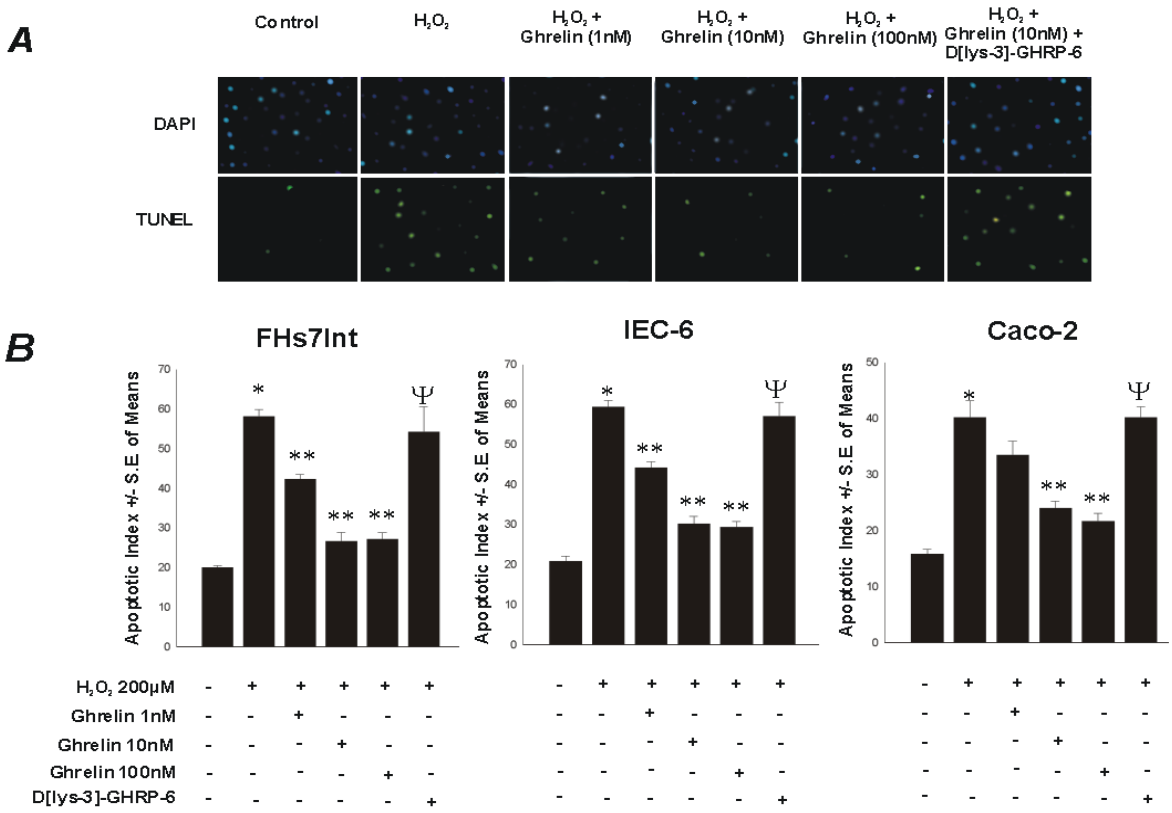
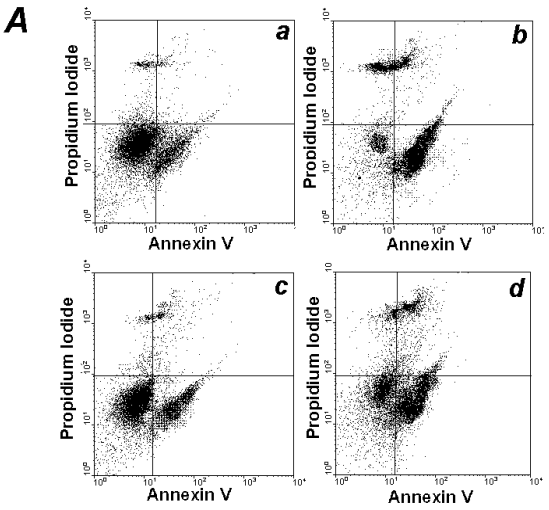


Figure 1. Representative TUNEL analysis showing ghrelin's anti-apoptotic effects on H2O2-induced apoptosis in intestinal epithelial cells. Intestinal epithelial cells were pretreated with ghrelin (1nM-100nM) for 4 hours along with or without ghrelin receptor antagonist, D[lys-3]-GHRP-6, apoptosis was stimulated by 24-hour treatment with 200µM H2O2 and was analyzed by TUNEL and DAPI staining. A, The upper panel shows DAPI staining of cellular nuclei in Caco-2 cells to mark the total number of cells; the lower panel is TUNEL staining. B, Quantitative representation of data; H2O2 potently induces apoptosis in FHs74Int, IEC-6 and Caco-2 intestinal epithelial cells (*p<0.05 vs. untreated controls), ghrelin pretreatment significantly inhibits the apoptosis (**p<0.05 vs. H2O2 200µM) and D[lys-3]-GHRP-6 pre-treatment abolishes ghrelin's anti-apoptotic effects (Ψ, p<0.05 vs. ghrelin10nM+ H2O2 200µM). Values have been presented in form of Means ± S.E. of at least three independent experiments; a p value <0.05 was considered to be statistically significant.



B	Agent / Peptide Treatment	No staining (% Living Cells Fraction)	Annexin V staining (% Apoptotic Cells Fraction)	PI staining (% Necrotic Cell Fraction)
	No treatment	75.88±3.7	15.85±3.38	8.27±0.89
	H_2O_2 treatment (200 µM)	15.94±1.9	58.60±4.80*	25.40±3.22$^{\Psi}$
	Ghrelin (10nM) + H_2O_2 (200 µM)	59.77±3.0	26.16±2.54**	14.05±4.41$^{¥}$
	D[lys-3]-GHRP-6 (1µM) + Ghrelin (10nM)+ H_2O_2 (200µM)	20.76±3.9	59.36±0.94§	19.87±3.46$^{\Phi}$

Figure 2. Representative flowcytometric analysis showing ghrelin's anti-apoptotic effects on H_2O_2-induced apoptosis in intestinal epithelial cells. Caco-2 intestinal epithelial cells were pretreated with 10nM ghrelin for 4 hours; apoptosis was stimulated by 24-hour

treatment of 200μM H_2O_2 and was analyzed by flowcytometric analysis followed by staining with Annexin V/ PI. A, Dot plot diagrams showing the induction of apoptosis by H_2O_2, and anti-apoptotic effects of ghrelin. A, The left lower quadrants in each dot plot panel represents living fraction of the cell (Annexin V-/PI-), right lower quadrant represents apoptotic fraction (Annexin V-/PI+) and upper right quadrant represents necrotic fraction of the cells (Annexin V+/PI-); A (a) un-stimulated control; A (b), H_2O_2 treatment; A (c), H_2O_2 + ghrelin (10nM); A (d), D[lys-3]-GHRP-6 + H_2O_2 + ghrelin. B, Table is quantitative representation of data; H_2O_2 potently induces apoptosis in Caco-2 intestinal epithelial cells (*p<0.05 vs. untreated controls), ghrelin significantly inhibits the apoptosis of epithelial cells (**p<0.05 vs. H_2O_2 200μM) and ghrelin anti-apoptotic effect is lost if we pretreat the cells with D[lys-3]-GHRP-6 (§p<0.05 vs. H_2O_2 200μM + 10nM ghrelin). Ghrelin also inhibits the necrosis of intestinal epithelial cells through GHS-Rs, significantly compared to H_2O_2 treatment (¥p<0.05 vs. H_2O_2 treatment). Values have been presented in form of Means ± SD of at least three independent experiments; a p value <0.05 was considered to be statistically significant.

Ghrelin stimulates the phosphorylation of Akt through GHS-Rs (Fig.3 A) and antagonism of GHS-Rs or PI3K by D[lys-3]-GHRP-6 or Wortmannin respectively leads to loss of ghrelin mediated Akt phosphorylation (Fig.3 A) and eventually loss of ghrelin's anti-apoptotic effects (**p<0.05 vs. H_2O_2 + ghrelin) (Fig.3 B).

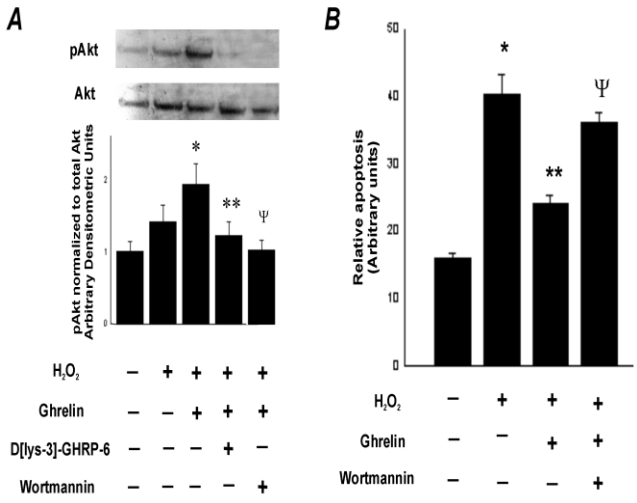


Figure 3. Ghrelin prevents Caco-2 intestinal epithelial cell apoptosis through PI3K/Akt dependent mechanism. A, Caco-2 intestinal epithelial cells were treated with H_2O_2 with or without ghrelin in the presence or absence of Wortmannin (1μM) and D[lys-3]-GHRP-6 (1μM). Ghrelin stimulates the phosphorylation of Akt in Caco-2 intestinal epithelial cells in the presence of H_2O_2, which is abolished following PI3K/ Akt and D[lys-3]-GHRP-6 pretreatment. Densitometric analysis complements the blot; ghrelin significantly stimulates phosphorylation of Akt in Caco-2 intestinal epithelial cells (*p<0.05 vs. untreated controls) and ghrelin-mediated Akt phosphorylation is lost if we pretreat the cells with D[lys-3]-GHRP-6 (**p<0.05 vs. H_2O_2 200μM + 10nM ghrelin) or Wortmannin (Ψ, p vs. H_2O_2 200μM + 10nM ghrelin). B, TUNEL analysis; Wortmannin pretreatment (60 minutes prior to ghrelin treatment) inhibits the ghrelin-mediated anti-apoptotic effects in Caco-2 intestinal epithelial cells. Values have been presented in form of Means ± SE of at least three independent experiments; a p value <0.05 was considered to be statistically significant.

Ghrelin's anti-apoptotic effect in the presence of H_2O_2 is associated with inhibition of mitochondrial cytochrome 'c' release into the cytosol: ROS structurally and functionally disable the mitochondria, which are the main sources of energy to the cells. Various oxidative agents including H_2O_2 are produced in the mitochondrial membrane and disrupt it to release cytochrome 'c' into the cytosolic compartment [30]. Cytochrome 'c' subsequently initiates the caspase cascade to promote the cellular apoptosis [30]. Therefore, we analyzed the release of cytochrome 'c' into cytosolic compartment through western blot analysis of cytosolic extracts of the cell lysates. Our data (Fig 4& B) reveal that H_2O_2 potently stimulates the release of cytochrome 'c' into the cytosolic compartment (Fig 4B; *p<0.05 vs. untreated controls). Ghrelin pretreatment inhibits the release of cytochrome 'c' into the cytosolic compartment (Fig.4 A&B), hence might prevent the initiation of caspase dependent apoptosis.

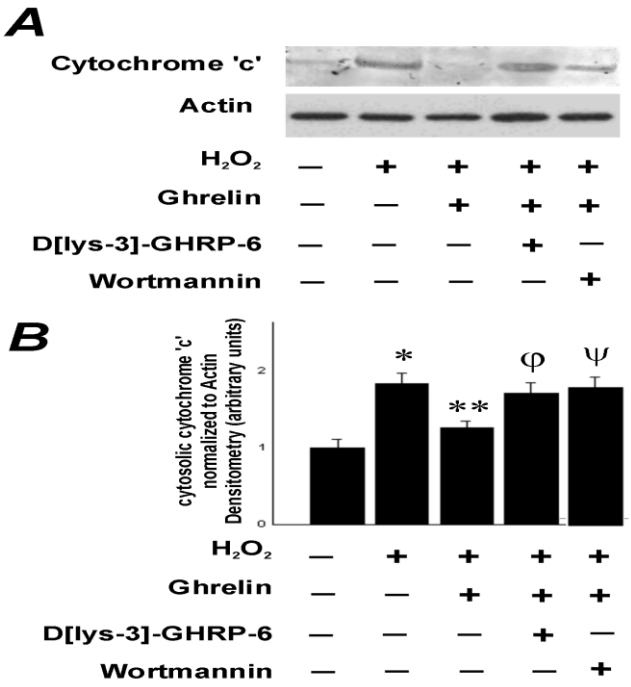


Figure 4. Ghrelin's anti-apoptotic effects are associated with inhibition of mitochondrial cytochrome-c release into cytosolic

compartment in Caco-2 intestinal epithelial cells. A, Caco-2 intestinal epithelial cells were treated with H_2O_2 with or without ghrelin (10nM) in the presence or absence D[lys-3]-GHRP-6 (1μM) and western analysis was performed with cytosolic fractions of the cell lysates. Ghrelin inhibits H_2O_2induced mitochondrial cytochrome-c release into cytosolic compartment, which is abolished following D[lys-3]-GHRP-6 pretreatment. B, representative densitometric analysis of three independent experiments normalized to Actin levels. H_2O_2 induces the release of mitochondrial cytochrome-c (*p<0.05 vs. no treatment); ghrelin inhibits the release of mitochondrial cytochrome-c release (**p<0.05 vs. H_2O_2). Values have been presented in form of Means ± SE; a p value <0.05 was considered to be statistically significant.

Ghrelin's anti-apoptotic effect in the presence of H_2O_2 is associated with inhibition of caspase-3 activation: Additionally, we analyzed the status of activation of caspase-3 in H_2O_2 activated Caco-2 cells by ELISA assay and by immunostaining the caspase-3/7 by a newly introduced technique (see the details in Materials and Methods section). Ghrelin inhibits the activation of caspase-3 (**p<0.05 vs. H_2O_2)(Fig.5 A&B), which is central effecter caspase molecule in caspase dependent apoptosis. Ghrelin mediates this caspase-3 activation through GHS-R because GHS-R antagonism leads to loss of ghrelin's cytoprotective role. Additionally, caspase-3 inhibitor also abolishes the ghrelin-mediated caspase-3 activation further confirming the involvement of caspase pathway in ghrelin-mediated anti-apoptotic mechanisms.

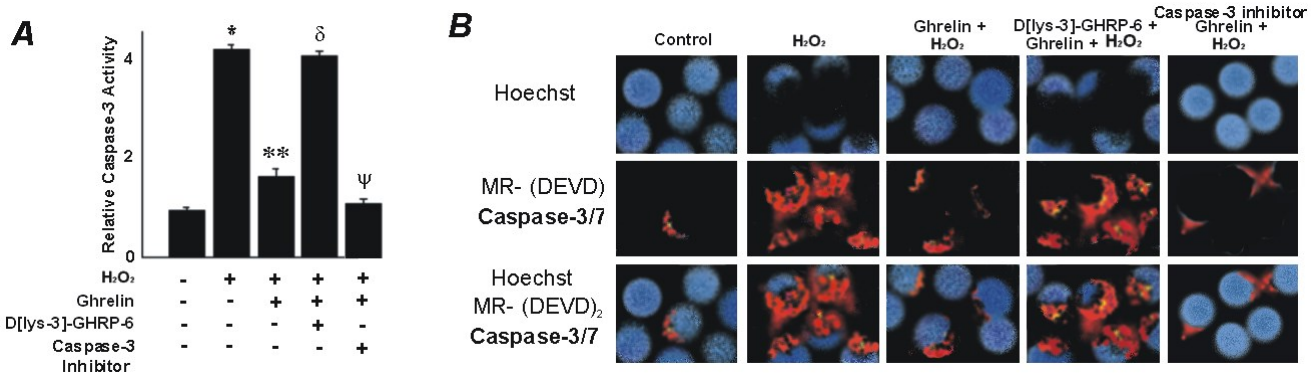


Figure 5. Ghrelin's anti-apoptotic effects are associated with inhibition of Caspase-3 activation in Caco-2 intestinal epithelial cells. A, Caco-2 intestinal epithelial cells were treated with H_2O_2 with or without ghrelin (10nM) in the presence or absence of D[lys-3]-GHRP-6 (1μM) and Caspase-3 levels were analyzed by ELISA. H_2O_2 stimulates the activation of caspase-3 significantly above the untreated controls (*p<0.05 vs. no treatment). Ghrelin pretreatment inhibits H2O2-induced caspase-3 activation (**p<0.05 vs. H_2O_2), and ghrelin mediated caspase-3 activation is abolished D[lys-3]-GHRP-6 pretreatment (δ, p<0.05 vs. H_2O_2+ ghrelin) or caspase-3 inhibitor (1μM) pretreatment (Ψ, p<0.5 vs. H_2O_2 + ghrelin). Values have been presented in form of Means ± SE of at least three independent experiments; a p value <0.05 was considered to be statistically significant. B, representative fluorescence staining of caspase-3/7 following various treatments; Upper panel represents the Hoechst staining of cellular nuclei, Middle panel represents the caspase-3/7 staining of the cells and in Lower panel, the Hoechst and caspase-3/7 stainings have been merged. H_2O_2induces the activation of caspse-3/7 in Caco-2 cells following H_2O_2 treatment; ghrelin inhibits the activation of caspase-3/7.

DISCUSSION

The intestinal epithelium functions as a highly selective barrier that allows the absorption of dietary nutrients yet restricts entry of the pathologic antigens [31]. The precision and balance in the absorptive function of this barrier function entails critical role in maintaining the mucosal immune homeostasis and epithelial integrity [32,33]. During the intestinal states associated with inflammation, ischemia and infection the intestinal barrier function is significantly compromised leading to the structural and functional abnormalities in the intestinal tract [32,33]. Reactive oxygen species (ROS) are one of the important pathologic products of the mucosal leukocytes during ischemia, infection and inflammation that lead to intestinal epithelial cell apoptosis and eventually intestinal barrier dysfunction [32,33].

