

Archives of Surgical Research

Bringing Surgical Science and Art Closer

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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

Editor in Chief: Prof Khwaja M Azim FRCS

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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

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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

Entrustable Professional Activities (EPAs) as a Measure for General Surgery Resident Evaluation

Sharjeel Mahmood, Tauseef Asghar, Asghar Nagi

IMPORTANCE Surgical training is going through a continuous process of evolution and instead of relying on subjective methods of evaluation and cognitive assessments, we are gradually shifting toward competency-based modes of assessment. Entrustable Professional Activities (EPAs) are rapidly complementing and replacing other means of assessment in order to declare a surgeon competent. American Board of Surgery and Intercollegiate Board in the UK have laid down a path for such a process and would likely become the main tool for surgical skill assessment in the future. College of Physicians and Surgeons is in process and can definitely follow the principles and plans to augment their surgical resident assessment for enhancing the quality of assessment.

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Editorial

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or many years, the assessment criteria being used for assessment and evaluation of the trainees and residents of general surgery rotation is "time-based" rather than an actual demonstration of the competency of the candidates. The methods of testing like selfassessment, exam performance, mentor assessment, and patient outcome have shown variable results. The General Surgery Residents are allowed to sit for the American Board of Surgery licensing exam based on surgical case volume, the time they spend in training and little weightage is paid to anything else, especially when it comes to assessing the competency of the residents¹. With time, in order to address the evolving surgical training environment, there is a need to shift towards new methods of assessing the competency of surgical trainees to hand over the tasks to them that they are able to perform independently depending on the level of their abilities. Especially with the onset of Covid-19, it was made evident that competencybased assessment is necessary for the appropriate determination of the trainees' readiness to enter the certification process and patient care independently. One such component of clinical assessment of the competencybased resident evaluation is the use of Entrustable Professional Activities (EPAs).

EPAs are "a unit of professional practice that can be fully entrusted to a trainee as soon as he has demonstrated the necessary competence to execute this activity unsupervised". EPAs incorporate several cognitive and behavioral factors that are critical for surgical care that is not being tested by the current model of resident assessment². Each EPA is a synthesis of multiple competency domains (e.g., medical knowledge, communication skills, and professionalism) and requires the integration of knowledge, skills, and attitudes. They provide an approach to assessing tasks that may require multiple milestones and otherwise, might not be assessable. When a general surgery resident has achieved an adequate number of EPAs, they would be deemed competent enough for further specialty training or independent practice.

One of the major advantages of using EPAs is that it was achievable in any context, relies on frequent micro-assessments instead of less meaningful and time-consuming end rotation evaluations, and teaches the trainees skills of implementation and improvisation required in the uncertainties of clinical practice.

The American Board of Surgery will launch its EPA program for general surgery residents in July 2023 and the residents will be assessed on the basis of EPAs. For this purpose, a pilot study was carried out in 2018 with 5 pilot index EPAs and they were tested across 28 different surgical residency programs from 2018-2020¹. After the pilot study showed fruitful results, a whole suite of 19 EPAs was defined that represented the core elements of general surgery practice. The general surgery residents will be evaluated against these 19 EPAs that would define the level of their abilities

1

to perform the tasks. The ABS has established several councils and working groups that are tasked with the development and implementation of the EPA initiative and under their supervision, the following EPAs are being implemented for the General Surgery Training:

- 1. RLQ pain/Appendicitis
- 2. Benign or malignant breast disease
- 3. Benign or malignant colon disease
- 4. Gallbladder disease
- 5. Inguinal hernia
- 6. Abdominal wall hernia
- 7. Acute abdomen
- 8. Benign anorectal disease
- 9. Small bowel obstruction
- 10. Thyroid and parathyroid disease
- 11. Dialysis access
- 12. Soft tissue infection
- 13. Cutaneous and subcutaneous neoplasms
- 14. Severe acute or necrotizing pancreatitis
- 15. Perioperative care of the critically ill surgery patient
- 16. Flexible GI Endoscopy
- 17. Evaluation/initial management of a trauma patient
- 18. Significant comorbid disease
- 19. Provide general surgery consultation¹

After defining the EPAs, the next step was to define a framework for demonstrating competence for a discrete general surgery consultation. Another study was performed and six critical steps, six performance traits, and five red flag behaviors were defined, against which the residents of the General Surgery programs would be tested³. The red flag behaviors would have a negative effect on the trustability of a resident for that consultation. In order to keep bias to the minimum and to involve and capture the preferences of different specialties, 23 teaching faculty were recruited from a range of surgical specialties. Cognitive task analysis and semi-structured interviews were used. The steps of a surgical consult were defined and furthermore, the assessment criteria based on the steps, traits, and negative impact of the red flag behavior were established. The steps in a surgical consult were defined as:

- 1) Receiving information,
- 2) bedside evaluation,

- 3) obtaining additional information,
- 4) decision making,
- 5) communication,
- 6) Documentation³.

Following is the list of some red-flag behaviors:

- 1) Failure to recognize patient acuity,
- 2) lying/deception,
- 3) missing critical details of the evaluation, workup, or presentation,
- 4) refusing to see the consult,
- 5) rudeness/disrespect3.

A similar competency-based training system is being implemented in the United Kingdom as well to cater to the needs of the developing surgical training resident programs.

Now, in reference to Pakistan, there is an urgent need to implement the competency-based assessment criteria for the General Surgery residents so that our trainees can be judged on the basis of their competency and their ability to handle the patients rather than on basis of systems that have shown variable results, are time-taking and less efficient. It helped us improve the Health Education System and our resident training programs in an effective manner and will improve patient care. The residents getting into specialty training and independent practice after passing through better and improved assessment criteria will have a deeper and more practical approach to patient care and will be able to provide better consultations.

Recommendations:

- Faculty development initiatives should be designed to make the faculty familiar with the concept of EPAs and their uses for workplace-based assessment.
- The EPA should be included in the curriculum to improve the standard of the products of General Surgery Resident Training.
- Further research should be done for mapping these selected EPAs with the pertinent competencies.
- A system assessing the residents based on their competency using the already defined EPAs should be implemented.

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The surgical consult entrustable professional activity (EPA): Defining competence as a basis for evaluation. *Am J Surg.* 2020;219(2):253-257. doi:10.1016/J.AMJSURG.2018.12.056

Archives of Surgical Research | Meta-Analysis

Proficiency-Based Progression Training: Key To Effective Clinical Procedural Teaching?

Hamza Azhar, Ehtisham Sohail Khan, Talat Waseem

IMPORTANCE Proficiency-Based Progression (PBP) training is a form of training in which the trainee has to achieve a benchmark that has been quantitatively defined. This is contrary to conventional training where progression benchmarks are arbitrary, This form of training may find its place in surgery and procedural medicine with some studies finding it to be effective while others claim to have seen no impact on trainees.

METHODS A systematic literature search was conducted on PubMed and Cochrane library and 15 eligible RCTs were extracted in which proficiency-based progression (PBP) training was compared with traditional surgical training methods.