Ghrelin has recently gained attention in relation to cytoprotection and mitogenesis in variety of in vitro cell systems [5,8,26]. It prevents apoptosis in endothelial cells and cardiomyocytes and cell death in adipose cells [21]. Though the detailed mechanism of ghrelin's cytoprotective activities has not been well characterized, however the preliminary studies indicate that ghrelin prevents cellular apoptosis through induction of various cytoprotective intracellular proteins including Akt and MAPK [13]. Here, we have examined the role of ghrelin in H_2O_2-induced

apoptosis in intestinal epithelial cells and subsequently have explored subcellular signaling events.

Hydrogen peroxide (H_2O_2) is also one of the oxidative agents, which promote both apoptosis and necrosis in intestinal epithelial cells [33,34]. It is believed to induce the intestinal epithelial cell necrosis and apoptosis through either the exogenous sources or through autocrine mechanisms of ROS overproduction triggered by the pro-inflammatory cytokines [33]. In current set of experiments, we have used the dose of H_2O_2 that is equivalent to the amount produced by the macrophages during intestinal ischemia-reperfusion injury or inflammation. Consistent with previous literature, exogenous H_2O_2 induces significant apoptosis and necrotic cell death following a 24-hour treatment. Our TUNEL analyses show that exogenous ghrelin treatment prevents H_2O_2-induced apoptosis in FHs74Int, IEC-6 and Caco-2 intestinal epithelial cells. This anti-apoptotic effect is mediated in a dose dependent manner through GHS-Rs, because ghrelin-mediated cytoprotective effect is lost in the presence of GHS-R antagonist, D[lys-3]-GHRP-6. In addition, our flowcytometric data corroborate our TUNEL assay findings. Ghrelin significantly reduces the apoptotic cell fraction from ~60% to ~25%. Flowcytometric analyses also indicate that ghrelin reduces intestinal epithelial necrosis significantly suggesting that ghrelin prevents apoptosis as well as necrosis in intestinal epithelial cells under oxidative stress.

Phosphatidylinositol 3-kinase (PI 3-kinase), a ubiquitous lipid kinase, along with Akt is involved in cell survival. Promotion of cell survival by the activation of PI 3-kinase/Akt occurs by the inhibition of proapoptotic signals and the induction of survival signals [35-37]. PI3K/ Akt also inhibits the production of endogenous ROS to limit the apoptosis by maintaining the mitochondrial integrity. Baldanzi et al have previously shown that ghrelin prevents doxourubicin-induced cell death in cardiomyocytes through activation of Akt [13]. Consistent with these previous findings our data indicate that ghrelin stimulates the phosphorylation of Akt in intestinal epithelial cells in the presence of H_2O_2 through GHS-Rs and chemical inhibition of PI3K-Akt signaling results in failure of the ghrelin to inhibit the oxidative stress-induced apoptosis.

Another mechanism of H_2O_2-induced apoptosis in intestinal epithelial cells is mediated through disruption of mitochondrial membrane. Ruptured mitochondrial membrane releases cytochrome 'c' into cytosolic compartment, which in turn activates caspase-9, an initiator caspase and caspase-3, an effecter endpoint caspase to promote apoptosis in intestinal epithelial cells [34]. Here we show that ghrelin inhibits the H_2O_2-mediated release of cytochrome 'c' from intestinal epithelial cells. The ghrelin-mediated inhibition of mitochondrial cytochrome 'c' release also affects the downstream caspase-pathway. Our data clearly shows that ghrelin potently inhibits the activation of caspases in the presence of H_2O_2 to prevent intestinal epithelial apoptosis.

In summary, we have clearly demonstrated that ghrelin has potent anti-apoptotic effects on intestinal epithelial cells under oxidative stress. Further, ghrelin's anti-apoptotic effects on intestinal epithelial cells under oxidative stress are associated with activation of PI3K/Akt and inhibition of release of mitochondrial cytochrome 'c' release and caspase-3 activity. Given, ghrelin has been found to be mitogenic, anti-inflammatory and anti-apoptotic, the therapeutic utility of ghrelin in intestinal conditions associated with mucosal barrier dysfunction warrants further investigation [38,39].

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Archives of Surgical Research | Original Research Communication

Enriching Operating Room Based Student Learning Experience: How Should We Structure It?

Nida Maryam, Zaitoon Zafar, Hassan Hafeez, Talat Waseem

IMPORTANCE The Operating Room (OR) is a high-pressure setting where multiple complex educational, and administrative facets interplay. The learning process, dictated by the operation list, is disparate, opportunistic, unstandardized, and at times suboptimal. Upon reviewing existing published literature regarding the learning experience in the OR setting, it was clear that this field is, to this day, unstructured and ambiguous, with many grey areas that need to be worked on. To achieve an optimized and enhanced theatre experience, it is of immense importance to recognize the pros and cons of available models that can be employed within this setting and deduce ways to improvise them into a most beneficial method. This study aims to recognize the role of a structured learning process for medical graduates in the setting of the OR. The study also explores pertinent questions; whether the learning models currently being used for residents are appropriate for medical graduates and how must we structure learning activities within OR settings.

METHODOLOGY The study involved an extensive literature review and thematic analysis to generate themes and subthemes, which were subjected to a modified Delphi technique where residents and teachers participated to identify debate and produce a consensus on the relative importance of each method when employed in Operation Theater based learning.

RESULTS While structured learning is essentially goal-oriented, student-friendly, and time-saving and provides qualitative outcomes, it, however, has drawbacks owing to a lack of faculty and resources. Various potential problems in the implementation of a structured learning process were identified and components in making the structured learning meaningful were formulated. The models each have their potential advantages and disadvantages when implemented in the OR for learning.

CONCLUSIONS Structured learning process within the OR setting should at least cover the minimum standards that a graduate essentially requires. It should be a balanced program according to the specialty. However, the quality of evidence to substantiate these aspects remains contextual with low external validity and generalizability.

KEYWORDS Operating Room; Operation Theater; Learning; Student; Simulation Lab; Surgical Education, Learning Models, OMP, Lyon's Model, Koen's Model, 4C/ID,

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Original Research Communication

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The role of a structured learning process for the medical graduate in the OR setting has been debated for years. As much as structured learning is appreciated, it comes with its problems. This study explores the merits of structured training, in comparison to traditional opportunistic learning. While structured learning is essentially goal-oriented, student-friendly, time-saving, and provides qualitative outcomes, it, however, has drawbacks owing to a lack of faculty and resources, time, and training, in addition to the unavailability of OR and surgical cases. A structured approach should at least cover the minimum standards that a graduate essentially requires. It should be a

balanced program according to the specialty. This study allowed participants to give their valuable input as to how we can structure learning activities within the OR.

Another critical question is whether the OR-based learning process should be standardized or opportunistic? Lyon's model and many others encourage students to apply self-regulated learning to maximize their learning experience in the OR (Lyon 2004a; Weinberg et al. 2015). However, this approach may lead to an unstandardized, opportunistic, and random learning process for medical graduates producing non-uniform student learning and healthcare safety issues. On the contrary, Roberts et al. (2009) emphasize a more structured approach towards OR-based learning.

This study further explores the potential role of various models currently being used for the training of surgical residents in OR-based learning of a medical student. Are the models currently being used for the residents learning appropriate for the medical graduates as well? The prevalent models of OR-based learning were studied in-depth and were critically appraised for their utility in the arena of medical graduates OR-based learning.

Another very important aspect of this study included the idea of synchronization of OR-based learning with simulated lab activities and the use of technology in this aspect. It is no secret that within a few years technology will dominate most of the OR activities. The need of training the faculty for the structured OR-based learning programs was also identified.

METHODOLOGY

Following ethical approval from the local institutional review, a board study was conducted between April to June 2020, consisting of two phases, which have been summarized in a flowchart in Figure 1.

In Phase 1, following the PRISMA flow chart (Figure 2), a literature search was done through Pub Med, ERIC, and Google Scholar. Thematic analysis and review were performed to analyze various models and their relevance in Operation Theater-based learning.

In Phase 2, Modified Delphi was used for analyzing the relative importance of identified models from the literature review. Modified Delphi Technique is a composite of qualitative and quantitative methodology and is especially useful in discovering the meaning that people give to events they experience (Bogdan&Biklen, 2007). Based on the Phase 1 literature review items, a Delphi questionnaire was developed for Round 1 for both students and teachers. The Delphi technique involved both qualitative and quantitative components. The quantitative component sought the participants' opinions on a Likert scale for measuring the relative value of the factors influencing students' OR-based learning. The quantitative component is appropriate for prioritizing the factors, and the Delphi approach itself was useful for consensus building. While taking a sample, a purposive sampling technique was used because of the specific nature of the research question (Fraenkel et al. 1932).

The consensus would be considered achieved once 70% of the participants agree on an issue (Trevelyan and Robinson 2015).The qualitative methodology allowed for an 'insider' view of participants under study. Thematic analysis was done for the qualitative data as described previously. The data analysis was done manually. Quality assurance was established through the maintenance of credibility, dependability, transferability, and conformability.

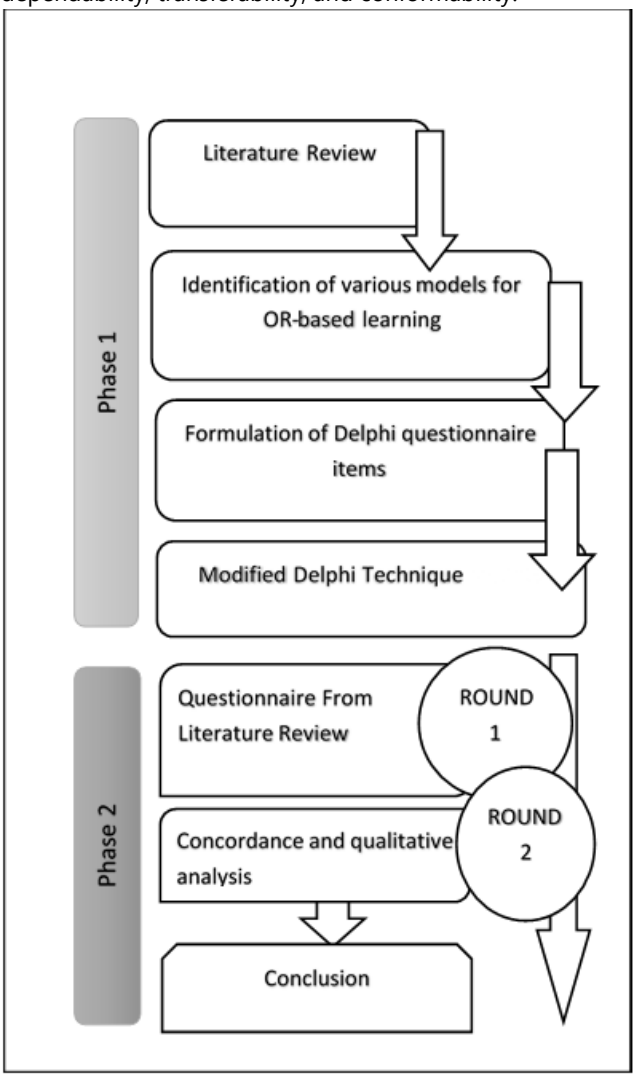

Figure 1: Methodology

In the Delphi study, participants included surgical teachers with extensive experience in medical education and medical students who had attended surgical rotations. 18 surgeons and surgical residents participated in this Modified Delphi Study. In the Delphi study, there are no hard and fast rules about sample size, as suggested by Linstone et al. (1978). It seems, therefore, that the decision about panel size is empirical and pragmatic, taking into consideration factors such as time and expense (Hasson 2000). Representation is assessed by the qualities of the expert panel rather than its numbers (Powell 2003). Therefore, in this study, the students and faculty members were purposively sampled to generate high-quality debate and opinions so that a meaningful scientific discussion could take place. Participants from the University of Lahore, the University of Health Sciences, King Edward Medical University, Riphah International Islamic University, Khyber Medical University, University of Dundee, and Queen Elizabeth Hospital Birmingham offering graduation in medicine were included for a diversity of opinion. All of these institutes are tertiary-level institutes with an excellent reputation and structured clinical programs. Faculty and undergraduate students from these institutes participated in this Delphi Study with the eventual aim of finding the optimal model for implementing in operating rooms based learning. Confidentiality was maintained, and participants' names were not used during any step; participants were given codes for their identity and analysis purposes. All of the participants were blinded from each other. Blinding ensured neutralization of the impact of higher positions of influence on the students. The foundations of research were maintained on ontological, epistemological, and methodological perspectives.

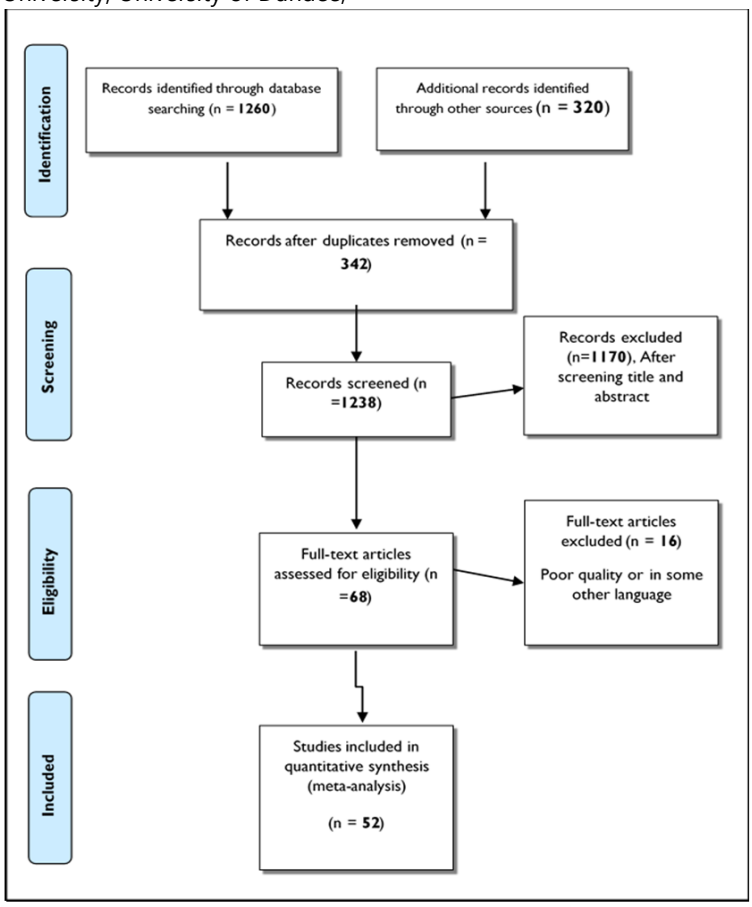

Figure 2: PRISMA Flow Chart for literature search

RESULTS

The results are presented in three phases as per sections of the study.

Phase 1: Literature Review on Factors Affecting Student Learning in OR: The literature search strategy identified a total of 1580 articles. 52 papers were included after the screening process by removing duplicates. Figure 2 explains

the process of literature search and article selection through a PRISMA flow chart. Selected papers were thematically analyzed for finding themes and subthemes affecting students learning in OR. The rest of the themes and subthemes emerged during the Delphi qualitative data input. If the literature review's detailed findings have been published elsewhere; their detailed overview has been omitted in this article to focus more on the Phase 2 findings here.

Phase 2: Modified Delphi Study Results: The study's participants were both faculty members with experience in teaching surgery and medical education and the participating students had undergone rotation in the surgery department. The participants belonged to diverse institutes, including local as well as institutes in the United Kingdom.

Relative Importance Of OR Based Learning Models—Quantitative Component

The participants evaluated the relative importance of learning models identified from the literature review through quantitative analysis of Delphi Round 1 and 2. The importance was scored on a scale of 0-5. The learning models most effective in OR-based learning of students discussed here in this study have been rated as either 'Quite Important' or 'Highly Important'. None were rated unimportant. The learning models were then prioritized based on scoring across 2 rounds of the Delphi technique.

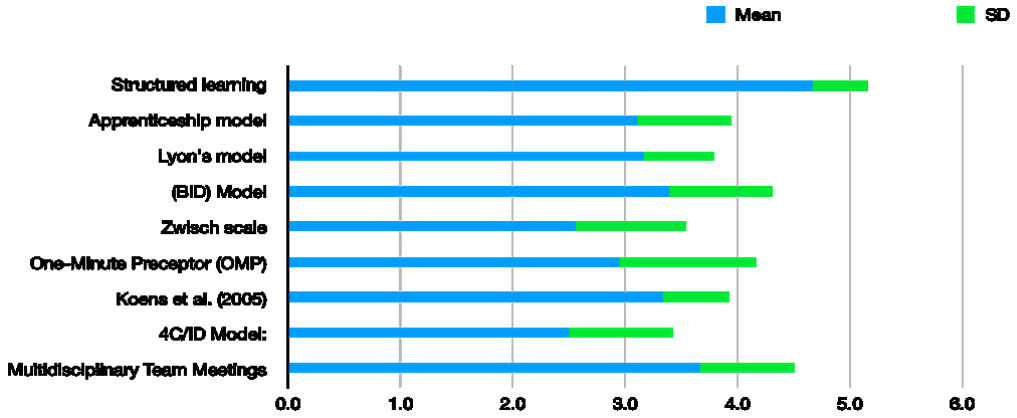

Figure 3: Quantitative Analysis of the Consensus Through Delphi Study: 18 experts with experience in surgical OR-related education participated in this first round of the study. Quantitative and qualitative analysis was done based on the filled Delphi questionnaire and the following observations were made. Most of the factors described based on the literature review were considered important. Most of the factors have been rated as either 'Quite Important' or 'Highly Important'. Only one factor related to student-driven personal learning objectives is considered 'Somewhat Important'. The relative rating is given in the table (Means±SD).

Relative Importance Of OR Based Learning Models—Qualitative Component

The qualitative analysis of emerging themes, subthemes, and axial codes through the Delphi Rounds was done and is presented in Table 2. Here we describe only the conclusions drawn from this analysis. The details of the final axial codes, themes, subthemes, and representative statements can be reviewed in Table 2.