RESULT 15 RCTs were included (412 participants from all RCTs). The PBP group demonstrated a reduced number of procedural errors as compared to the non-PBP group (Weighted Mean Difference: -6.14 errors, 95% Confidence Interval (CI) -8.63 to -3.65, p < 0.00001), as well as a reduction in procedural time in the PBP group as compared to the non-PBP group (Weighted Mean Difference: -5.46, 95% Confidence Interval (CI) -8.56 to -2.37, p = 0.0005) but the non-PBP group performed more procedural steps than the PBP group (Weighted Mean Difference: 2.18, 95% Confidence Interval (CI) -1.31 to 5.66, p < 0.00001).

CONCLUSION Our meta-analysis shows that PBP-trained groups outperform their traditional counterparts by completing procedures quicker and making fewer errors. This model of training may be an effective training tool of the future.

KEYWORDS PB; Traditional Surgical training; Simulation training; Proficiency based progression; Meta-analysis.

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roficiency-Based Progression (PBP) training is a form of training in which the trainee has to achieve a benchmark that has been quantitatively defined, this is contrary to conventional training where progression benchmarks are arbitrary, this form of training has found its place in surgery and procedural medicine¹. A study by Satava et al was the first to propose the use of this method of simulation training in surgery and demonstrated favorable results². One of the pioneer studies carried out in 2002 by Seymour et al showed that trainees taught through PBP methods outperformed their traditionally trained counterparts³. Proficiency-based simulation has proved to not only improve skill acquisition but also maintenance of skills over an extended period of time⁴, such form of simulation training has especially had a positive impact on and is widely used in laparoscopic training⁵. With

advancements in technology and the introduction of robotic surgery this form of proficiency-based simulation training may have an even more integral role in training^{6,7}. Previous review studies on the matter make an attempt at highlighting the significance of such a form of training but are mostly focused on laparoscopic procedures^{8,9} but these studies showed limitations in which they focus more on process measures, and do not adequately assess the quality of the studies and focus minimally on patient outcome. Many studies and trials, as of now, have concluded that PBP training has shown to be a more effective and efficient method of training compared to conventional methods of training, while some studies show no significant impact on the trainees. Our meta-analysis attempts to compare and analyze the outcomes of a number of high-quality studies which compare and contrast PBP training and traditional training.

METHODOLOGY

We used PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines to do the literature search for our meta-analysis.

Literature search: PubMed and Cochrane library was used to carry out our literature search. Only Randomized controlled trials were included in the search. We conducted our search from 1st March 2020 to 1st July 2022 according to the PRISMA devised guidelines. We used these search terms for our literature review: (Proficiency-based AND progression AND training) OR (Proficiency AND based AND progression) OR (Proficiency-based AND training). Only randomized controlled trials (RCTs) published between 1st March 2020 and 1st July 2022 were selected. We also searched the reference lists of the relevant articles to include RCTs in our study.

Inclusion of studies: A literature search according to PRISMA guidelines was done and 16 articles were found in PubMed's database, 64 articles were found in the Cochrane Library database and 12 studies were identified through other sources. Duplicates were removed and a total of 88 studies were screened after the exclusion of 63 articles, 25 articles were selected after reading their titles and abstracts. Full-text assessment of these 25 articles was done and out of these 25 studies, 10 studies were excluded because they did not meet our inclusion criterion i.e. studies other than randomized controlled trials (RCTs), unavailability of full text, poor MERSQI scores and studies which did not compare the outcomes of our interest. After exclusion of these 10 studies, we were left with 15 randomized control trials which were then included in our final analysis.

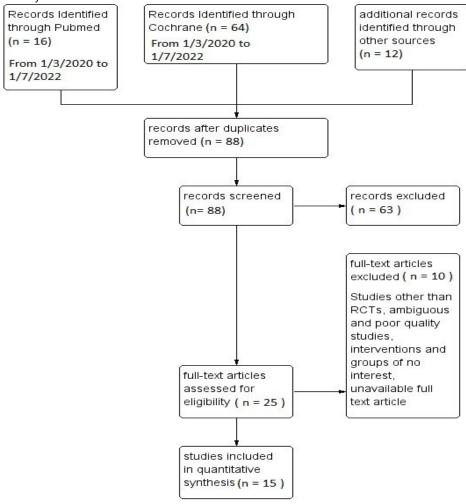


Figure 1: Showing PRISMA Flow diagram

Quality assessment and Risk of Bias: The quality of trials was assessed using the Medical Education Research Study Quality Instrument (MERSQI) scoring system, which contains the following judgment criteria: study design, institutions studied, response rate,

type of data, internal structure, content, relationship to other variables, appropriateness of analysis complexity of analysis and outcome. Only high-quality studies were included in the quantitative analysis.

Study	Study design (1-3)	Institutions studied (0.5-1.5)	Response rate, %: (0.5-1.5)	Type of data (1 or 3)	Internal structure: (0 or 1)	Content (0 or1)	Relationships to other variables: (0 or 1)	Appropriateness of analysis: (0 or 1)	Complexity of analysis: (1 or 2)	Outcome (1-3)	Final score
Ahlberg et al. 2007	3	1.5	1.5	3	1	1	0	1	2	2	16
Ahmed et al. 2018	3	0.5	1.5	3	1	1	0	1	2	2	15
Angelo et al. 2015	3	1.5	1.5	3	1	1	0	1	2	2	16
Breen et al. 2019	3	0.5	1.5	3	1	1	0	1	2	2	15
Cates et al. 2016	3	0.5	1.5	3	1	1	0	1	2	2	15
Jensen et al. 2015	3	1.5	1.5	3	1	1	1	1	2	2	17
Palter 2012	3	0.5	1.5	3	1	1	0	1	2	2	15
Pedowitz et al. 2015	3	1.5	1.5	3	1	1	0	1	2	1.5	15.5
Peeters et al 2015	3	1.5	1	3	1	1	0	1	2	2	16.5
Seymour 2002	3	0.5	1.5	3	1	1	0	1	2	2	15
Srinivasa n et al. 2017	3	0.5	1.5	3	1	1	1	1	2	3	17
Van Sickle et al. 2008	3	0.5	1.5	3	1	1	0	1	2	1.5	14.5
Gurung PMS et al 2019	3	0.5	1.5	3	1	1	0	1	2	2	15
Puliatti S et al 2021	3	0.5	1.5	3	1	1	0	1	2	2	15
Cassidy DJ et al 2021	3	1.5	1.5	3	1	1	0	1	2	2	16

TABLE1: MERSQI scores of the 15 studies included in the final quantitative synthesis

Data extraction and Statistical analysis: The relevant data was collected and sorted in a structured way. Three outcomes were used for analysis i.e. procedural errors, number of procedural steps and procedural time. The outcomes of The Proficiency Based Progression (PBP) group and Non Proficiency based progression (Non PBP) group were compared. We used continuous and dichotomous variables to compare the outcomes. In cases of continuous variables, we used mean difference with inverse variance while odd's ration with Mantel-Haenszel method with 95% confidence interval was used for the calculation of

dichotomous variables. Heterogeneity of the data was calculated and random effect was used when the heterogeneity of the data was more than 50% while fixed effect was used when it was less than 50%. 2x2 chi-squared test was applied to carry out our meta-analysis in Review manager 5.4.