The participants here clearly argue for more structured learning within the OR than the traditional opportunistic learning. A structured approach should at least cover the minimum standards that a graduate essentially requires. It should be a balanced program according to the specialty. The participants identified the advantages and disadvantages of a structured learning program. While structured learning is essentially goal-oriented, student-friendly, time-saving, and provides qualitative outcomes, it, however, has drawbacks owing to a lack of faculty and resources, time, and training, in addition to the unavailability of OR and surgical cases. The participants identified potential problems in the implementation of a structured learning process. The participants formulated components in making the structured learning meaningful. The participants also explored the idea of synchronization of OR-based learning with simulated lab activities and the use of technology in this aspect. The participants also emphasized the need for training the faculty for the structured OR-based learning programs. The participants reached a consensus on the usefulness of the traditional Apprenticeship model but also realized the drawbacks of it such as lack of interest and commitment from either student or the teacher, it being time-bound and the dire need of the training of the faculty for this model to work. Lyon's model (P Lyon 2004) was well

accepted among the majority of participants as highly useful. Regardless of it being a convenient form of learning, it was effective only if the resident could self-regulate. The Briefing-Intraoperative teaching-Debriefing (BID) model (Roberts et al. 2009) was much appreciated by the participants because it was useful in teaching larger audiences and post-simulation discussions were very effective. The Zwisch model, originally designed by Dr. Joseph Zwischenberger in 2013, was not very appreciated although it was largely identified as a useful modality to be used within resident training. The One Minute Preceptor (OMP) model (Lap Ki Chan and Jeffrey Wiseman 2011) made efficient use of time and could be used in theater as well as in simulations. Koen's model (Koens et al. 2005) was highly appreciated by the participants due to its usefulness in the application of surgical knowledge. Koen's model employed the technique of virtual patients for learning. The Four-Component-Instructional-Design (4C/ID) model (Vandewaetere et. al 2014) was not popular with the participants as it was difficult to implement. Multi-disciplinary Mortality and Morbidity meetings were a much-preferred form of learning model amongst all participants.

DISCUSSION

Standardized graduates are need of the hour so that they can function anywhere in the world optimally, and a uniform level of healthcare can be provided. However, standardization has an inherent flaw in that it is usually done for leveling the average. Hence, standardized learning strategies do not account for differently gifted students. Another drawback of this approach is the potential loss of diversity in medical education.

Moreover, personal learning objectives are essential for the sharpening of focused minds. Hence, the structured learning process should have a window of consumption for exceptional minds. The curricula need to have room for a self-driven intellectual brought up through personalized learning objectives and create opportunities in this regard. In summation, a predominantly structured program with well-organized lessons would likely be an optimal option for an adequate learning experience in the operating room. However, for some segments of learning and for students who take initiative, opportunities for personal learning objectives and self-driven learning should be encouraged.

Many models are currently being used for the student and resident learning in OR, which varies based on agenda – the freedom for the student to decide learning objectives and modalities of learning.

The apprenticeship model has been the mostly applied informal way of teaching and learning in the field of surgery. This model is based on the "principle of shadowing", which means the resident follows the trainer in terms of practice, follows his cues, and over time the skill is inculcated into the resident. Residents typically follow the 'see one-do one' approach. The teachers have a dominant role within the OR setting. Their interest, competence, attitude, quality of feedback, and encouragement positively influence OR-based learning. Fear, intimidation, and bullying negatively affect student learning and should be discouraged. Teachers and staff's welcoming attitude has a positive impact. Considering the teachers' rate-limiting role within the OR setting, it remains imperative to focus on faculty training.

Many authors (Lyon 2004b; Weinberg et al. 2015) have previously argued for student-led education in operating rooms. Lyon's model of learning stands on the principles of andragogy and adult learning. The authors argue for student-driven learning in the operating room as surgeons are often busy due to competing responsibilities and activities (P. Lyon, 2004b). Lyon et al. have identified various challenges posed to a student in the OR environment which are conceptualized around 3 key domains: the challenge posed by the physical environment; the challenge of the educational task, and the challenge of negotiating a role as a student participant within operating rooms. This model provides diversity and opportunities for students to drive the learning process. However, this model defines the benefits of standardization of medical graduates.

Students usually prefer Robert et al.'s Briefing-Intraoperative Teaching-Debriefing (BID) model for teaching at the resident and student levels. The BID model, is not something new but knowingly or unknowingly has been part of traditional OR-based learning over centuries. It constitutes a three-step process of OR-based learning i.e. Briefing, Intra-operative Teaching, and Debriefing. 'Briefing' is a short 2-3 minutes interaction with learners before an operative procedure, which encompasses learning objectives, learning need assessment, and process of learning activity. Intraoperative teaching is primarily a didactic walk of the procedure, which is a two-way productive interaction between the learner and the teacher, with the ultimate goal of skill transfer and independence of the learner in terms of performing the procedure. The Debriefing session consists of feedback and reflection provided by both the learner and the teacher with the ultimate aim of achieving conceptual clarity. This technique is quite useful for imparting learning about surgical procedures—many of the participants of our study concur with this model's utility.

Table 1 Qualitative responses were analyzed by thematic analysis given in the table below. Highlighted items are subthemes that emerged through this thematic analysis.

IMPORTANCE RATING OF THEMES AND SUBTHEMES OF QUALITATIVE ANALYSIS

Themes	**Subthemes**	**Relative Importance on Likert Scale (1-5) Mean±SD**	**% of participants who rate factors either Quite or Highly relevant**	**Qualitative Analysis: Final Codes**
Learning in OR	Should OR-based learning be structured or opportunistic?	4.7 ± 0.5	100%	**Requisites/Essentials of the structured approach** 1. A structured approach should at least cover the minimum standards that a graduate essentially requires. 2. It should be a well-balanced program according to specialty and cases for operation available. 3. To diversify the learning process, the curriculum must have some space for self-regulated learning as well but that should not replace the minimum essential structured component. **Provision of opportunities** 1. Structured learning provides equal opportunities for the students to learn and establish themselves as equally competent graduates. 2. It paves the way for the best opportunities. **Assessment Tool** It helps gauge the learning experience of students.
	Advantages and disadvantages of structured learning	NA	NA	**Advantages :** **Student-friendly approach** ● Structured learning keeps the students focused ● It develops the interest of students **Goal-oriented learning** ● Students know what to expect on the day and in the environment and students can prepare for it in advance. ● Helps mark the milestones which a student needs to cover ● Helps students realize that this much learning is expected of them ● Provides a guideline in the form of a curriculum **Assessment Tool for Students** ● Helps the student mark what he does know and does not know ● Helps students to identify and focus on areas they are deficient in. ● Early recognition of the learner's mistake and timely resolution of faults ● Structured formative assessments are possible **Time-Saving** ● Most procedures and techniques don't need repetition **Provision of opportunities** ● Equal opportunities for all **Quality of product** ● Outstanding surgeons will be produced **Disadvantages:** **Lack of faculty and resources** ● More faculty engagement especially in setups where they are already over-burdened and have limited resources. ● More gadgets required to observe surgery **Lack of time** ● Structured training programs are difficult to implement in public or busy setups because the workload is huge ● Lots of time required to implement structured training **Lack of training** ● Training of the trainers required ● Lack of uniform facilities and trainers at different centers

				Unavailability of OR and cases ● The ORs are day and time-bound Availability of cases in correspondence to the structured program may not always be possible
	Potential problems in the implementation of the structured learning process	NA	NA	**Potential problems:** **Unavailability of cases** ● Clinical cases may not always be available at the time of teaching of that particular topic **Inapt circumstances in OR** ● Operation theater is a high-pressure setting where surgeons have to deliver at multiple fronts so implementing any structured learning process would require special arrangements, dedication, and conviction to make it work. **Need for compatibility and cooperation** ● The system would have to adapt to the learning requirements and has to be compliant with the needs of the learning process and at this point, the surgical operation theater leadership has to play a constructive role. The teachers responsible for curricular design need to liaise with the stakeholder effectively
	Components in making structured learning meaningful	NA	NA	**Components:** **Planned curriculum and learning objectives** ● A predefined list of procedures and techniques to observe at emergency and elective OR/ a set syllabus or curriculum for the students to complete ● Active and passive learning with smart and well-aligned objectives **Surgical ethics and protocol** ● Development of attitude and surgical ethics ● Comprehension and compulsion of aseptic techniques and subsequently building habits **Learning and practicing skills** ● Skill acquisition through engaging students in operation theaters ● Hands-on experience of specific techniques **Roles in Operating Room** ● Operating room's leadership ● Interdisciplinary approaches **Group and inter-group discussions** ● Cognitive development through preoperative case discussions ● Discussions among the students of various specialties and disciplines ● Discussions among students and residents and professors at all tiers and levels ● Panel discussions **Reporting and recognizing errors** ● Reporting of any complication if it occurs ● Mortality and morbidity meetings aiming to find what could have been done ● Audits; qualitative and quantitative **Attendance and assessment** ● Compulsory attendance of the elective and emergency ORs for specific periods ● Regular evaluation of students and residents after specific intervals **Feedback before and after the session** ● Students input when the composition of the content of the program is made Feedback from the students after going through the program
	Synchronization of OR-based learning with simulated lab-based activities	NA	NA	**Unrestricted access to labs** ● Simulation labs are not time-bound and could be used at odd hours **Learning and practicing skills** ● Simulations could be a way to introduce the students to some particular skills ● Simulation-based learning covers the psychomotor and affective domains of OR-based learning. ● Step by step learning will create an order to appraise the lag of learner ● A logbook can document the amount of time spent on learning specific skills under supervised guidance **Learning from observation and demonstration** ● Synchronization by practicing in simulation labs whatever has been observed in ORs

				• See one, do one, and teach one principle that can be easily applied in simulation labs. For example, trainers can demonstrate laparoscopic suturing in simulation labs over and over again **Constructive feedback** • Instant feedback to the student with suggestions for improvement **The safe and risk-free practice of skills** • Simulations help students practice without guilt and without unnecessarily risking patient safety until they perfect a particular skill so it can be performed on real patients No inadvertent harm to real patients which is highly likely with inexperienced trainees or students
	Use of technology in OR-based learning	NA	NA	**Latest technology in OR - a healthcare necessity** • Technology in many forms is revolutionizing the OR environment and students need to not just familiarize themselves but learn it all • The need for the latest technology and facilities for diagnosis and management of patients • 3D imaging **Tele-education and E-learning** • Live surgery telecasts in classrooms and on social media enhance learning for large groups while staying at a safe distance • Visual memory is enhanced for many people at a time • Creates a learning environment • Recorded videos can be used for teaching • Online teaching sessions **Intraoperative teaching using a visual aid** • Anatomical drawings and atlas projections while performing corresponding surgeries for a better grasp and understanding of students **Hands-on learning** • Simulations based learning Skills lab
	Training of faculty for OR-based learning of medical students	NA	NA	**Training of faculty** • Faculty development programs • Training the trainers formally. • Direct supervision of training faculty **Essentials of the training** • By encouraging the trainers to review literature • Attending online courses and international courses • Encouraging more time to be spent in simulation labs • Role modeling **Objectives for the trainers** • A curriculum should be devised • Preplanned instructor manual • The teaching roster of the trainers set and thoroughly implemented **Using online platforms and soft wares** • Moodle like platforms **Appreciation of the trainers** • Certificates and diplomas in medical teaching Feedback of the trainers from the students and residents

DIFFERENTIAL EXAMINATION OF OR LEARNING MODELS

Models	Apprenticeship model "Principle of Shadowing"	3.1 ± 0.8	72%	**Advantages**: • A well known, traditional, and effective way of teaching • Positively affect the students' learning • Students can find mentors and guidance Students can participate in more advanced individual activities **Disadvantages**: **Lack of interest and commitment**

				• Medical students on rotations may not be aiming for that specialty and may not show an active interest in it • Lack of commitment on students' behalf • The learning graph isn't rapidly progressive • The student may not have good observational quality **Time-bound learning** • Medical students on rotations come for a limited period so this model is difficult to apply for them • Longer and meaningful exposure is required • A limited number of residents/students get the chance to learn maximum **Problems related to trainers** • The trainer's training quality can affect the learning • The trainer may be busy or overworked • Lack of commitment on trainers' behalf • Requires designated faculty with specific students More entrustment is required
	Lyon's Model	3.2 ± 0.6	88%	**Advantages**: **Convenient learning** • Discussions with colleagues are easier and comfortable in comparison to those with condescending seniors • It could be used for student's "additional" personal learning objectives **Dependent factors** • It is effective only if the resident can self-regulate • It depends on the type of OR. Capacity, types of cases operated, number of students and their attitude and aptitude **Making Interpretations** • Interprets learning and teaching in OR Learning involves interpreting the student and surgeons' behavior, style, attitude, and consequences of the decision **Disadvantages**: **Lack of interest** • Undergraduates usually don't show much responsibility towards their learning in OR **Downsides of self-regulated learning** • Self-regulated learning may not be able to produce standardized graduates and many components of graduate learning may be missed in a self-dictated learning **Surgeon's priorities** • OR environment is very demanding. While most of the focus is kept on the patient's wellbeing, safety, and avoiding complications, the students are often ignored Time restraints from the surgeon and academic point of view
	Briefing-Intraoperative teaching-Debriefing (BID) Model	3.4 ± 0.9	72%	**Advantages:** • Teaching a larger audience • Much helpful in comparatively large setups • Good for rotations of a medical student as many students can be accommodated • Post-simulation discussion • Could be effectively used after simulation-based learning **Disadvantages:** • Surgeon's disregard • As teachers, surgeons don't intend to train students, so it is not that pertinent • Insufficient teaching/training • Residents require deeper knowledge. This model will not suffice their needs
	Zwisch model	2.6 ± 1	55%	**Advantages:** **Learning basic skills and instruments** • Effective for basic techniques such as gloving, scrubbing, stitch removal, and different types of dressings

				• Extremely useful for initial training of the interns and residents Producing competent and confident residents • Assesses and analyzes the competence level of residents and the faculty can delegate the autonomy to the resident accordingly • Boosts the confidence of the resident **Disadvantages:** **Limited to few skills** • Can be applied to learning only a few techniques **Lack of consideration for undergraduates** • Students are almost novice in the field and not much work at student levels • Surgeons avoid delegating autonomy to undergraduate students for the safety of patients so this model has the least implication
	One-Minute preceptor (OMP)	2.9 ± 1.2	61%	**Advantages:** **Time productivity** • A very effective way to use the time between the procedures Incorporating OMP in OR learning • There are always some important learning moments in OR-based learning which needs to be harnessed effectively and OMP can be a wonderful strategy for that **Incorporating OMP in simulation training** • If this technique is applied with simulation-based learning, it will be very effective **Disadvantages:** **Inapt circumstances in OR** • Considering the workload of OR, the way they work, it is quite difficult
	Koens model	3.3 ± 0.6	94%	**Advantages:** **Application of knowledge practically** • Helps to comprehend the knowledge learned in classrooms and wards • The combination of practical and clinical knowledge implemented with theoretical knowledge enhances the learning and better understanding of salient points • Reduced and enhanced ends are crucial in learning to analyze progress **Use of virtual patients for learning** • Virtual patients make a good example and if employed effectively, they can improve the clinical decision-making process of students **Disadvantages:** **Unequal chances at learning** • Not all students can have a chance or opportunity to see the same thing closely. Only a limited number of students or residents can work as assistants so limited chances. **Difficult to carry out** • They are difficult to construct and a lot of effort is required by the faculty members
	Four component instructional design model (4C/ID)	2.5 ± 0.9	33%	**Advantages:** **Learning in sections/components** • Most procedures and techniques are learned better if divided into components Long term committed teaching • If applied for cases of continuous and more committed teaching on a long term basis where a long term plan can be made **Precision by repetition** • Repetitive difficult tasks and repetitive feedback will make learning meticulous **Disadvantages :** **Unfitting and difficult** • Small procedures and techniques might not need compartmentalization so cannot always be utilized • Difficult
	Multidisciplinary Team Meetings and Mortality and Morbidity Meetings	3.7 ± 0.8	88%	**Advantages:** **Learning by a multidisciplinary approach** • The involvement of consultants of different specialties enhances learning by giving deep insight into different aspects of procedure and management protocol **Participation of students**

				• Even at lower levels i.e. students can attend these meetings, listen to discussions and get learning points and relate that to relevant cases later on. **Case discussions and decision making as a team** • It helps in reviewing the case to case studies. • Individual cases help to develop a rational decision, helps in teamwork and leadership skills with feedbacks regarding decision making with equal responsibilities **Disadvantages:** **Lack of experience for active participation of students** • Students require more in-depth knowledge and experience to participate effectively in these meetings **Incompatibility of cases with clinical rotations** • It cannot work out as a planned syllabus manner because the types of cases cannot be predicted for the period students are allocated to the very clinical rotation
	Any other model, modality, and technique that can be helpful	NA	NA	• Designate PGs to teach • Structured learning of most importance • Simulated environments • Learning first, then teaching • Residents should be regularly evaluated • Feedback should be regularly taken and reviewed seriously

In line with Roberts et al., this study finds that students prefer a more structured learning plan. They feel that teachers can more appropriately choose learning objectives corresponding to the expected skill set required by a graduate, with more experience in this field and having gone through this experience themselves beforehand. Moreover, they are more comprehensively exposed to various aspects of medical learning and patient care and are likely to make better decisions in favor of their patients. However, they would like to participate in selecting modalities to be used for achieving these learning objectives.

To assess and calibrate a resident's level of competence and to delegate autonomy of the operative work with patient safety the concept of EPAs and Zwisch scale has been developed. The resident is evaluated for any surgical intervention on a scale of "Show & Tell," "Smart Help," "Dump Help," and "No Help" in terms of senior support required and then is given autonomy based on that. The model provides both faculty and residents a lexicon with which to discuss the expected role of autonomy in the future of surgery.