RESULTS

A PRISMA compliant literature search was done on databases of PubMed and Cochrane library and 15 Randomized controlled trials (RCTs) were selected and included in the final quantitative synthesis^{3,10-23}. A thorough summary of each study has been given in the table. Each study was an RCT and they gave a comparison of different outcomes for PBP and non PBP group. The participants of these studies included surgical residents, surgical attending, medical students and nursing students. A total of 412 participants

from all RCTs were included in the analysis. The table 2 shows the comparison arm, procedure/ task trained, intraoperative patient performance, compared outcomes and MERSQI score of each study.

Study	Subjects(N); Comparison Arm Type		Task/Procedure Trained	Intraoperative Patient Performance	Outcomes Compared	Other Scale Used	MERSQI
Ahlberg et al	13;Residents	Swedish National Surgical Residency Training Program	Laparoscopic Cholecystectomies	Yes	Errors	_	16
Ahmed et al	18;Medicine Students	Self-Guided Ultrasound-Guided Peripheral Nerve Block Simulation Practice	Ultrasound-Guided Peripheral Nerve Block	No	Errors, Steps	_	15
Angelo et al	44; Residents	ACGME approved Orthopedic Residency & Arthroscopy Association of North America Shoulder Course	Arthroscopic Bankart Procedure	Yes	Errors, Steps, Time	_	16
Breen et al	90;Medicine and nursing students	National and certified ISBAR training Program	Clinical Communication	No	Errors, Steps	_	15
Cates et al	12;Attendings	Industry sponsored CASES education and training system	Carotid Artery Angiography	Yes	Errors, Time	_	15
Jensen et al	16;Residents	ESC Core Curriculum for the General Cardiologist	Coronary Angiography	No	Errors, Steps, Time	_	17
Palter, et al	25;Residents	ACGME approved General Surgery Residency Training Program	Laparoscopic Right Colectomy	Yes	Steps	OSATS	16
Pedowitz et al	44;Residents	ACGME approved Orthopedic Residency & Arthroscopy Association of North America Shoulder Course	Knot-Tying	No	Errors	_	14.5
Peeters, et al	10;Residents	National Obstetrics and Gynecology Residency Program	Fetoscopy Laser Surgery	No	Steps, Time	_	16.5
Seymour et al	16;Residents	ACGME approved General Surgery Residency Training Program	Laparoscopic Cholecystectomy	Yes	Errors, Time	_	15
Srinivasan et al	17;Residents	Irish National Anesthesia Training Program	Epidural Analgesia	Yes	Errors	GRS, TSCL	17
Van Sickle et al	22;Residents	ACGME approved General Surgery Residency Training Program	Nissen Fundoplication	Yes	Errors, Time	_	14.
Gurung PMS et al 2019	16; MS3 Medical students	conventional proficiency-based training protocol (CTP)	Robotic surgical simulation training	No	Steps	_	15
Puliatti S et al 2021	47; Medical students	Quality assured online learning for robotic suturing and knot tying in ORSI academy	Robotic vesico- urethral anastomosis	No	Steps, Errors	_	15
Cassidy DJ et al 2021	22; Residents	Repetition based VR training program for Fundamentals of Endoscopic Surgery (FES) program	Porcine endoscopy and colonoscopy	No	Time	_	16

TABLE 2: Summary of Studies

Procedural Errors: A total of 9 RCTs gave the comparison of procedural errors between the PBP and non PBP group. 89 participants were included in the PBP group while 85 participants were included in the Non PBP group. The lesser statistical analysis revealed that the PBP group committed a

Number of procedural errors in comparison to non PBP group (Weighted Mean Difference: —6.14 errors, 95% Confidence Interval (CI) —8.63 to —3.65, p < 0.00001). A high heterogeneity of 97% was observed so random effect model was used.

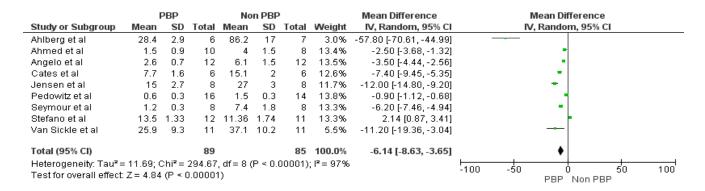


Figure 2: Showing forest plot of comparison of Procedural Errors between PBP and Non PBP group

Procedural Steps: 7 RCTs reported this outcome. 80 participants were included in the PBP group and 77 participants were included in the Non PBP group. The analysis showed that Non PBP group performed more

Procedural steps than the PBP group (Weighted Mean Difference: 2.18, 95% Confidence Interval (CI) —1.31 to 5.66, p < 0.00001). 99% heterogeneity was observed therefore random effect model was used.

		PBP		N	on PBP			Mean Difference		-	Mean Differer	nce	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV	, Random, 95	5% CI	
Ahmed et al	15	1.2	10	4	3.6	8	11.2%	11.00 [8.40, 13.60]			-		
Angelo et al	42.6	0.6	12	38.6	0.9	12	11.9%	4.00 [3.39, 4.61]			-		
Jensen et al	70.5	5.8	8	45.5	3.3	8	9.9%	25.00 [20.38, 29.62]			-	•	
Palter et al	15.7	1.3	9	10.4	2.1	9	11.7%	5.30 [3.69, 6.91]			-		
Peeters et al	47.7	2.9	5	36.2	4.1	5	10.1%	11.50 [7.10, 15.90]			-		
Pratik (Task 1)	7.88	1.25	8	21.63	3.34	8	11.3%	-13.75 [-16.22, -11.28]			+		
Pratik (Task 2)	10.38	2.67	8	23.5	3.29	8	11.0%	-13.12 [-16.06, -10.18]			-		
Pratik (Task 3)	12.75	2.82	8	20.5	3.38	8	11.0%	-7.75 [-10.80, -4.70]			+		
Stefano et al	2.75	0.41	12	2.18	0.515	11	12.0%	0.57 [0.19, 0.95]			t		
Total (95% CI)			80			77	100.0%	2.18 [-1.31, 5.66]			•		
Heterogeneity: Tau² = Test for overall effect				, df = 8 ((P < 0.0	0001);	l²= 99%		-100	-50		50	100
restror overall effect	1.22		5.22)								PBP Non	PBP	

Figure 3: Showing forest plot of comparison of Procedural Steps between PBP and Non PBP group

Procedural Time: A total of 7 RCTs provided the comparison of procedural time between PBP and Non PBP group. PBP group contained 83 participants while Non PBP group also contained the same number of participants. The analysis showed a reduction in procedural time in the PBP

Group in comparison to the non PBP group (Weighted Mean Difference: -5.46, 95% Confidence Interval (CI) -8.56 to -2.37, p = 0.0005). Heterogeneity of 62% was observed and random effect model was used for analysis.