One-Minute Preceptor (OMP) model for teaching micro-skills: for a smaller subset of skills in the operating room, OMP can be a very useful strategy both for residents and medical students. Short activities can be carefully planned in a typical moment of learning in OR and this learning modality has demonstrated a track record of being productive. This modality is based on a 5-step process, consisting of (1) getting learner commitment, (2) probing for clinical reasoning, (3) teaching of general rules, (4) reinforcing good performance or providing positive feedback, and (5) correcting poor performance. Thus, OMP is an effective strategy for clinical encounters within an ambulatory setting, operating theater, and simulation lab.

Koens et al. (2005) developed a model for considering the role of the context within medical education. The model is based on principles of experiential learning. For a learning activity to have a stronger impact on the learner and more enhanced cognitive and psychomotor retention, physical, sematic, and commitment contexts need to be added. For example, studying the anatomy of the inguinal canal, alone in the library, will be at the reduced end. In contrast, learning within the OR as a surgeon operates on a hernia when the learner can see the anatomy, will be at an enhanced end. The semantic or cognitive dimension provides a relationship between the learner's knowledge and the learning task. For example, a simple task of learning facts, such as three causes of splenomegaly, will be at the reduced end. In contrast, to see patients undergoing splenectomy for idiopathic thrombocytopenic purpura (ITP) will be at the enhanced end. The commitment dimension deals with the learner's motivation.

The 4C/ID model's utility can be employed successfully for learning skills within the simulated or standardized environment. This model is a structured modern form of the apprenticeship model for operative learning. The four-component instructional design model (4C/ID) stands on chunking repetitive difficult tasks to smaller more manageable components with repetitive feedback which is gradually replaced with reflection as the learner gains expertise. This model follows motor learning theory and theories related to feedback and reflection. This approach deals with persistent problems like compartmentalization; separation of a whole competence in distinct parts or categories like declarative knowledge, procedural knowledge, and attitudes; fragmentation, breaking complex skills or competencies in smaller parts without taking into account the interactions between the parts; and the transfer paradox, when students learn complex tasks in an isolated manner, it will be more difficult for them to transfer what they have learned to the reality of the work settings because what works well for reaching isolated, specific objectives often does not work when it comes to reaching integrated objectives (Vandewaetere et al., 2015). However, this model's application or the apprenticeship model for students may not be practically feasible considering the number of students, safety and ethical issues, and time constraints. Hence for every learning encounter or designed activity, an appropriate model would require selection, and the encounter's structure would change accordingly.

Likewise, students' motivation and desire to learn, preparedness, and skill to use self-regulated learning can influence their quality of learning experience. The organization needs to be supportive in infrastructure and adequate visual and skill lab support to improve OR learning experience.

LIMITATIONS

Although there is a reasonable amount of literature available related to factors that influence medical students learning, the data is contextual. The data is based on opinions without sound scientific evidence and may not be generalized. Some studies have a low response rate signifying non-response bias that limits both the studies' reliability and validity.

This study is also based on the participants' perceptions and thoughts. It possesses inherent flaws of the Delphi technique, which is again opinion-based data collection that

cannot completely exclude personal biases. In the future, it would be necessary to explore various models of learning and teaching within the OR setting.

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Archives of Surgical Research | Clinical Audit

Clinical Audit of Compliance with WHO Surgical Safety Checklist in a Private Tertiary Care Surgical Facility

Hamza Azhar, Nouman Zaib, Haseeb Arif, Fatima Jamil, Talat Waseem

IMPORTANCE WHO safe surgery checklist was designed to reduce avoidable surgical errors. Literature has shown that after applying this checklist in hospitals a significant drop in complications, mortality and morbidity is observed.

METHODS It is a prospective study carried out at a tertiary care hospital after approval of the institutional review board. The study was divided into two phases. In the first phase, we developed a questionnaire based on the WHO safe surgery checklist to see the compliance of our anesthesia, nursing, and surgical staff to the checklist. The results were shared with the relevant departments. A re-audit will be done in the second phase.

RESULTS AND DISCUSSION 123 patients were included in the first phase of the study. The sign-in checklist was fully implemented in 35 of 50 total patients (70%). The time-out checklist was fully implemented for 1 of 39 total patients (2.6%) and the Sign out checklist was fully implemented for 0 of 34 total patients (0%).

CONCLUSION Poor compliance was observed with the "Time out" section of the safe surgery checklist in our study. This information can help us identify the problems which can be amended in the future.

KEYWORDS Audit, surgical audit, WHO safety checklist, WHO, Safe surgery, WHO surgical safety checklist

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Clinical Audit

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It is reported that approximately 234 million people need surgical treatment for different medical reasons every year and that 14% of these people experience an unwanted event [1]. In 2008, the World Health Organization (WHO) initiated a campaign called "Safe Surgery Saves Lives" in order to draw attention to all these unwanted events resulting from surgical procedures and to improve the safety of surgery and consistency of surgical care based on the fact that at least half of surgical errors can be prevented with safe surgical practices. Therefore, the WHO Safe Surgery Checklist (SSC) was developed to improve teamwork among OR staff, to reduce mortality and complications in the perioperative process, and to ensure the consistent use of procedures for safe surgery [2].

WHO Surgical Safety checklist has 3 main components i.e. Sign – In (Before Induction of Anesthesia, Time – Out (Before Skin Incision), and Sign – Out (Before the patient leaves the operating room). These components are designed to analyze compliance. This process involves OR Nursing team, Anesthesia, and Surgery team. This study aims to help us understand the compliance of all three components of the WHO Surgical safety checklist in our tertiary care facility. It can help us minimize the risk of surgical errors and complications in other surgical patients in the future.

METHODS

It is a prospective study that was carried out at our tertiary care facility. It was divided into two phases. After approval from the Institutional review board (IRB) the first phase of this study was started. In the first phase, compliance with the WHO safe surgery checklist was observed for 1 month. A total of 123 patients were included in the first phase. All the consenting patients who underwent any surgical procedure in that month were included in the study. A questionnaire based on the WHO safe surgery checklist was used to check the compliance. The questionnaire was designed in English as well as in our local language. The nursing staff, anesthesia team, and surgical team were educated regarding the questionnaire. The questionnaire was divided into three parts i.e. sign in (before the induction of Anastasia), time out (before the skin incision),

and sign out (before the patient leaves the operating room). A total of 31 components i.e. 11 components of sign in, 11 components of time out, and 9 components of sign out were included in the study. After the completion of the first phase, a presentation was done in which results were shared with relevant professionals. The second phase of the study will be carried out to assess the change in compliance after our surgical audit. Statistical analysis was done using SPSS with a t-test. A P-value of less than 0.05 was considered statistically significant.

RESULTS

The study included a total of 123 patients, the 'Sign in' checklist compliance was checked in 50 of these patients, the 'Time out' checklist compliance was checked for 39 patients and the Sign out checklist compliance was checked in 34 patients. The sign in checklist was fully implemented in 35 of 50 total patients (70%). The time out checklist was fully implemented for 1 of 39 total patients (2.6%) and the Sign out checklist was fully implemented for 0 of 34 total patients (0%).

Most skipped components (questions) in the SSC: (# of patients; percentage of patients in the cohort)

Sign in:

• Site o/ procedure marked? (9 patients; 18%)

• Blood loss (>500mL) risk assessment done? (9 patients; 18%)

SIGN IN CHECKLIST:

- Was sign in of WHO checklist performed in pre-op (transfer) area?
- Were questions from sign in part of WHO checklist asked and ticked off immediately?
- Identity of the patient confirmed?
- Site of procedure marked?
- Procedure name confirmed?
- Consent form signed by patient and attendant?
- Anaesthesia safety check completed?
- Pulse oximeter attached on patient and vitals monitoring done?
- Difficult airway/aspiration risk assessment done?
- Blood loss (>500mL) risk assessment done?
- History of any drug allergy confirmed by patient?

The sign in checklist: components filled for all patients (green), components unfilled in at least 1 patient (red)

Time out:

• Did OR members introduce each other and confirm their roles? (34 patients; 87.17%)

• Were answers audibly verified and immediately written documentation upon response was done? (17 patients; 43.6%)

Sign out:

• Was there any equipment/instrument issue addressed by team? (31 patients, 91.2%)

• Was sign out performed before skin suture? (26 patients, 76.5%)

TIME OUT

- Was time out performed in OT before skin incision?
- Did all the OR team members introduce themselves to each other and confirm their roles?
- Did the surgeon, anaesthetist and nurse verbally confirm the patient, site and procedure?
- Did the surgeon review the operative duration, critical steps and anticipated blood loss during surgery?
- Did the anaesthetist review any patient-specific concerns?
- Did the nursing team review the necessary equipment and confirm sterility?
- Was antibiotic prophylaxis given to the patient within last 60 minutes?
- Was essential imaging (X-ray, CT scan etc.) displayed?
- Were checklist items ticked off immediately afterwards?
- Were the answers audibly verified and immediate written documentation upon response was done?
- Was the end of time out announced audibly

The time out checklist, filled components (green), unfilled

SIGN OUT:

- Was sign out performed before skin suture
- Was there an audible announcement of sign out by an OT team member?
- Did the OR nurse confirm the name of the procedure with the team?
- Did the OR team confirm the name of procedure with the team?
- Was the specimen labelled correctly including patient name?
- Was the any equipment/instrument issue addressed by team?
- Did the surgeon, anaesthetist, and nursing team review the key concerns about recovery and management of the patient?
- Were the checklist items ticked-off immediately afterwards?
- Was the end of sign out announce audibly by the surgeon and confirmed by the Anaesthetist or operation theatre nurse?

The sign out checklist, filled components (green), unfilled components (red)

DISCUSSION

In our study, the compliance with the checklist was highest for the sign-in, lower for the time-out and no successful

completions of the checklist were observed for the Sign out checklist. Reshma Ambulkar et. al. conducted an observational study in a tertiary level cancer hospital in India to evaluate the implementation of the adapted SSC checklist in 352 patients undergoing surgery [3]. Compliance in that study was highest for the first part (100%), lower for the second part (78%) and lowest for the third part (76.5%). This reduced compliance for the third part of the checklist is consistent with the results from studies done in the Western world where the completeness of the checklist was lowest for the third part. Ambulkar et. al. concluded that Members of the OT team 'relatively unoccupied' for sign-in and occupied with a sensitive surgical procedure for the other parts hence the reduced compliance in those sections. The results of this study, therefore, had a similar pattern to our study except the compliance rates were higher for all 3 parts of their checklist.

In a local study, Mariyah Anwer et.al evaluated the compliance and effectiveness of the SSC at the Jinnah postgraduate medical center (JPMC), Karachi. The study included 3638 patients and was performed over four years[4]. The study successfully used three main methods of improving compliance with the SSC over the four years; the SSC was made a part of the ward file, surgical teams were educated by presentations on filling and files were later checked for compliance. The study showed a dramatic improvement in compliance with the SSC over four years (20.4% to 89.9%). This was associated with a reduction in surgical site infections (SSI) in patients over the four years as well from 7.5% in the first year to 2.12% in the fourth year. It was also concluded that the evaluation of the team's compliance was as important as the outcome. Therefore it is evident that simple measures can be implemented to improve compliance with the SSC with benefits such as a reduction in SSI and patient morbidity.

Brigid Brown et al conducted a study that used the quality improvement principles of identifying the problem and designing strategies to improve SSC compliance at Flinders Medical Centre (FMC), Adelaide, South Australia[5]. This study also showed poor compliance with the SSC with the poorest adherence to the third stage of the checklist. The study found that the SSC process was conducted correctly and in its entirety in just 3.5% of surgical cases but documented as 100%. A staff-wide education program was performed concurrently with an overhaul of the existing SSC checklist including the creation of a new form with modifications for better compliance with WHO standards. A laminated secured form of the SSC was attached to metal boards in all operation theatres to be filled during each procedure to promote better team participation and coordination in filling the SSC. Four separate assessment and improvement cycles (PDSA cycles) were performed for improvement and assessment. These focused on educating the staff, receiving feedback, specifically improving compliance to particularly overlooked elements of the SSC, and assessing the benefits of the program. The compliance to the SSC was improved from 3.5%- 63%, with stage 1 compliance ultimately improving to 99%. Staff specifically commented that all teams were more involved in the process and that verbalizing team members' names were useful, noting an improved knowledge of their team. The study showed a reduction in near-miss events such as lack of consent, wrong surgical site, and faulty equipment. Similar methods could be implemented in all health institutions to improve surgical safety through the implementation of the SSC.

CONCLUSION

Our study found that the overall compliance to the SSC at Shalamar Hospital was poor with the 'Time out' section being completed in none of the patients that were observed. Similar patterns have however been observed in institutions around the world and significant improvement can be made through the implementation of measures to improve SSC compliance. The improvement of SSC compliance is essential in preventing potentially disastrous outcomes in all surgeries

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Archives of Surgical Research | Review Article

Role of Artificial Intelligence in Management of Thyroid Nodule

Muhammad Wakeel, Rabia Maryam, Muhammad Waleed Amjad, Hira Ashraf

IMPORTANCE Prevalence of thyroid diseases is increasing globally. Detection of thyroid nodules using diagnostic imaging relies heavily on physicians' expertise. Development of artificial intelligence (AI) approaches has led to significant advancement in visual identification. Machine learning and radiomic are approaches of artificial intelligence that have the potential to improve clinical diagnosis. AI approaches can be used to detect biological anomalies, diagnose neoplasms, and predict response to therapy. However, diagnostic accuracy of these approaches is still a point of contention. Aim of this article is to give a general review of aspects, limits, and key challenges in use of artificial intelligence for thyroid imaging. Core principles and process parameters of learning algorithms, cavernous learning, and technological frontier as well as data processing criteria, distinction between AI approaches, and their constraints are discussed in this article.

KEYWORDS Artificial intelligence, thyroid nodule, imaging evaluation, radiomic, diagnosis.

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Review Article

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Role of medical imaging in healthcare has shifted from a screening tool to a significant contributor in early diagnosis and assessment of illness, patient management, and surveillance[1]. Medical imaging is a non-invasive, reproducible method of obtaining information about properties of human tissues[2]. In recent years, advancements in medical imaging focused on equipment modification (hardware) and analytical techniques. Primary application of medical imaging in clinical practice is qualitative evaluation of anatomical locations[3]. Furthermore, images characterized by a large amount of statistical information, and quantitative assessment create ability to detect possible links between statistical information included in digital photos and tissue pathology. Statistical method aims to extract details from images obtained through magnetic resonance imaging (MRI), computed tomography (CT), ultrasound imaging (US), and positron emission tomography (PET), which otherwise pose difficulty in quantifying health outcomes with naked eye observation[4].

Image characteristic analysis in medical imaging has become a topic of interest[5]. Attributes of imaging are evaluated in most studies with goal of detecting and diagnosing aberrant locations inside body tissues. Computer-aided detection (CAD) and computer-aided diagnosing (CADx) technologies are terms used to describe these operations. Doctors employ CAD assessment output in identifying lesions or making diagnoses with aim of boosting diagnostic performance and decreasing picture-processing duration[6].

Radiomics has emerged as a promising world of clinical study because of a more comprehensive development linked with statistical medical image analysis[7]. Radiomics tries to obtain relevant information regarding tissue damage and reaction through large set of numerical parameters of personalized medication[8]. Artificial intelligence (AI) technology is used to achieve partial or full automation of different aspects of medical image processing procedures. A complete understanding of its functioning principles is required to create effective forecasting analytics and customized treatments[9]. Goal of this article is to study benefits and drawbacks of many AI-based methodologies used to assess pathological status of thyroid[10].

RELATIONSHIP BETWEEN ARTIFICIAL INTELLIGENCE AND MEDICAL IMAGING

In 1950s artificial intelligence (AI) described an area of computer engineering which used statistical procedures

requiring human cognitive processes to execute activities [11]. AI applications have had tremendous growth over the last decade because of advances in computer capacity and datasets accessibility. Artificial intelligence is used in healthcare to construct models that may increase diagnostic performance, prediction, and medical imaging interpretation[12]. In the subsequent sections, we will go through two separate machine learning (ML) approaches that are used for assessment of diagnostic imaging[13].

MACHINE LEARNING

Machine learning (ML), named by Arthur Samuel[14] is a type of artificial intelligence in which computers are trained to predict outcomes based on exposure to previous examples and observations. Machine learning algorithms are essential component of CAD systems and radiomics research. Unsupervised learning and supervised learning are types of machine learning. A tagged database or a set containing input information with matching output (labels) is required for reinforcement. Unsupervised machine learning works without labelling input sequence. This machine learning technique uses patterns and regularities in raw data to divide it into subgroups with similar attributes[15]. We concentrated on reinforcement methods in this review article because it is the most common strategy used to analyze medical images[16].

Output label can be used to differentiate benign and malignant tumors, categorize diseases, or study response to treatment, such as recurrence or longevity. Prediction model distinguish between two types of machine learning tasks: categorization and extrapolation. In classification techniques, a binary classifier is used to judge from a narrow and distinct set of options, such as determining benign and malignant tumors. Prediction model is used to estimate continuous output results, such as disease intensity evaluation. Machine learning algorithms are used in CAD systems for categorization. This technique is employed as a stage in radiomic assessment[17].

A guided machine-learning model has two main phases: training and implementation. Prediction model is trained by using sets of input photos and their corresponding labels. Qualified physicians draw region of interest (ROI) from source images either physically or semi-automatically. Subsequently, a series of feature representation is retrieved, such as morphological and grey threshold characteristics. Identification and evaluation of picture characteristics in ML algorithms is done manually by an experienced personal. It is a necessary step in determination of significant features linked to clinical outcome. Characteristics employed in design tools are used in diagnosing lesions[18]. These features are then fed to the machine-learning model.