	1	PBP		No	n PBP	•		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Angelo et al	80.4	5	12	81	8	12	14.8%	-0.60 [-5.94, 4.74]	
Cates et al	26.9	5.3	6	32.3	4.8	6	13.9%	-5.40 [-11.12, 0.32]	
Douglas (Advanced Mucosal Evaluation 1)	43.5	20.9	11	68.5	22.4	11	2.6%	-25.00 [-43.10, -6.90]	←
Douglas (Endoscopic Navigation)	43.1	25	11	70.6	17	11	2.7%	-27.50 [-45.37, -9.63]	←
Douglas (FES)	170	66.3	11	242.2	48.6	11	0.4%	-72.20 [-120.78, -23.62]	•
Jensen et al	22.6	2.2	8	27.1	2.5	8	23.1%	-4.50 [-6.81, -2.19]	
Peeters et al	36.2	5.6	5	39.1	8.1	5	8.7%	-2.90 [-11.53, 5.73]	
Seymour et al	14.5	5.5	8	20.5	10	8	9.7%	-6.00 [-13.91, 1.91]	
Van Sickle et al	8.7	3.2	11	13.1	0.3	11	24.1%	-4.40 [-6.30, -2.50]	
Total (95% CI)			83			83	100.0%	-5.46 [-8.56, -2.37]	-
Heterogeneity: Tau² = 9.42; Chi² = 21.17, df =	8 (P = 0	.007);	I = 629	Х.					-10 -5 0 5 10
Test for overall effect: Z = 3.46 (P = 0.0005)									PBP Non PBP

Figure 4: Showing forest plot of comparison of Procedural Time between PBP and Non PBP group

DISCUSSION

In this meta-analysis, we attempted to draw out the differences in training outcomes of proficiency-based progression simulation training as opposed to more classical or traditional methods of training. This analysis included only prospective, randomized, and blinded clinical studies, after scouring for literature on 2 main search platforms (PubMed, and Cochrane) while also searching through additional sources, the results of 15 studies were included. The quality of studies analyzed was high, based on the MERSQI scoring instrument, no study scored below a score of 14.5.

Proficiency-Based-Progression training is effective, as it sets performance metrics that are developed by experienced surgeons and clinicians and an accumulation of validated evidence derived from them^{24,22} the method is based on strict performance metrics such as procedural steps, time, and errors or deviation from optimum performance. These set objectives allow trainees to have more deliberate practice instead of undirected repetitions²⁵ such deliberate practice is vital to achieving proficiency⁴. And these are the exact metrics explored in this study.

In the past few meta-analyses have been taken up on the topic. Mazzone et al²⁶ in 2020 compare similar outcomes of procedural error, steps, and duration but feature fewer studies than in this paper. While other meta-analyses present focus more on specific fields such as laparoscopy²⁷ or dental procedures²⁸ and do not focus on the implications of such methods as a whole on surgical training.

Our analysis shows that PBP groups have outperformed Non-PBP groups making fewer procedural errors and requiring less time to complete procedures, which is validated in other such analysis²⁶. But our study differs in its finding of PBPs effect on procedural steps completed as we found Non-PBP groups completed more steps, however, this metric isn't an appropriate measure of quality, for example, a procedure with all its steps completed but done inadequately or a procedure may be completed swiftly but not done safely or steps skipped to achieve faster times^{12,29,30}. Hence the number of procedural errors in the PBP methodology gives the most reliable and quantitatively measurable index of the quality of the procedure.

Even with the results of the study favoring PBP training and the inclusion of high-quality trials the study was not free of limitations. Despite this inclusion of more RCTs than previous such studies (15 RCTs), the number is still insufficient and more additions are still required, as a limited number reduces the general application of the findings and elevates the risk of residual biases. Furthermore, despite the use of a random-effect model, which accounts for within-study as well as between-study variations, there is residual heterogeneity between studies due to differences in population, study protocols, and tasks/procedures which may have remained unaccounted for. However, it is important to note that only high-quality RCTs were used, a factor that supports our strong findings.

CONCLUSION

Our meta-analysis found that PBP trained groups outperform their traditionally trained counter parts, by not only completing procedures quicker but also making fewer errors, our study did however show that traditional (Non PBP) groups complete more number of steps but having said that there is significant evidence based on the results of this review to consider the integration of the PBP training method into current surgical training.

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Archives of Surgical Research | Systematic Literature Review

Utility of Workplace-Based Assessment Among Surgical Residents: A Systematic Literature Review

Nabila Talat, Muhammad Usama Aziz

IMPORTANCE This review article aims to assess the usefulness of Workplace-Based Assessment (WBA) among surgical residents. Multiple studies have been done in the past to determine the utility of WBAs across different fields of medicine. But it hasn't been done among surgical specialties on large scale, and the present paper fills in this research gap.

METHODS Articles were searched using PubMed and Google Scholar databases up to 30th June 2022. Following headings were used for the literature search i.e work-based assessment or workplace-based assessment or WBAs or direct observation of procedural skills or DOPS or procedure-based assessments or PBA or Case-based discussion or CBD or clinical evaluation exercise or CEX or Mini CEX, and surgical training. The utility formula of Vleuten was used to assess the usefulness of WBA. It is a product of validity, reliability, educational impact, acceptability, cost-effectiveness, and feasibility.

RESULTS For reviewing purposes, 29 studies were selected. There were 8 studies on PBA, 2 on Mini-CEX, 2 on CBD, 6 on DOPS, and 11 studies on multiple methods of WBA. PBA had positive satisfaction levels and was valid, reliable, feasible, and acceptable. CBD. Mini-CEX and CBD had very few studies in which they were proved to be reliable and valid but had mixed responses in terms of satisfaction levels. DOPS had a level 1 educational impact and also proved to be valid. When all components of WBAs were used together, a negative level 1 educational impact was observed. The concerns that were identified include lack of time, training and evidence of validity, design of the tool, and perception of WBA as a summative tool.

DISCUSSION Work-based Assessments should be implemented and used properly after the training of faculty. The focus should be on the quality of the assessments, not on the quantity. Large-scale studies should be done to assess level 3 and 4 of educational impact from WBAs.

KEYWORDS Work-based assessment, Surgical resident, Utility, Procedure based assessment, Case-based discussion, Clinical Evaluation Exercise, Direct Observation of Procedural Skills **HOW TO CITE** Talat N, Aziz MU. Utility of Workplace-Based Assessment Among Surgical Residents: A Systematic Literature Review. *Archives of Surgical Research*. 2022, 3 (2):11-18. https://doi.org/10.48111/2022.02.03

Systematic Literature Review

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he 21st century is bringing new challenges. There are expected rapid changes in surgical knowledge and understanding of diseases, new and better technologies, and surgical procedures. To keep pace with the modern world of science, training institutions need more active scrutiny and error judgment in their training programs¹. In the modern world, the current module of surgical training has been shaped by different modifications in medical education and training like modernizing medical careers and postgraduate education².

In the past, trainee doctors were mostly assessed for their knowledge using theory examinations and stimulated clinical assessments at the end of their training period. More emphasis was given on what a person knows rather than what he or she does in practice. However, doctors have multiple attributes besides specialty knowledge and skills, but also attitudes and generic skills like integrity, honesty, communication, and teamwork. Actual performance is the only reflection of the competence, i.e., day-to-day behavior and performance of a person in practice³. Workplace-based assessments (WBAs) are the skills that need to be assessed in clinical settings. Strong emphasis has been given to the assessment of trainees at the workplace⁴.

WBAs deal with all forms of work a resident usually does at his workplace⁵. The reason behind implementing the WBAs is to make sure that a trainee learns and develops through evidence-based progression to attain clinical competency⁶. Assessment of clinical skills in WBA correlates with the "Does" level in Miller's Pyramid (Fig 1)⁷.

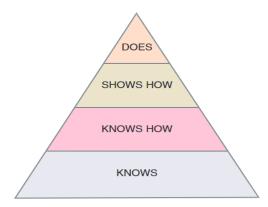


Fig 1. "Miller's Pyramid"⁷

There is always an emphasis on formative assessment of trainees and WBAs are a source of it. They provide feedback to improve trainees' development and learning⁸. Consultants or trainee's supervisors should carry out WBAs who assess skills, knowledge, and behavior during multiple daily tasks in a hospital⁹. (Fig 2)

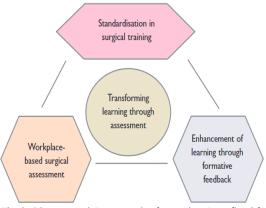


Fig 2. "Conceptual Framework of Learning Benefits Of Workplace-Based Surgical Assessment" ¹⁷

The working environment for Surgical Training is unlike other training programs. The surgical resident performs multiple tasks such as treating patients in wards as inpatients as well as patients in outpatient clinics, doing surgical procedures, and seeing patients pre and postoperatively. They require special surgical skills to complete their training which is not seen in other specialties. Some of the tasks can be performed independently by the surgical trainee at workplace in which he is competent enough, but direct observation of a

consultant is required for most of the surgical procedures. All types of work that a trainee do in his day-to-day tasks, should be included in WBAs¹⁰.

The WBAs include procedure-based assessments (PBA), case-based discussion (CBD), clinical evaluation exercise (CEX), and direct observation of procedural skills (DOPS). (Table 1)^{5,11–13}.

Procedure- Based Assessment (PBA)	(Orthopedic Proficiency Assessment Project (OCAP) initially produced PBA which was then introduced in other fields of surgery. PBA form includes feedback from instructor and trainee, several competencies, and a worldwide assessment. In case a trainee can perform the procedure with no guidance and deal with it on his own, then it means that this individual has attained the highest competence degree.
Clinical Evaluation Exercise (CEX)	American Board introduced CEX in medical specialties. It was then modified to mini CEX to suit the surgical clinical activities. The trainee is evaluated while wearing interactions with patients such as taking history, medical examination, communication skills, and professionalism. ¹¹
Case-Based Discussion (CBD)	CBD is an in-depth discussion with the trainee about the management of a patient. The trainee is assessed in terms of clinical knowledge, reasoning, and judgment. ¹²
Direct Observation of Procedural Skills (DOPS)	Initially, the Royal Colleges of Physicians developed a tool to assess operative, technical and professional skills in diagnostic and interventional procedures. Several modifications have been done to include different surgical procedures in it. ¹³

Table 1: Types of Workplace-Based Assessment

For more than 10 years, WBAs have been in use in general surgery training. Since its implementation, multiple studies have been published in the literature on the utility of WBAs in training. However, in surgery, there are not a lot of studies, especially on DOPs, CBD, and Mini CEX¹⁰. Due to the heterogenicity of the methods and outcomes of the previous studies, it is expected that there are very metastudies available in the literature. Saedon et al. stated in their systematic review that WBA provides valuable feedback which has a constructive effect on clinical practice. But it involved studies from all medical and surgical specialties⁸. Similarly systematic reviews of Barette et al. and Miler et al. also included articles from all medical specialties^{14,15}. Aryal et al. published 2 systematic reviews in 2019 and 2021 that focused on the educational impact and utility of WBAs in higher surgical training residents 10,16. But medical knowledge is everchanging so we needed an updated review about WBA and its components. This systematic review was done to assess the insight of the utility of WBA's among consultants and their trainees. This study reviews published articles on the utility of WBAs among residents of general surgical and surgical specialty training.

METHODS

This study has been reported following the guidelines of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)¹⁸. Literature was searched on the databases Pubmed and Google Scholar up to 30th June 2022. The literature search was done under the headings of work-based assessment or workplace-based assessment or WBAs or direct observation of procedural skills or DOPS or procedure-based assessments or PBA or Case-based discussion or CBD or clinical evaluation exercise or CEX or Mini CEX, and surgical training.

Inclusion criteria included quantitative or qualitative studies published in the English language, involving post-graduate surgical specialties trainees or trainers. Following surgical specialties were included: General Surgery, Orthopedic Surgery, Urology, Plastic surgery, Neurosurgery, Cardiothoracic Surgery, Vascular Surgery, Pediatric Surgery, Oral and Maxillofacial Surgery, Otolaryngology, and Ophthalmology. Studies involving, gynecology, pediatrics, anesthesia, endoscopy, dental, histopathology, medical students, nursing, and other specialties were excluded.

According to the inclusion and exclusion criteria, both authors did the initial scrutiny of the articles by titles and abstracts. Then full text of the selected articles was reviewed. Only those articles were selected which described the utility or usefulness of WBAs in surgical training. The final selection of the studies was also done by both authors. The usefulness of WBA is assessed by the utility formula of Vleuten. Utility= Validity x Reliability x Educational Impact x Cost effectiveness x Feasibility x Acceptability¹⁹.

"Extent to which a test measures what is intended to be measured and nothing else" is known as validity²⁰. Reliability is "a measure of the consistency and precision with which a test measures what it is supposed to assess"²¹. Educational impact may have 4 levels; Satisfaction, Learning, Behavior, and Results with better patient outcomes²². Cost-effectiveness of assessment means evaluating the benefits of a particular assessment against its cost⁷. Acceptability means the assessment tool is acceptable to the participants. Availability of sources, time, and personals will determine the Feasibility²³.