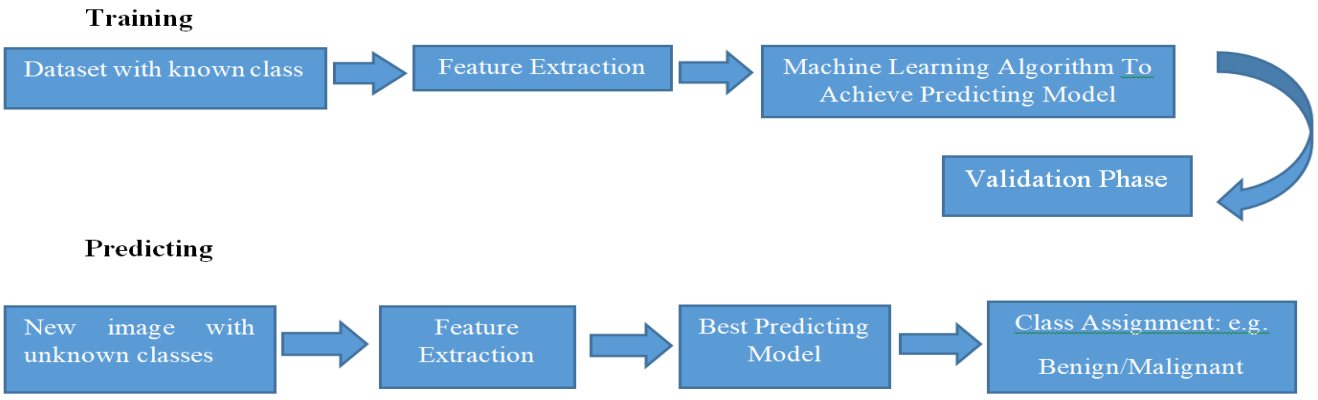

Figure 1. Schematic flowchart of the machine learning model implementation and application for medical image classification purpose.

Logistic regression analysis supports vector machine. Regression trees, and artificial neural are common examples of functionality supervised learning methods. Support vector machine (SVM) approach is extensively employed in biological binary classifier issues and it is an example of these functionality ML techniques. SVM is a classification method used to find maximum margin or higher dimensional space to optimize separation distance between two classifications. Minimization of boundary condition enhances distance between the two categories, classifier's generalization ability and matching efficiency.

This framework is then used to describe input values with undetermined label in the testing stage. It is worth noting that continuing to practice fully specifies classifier's conditional probability, but testing set is merely used to assess effectiveness of the algorithm. It can create a design that fits adequately once implemented to a new dataset.

Supervised learning should be vastly adequate. Testing set ought to be reasonably extensive to provide a consistent and trustworthy assessment of model's effectiveness. A k-fold cross-validation framework[19] is generally used because it's hard to fulfil requirements in medicine by simply partitioning existing evidence into training and testing sets. Database is partitioned into K equal-sized subgroups for K-fold testing data. Model trained on (k 1) observations with one subset is kept for testing. The process is rehashed k times among each fraction employed once as a testing dataset. Model's total effectiveness is then evaluated as standard result across K iterations. Forecasting is generated from minimal datasets. Machine learning algorithms are useful in clinical picture assessment. Furthermore, these approaches are frequently subjected to interpretation for obtaining information regarding a form of anticipation.

Description	Cohort	Method	Performance	Reference
Classification Benign/ Malignant Thyroid Nodules US	106 Patients	SVM	Accuracy 82% Sensitivity 91% Specificity78%	[20]
Classification Benign/ Malignant Thyroid Nodules US	286 Patients	SVM	Accuracy 75.9% Sensitivity 90.4% Specificity 58.8%	[21]
Classification Benign/ Malignant Thyroid Nodules US	826 Patients	SVM	Accuracy 83% Sensitivity 86.1% Specificity 82.7%	[22]
Classification Benign/ Malignant Thyroid Nodules US	50 Patients	SVM	Accuracy 84.6% Sensitivity 80% Specificity 88.1%	[23]
Classification Benign/ Malignant Thyroid Nodules US	118 Patients	SVM	Accuracy 98.3% Sensitivity N/A Specificity N/A	[24]

Table 1. Machine learning (ML) based studies.

Professionals should execute preliminary phase of the process, such as defining attributes to be retrieved from photos and selecting clinical objects of interest. Furthermore, all guided machine-learning approaches are influenced by imbalanced datasets. It occurs when prediction model precisely understands training dataset but fails to fit fresh data from validation dataset. Nevertheless, this problem can be mitigated by using a cross-validation setup and feature selection technique.

DEEP LEARNING

Deep learning (DL), named by Rina Dechter in 1986, is a new approach of machine learning (ML) established through growth of convolutional neural networks. DL is based on networks of computing elements, such as neural units stacked in levels, that retrieve greater features from input information. These frameworks automatically analyze exclusion characteristics from information, thereby, allowing to mimic complex non-linear relationships with enhanced precision. Unlike previous feature-based ML techniques, DL can accomplish diagnostic mechanization without need for human interaction. DL methods are used for detection and evaluation of tissue lesions, and investigation of pathogenicity. Amongst numerous DL architectures is LeCun's introduction of convolutional neural networks (CNNs)[25].

CNNs maintain spatial relations in 2D data and exceed alternative topologies in picture pattern classification which is commonly used in object recognition and computer vision. CNN's feed is organized in a grid layout and analyzed through convolution operation layers to maintain associations. Based on characteristics collected mechanically by convolution section, the layers are often linked intrinsically and it is considered multi-layer discernment classifier. The system is designed to spot similarities and responses to a set of labelled training data. Network weights is tweaked during learning until connections are detected by system to reflect decent training data. System uses additional data in testing set to create forecasts[26].

Convolution is a space-invariant continuous procedure on 2D grids analogous to filtering images. Filters are dragged across source images and results are multiplied by image pixel values. They are combined to measure value of extracted feature map's associated place. Figure 3a provides an illustration of Fourier procedure. CNN hyper parameters including quantity and quality of filtration are often not tuned during acquisition. Increasingly efficient networks raise danger of overloading with greater number of variables to tune which result from bigger filters [27].

Activated function is applied component by component to calculated combination of output, utilizing map as an input for next step of system. Rectified linear unit (ReLU) is amongst the most utilized kernel function and has shown to speed up learning process statistically[28]. Affirmative inputs are linear and map unmodified to the next level while lower values are blocked. ReLU can be stated

mathematically (x) = max (0, x) (4) where x is a result gathered from last layer's activity[29].

Some clustering algorithms consider pooled procedures. This procedure takes tiny sections of input map in account and returns a single statistic. It lowers dimension of feature map and number of pixels to be analyzed in network's subsequent layers[30]. Neuron stimulation values indicate increasingly higher and significantly bigger fractal geometry in input as we travel further in the networks and demand lesser spatial resolution. A completely connected layer describes final component of CNN model, i.e., each neural component in current layer is linked to neural unit in next layer. The subset of features is compressed into a column vector and linked to one or even more fully associated levels. Features extracted from last fully linked layer represent an array of unnormalized probability. Soft-max function is defined as CNN's last convolution layer which convert values of k vector to a range of values (zero;1).

Neural units that make output layer of CNN represent chances for each category. Analysis of relevant literature points at a growing interest in using DL for medical image representation[31]. Simplified functionality ML algorithms, such as SVM methods, are easier to interpret and much

more efficient for specified set of image elements. Set back in using DL is requirement of enormous datasets for training the model. Medical datasets in United States are scarce compared with standard datasets in other fields. Numerous investigations looked in pre-trained architecture constructed with ImageNet (a huge and labelled library of low-resolution color photographs) to meet information requirement[32]. Till date, there is no DL architecture on high-resolution medical images. Therefore, a large collection of medical images is required to improve performance.

Description	Cohort	Method	Performance	Reference
Malignancy risk thyroid nodules	757	CNN	Accuracy 85.1% Sensitivity 81.8% Specificity 86.1%	[33]
Classification Benign/ Malignant Thyroid Nodules US	1396	CNN	Accuracy 82% Sensitivity 85% Specificity 78%	[34]
Classification Benign/ Malignant Thyroid Nodules US	695	CNN	Accuracy 80.3% Sensitivity 80.6% Specificity 80.1%	[35]
Classification Benign/ Malignant Thyroid Nodules US	221	CNN	Accuracy 75% Sensitivity 84.9% Specificity 69%	[36]
Nodule detection predicted malignancy level stratification	1230	CNN	Accuracy N/A Sensitivity 87% Specificity 52%	[37]
Classification Benign/ Malignant Thyroid Nodules US	519	CNN	Accuracy 87.3% Sensitivity 90% Specificity 82%	[38]
Classification Benign/ Malignant Thyroid Nodules US	286	CNN	Accuracy 86% Sensitivity 91% Specificity 80%	[21]
Classification Benign/ Malignant Thyroid Nodules US	276	CNN	Accuracy 90.3% Sensitivity 90.5% Specificity 89.91%	[39]
Classification Benign/ Malignant Thyroid Nodules US	17627	CNN	Accuracy 86% Sensitivity 84% Specificity 87%	[40]
Classification Benign/ Malignant Thyroid Nodules US	592	CNN	Accuracy 96.3% Sensitivity 82.8% Specificity 99.3%	[41]
Classification Benign/ Malignant Thyroid Nodules US	4782	CNN	Accuracy 83% Sensitivity 82.4% Specificity 84.9%	[42]

Table 2. Deep learning (DL) studies.

RADIOMIC Radiomic is a new discipline that uses automatic extracting methods for extraction of huge numbers of measured values (200+) from medical imaging. Quantitative imaging is another term for radiomic and it can be applied to any medical image. It is used to treat tumor subareas, metastatic lesions and healthy cells[43].The

term feature refers to descriptor of an image, such as parameters generated from grayscale intensity, shape of tumor or healthy tissue. Radiomic is based on machine diagnostic techniques albeit methodological approach and implementations are different. It is about extracting quantifiable features from medical pictures that are linked to biological objectives and clinical relevance. Radiomic uses digital information stored in images to create diagnosing, predicting, and prognosis methods that can help clinicians in judging and arranging more individualized treatment. Primary distinction between radiomic and CAD technologies is the connection that radiomic must establish among current features and progression of tissue lesions to customize treatments[44]. Depending upon AI methodology two procedures are used to undertake radiomic experiments. In traditional or ML-based radiomic characteristics are preset for retrieval, while, in DL-based radiomic characteristics are not specified and retrieved from data autonomously.

Region of interest (ROI) is selected from USG, CT, MR, and/or PET images and subsequently lesion is segmented manually, i.e., delineated with computer-assisted remodeling performed by a skilled practitioner[45]. Picture data is subjected to preprocessing, such as gray-level partitioning, to improve reproducibility of results. Characteristics of spatial interaction between various saturation levels, diverse structures, shape, and links of tissue lesion with surrounding structures are all employed to extract statistical imaging features. Most significant predictive characteristic is subsequently identified using a feature evaluation approach. A characteristic profile, also known as quantitative imaging biomarker, has several benefits with predictive or qualitative research. Selected traits are examined to create categorized models for predicting consequences alone or in conjunction with other data, such as demographics, comorbidities, or genetic data[46].

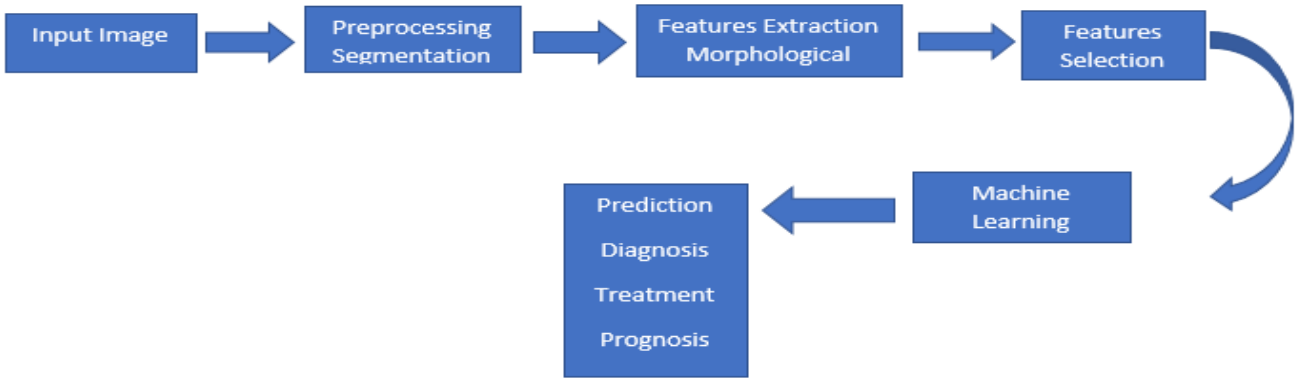

Figure 2. Schematic flowchart of radiomic approach.

Segmentation is an essential requirement in radiomics since many retrieved characteristics are dependent on region of interest[43]. Specialists physically draw ROI in various radiomic investigations. A few methods have been devised for semi-automatic categorization. Use of geographical area algorithm and grey-scale cutoff point method is common for ROI identification. Manual demarcation by a professional is considered gold standard despite time-consumption and sensitivity to interobserver heterogeneity. Team of physicians or multiple methods can be utilized to eliminate potential bias.

Radiomic properties are classified as morphological. It is predicated on the ROI's geometric parameters, such as volume, largest surface area, and circumference[47]. First-order estimates, also known as histogram statistics, characterize dispersion of grayscale intensity using histograms without regarding spatial relationships within ROI. Grey level refers to maximum, minimum, and percentiles. GLCM displays number of times same intensity combinations appear in two pixels divided by certain length in a particular direction[48]. Wavelet or Fourier transformations are examples of transformation and filtration that show recurring motifs, histogram-oriented trends, or local derivative patterns. Image biomarker standardization initiatives (IBSI) provide explicit definition of radiomic characteristics[48].

To avoid overfitting learning precision is enhanced and calculation time is decreased. Radiomic features are exposed to a feature representation. Glitchy, non-informative, or duplicate characteristics should be

eliminated throughout recruitment process. Method of selection is divided into three categories. Methods which evaluate utility of a given feature using range of data tests to determine relationship with end characteristic are discussed in this article.

Wrapper procedure scores distinct subsets of features. These features are predicated on their classification results using an exterior classification technique. It is an engrained method where feature extraction is innate to model training, i.e., features are selected to optimize performance of proposed learning algorithm[49]. Filter approaches are simple, clear, and efficient but they treat characteristics as separate entities without interactions. Wrapper approaches have lesser risk of generalization but require more computing power[50]. Embedding is more efficient and robust since selection technique is part of training process. Least absolute contraction and choice activator is a common integrated algorithm used in radiomic investigations.

Selected attributes used to create a statistical model can predict the known medical outcomes. Selection of a good modelling methodology has a certain criterion, including sample and study outcome. It is beneficial to add variables in the model other than radiomic, such as clinical data and/or other "-omics" including genetic information[51]. Mathematical formula makes it easier to construct a personalized care by incorporating data from numerous sources, such as medical imaging, disease conditions, therapy, and follow-up details. As previously stated, radiomic investigations are used to determine either a current characteristic (tumor phenotype) or forecast a prospective (therapeutic efficacy)[52]. Characteristically,

radiomic research employs feature-based ML algorithms. In functionality ML algorithms link input data and intended outcome through training process. SVM algorithm is amongst the most commonly used. Use of DL-based radiomic enables extraction of feature representation to give desired outcome. All processing stages outlined in ML-based model are performed by various components of DL framework including extraction features, choice and model execution[53]. Most popular design used in radiomic investigations is CNNs. Evaluation is an essential part of both traditional and DL-based radiomic. Before use training set should be evaluated by cross-validation.

Description	Cohort	Method	Performance	Reference
Classification Benign/ Malignant Thyroid Nodules 730 features extracted and 66 selected US	1609 Patients	ML-Based Radiomic	Accuracy 77.8% Sensitivity 70.6% Specificity79.8%	[54]
Classification Benign/ Malignant Thyroid Nodules US	8339 Patients	DL- Based Radiomic	Accuracy 89.1% Sensitivity 94.9% Specificity 81.2%	[55]
Evaluation of extrathyroidal extension (ETE) in patients with papillary thyroid carcinoma; 479 features extracted; 10 features selected US	132 Patients	ML-Based Radiomic	Accuracy 83% Sensitivity 65% Specificity 74%	[56]
Evaluation of extrathyroidal extension (ETE) in patients with papillary thyroid carcinoma MRI	102 Patients	ML-Based Radiomic	Accuracy 79% Sensitivity 75% Specificity 80%	[57]
Classification Benign/ Malignant Thyroid Nodules US	106 Patients	ML-Based Radiomic	Accuracy 75.5% Sensitivity 69.7% Specificity 78.1%	(Zhao et a., 2021)

Table 3. Radiomic studies.

AI AND RADIOMIC IN THYROID DISEASES

Ultrasound imaging is the preferred approach for identification and treatment of thyroid abnormalities due to cost effectiveness, efficacy and lack of radiation exposure. It is widely recognized as the first imaging tool for detection of thyroid diseases. Artificial intelligence (AI) technologies are gaining popularity in medicine and playing a role in decreasing invasive diagnostic practice[58]. AI algorithms are mostly used to classify thyroid nodules as benign or malignant. Conclusion of these investigations contrast to radiologists' diagnoses. A study shows DL ability in capturing complicated patterns owing to significantly improved selectivity and precision when compared to feature-based ML traditional applications[59]. DL algorithms have shown results comparable to radiologists' conclusions in various investigations. Moreover, Jin et al. stated that

application of computer algorithms enhances detection accuracy of novice radiologists and makes it comparable with transitional radiologists[60].

Radiomic is a viable tool for incorporating personalized medicine based on patient's personal qualities. CAD system focuses on distinguishing benign and malignant thyroid lesions, while, radiomic expands assessment to prediction and treatment success[57]. In addition, radiomic algorithms are used to examine prognosis and detect thyroid cancer with excellent precision (about 85 percent). Use of radiomic to ascertain tumor phenotypes or genetic mutations can be beneficial.

Radiomic characteristics have been studied to assess prevalence of metastasis or disease-free longevity[61]. Radiomic investigations aiming at classifying types of thyroid nodules are less reliable than traditional ML approach. It is worth mentioning that studies on thyroid lesions are still restricted. Table 3 enlists relevant studies of radiomic application for thyroid lesions.