RESULTS

Initially, 257 studies were identified through a database search. Titles and abstracts of these articles were screened and 208 studies were excluded. Full-text review of 49 articles was done and out of which 29 were included in this study. (Fig 3)

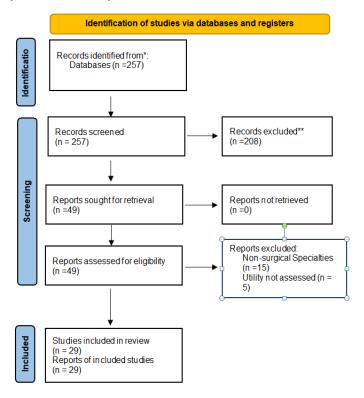


Figure 3. PRISMA 2020 flow diagram

Procedure-Based Assessment (PBA): We found 8 publications in surgical specialties describing PBAs (Table 2). Medeiros et al. showed high validity, reliability, and feasibility of PBA among urology residents²⁴. Rhamhamdany described a modified version of PBA for orthopedic trainees which had a better formative assessment of surgical skills. At the same time, it was not much acceptable due to the lengthy tick box activity²⁵. Shalhoub et al. stated that PBA has a high educational value but it should be perceived as formative tool²⁶.

Roushdi et al. found a high level of confusion among trainees and trainers regarding the use of PBA²⁷. Hunter et al. showed that PBA is a useful tool for feedback and learning but the focus should be on quality, not quantity²⁸. PBA was proved to be valid, reliable, acceptable, and feasible with a good satisfaction level in other ^{studies29–31}. Overall, PBA showed excellent utility and positive satisfaction among surgical residents.

Author	Study Design	Values Assessed	No of Participants	Subject Area	Results
Medeiros et al., 2021 ²⁴	Prospective, action- research study	Validity, Reliability, Feasibility	6 trainees 10 trainers	Urology training	PBA has high validity, reliability, and feasibility
Ramhamadany, 2020 ²⁵	Quantitative survey	Validity and acceptability	12 trainees	Orthopedic surgical residents	A modified version of PBA is a better formative assessment of surgical skill. Lengthy tool and prolonged tick box exercise questions its acceptability
Shalhoub et al., 2017 ²⁶	Qualitative semi- structured interviews	Validity, Educational impact	10 trainees	Different Surgical Specialities	"PBA has significant educational value when used as a formative tool"
Roushdi et al. 2015 ²⁷	Quantitative survey	Validity, Educational impact	39 trainees 21 trainers	Orthopedic Surgical Training	High level of confusion among trainers and trainees about both the purpose of PBA and the correct method of using them
Hunter et al., 2015 ²⁸	Quantitative Survey	Educational Impact	616 trainees	Orthopedic Surgical Training	Most residents found PBAs useful as a learning tool for the delivery of feedback. Quality should be improved rather than quantity
Marriot et al., 2011 ²⁹	Quantitative, Observational	Validity, reliability, acceptability	81 trainees	6 surgical specialties	Overall high validity and acceptability, and reliability
Beard et al., 2011 ³⁰	Quantitative, Observational	Acceptability, Reliability, Validity	85 trainees	6 surgical specialties	High acceptability, validity, reliability, and user satisfaction.
James et al., 2009 ³¹	Quantitative, Observational	Educational impact, feasibility	3 trainers 2 trainees	Higher surgical training	Feasible "Focused feedback and targeted training"

Table 2: PBA

Clinical Evaluation Exercise (mini-CEX):

We only found 2 studies evaluating mini CEX among postgraduate trainees in general surgery (Table 3). It

proved to be a valid, reliable, acceptable, and feasible tool and showed positive satisfaction among trainees and trainers^{32,33}.

Author	Study Design	Values Assessed	No of Participants	Subject Area	Results
Deshpande et al. 202132	Quantitative Observational	Educational impact, Validity, Reliability, Acceptability, Feasibility	18 trainees 10 trainers	Orthopedic surgical training	Mini-CEX improves technical and non-technical skills It is a valid, reliable, acceptable, and feasible tool
Joshi et al., 201733	Quantitative survey	Acceptability, feasibility	16 trainees 9 trainers	Higher surgical training	Mini-CEX is feasible and well accepted by trainees and trainers

Table 3: Mini-CEX

Case-Based Discussion (CBD)

The utility of CBD has been discussed in 2 studies for surgical specialties which include only trainees (Table 4).

These studies showed that CBD is reliable and valid with good educational impact but promotes tick box mentality^{34,35}.

Author	Study Design	Values Assessed	No of	Subject Area	Results
			Participants		
Philips et al.,	Quantitative survey	Utility, Educational	42 trainees	Surgical training	Provides feedback., Improves learning
201634		impact			Promotes tick-box mentality
Awad et al.,	Retrospective	Reliability, Validity	46 trainees	Otolaryngology	Case-based discussion is a reliable and valid tool
201535	database analysis				

Table 4: CBD

Direct Observation of Procedural Skills (DOPS)

Among DOPS, 6 studies are identified (Table 5). Inamdar et al. showed that DOPS is a feasible, acceptable, and effective tool³⁶. A study in Ophthalmology showed positive satisfaction among trainees³⁷. DOPS have helped improve surgical skills in multiple studies^{38,39}. Mathew et al. modified the DOPS tool into Surgical DOPS (S-DOPS) which showed

good uptake and construct validity as compared to the original version of the tool¹³. Awad et al. had a view that DOPS can differentiate between senior and junior residents⁴⁰. Overall DOPS proved to be valid, acceptable, and reliable with a good educational impact in surgical training.

Author	Study Design	Values Assessed	No of Participants	Subject Area	Results
Inamdar et al., 202136	Quantitative	Educational Impact, Feasibility, Effectiveness, Acceptability	30 trainees	Surgical training	DOPS is a feasible, acceptable, and effective tool
Sethi et al., 201937	Quantitative	Educational impact	115 trainees	Ophthalmology	Improvement in clinical skills with repeated DOPS
Hussain Waqar et al., 201638	Sequential mixed-method study	Educational impact, validity, feasibility	48 trainees	Surgical training	Improved surgical skills. Shortage of time and lack of training are the main concerns
Ali et al., 201939	Comparative study	Educational impact, Effectiveness	20 trainees 4 trainers	Urology training	DOPS is an effective tool for assessing and improving the surgical skills
Matthew et al., 201413	Quantitative	Construct validity, DOPS uptake	Phase 1, 1370 trainees Phase 2, 16 assessors and 15 trainees Phase 3, 3525 trainees	Surgical training	Good uptake and construct validity of the new S-DOPS.
Awad et al., 201440	Quantitative	Validity, Reliability	767 DOPS Trainees not mentioned	Otolaryngology	Reliable and internally consistent. Differentiates between junior and senior trainees

Table 5: DOPS

Multiple WBA Methods

When we searched for WBAs having all or maximum of its components within the same study, a total of 11 studies were found that highlighted the use of all or most of the components of WBAs within the same settings(Table 6). All of these studies highlighted several problems including negative satisfaction levels on educational impact. PBA was

identified as the most useful tool of assessment among all WBAs and CBD was at the 2nd spot. There were concerns about lack of time, training and evidence of validity, design of the tool, and perception of WBA as a summative tool. Multiple WBAs when used together can lead to confusion and negative satisfaction levels among trainers and trainees^{17,41–50}.

Author	Study design	Type of WBA	Value assessed	No. of Participants	Subject Area	Results
Aryal et al., 202041	Mixed method study	CEX, CBD, PBA, DOPS	Educational impact, Validity	Phase 1 - 27 trainers, 38 trainees Phase 2 - 5 trainers and 5 trainees	General surgical training	PBA was the most useful WBA. Useful when practiced with face-to- face validation, and trainer trainee engagement. Require time and training
Nathoo et al., 202042	Qualitative	WBA	Educational impact	4 trainees 9 trainers	Ophthalmology	WBA is an excellent feedback tool but needs to be designed well
Gaunt et al., 201743	Qualitative interviews	PBA, DOPS, CBD, mini-CEX	Educational impact	42 trainees	Surgical specialties	Negative feedback by trainees.
Gaunt et al., 201644	Quantitative survey	PBA, DOPS, CBD, mini-CEX	Perception of WBA	178 trainees 147 trainers	General Surgical training	Both trainers and trainees perceive WBA as a summative assessment tool
Pentlow 201545	Quantitative survey	PBA, DOPS, CBD, CEX	Educational impact	61 trainers 46 trainees	Orthopedics Training	Only PBA was perceived to be educationally valuable
Philips et al., 201546	Quantitative survey	PBA, DOPS, CBD, mini-CEX	Utility	64 trainers	General Surgical training	PBA and CBD were the most useful tools
Eardley et al., 201347	Qualitative	PBA, DOPS, CBD, mini-CEX	Validity, Reliability, Educational impact	No. of trainees not mentioned	Surgical specialties	PBA is the best tool for assessment. Concerns include proper training, time management, and lack of reliability and validity
Ali et al., 201248	ISCP portfolio	DOPS. PBA	Educational impact	170 trainees	Surgical specialties	Lack of feedback is recorded and when recorded, it is not of good quality
Pereira et al.,	ISCP portfolio	PBA, DOPS,	Educational	359 trainees	General surgical	Negative satisfaction.

201349	Quantitative	CBD, mini-CEX	impact		training	Inadequate evidence of validity
	Survey					
Stepathy et al.,	Qualitative	PBA, DOPS	Educational	4 trainees	General surgical	Concerns about validity and
201117	interviews		impact	14 trainers	training	feasibility of assessment tools
Pereira et al.,	ISCP portfolio	PBA, DOPS,	Educational	539 trainees	General surgical	Poor validity.
200950	Quantitative	CBD, mini-CEX	impact		training	41% reported a negative impact
	Survey					overall upon their training

Table 6: WBA

DISCUSSION

There is a vital role of assessment in trainees' progression. To improve their clinical skills, several tools have been developed. Their cognitive knowledge has been assessed by Written and oral exams, while their clinical skills are assessed by work-based assessment (WBA) methods. These methods either use real-life patients or simulated patients or also provide constructive feedback⁵¹.

Out of these 29 studies, only 10 studies discussed purely general surgery. PBA has been discussed in most of them. Among these WBAs, PBA appears to be most useful and then CBD⁴⁶. PBA is designed to assess the surgical competencies of trainees by direct observation and to provide feedback. PBA is a reliable, valid, acceptable, and feasible tool to assess trainees learning. PBA has significant educational value when used as a formative tool. Trainees perceive it as a means of targeted feedback and training^{24–31}.

But still, a high level of confusion among trainers and trainees exists about both the purpose of PBA and the correct method of using them. Many of them perceive PBA as a lengthy tool and prolonged tick box exercise which questions its acceptability. Emphasis should be on quality rather than quantity^{27,28}.

CBD is a performance-based assessment tool that is used to evaluate clinical assessment and reasoning, management, communication, and professionalism. CBD is regarded as a tool for learning because it allows discussion of complicated cases, and promotes higher-order thinking. CBD is regarded as a reliable and valid tool. It promotes feedback and evidence-based learning^{34,35}.

DOPS is used to test the "Does" level of the Miller's Pyramid. In DOPS, a trainee is observed for consent taking, the indication of the procedure, clinical awareness, handling complications, and communication skills, and then immediate constructive feedback is provided by the assessor. According to the Royal College of Physicians, DOPS is a valid and reliable tool in contrast to the old methods of assessments such as logbooks. DOPS is an effective tool for assessing and improving surgical skills.

DOPS is a feasible, acceptable, and effective tool. Major concerns were the shortage of time and lack of proper training^{13,36–40}.

MINI-CEX tool has been suggested for clinical assessment as well as teaching because it allows the observation of a trainee by different observers at different stages of their training and it also provides effective feedback. As a formative assessment tool, MINI-CEX is well accepted by the trainers and trainees. Mini-CEX improves technical and non-technical skills. It is a valid, reliable, acceptable, and feasible tool^{32,33}.

In most of the centers, 40 WBAs per year are being used. One study suggested that 18 WBAs were used in their training program every year²⁸. Their quantity should be adequate to maintain reliability as well as their quality. Some centers use 80 numbers but they may decrease their quality¹⁰. These studies showed that WBAs should be used as a formative tool to improve their value.

Miler and Archer stated in their review that WBA leads to improved performance of residents but several factors like the presence of facilitation and the design of the feedback tool can have effects on the response. When multiple tools (PBA, CBD, DOPS, Mini-CEX) were used together, it did not show any improvement in the performance although it had a positive educational impact¹⁵. Saedon et al. had a view that if feedback from workplace-based assessments is well implemented, it can lead to a positive effect on practice⁸.

The concept of WBAs among trainees and trainers is gaining popularity day by day. As most of their users are certain that they help to develop and improve their clinical skills if used correctly. WBAs, when used alone or as a component, they had an excellent validity, utility, reliability, acceptability, and high educational impact. But it is not the same scenario when these tools are used together. The possible reasons for this are that WBAs are not used properly, there is always a shortage of time, avoidance of face-to-face feedback, lack of faculty training, and use of WBA as a summative feedback tool^{17,41–50}.

The medical field is an everchanging world, which always demands you to improve yourself and one of the best ways

to improve is by feedback and assessment. There will always be a need for a professional assessment of the trainee and WBAs should be used for this assessment so that there will be continuous development of clinical skills. But the point is that they should be properly used so that most of the benefits can be achieved. We need studies on larger scales to assess these tools and to define their role in the training of general surgery residents.

CONCLUSION

Work-based Assessments should be implemented and used properly after the training of faculty. All components or methods of WBAs should not be incorporated or used simultaneously. The focus should be on the quality of the assessments, not on the quantity. Large-scale studies should be done to assess level 3 and 4 of educational impact from WBAs.

Recommendation: We recommend that WBA should be implemented in all public and private hospitals. The model of WBA in the UK can be used as a template for this purpose. Specialty-based relevant methods and tools should be opted and utilized rather than implementing all tools together. We also suggest that undergraduate students should also be included in this setup.