DISCUSSION

Imaging techniques provide thorough details about tumors and play a crucial role in early-stage diagnosis, differentiate benign and malignant lesions, quantify risk and improve treatment outcome. Imaging is a non-invasive technique while biopsies being invasive techniques have risk of exposure to pathogens. Since past few decades medical images are transformed into statistical data and evaluated with AI techniques. Tumor samples gathered by biopsy may not accurately reflect changes in tumor since neoplasms exhibit intra-tumoral diversity62. AI approaches analyze entire image of a disease and have the capability to capture heterogeneity of tumors. AI can serve as a bridge between imaging and biopsy. However, AI systems require data of case-to-case variation for training. Inter-variability in patients makes it challenging to develop an AI system with accurate diagnosis of pathological conditions. Furthermore, prediction model is constructed using a constrained classification model[63]. Since, living cells have distinguished heterogeneity in inter-subjects and intra-subjects, limited training dataset cannot adequately represent range of cases that can arise in healthcare. Research is required to enhance generalization and precision of AI-based models. Dependence on AI technology for diagnosis is discouraged in healthcare system.

Various researches recommend that assessment of lesions should be done by both clinicians and use of ML or DL methods[64]. AI researches on thyroid diseases have used prospectively obtained data. In contrast, a few researches in this field have systematically tested AI prediction models for thyroid disease assessment. In retrospective research, cohorts are chosen amongst patients diagnosed with histological evaluation[21].

Additional research on AI models is required to reduce risk of generalization and enhance consistency of treatment outcomes. AI approaches rely on study of visual information to construct prediction models. ML is mostly used to distinguish between benign and malignant thyroid nodules. A study shows that TI-RADS method is effective in distinguishing benign and malignant thyroid nodules. Certain traits, such as calcifications and internal material, constitute a component that enhances reliability[56].

Retrieved characteristics in this research are morphological, first-order analytics, sensory, and elevated statics[65]. Wang and coworkers found that ETE diagnosis improves when factors associated to PTC diversity are considered. Guo et al., 2020 studied thyroid cartilage infiltration from laryngeal and hypopharyngeal squamous cell carcinoma and examined tumor interstitials while considering tumor heterogeneity. BRAF mutation can be studied using histogram-based and texture characteristics that indicate location of echogenicity and heterogeneity[66].

Various researches compare effectiveness of AI-based algorithms and capability of experienced doctors. Research shows that performance of DL algorithms is generally comparable to medical practitioners[67]. AI applications may improve precision of thyroid diseases diagnosis, particularly for junior radiologists. Evaluation of medical imaging by radiologists is strongly dependent on level of expertise. Responsiveness of junior radiologists is around 40% and 100%. While, precision ranges from 50 percent to 100 percent. Use of AI algorithms for characterization of thyroid lesions increases precision of junior radiologist from 82% to 87%. Peng and associates reported that using AI as feedback decreases fine needle aspiration by 27% and number of undetected cancers by 2%. Moreover, level of expertise of doctors has significant impact on performance of AI-based approaches[68].

ROI serves as input information for AI algorithms. Due to inter-operator heterogeneity in capturing images and classifying them it is widely regarded as essential sub-process[47]. Current findings suggest that semi- or completely automated approaches can increase performance of algorithms, however, detection and segmentation by specialists is still the most common practice. Most of ML-based thyroid investigations are

associated with manual ROI segmentation. ML-based studies have established a semi-automated strategy in which initial automatic classification of a box-interconnected world relies on manual contouring by trained clinicians. In contrast, studies based on DL algorithms for imaging of thyroid gland used a manually selected box in area of interest[69]. Radiomic findings focused on hand contouring along boundary of thyroid tumors in order to eliminate artefacts [70].

Gilies and collaborators[44], provide an empirical rule to limit size of data in radiomic studies to avoid overfitting. It stated that roughly 10–15 patients are required for each radiomic feature under investigation[71]. AI approaches can help clinicians improve their diagnostic choices in future. When these approaches are combined with other "-omic" information they can help improve health risk assessment for personalized illness survival prediction[72]. Several initiatives have been taken to increase availability of an open-access library of annotated medical pictures to aid in the development of Intelligence forecasting analytics[73]. Improvement in Intelligence performance is a field of interest in United States[72]. Ultrasonography (USG) is widely recognized as the most important imaging method for evaluating thyroid nodules. US's has high sensitivity and specificity in differentiating benign and malignant thyroid lesions.

Significant number of thyroid goiters are found incidentally during non-thyroid imaging assessments (e.g., CT, MR, and PET/CT)[74]. These imaging processes have a poor or subpar ability in identifying benign and malignant tumors in adrenocortical thyroid epistasis, hence, substantial effort is being made to enhance their potential in recognizing patient's need for an urgent or non-urgent endocrine evaluation coupled with in-office US examination.

CONCLUSION

Medical imaging has a significant role to play in healthcare. Medical imaging assists doctors in deductive reasoning, understanding of pathological processes and assimilation of findings from previous investigations. Detection of thyroid nodules using diagnostic imaging relies heavily on physicians' expertise. Development of artificial intelligence (AI) approaches has led to significant advancement in visual identification. AI techniques can be used in healthcare to improve assessment of medical imaging. AI approaches can be used to detect biological anomalies, diagnose neoplasms, and predict response to therapy. However, diagnostic accuracy of these approaches is still a point of contention.

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Archives of Surgical Research | Perspective

Surgical Training in Pakistan: Time to Move to Specialty Based Practice

Awais Amjad Malik

IMPORTANCE Surgical training in Pakistan has been following the Halstedian model of training. Today the number of hospitals training surgeons in Pakistan has increased. Although commendable this has a huge downside to it. There is a growing perception among the surgical community that we are not moving fast enough to adapt to the rapidly changing needs. College of Physicians and Surgeons of Pakistan (CPSP) has commendably incorporated such elements of the structured training program however quality assurance of these programs at the training institute level has struggled. There is a growing need for improving the quality assurance of residency programs especially at the training institute level.

KEYWORDS Surgical Training; Pakistan; Structured training.

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Perspective

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Pakistan is a country where the burden of surgical conditions is increasing. With more and more people having access to health care there is a need to provide adequately trained surgeons to the system[1]. This has led to an increasing number of hospitals providing training in surgery. At the time of its establishment in 1947, Pakistan had only three undergraduate medical colleges and no local pathways for postgraduate certification[2]. Today the number of hospitals training surgeons in Pakistan has increased to 123[3]. Although commendable this has a huge downside to it. There is a growing perception among the surgical community that we are not moving fast enough to adapt to the rapidly changing needs.

Training in Pakistan was considered to be at par with internationally trained surgeons in the 80s and 90s. But we have failed to adequately adapt to changing times. Why is our surgical training lagging behind and how can we quality assure it? There is a multitude of reasons being cited. Is it the system, the trainers, or the trainees? While all factors can be accounted for and there is extensive debate regarding this suboptimal adaptation to change; however, one thing is unanimously agreed that the system needs to improve. In fact, this change has now become inevitable.

Surgical training in Pakistan has been following the Halstedian model of training[4]. The "see one, do one, teach one" model of training has been training surgeons for almost 100 years. The acquisition of surgical skills in this model relies on a model based on apprenticeship. Trainee surgeons spend a fixed amount of time in a surgical unit and rotate through a few other specialties to acquire surgical skills. During these attachments, surgical trainees are supervised by senior trainees and the consultants running the unit. The acquisition of skills through this method is difficult to guarantee, measure and test. There are a lot of varying levels of training among units and the system has struggled with standardization. The exposure to laparoscopic and minimally access surgery and recent advances in neither standardized nor optimal. The assessment methods need improvement and need to test the skills and clinical judgment apart from a cognitive portion of learning in a more robust manner. Failure to do so affects the overall performance of an independent surgeon or consultant, especially in the periphery where supervision and lateral support is minimal or none.

There is a growing thought and inclination to change our residency structure in the surgical community and everyone feels the need for it. Fortunately, we can look at the West and the Far East for incorporating changes in our residency programs. Although, there are differences in the dynamics of our healthcare structure, however, still these structural changes can be adapted to our requirements. Surgical training in the UK has undergone major reforms over the last few decades. The UK has given up on the Halstedian model. They have not completely abolished it but have defined goals. The long protracted unstructured career path has been slowly replaced by a shorter more structured surgical

curriculum. The program has been improvised by the achievement of competency-based education, simulation-based training, periodic assessment, and non-technical skill enhancement. The introduction of the Specialist Registrar grade in 1993 was the first step in these reforms[5]. This was followed by the introduction of the new Intercollegiate Surgical Curriculum Program (ISCP) in 2007[6].

Another very important step taken up by the NHS is how the in-training doctors are assessed. One single exam can never assess surgical competence. The move towards work placed based assessments has increased accountability among the surgeons and has led to better-trained surgeons. Workplace-based assessment (WPBA) has ensured that each trainee is evaluated while in training. This puts pressure on the supervisors as well as the trainees and leads to improvement in training. WPBAs ensure that the system produces adequately trained surgeons with a focus on competence rather than just volume[7].

College of Physicians and Surgeons of Pakistan (CPSP) has commendably incorporated such elements of the structured training program however quality assurance of these programs at the training institute level has struggled. There is a growing need for improving the quality assurance of residency programs especially at the training institute level. The training units need to have an adequate number of these procedures which have been defined as part of their curriculum. Another issue is the number of trainees. What used to be 4 to 6 residents per unit is now 20 plus residents in each unit[8].

Another important issue is the duration of training. Pakistan has one of the shortest training time for becoming a surgeon, which leads to under-exposure to the number of procedures required to achieve the required competence level. Elsewhere the training period ranges from 5 to 7 years[9]. The UK has introduced a 2-year foundation training followed by 3 to 4-year specialty training. The introduction of specialty training came with improved evaluation and assessment of surgical training. This new curriculum added the concept of competency-based training and assessment. The curriculum has set standards for what trainees should know, be able to do, and be committed to. The training program assesses the progress of trainees in terms of clinical judgment, technical and operative skills, specialty-based knowledge, and generic professional skills.

So how do we bring about an acceptable change in the system? One preposition which has been abuzz for a few years among the surgeons across the country but has never been taken seriously is to make a dynamic shift from General Surgery to supra specialty surgery. The main reason for not having further training programs is the lack of specialized units. The idea is to limit every surgeon to focus only on one supra specialty. So each hospital instead of having different general surgery units will have specialty-based units namely colorectal, upper GI, breast and endocrine, vascular, HPB, and transplant surgery. Each unit will still be dealing with surgical emergencies and basic surgical procedures such as cholecystectomies and hernias. Similarly, one hospital might not have all the specialties and will need to refer special cases to other hospitals. Such as transplant surgery, vascular surgery, etc.

This has a lot of advantages. It will enable the units to develop into high-volume units for a chosen specialty. Higher volumes improve surgical outcomes[10,11]. The residents will be a part of a common pool and will be required to rotate for the first 2 years in their parent unit and then for 3 or 6 months through each of the specialties; namely, colorectal, upper GI, breast and endocrine, vascular, thoracic, HPB and transplant surgery. So a resident must complete all his rotations and be adequately exposed to all specialties. The rotations can be on-site or at another hospital but no resident should be allowed to sit the exam unless he/she has completed all the rotations in supra-specialties and scrubbed in a minimum number of required cases to achieve competence.

Similarly having dedicated units can pave the way for supra-specialty training or fellowships in these fields. Currently, CPSP offers supra specialty training in Vascular Surgery, Breast Surgery, and Surgical Oncology[12]. Only breast surgery is being offered in public sector hospitals. No public sector hospital is offering training in surgical oncology or vascular surgery.

The first step thus has to be division of patients among unit on the basis of specialties. This is a big sacrifice on the part of the currently 'in practice' surgeons but that is the only way forward. There is a fear that giving up on general surgery practice will lead to loss of skills and have a negative effect on practice but it has been proven time and again that focusing on supra specialty not only improves outcomes but leads to more referrals and is actually good for practice as well as training[13].

Everyone agrees that you cannot be good at every type of case you operate. The old saying of "Jack of all trades and King of none" holds true for the surgeons as well. Modern-day practice expects the highest possible standards in

patient management. These expectations are unlikely to be met by a general surgeon. If we want to excel and be at par with international surgeons we have to shift towards specialty-based practice. This is not only going to be good for the surgeons but also for the system and most importantly for the surgeons in training.

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Archives of Surgical Research | Perspective

National Licensing Exam: Medical Students' Perspective

Tausief Fatima

IMPORTANCE Assessments play an important role in the process of learning and help in motivating learners. All assessments have different effects during the education process like decisions about grades, the effectiveness of curriculum, placement, instructional needs, advancement, and in some cases funding. Recently Pakistan Medical Commission has started National Licensing Examination (NLE) 2021 under PMC ACT. The PMC is struggling to achieve centralization and standardization of medical education with this exam. There are opposing arguments whether this exam would be able to achieve its objectives. Here, we present the student perspective in this short communication.

KEYWORDS National Licensing Exam, Medical Education, Student Perspective,

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Perspective

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Assessments play an important role in process of learning and help in motivating the learners. All assessments have different implications in the educational process like instructional needs, decisions about grades, the effectiveness of curriculum, placement, advancement, and in some cases funding1. Licensing exams are high-stake exams in medicine to assure the quality of educational goals and learning objectives. In other words, they primarily aim at judging whether students are able to save another life or not. It's not only high-stake for the learner and administration but for the whole society. Medical students take countless high to mid-stakes exams during 5 years of MBBS. Recently Pakistan medical commission started conducting licensing examinations for the 1st time. The National Licensing Examination (NLE) 2021 has been designed under PMC ACT Section 20. It has been developed and will be administered to gauge the ability of MBBS graduates to practice independently2. Passing the NLE (both the theory and clinical skills examination components) is mandatory for obtaining a full license to practice as General Practitioner. The PMC, however, is struggling to achieve centralization and standardization of medical education with this exam.

The major stakeholder in this stance is the medical student and the medical faculty. So, we conducted a survey to assess the perspective of two batches of final-year medical students (outgoing and new). The data regarding the perspective of MBBS students about NLE was collected through WhatsApp. The data was analyzed and is being reported below.

Students mentioned many discussions that have been done in connection with the NLE exam. The purpose of the NLE and final MBBS exam seems similar which is making sure the competencies of the graduating students as a general practitioners. The strongest argument in support of NLE is that it might solve the problems regarding the standardization of the final MBBS exam in medical education in Pakistan. It appears to be the right reason for giving a national-level exam, but this is the wrong way to achieve standardization. Why not make the already existing exam up to the standard? The number of exams given to assess the same objectives will not add to the quality of medical education and will not help in the standardization of this and for that matter any assessment.

Students mentioned many problems with the assessment system of the current medical education in Pakistan. One of these problems is that these exams are based on testing the knowledge component of the learners and these assessments do not assess the workplace-based competency of medical students but just a mere portion in form of "shows how". They mentioned a lack of real skill in teaching and assessment. According to them, NLE will not solve this problem either.

The faculty that constructs the MCQs for the final year MBBS exam is the faculty asked to construct MCQs papers for NLE with the same learning objectives. What difference will it create except to burden the already burdened undergraduates and the faculty? The medical education

system is already troubled from all sides. There is a need to devise policies to make the system better rather than increasing the number of exams but flouting the quality and purpose of the exams.

If we compare the NLE with international exams, it is correct that all developed countries have comparable exams. But the difference lies in the system. USMLE is embedded in the undergraduate program of medical education in the USA. USMLE Step 1 is taken halfway through medical school, then Step II is closer to the end of medical school, and Step III is before the end of their internship (house job) year. It is also worth mentioning that like the USMLE, the UK's licensing examination is introduced and undertaken as part of the medical school degree program. It is not a sequestered examination with an unknown layout and unprofessed outcomes, forced suddenly after graduation. This is what National Licensing Exam is!

The NLE will be conducted twice a year with unlimited attempts if failed by the student and each attempt will cost Rs. 12000/-. Will these six months not be a waste of energy and working hours for doctors and the administrative staff in a resource-depleted country? This is the time for them to work in the periphery, fill the empty seats of doctors, provide health care facilities to the neediest and prepare for further specialty in field of their choice. They will be deprived of practicing the knowledge and skill they achieved in 5 years. There is a need to give motivation to students for this assessment. Either link this to the exam which helps them to pursue the specialty training, or it can replace the final exam of MBBS/BDS.

Another issue that students highlighted about NLE is the sudden implementation of the exam. They claim that this new PMC act cannot be applied to these students as it came into existence after their admission to medical colleges. When we compare this haste with international standards, we see that the Professional and Linguistic Assessments Board test was suggested for the test in 2005 in the UK for the first time and it was officially announced in 2017 which is almost 6 years before the actual exam was conducted. It's quite contrary in Pakistan; the exam is announced and implemented in less than a year. Things done in haste and without taking stakeholders on board are the things that fared even worse.

These are some objections examined here raised by the students and all indicate that NLE is going to be a problem. We cannot stress more on standardization and centralization of assessment of medical trainees. But due to all the reasons mentioned above, it seems a struggle to do the right in a tiring and erroneous way. As a nation we need to meet the world standards, and to do so we need to systematize our medical education to come at par with the international community or Pakistani medical graduates will not be able to practice globally. We might lose the recognition of our medical degree internationally. This would be an alarming situation.

Before I deduce, it is worth mentioning that it is very discouraging for doctors and medical graduates to be treated so amateurishly. They are not only the country's most intelligent, ambitious professionals but also fight on the front line against all diseases. For them to not be heard and simply forced to abide by useless and poorly conceived laws is quite unacceptable.

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Archives of Surgical Research | Case Report

Anesthetic Management of Previously Right Sided Pneumonectomy Patient For Laparoscopic Transabdominal Hysterectomy

Aamir Bashir[1], Muhammad Naveed Azhar[2]

IMPORTANCE Preoperative pulmonary disease is one of the recognized risk factors for postoperative respiratory complications. Lung resection surgeries especially pneumonectomy can lead to significant respiratory complications and can have grave consequences intra-operatively as well as postoperatively. Increasing number of patients require general anesthesia after pneumonectomy but very limited data is available to guide anesthetists. We present a case of 41 years old female who underwent laparoscopic transabdominal hysterectomy and bilateral salpingo-oophorectomy at a tertiary care cancer hospital with previous history of right sided pneumonectomy due to pulmonary tuberculosis. A thorough knowledge and understanding of anatomical and physiological changes after lung resections can help anesthetist to manage these difficult surgical patients to have a safe and uneventful perioperative outcome.

KEYWORDS pneumonectomy; laproscopic surgery; anesthesia management;

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Case Report

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Lung resection especially the pneumonectomy leads to significant respiratory insufficiency in selected number of patients if they have been planned for another surgical procedure. This can lead to increasing risk of postoperative prolonged hospital stay, morbidity and mortality when compared with limited lung resection cases. Considering post pneumonectomy five-year survival rates of more than 75% for benign disease and 40% for malignant disease, published data to guide anesthetist regarding management of laparoscopic surgeries after pneumonectomy is scarce[1]. Considering pneumonectomy, post-operative complications rate could be as high up to 40-60%[2]. Robust preoperative evaluation, optimization, intraoperative invasive monitoring, careful fluid administration and postoperative analgesia planning are key to success. The main aim is to avoid hypoxia, hypercarbia and pulmonary edema along with providing optimum pain control and judicious fluid management.

CASE PRESENTATION

A 41 years old lady with history of lower abdominal pain from last one month, presented for laparoscopic transabdominal hysterectomy and bilateral oophorectomy at Shaukat Khanum Memorial Cancer Hospital and Research Center Lahore, Pakistan. Previous history was significant of pulmonary tuberculosis, thoracolumbar scoliosis and right sided pulmonary decortication followed by right sided pneumonectomy. Detailed pre-operative evaluation, history, clinical examination, and investigations including routine blood investigations, arterial blood gas analysis, chest x-ray and CT scan were done. Anesthetic plan was formulated and discussed with patient and she signed informed written consent for general anesthesia and epidural.

Following WHO safety check list, standard anesthetic monitoring, and lower thoracic epidural catheter was placed. After pre-oxygenation with 100% oxygen, general anesthesia was induced with midazolam, fentanyl, propofol and atracurium, oxygen and sevoflurane. Easy bag mask ventilation, endotracheal intubation with ETT 7.5 mm, confirmed with capnography and secured at 20cm at lips. Mechanical ventilation was commenced with pressure control ventilation with target exhaled tidal volume of 400 ml approximate. Peak pressures were less than 25cm H20. Arterial line was inserted at left radial artery to aid invasive monitoring and frequent arterial blood gas analysis. Pneumo-peritoneum was maintained with at 12-14cm H2O along with progressive Trendelenburg position to avoid sudden increase in airway pressure. Rise in peak pressure was managed by reducing intra-abdominal pressure and tidal volumes. Epidural was loaded with Bupivacaine 0.125%-

10 ml followed by continuous infusion for pain relief. Arterial blood gas analysis was done intra-operatively to guide ventilation strategy. Restricted intravenous fluid was given; urine output was adequate. Moreover, she was given paracetamol and ketorolac along with anti-emetics. Few boluses of phenylephrine were required to maintain blood pressure. The procedure lasted for 3 hours and 40 minutes. At the end of the surgery, after reversal of muscle relaxants, she was extubated fully awake with good head lift. Arterial blood gas was repeated in recovery room, which was within normal limits. After two hours of recovery, she was shifted to Intensive care unit for postoperative monitoring and pain management.

Fig 1: X-ray chest

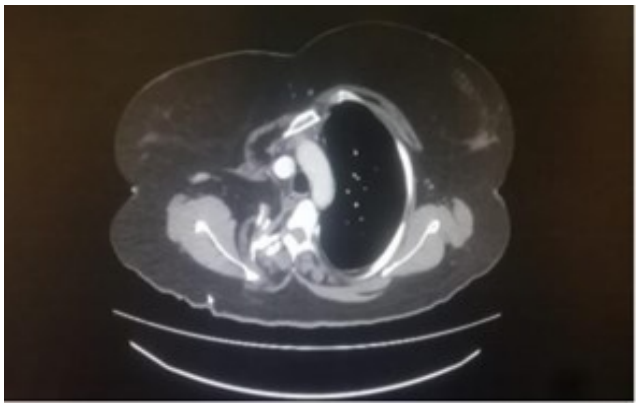

Fig 1b: CT Thorax

	Intra operative	Post Operative
FiO2	0.45	0.4
pH	7.45	7.39
PO2 (mmHg)	88	158
PCO2 (mmHg)	38	38
HCO3 (mmol/L)	25.8	23.1
BE (mmol/L)	1.7	-2.0
HCT (%)	42	33

Table 1: Arterial blood gas analysis

DISCUSSION

Lung resections surgical procedures ranging from video assisted biopsy to more invasive lung lobectomy or total pneumonectomy are performed at specialized centers. These patients are on risk of respiratory compromise during post-operative period and that range from immediate post-operative period to long term complications. These long term complications include various anatomic and physiologic changes as well as mediastinal deviation towards surgical side. There is also compensatory hyperinflation of remaining lung and its herniation across midline. Pneumonectomy also leads to anatomical changes in throracic spine and mild degree of thoracic scoliosis is common in lung resection patients[3] which we saw in our patient as well. Scoliosis also compromise lung functions and leads to difficult epidural catheter placement in such patients. Anatomic site of lung resection surgery also has a significant impact on postoperative complications as for example, right pneumonectomy is associated with a threefold greater chances of mortality when compared with left pneumonectomy[4]. Other postoperative complications after pneumonectomy include broncho-pleural fistula, empyema, pulmonary edema, cardiac arrhythmias, pulmonary artery thrombosis, and the post-pneumonectomy syndrome. One of the major post-pneumonectomy complications is pulmonary edema and it indicates the early onset of hypoxia and respiratory insufficiency. Brunelli and colleagues suggest a routine cardiopulmonary exercise testing before pneumonectomy. Pre-operative evaluation also includes assessment of cardiac status of the patient with the help of echocardiography and more invasive testing where indicated to rule out right heart failure and pulmonary hypertension[5]. Considering surgical options for post pneumonectomy patients, minimally invasive surgical techniques like laparoscopic surgery, would be more appropriate keeping in view the risk of respiratory complications secondary to large abdominal incision and splinting and leading to respiratory insufficiency and respiratory failure. However, carbon dioxide pneumo-peritoneum presents a challenge in a patient with decreased functional reserves and the raised intra-abdominal pressure further compresses the lung, reducing diaphragmatic excursion, lung compliance, and functional residual capacity. Endotracheal intubation is the key to maintain airway but endobroncheal intubation must be avoided. It is necessary to hyperventilate the patient to maintain acid base balance. The intraoperative use of PEEP depends upon patient condition and airway peak and plateau pressure. Functional changes in esophageal motility are common in patients with

a history of pneumonectomy[6], although most patients do not report dysphagia. It is unclear whether these patients are at increased risk of aspiration during anesthesia but the remaining lung should be protected from any insult.

CONCLUSION

We concluded that, a thorough knowledge and understanding of anatomic and physiologic changes due to pneumonectomy and carbon dioxide pneumo-peritoneum can help us to devise and apply various measures to manage these patients and to improve their perioperative outcome.

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Archives of Surgical Research | Case Report

Huge Retroperitoneal Liposarcoma: Old Beast in Modern Era

Iqra Imtiaz, Ahmad Kaleem

IMPORTANCE Retroperitoneal liposarcomas are amongst the commonest soft tissue sarcomas in the retroperitoneum. They can reach enormous sizes before presentation to a hospital. Contrast-enhanced CT scan is of utmost importance in estimating the location, extent, and depth of the malignancy. An image-guided biopsy can be of great help in the planning of treatment plans and in clinically equivocal cases. Complete Ro resection is of paramount importance in treating this aggressive disease entity. Radiotherapy and chemotherapy in the pre-operative stage can help in sensitive tumors. Molecular therapies are in the trial phase to strengthen treatment options. Here we present an interesting case, discuss its management and provide a literature review.

KEYWORDS Retroperitoneal liposarcoma, Enbloc resection,

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Case Report

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Soft tissue sarcomas constitute 1% of all adult malignancies.10-15 % of these are in the retroperitoneum. Liposarcomas are the most common variant comprising 20% of all soft tissue sarcomas and 50% of retroperitoneal variety. Most of these sarcomas do not have a clearly identified cause with possible etiology including genetic changes and exposure to ionizing radiation and chemical substances[1].

The median age at diagnosis is 56 years with equal gender distribution or slight female preponderance. They have been associated diabetes mellitus in 25% of cases. According to ESMO, only 10% of these malignancies metastasize but these are probably one of the largest neoplasms in the human body. Amongst the four types of retroperitoneal liposarcomas, the well-differentiated subtype is the most common variant of RPS (46%), followed by the myxoid (28%), dedifferentiated (18%), and pleomorphic subtypes (8%). They are generally discovered as abdominal mass (66-80%) or vague abdominal pain as they can grow for a long time in an expandable retroperitoneal space. The symptomatology can vary from gastrointestinal, urological, and neurological compressive symptoms[2].

The most common genetic mutations seen in retroperitoneal liposarcomas are MDM2/CDK4 amplification (12q13-15), presence of FUS-DDIT3 fusion gene, HMGA2 mutation, FRS2 amplification and downregulation of genes such as LIPE, PLIN and PLIN2[3]. Mortality rates for patients with liposarcoma range from 1% to 90%, and recurrence rates range from 5% to 83% depending on the histologic subtype and location[4]. Contrast enhanced CT scan abdomen, chest and MRI abdomen plus pelvis are the most invaluable investigations in these malignancies to determine origin, extent of local and distant organ involvement[5].

The differential diagnoses of retroperitoneal tumors are: lymphomas, testicular carcinomas and germ cell tumors, among others[6]. Surgical resection with negative margins of these tumors is the mainstay of treatment. Radiotherapy and chemotherapy are planned with multidisciplinary meetings[7].

CASE REPORT

A 54-year-old male presented to us with eight months history of gradual onset large abdominal swelling with significant unintentional weight loss. He had complaints of back pain but no history of altered bowel or urinary habits, fever or night sweats with itching and lumps in the body. There was no family history of such swellings or tumors of digestive, respiratory or biliary tracts. Family history for soft tissue malignant tumors was negative. He did not have any history of exposure to ionizing radiations.

The patient had a medical history of diabetes mellitus, hypertension, and ischemic heart disease with good compliance and control. On abdominal examination, there was a large abdominal swelling 30 x 25 cm, occupying most of the right hypochondrial, lumbar and iliac regions with prominent overlying abdominal veins. The swelling was firm in consistency and not moving with respiration. It was not falling forwards in the knee-elbow position. There was no evidence of free fluid or organomegaly in the abdomen. Normal bowel sounds were heard to the left of the umbilicus. Lymphadenopathy was not present. There was no evidence of varicocele, hernial orifices were intact and testicular examination was unremarkable. The distal neurovascular status was intact, and examination of spine was unremarkable. The chest examination was unremarkable, and jaundice was not present. Right ankle edema was present. His laboratory investigations were unremarkable except Hb of 10.3g/dl. A contrast enhanced CT scan of abdomen and pelvis revealed a large 27 x 24 x30 cm heterogeneous mass seen originating from the right retroperitoneal space, displacing the right kidney anteriorly and medially, filling almost the entire abdominopelvic cavity with displacement of the bowel loops on the left side. Inferiorly, the mass was seen reaching up to the level of the lower sacral piece approximating the distended urinary bladder. There were fatty areas with enhancing septae and soft tissues in the mass. A core biopsy of the mass confirmed CT scan impression of retroperitoneal sarcoma with positive CD34 and S-100 cells. Clinical TNM stage was IIIB (T4, N0, M0). After anesthesia clearance for surgery, enbloc resection of retroperitoneal liposarcoma with right nephrectomy of grossly involved kidney was carried out.

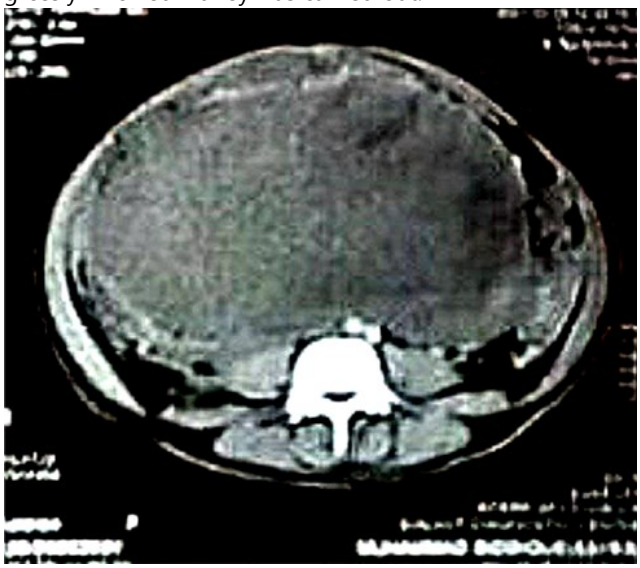

Figure 1: CT scan abdomen showing large retroperitoneal tumor displacing bowel loops

Figure 2: A CT scan image (upper slice) showing tumor displacing right kidney.

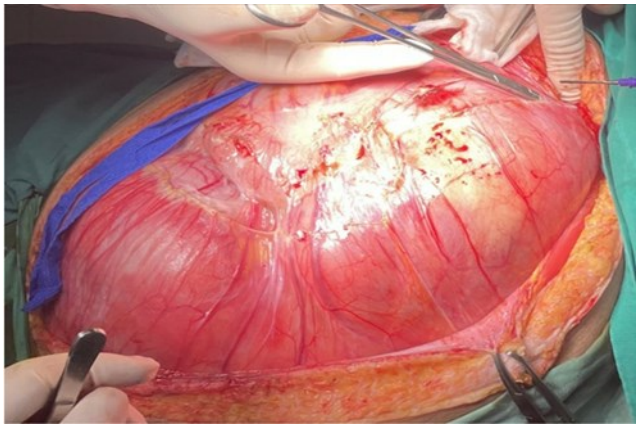

Figure 3: Intraoperative view of huge retroperitoneal sarcoma.

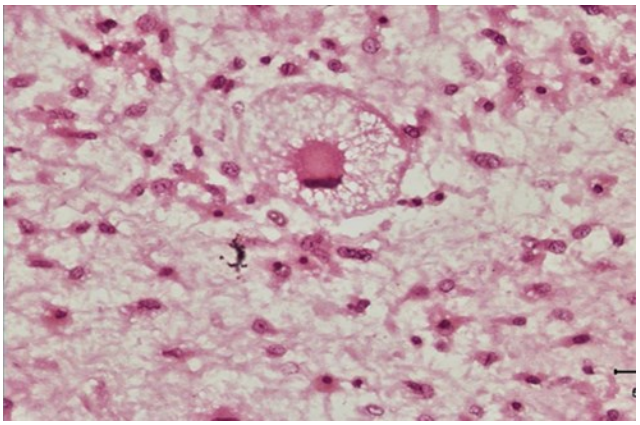

Figure 4: Microscopy reveals many lipoblasts with a central nucleus and vacuolated cytoplasm in a loose myxoid stroma.

Figure 5: Cut section reveals solid tumor with variegated appearance with hemorrhagic and yellowish fatty areas.

Histopathology report revealed a huge (44x36x34cm) retroperitoneal myxoid liposarcoma with positive S-100 and p 53. No lymphovascular invasion, necrosis was identified. Pathological TNM was T4, Nx, Mx with grade 2 to 3.

The post-operative course remained uneventful, and patient was discharged for follow up (through imaging of chest, abdomen every 3-6 months for 2 years, then every 6 months for the next 2 years, then annually) and referred for further care to department of medical and radiation oncology.

DISCUSSION

The average annual incidence of retroperitoneal sarcomas is 2.7 cases per million population. It has 36-58% over all 5-year survival rate with a natural history characterized by late recurrence. Locoregional recurrence remains a frequent cause of death. Only 28% of patients do not experience recurrence in 5 years[8].

We found case report of retroperitoneal sarcoma of size 30cm in literature[9]. On the contrary, in our case, maximum size dimension of tumor was 44cm. Cases of local progression with colonic perforations have been reported which require implementation of judicious clinical workup strategies for prevention[10].

Liposarcomas have got a different behavior from other sarcomas in being indolent and death occurring principally from local progression than distant metastasis. Seventy percent of these require multivisceral resection, most commonly of kidney (32%) and colon (25%). Studies focusing on growth rate of these tumors have found that the ones with growth of 0.9cm per month had improved survival after aggressive resection of local recurrence[11].

In our case, we removed right kidney enbloc with the tumor because of its involvement. Liberal visceral enbloc resection has been able to achieve good local control[12].

The mainstay of management for liposarcomas is surgical resection with negative margins. Complete resection has been associated with a 5-year survival rate of 70%[13]. The post-operative margin status is single most important prognostic factor for disease free survival. One study reports 72 month median overall survival in primary retroperitoneal tumors, 28 months for recurrent cases and 10 months for metastatic disease[14].

The tumor may be deemed unresectable when it invades aorta or inferior vena cava, viscera, spinal cord, root of mesentery and peritoneal implants[15]. Perioperative radiotherapy, in particular pre-operative variety, has been able to lessen recurrence with no effects on distant metastasis and overall survival[16]. Chemotherapy, particularly in neoadjuvant form may be deployed in chemo sensitive tumors in which complete resection is uncertain[17]. Novel therapies such as CDK4/6 inhibition, PPAR-γ agonists, MDM2 inhibitors, PI3K and mTOR inhibitors, and inhibition of selective nuclear export inhibitors, multikinase inhibitors and immunotherapy are also in use in trial phases[18].

In a study, 1- year, 3- and 5-year survival rates have been reported to be 86%,66% and 57% respectively. The median overall survival is around 6 years. Important factors involved in predicting decreased survival are high grade, tumor rupture, gross disease and positive resection margins. Compartmental resection by high volume surgeons is of paramount importance in lowering recurrence rate to 3.29-fold compared with simple resection[19].

To conclude, retroperitoneal liposarcomas can reach enormous sizes before presentation. Enbloc compartmental resection is the way to go in curative approach to these malignancies.

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Archives of Surgical Research | Letter to the Editor

Re: Harnessing Power of Artificial Intelligence in Surgery

Sharjeel Mahmood, Abu Huraiyra Sabir, Minhaj Rafi

The role of artificial intelligence in surgery is growing with every passing day. In the past, there has been a lack of information regarding the possibilities of its application in the surgical field which was mainly centered on the belief that robots are replacing the human surgeons but their role is more of supplementing the surgeons, instead of replacing them. The change in this mindset has given dawn to several new avenues in the field of robotic and AI supplemented surgeries. Even though it took longer to look into its promising outcomes, the ever-growing research in this field has changed the face of healthcare over the last few years.

The use of robots in minimally invasive surgery is already of major importance as it has significantly reduced the surgical complications due to trauma and enhanced patient recovery, making their hospital stay shorter. The use of AI in storing and studying the reports of the patients and analyzing the reports has also proved to be beneficial to a certain extent.

The conventional robots have supplemented the surgeons by transferring the actions of the surgeon's hands to the surgical target through tremor-filtered movements of the surgical instruments. This has significantly reduced the occurrence of intra-operative trauma to the patient. Further research in this field has shown promising outcomes with elements of Machine Learning like Learning from Demonstration and Reinforcement Learning that has brought forward new opportunities for surgical robots to adapt to the human actions. This major breakthrough is due to the recent advancement in the cloud computing, big data analytics, and artificial intelligence.

AI assisted robots have already been used in several surgical scenarios. Surgical robots that work based on the head movement of the surgeon's head are assisting in laparoscopic surgeries. Similarly, examples of robots that work based on gestured, gaze and face movements are available in literature. AI assisted robots have been used in suturing the blood vessels, in hair transplant surgeries and in cardiac surgery as well.

Clinically feasible surgical robots are likely to be realized by the end of the 21st century. The combination of artificial intelligence with surgical robotics can enable the expansion of surgical capabilities to optimize outcomes and increase access to care. We agree with the authors and look forward to enhancing role of AI in surgery in future.

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The journal aims to uphold the highest standards at the cutting-edge of research, provide a focus for evidence-based medicine through the publication of review articles and special issues, and give the findings context through the publication of editorials, commentaries and letters from the surgical community. We encourage enforcement of reporting guidelines and encourage the registration of all research involving human participants in a publicly accessible research registry.

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This journal is reviewed using a *double blind* method through OJS. The following categories the journal will accept, out of guest editorials, original articles, review articles, case reports, clinical updates, short communications, book reviews, case studies, clinical notes, Continuation of Medical Education (CME), obituaries , letters, Knowledge-Attitude-Practice (KAP) studies, routine surveys and cross sectional studies. The authors are required to suggest potential refrees for the review process. The journal however would have to discretion to get the article reviewed by the suggested faculty or not.

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Compliance with the relevant reporting guideline is mandatory for submission of the following guidelines:

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Maximum length of the original manuscript should not exceed *4000* words including title page, table and references. For review articles, the maximum word count is *3500,* however considering the demand of the subject it can be up to 8000 words. Maximum number of tables & illustrations should not exceed 5. Short reports of cases, clinical experience, drug trials and their adverse effects can be submitted. Maximum length of these case reports should not exceed *800* words, *5* maximum number of references, and *2* table or illustrations. For letters, maximum words are *600* with *5* references. Extra charges will be applicable for lengthy manuscripts.

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Système Internationale (SI) units should be used, with the traditional equivalent in parentheses where appropriate. Avoid non-standard or uncommon abbreviations, but if necessary they must be defined at their first mention. Submit math equations as editable text. Add simple formulae in line with normal text where possible and use the solidus (/) instead of a horizontal line for small fractional terms, e.g., X/Y. Variables are to be written in italics. Powers of e should be denoted by exp. Any equations that have been presented separately from the text (if referred to explicitly) must be numbered consecutively.

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Make sure to use uniform lettering and sizing of original artwork. For original illustrations, use Arial, Courier, Times New Roman, Symbol, or a font that looks similar. Number the illustrations according to their order in the text with a logical naming convention for the artwork files. Provide captions to illustrations separately. Size the illustrations close to the desired dimensions of the published version, avoiding any files that are disproportionately large. Submit each illustration as a separate file. If the electronic artwork is created in a Microsoft Office application (Word, PowerPoint, Excel) then please supply in the native document format without alterations or conversions. If the application used is not part of Microsoft Office, convert the images to one of the following formats (note the resolution requirements for line drawings, halftones, and line/halftone combinations given below):

- EPS (or PDF): Vector drawings, make sure to embed fonts.
- TIFF (or JPEG): Color or gray-scale photographs (halftones); ensure a minimum of 300 dpi.
- TIFF (or JPEG): Bitmapped (pure black & white pixels) line drawings; ensure a minimum of 1000 dpi.
- TIFF (or JPEG): For combinations of bitmapped line/half-tone (color or gray-scale), ensure a minimum of 500 dpi.

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Tables

Submit tables as editable text and not as images. Tables can be placed either next to the relevant text in the article, or separately at the end in an appendix. Number tables consecutively according to their sequence in the text and present any table notes below the table body. Keep the use of tables to a minimum and ensure that the data included in them is not repeated in results described elsewhere in the article. Avoid using vertical rules and shading in table cells.

Supplementary Material, Research Data, and Video

Supplementary material such as applications, images, and sound clips, can be published with the article to enhance it. Submitted supplementary items are published exactly as they are received (Excel or PowerPoint files will appear as such online). Submit this material with the manuscript and supply a concise, descriptive caption for each file. If you want share data that supports your research publication, where appropriate, interlink the data with the article. Research data refers to the results of experimentation that validate research results. To enable reproducibility and data reuse, share the software, code, models, algorithms, protocols, methods and other useful materials related to the project. If you have made your research data available in a public data repository, link the dataset directly into your article. To enable transparency, we require you to state the availability of data in your submission if your data is unavailable to access or unsuitable to post. Authors who wish to submit video files with their article are encouraged to include links to these within the body of the article. This can be done in the same way as a figure or table by referring to the video or animation content and noting in the body text where it should be placed, or separately at the end. Keep the file in one of the recommended file formats with a preferred maximum size of 150 MB per file, 1 GB in total.

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- Conflict of interest: a conflict of interest exists when a manuscript's or journal's author, editor, reviewer have a financial or personal relationship that may influence their intentions or bias.
- Redundant publication : when a published work (or substantial sections from a published work) is/are published more than once (in the same or another language) without adequate acknowledgment of the source/cross-referencing/justification (https://publicationethics.org/category/keywords/redundant-publication)

Any allegations of misconduct brought to the journal's attention will be dealt with immediately and seriously. ASR

will not accept articles that violate research & publication ethics, any manuscript not in compliance will be rejected.

ASR utilizes Turnitin to assess all submitted manuscripts, a plagiarism percentage upwards of 24% is unacceptable and articles not in accordance with this rule will be rejected.

In cases of citation manipulation, relevant COPE guidelines will be followed.

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1. rejection of their submitted manuscript
2. communication of the authors' misconduct will be made to relevant institutions and regulatory bodies
3. black-listing of the authors from ASR for all future submissions

This is in accordance with COPE guidelines.

We follow the COPE Guidelines for sharing information regarding any misconduct with other journals. We also follow the COPE Retraction Guideline. We as a journal have policy to refer such cases to COPE if required.

In case of suspicion of image manipulation in a manuscript, COPE flowchart will be followed.

In cases of redundant publications, COPE flowchart will be followed.

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All authors are required to submit a Disclosure of Interest form, which can be found here: http://www.icmje.org/disclosure-of-interest/. In case of an undisclosed conflict of interest, COPE guidelines will be followed.

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Archives of Surgical Research (ASR) follows COPE guidelines in case of appeals to the journal's editor's decisions and complaints about ASR's journal management of the peer review process.

If authors wish to file a complaint or appeal against an editorial decision, they are encouraged to email: editorial@archivessr.com, with the subject heading mentioning "COMPLAINT" or "APPEAL". We have dedicated Ombudsperson for handling such appeals.

Furthermore, Archives of Surgical Research (ASR) consults COPE guidelines if a reviewer is suspected of appropriating or mismanaging author material and may refer such cases to COPE if required.

Data and reproducibility

Archives of Surgical Research (ASR) follows ICMJE data sharing guidelines.

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To Improve transparency, we encourage use of and link to international standard reporting guidelines such as those listed in the EQUATOR Network. We encourage pre-registration of clinical trials (and other study designs) in an online clinical study database before data are collected (eg, ClinicalTrials.gov). We encourage journal pre-registration and peer review of study protocols before data are collected (eg, as promoted by the Center for Open Science).

We have system of scruitiny to find such data manipulations, if found may result in:

1. Rejection of their submitted manuscript
2. Communication of the authors' misconduct will be made to relevant institutions and regulatory bodies
3. Black-listing of the authors from ASR for all future submissions

This is in accordance with COPE guidelines.

In case of suspicion of image manipulation in a manuscript, COPE flowchart will be followed.

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Archives of Surgical Research (ASR) follows COPE guidelines for ethical oversight, wherever applicable. ASR has it's own consent form for case reports, which is mandatory along with the submission of the manuscript. The consent form is adapted from BMJ Case Reports and is in line with COPE guidelines. To determine whether a study requires ethical approval or not, ASR looks to COPE guidelines.

Furthermore, ASR requires a transparency declaration from the lead author of an original study guaranteeing honesty and accuracy (as published & implemented by the BMJ and endorsed by the EQUATOR network).

Post-publication Review and Audit

If authors whose work has been accepted and/or published wish to retract/correct/revise their articles, please email: editorial@archivessr.com, with the subject heading mentioning "RETRACTION" or "CORRECTION" or "REVISION".

Conflict of Interest Policy

Adopted from Conflict of Interest in Peer-Reviewed Medical Journals which is prepared by WAME Editorial Policy and Publication Ethics Committees.

Articles would be published with statements or supporting documents declaring:

Authors' conflicts of interest

Sources of support for the work, including sponsor names along with explanations of the role of those sources if any in study design; collection, analysis, and interpretation of data; writing of the report; the decision to submit the report for publication; or a statement declaring that the supporting source had no such involvement; and Whether the authors had access to the study data, with an explanation of the nature and extent of access, including whether access is on-going.

To support the above statements, editors may request that authors of a study sponsored by a funder with a proprietary or financial interest in the outcome sign a statement, such as "I had full access to all of the data in this study and I take complete responsibility for the integrity of the data and the accuracy of the data analysis."

Disclosure form is available from the website, which has been adapted from ICMJE Disclosure Form and should be filled at the time of acceptance of manuscript. Disclosures are also obtained whenever deemed necessary at the time of review and editorial tasks.

9. EDITORIAL POLICIES

Principles of Transparency and Best Practice in Scholarly Publishing are followed as per ICMJE guidelines. This Journal strives to adhere to the ***Principles of Transparency and Best Practice in Scholarly Publishing*** which could be found in the **DOAJ** Web site completely,

This Journal has established a guideline for editorial independence as delineated below. The guideline generally follows that created by the World Association of Medical Editors.

1. This Journal is operated by Pakistan Endocrine & Thyroid Surgeons Association (PETSA), which is publishing organization.
2. The Chief Editor is responsible for independent leadership of This Journal editorial operations. The General Publishing Editor reports to the Editor-in-Chief for all editorial matters.
3. The Editor-in-Chief has full authority over the content of this Journal and its related offerings. This includes summaries and comments on recent medical advances, opinions, blogs and news.
4. Content-related decisions are based on quality, importance, and value to the users of this Journal. Contributing authors, editors, This Journal staff are free to express responsible positions -even if these views are not in agreement with interests, policies or published research, editorial or commentary of PETSA.
5. This Journal actively seeks input regarding editorial matters from the physician Editors-in-Chief in an advisory capacity, as well as from the other editorial board members, internal editorial staff, and readers.
6. Editors-in-Chief of this Journal is empowered to create content and commentary free of commercial and organizational influence. All authors and editors operate without conflict of interest and all potential conflicts are disclosed (please also see Conflict of Interest Policy).

10. PEER REVIEW POLICY

We follow ICMJE recommendations on the manuscript handling. The practice of peer review is to ensure that only good science is published. It is an objective process at the heart of good scholarly publishing and is carried out by all reputable scientific journals. Our referees play a vital role in maintaining the high standards Review Policy and all manuscripts are peer reviewed following the procedure outlined below:

Initial manuscript evaluation

The Editor first evaluates all manuscripts. It is rare, but it is possible for an exceptional manuscript to be accepted at this stage. Manuscripts rejected at this stage are insufficiently original, have serious scientific flaws, have poor grammar or English language, or are outside the aims and scope of the journal. Those that meet the minimum criteria are normally passed on to at least 2 experts for review. Most of the submitted manuscripts are reviewed except few invited or editorial content.

Type of Peer Review

Policy employs double blind reviewing, where both the referee and author remain anonymous throughout the process.

How the Referee is selected

Whenever possible, referees are matched to the paper according to their expertise and our database is constantly being updated. The referee is selected both from the editorial team and outside and depending on the author suggestions.

Referee Reports

Referees are asked to evaluate whether the manuscript: - Is original - Is methodologically sound - Follows appropriate ethical guidelines - Has results which are clearly presented and support the conclusions - Correctly references previous relevant work. This is a systematic process and works on the well-designed Peer Review Proforma. The confidentiality of the peer review is ensured. Reviewers are encouraged to report conflict of interest, ethical misconduct etc.

Language correction is not part of the peer review process, but referees may, if so wish, suggest corrections to the manuscript.

How long does the review process take?

The time required for the review process is dependent on the response of the referees. Should the referee's reports contradict one another or a report is unnecessarily delayed, a further expert opinion will be sought. The Editor's decision will be sent to the author with recommendations made by the referees, which usually includes verbatim comments by the referees. Revised manuscripts might be returned to the initial referees who may then request another revision of a manuscript.

Final Report

A final decision to accept or reject the manuscript will be sent to the author along with any recommendations made by the referees, and may include verbatim comments by the referees.

Editor's Decision is Final

Referees advise the editor, who is responsible for the final decision to accept or reject the article.

Conflict of Interest

All reviewers and editors have to declare any potential conflicts of interest if any. We follow COPE and ICMJE guidelines in this regard.

Editorial and Peer Review Processes Generally Follow these Steps:

We follow and request from authors, reviewers and editors the "ICJME Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals". Editorial reviewer policy is independent of any financial, academic or any other interest.

- When an article is submitted to Archives of Surgical Research, Editor makes the first check of submitted articles (structure, plagiarism, scientific quality).
- Article may be rejected, sent back for structural revision, or sent to at least two reviewers for peer review.
- After peer review process, articles may be rejected, sent back for revision requested by reviewers or accepted for publication.
- Revised articles by authors may be accepted, resent to reviewers, resent to authors for additional corrections/revision or rejected.
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- Accepted articles are forwarded to publishing process.
- Editor(s) may require additional materials or changes from authors during copy editing, composing, grammatical editing and/or proof reading steps.
- A fast track review system is in place upon deposition of additional processing fee (Rs. 20,000), however we do not encourage such route and should be employed only in significant circumstances. Moreover, this does not ensure that manuscript if accepted would be published on priority.
- Post-publication review and peer review is encouraged and is managed through letter to the editors.

11. STATEMENT OF INFORMED CONSENT

We follow ICMJE and COPE Guidelines for appropriate consenting. Patient's privacy should not be breached without taking consent. In written descriptions there should not be any specifications regarding patients including names, hospital numbers, photographs or pedigrees unless the information is needed for scientific purposes and the patient allows for publication with written informed consent. It should be disclosed by authors to the patients that any identifiable material could be available on the Internet or in printed form after publication. Patient consent ought to be written and archived with the journal, the authors, or both, as settled by local rules and regulations. Applicable laws vary from territory to territory, and journals should make their own policies with legal guidance. Since a journal that archives the consent will be aware of patient identity, some journals may decide that patient confidentiality is better guarded by having the author archive the consent and instead providing the journal with a written statement that attests that they have received and archived written patient consent.

Nonessential identifying details should be omitted. Informed consent should be obtained if there is any doubt that anonymity can be maintained. For example, masking the eye region in photographs of patients is inadequate protection of anonymity. If identifying characteristics are de-identified, authors should provide assurance, and editors should so note, that such changes do not distort scientific meaning.

The requirement for informed consent should be included in the journal's instructions for authors. When informed consent has been obtained, it should be indicated in the published article.

- International Committee of Medical Journal Editors ("Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals")

12. GUIDELINE FOR REVIEWERS

Peer review in all its forms plays an important role in ensuring the integrity of the scholarly record. The process depends to a large extent on trust, and requires that everyone involved behaves responsibly and ethically. Peer reviewers play a central and critical part in the peer-review process, but too often come to the role without any guidance and unaware of their ethical obligations.

Archives of Surgical Research follows COPE Guidelines for educating the reviewers for the review process.

13. ETHICAL EDITING FOR EDITORS

Becoming an editor of Archives of Surgical Research is an exciting but daunting task, especially if you are working alone without day to day contact with editorial colleagues. This short guide aims to summarize key issues and to provide links to relevant pages of the COPE website as well as those of other organizations. We encourage the editorial team to consult COPE and ICMJE resources frequently for their training and handling of the manuscript and various editorial issues.

14. GUIDELINES FOR JOURNAL MANAGEMENT

We believe that Archives of Surgical Research serves as an important part of the scientific literature. Hence, its management should be of the highest quality and ethically sound. We follow COPE Guidelines to manage the top hierarchy in terms of conflicts of interest and ethical considerations. We also following COPE Guidelines for maintaining relationship of journal management to the Pakistan Endocrine & Thyroid Surgeons Association to ensure editorial independence. The journal editorial teams meets periodically at least biannually. The editorial team is independent of the society and is managed by a transparent process two yearly as per the ethical confines suggested by COPE, ICMJE and local guidelines.

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Archives of Surgical Research
A Peer Reviewed Surgical Journal

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