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Archives of Surgical Research | Systematic Literature Review

The Role of Tranexamic Acid in the Prevention of Perioperative Hemorrhage

Igra Imtiaz, Sana Fatima, Abu Haraira Sabir, Hira Ashraf

IMPORTANCE Significant blood loss can occur as a result of trauma, surgery, anticoagulation, obstetric complications, and hemostatic disorders. As there are many diverse causes of hemorrhage, the availability of a clinically safe and effective hemostatic agent is the need of the hour. Tranexamic acid is one of the most commonly used and widely researched anti-fibrinolytic agents. Its role in trauma-associated, postoperative, and postpartum hemorrhage has been well recognized. However, the utility of tranexamic acid goes farther than these common indications, supported by accruing data suggesting its ability to reduce blood loss along with improvement in clinical outcomes in many hemostatic challenges without increasing thromboembolic risk.

OBJECTIVE To review the clinical application and effectiveness of tranexamic acid in the prevention of intraoperative hemorrhage.

METHODS: Secondary data were selected by utilizing three steps; identification of 490 articles, recruitment of 116 articles, and selection of 61 articles for the systematic review. Inclusion and exclusion criteria were designed according to PRISMA protocol.

RESULTS Tranexamic acid has reduced perioperative hemorrhage and blood transfusion requirements in elective surgical procedures. Many studies established the efficacy of tranexamic acid and its safety without raising thromboembolic risk, precipitating kidney failure, or their complications.

CONCLUSION In multiple clinical scenarios, tranexamic acid has proven to prevent hemorrhage without increasing thromboembolic risk and has broad-spectrum clinical indications. However more caution and regulatory guidelines need to be established to prevent the rare incidence of complications so as thromboembolism and seizures.

KEYWORDS Tranexamic acid, Prevention of haemorrhage, Intraoperative, General surgery, Anti fibrinolytic

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ranexamic acid, a synthetic amino acid has shown to be effective at preventing complications of bleeding in various hemostatic challenges due to its antifibrinolytic activities and reducing mortality rate with negligible side effects. 1-7 In one study, tranexamic acid has shown to decrease bleeding by nearly one-third as compared to placebo. 8 A hemostatic agent, such as tranexamic acid, with wide-ranging applicability and insignificant side effects is desirable as a part of supportive care protocol for hemorrhage. 3

Massive blood loss following severe trauma or surgical intervention remains one of the most common life-threatening emergencies. Haemorrhagic shock associated with trauma is the recurrent cause of preventable

mortality, along with hyper-fibrinolysis at the time of hospitalization is a well-known predictor of mortality. 12-14 Tranexamic acid has been extensively used for the prevention and treatment of hemorrhages and hyper-fibrinolysis. Clinical data has shown that timely administration of tranexamic acid following severe trauma can significantly improve the rate of survival. Studies are focused on the intravenous administration of tranexamic acid. However oral preparations have the same efficacy and safety. 15-18

The decrease in intraoperative hemorrhage and the consequential decline in blood transfusion requirement has prompted the European Society of Anaesthesiology and Task Force for Advanced Bleeding Care in Trauma to issue a 1A recommendation in their guidelines for use of tranexamic

acid in the event of perioperative and trauma-associated hemorrhage. ^{10,11}

METHODS

Search engines employed to obtain scientific data for this review were; PubMed and Google Scholar. After recruitment, data were carefully chosen based on the inclusion criteria.

Search Strategy, Data Extraction, and Inclusion Criteria:
We searched the Pubmed database using the terms: Search:

We searched the Pubmed database using the terms: Search: (tranexamic acid) AND (perioperative hemorrhage) Filters: Free full text, from 2018 - 2022 Sort by: Most Recent. The Google Scholar database was also searched using the term: "tranexamic acid and perioperative hemorrhage." PRISMA

guidelines were used for the inclusion of data in this systematic review. For inclusion, the procedure was divided into three steps; identification, primary selection, and final selection. In the first step, 490 articles were identified. 16 articles were selected in the second step. In the final step, 11 most relevant and admissible articles were selected. The selected articles, based on randomized trials, contained clear abstracts, and no older than five years, and were peer-reviewed.

Exclusion Criteria: Articles published more than five years ago and articles without any abstract or background information were excluded. Articles with fewer references and a lack of proper author information and affiliation were also excluded.

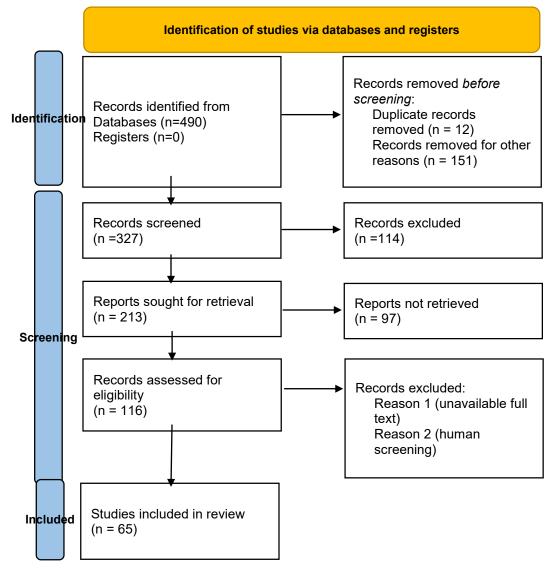


Figure 1: Article selection process through PRISMA flowchart; (From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71)

RESULTS

Bleeding remains one of the top perioperative complications in many surgical operations, including liver surgery. It has reduced the blood transfusion requirement and reoperation rate following hemorrhage. Tranexamic acid has been used intraoperatively in different surgical fields to reduce blood loss and maintain hemostasis. The potential of tranexamic acid in avoiding bleeding during and after surgery has been a subject of interest. The most important benefit of treatment is the absence of deaths. Delayed administration of tranexamic acid reduces treatment benefits.³

Year	Author	Country	Research Method	Themes Identified	
2022	SJ (SJ et al., 2022)	India	Cohort	Administration of tranexamic acid effectively reduces the need for blood transfusion.	
2022	Zha (Zha et al., 2022)	People's Republic of China	Observational study	Preoperative administration of tranexamic acid reduces the need for blood transfusion without an increase in risk for DVT.	
2022	Kukreja (Kukreja et al., 2022)	USA	Cohort	The use of a tourniquet to control hemorrhage in a limb is superior to using tranexamic acid peri-operatively.	
2022	Koh (Koh et al., 2022)	UK	Systematic review and meta- analysis	Administration of tranexamic acid effectively reduces the need for blood transfusion in elective extrahepatic abdominopelvic surgery.	
2022	Ek (Ek et al., 2022)	Australia	Cohort	Administration of tranexamic acid effectively reduces bleeding without any change in postoperative pain or range of motion.	
2022	Compton (Compton et al., 2022)	USA	Comparative study	Administration of tranexamic acid effectively reduces the need for blood transfusion.	
2022	Regan et al.	USA	Expert analysis	Tranexamic acid is highly effective in reducing bleeding but increases cardiovascular risk, due which an individualized approach should be used mind while administering it.	
2021	Liu (Liu et al., 2022)	People's Republic of China	Cohort	There are various fibrinolytic phenotypes, only some of which demonstrate a response to tranexamic acid transfusion.	
2021	Huynh (Huynh et al., 2021)	USA	Retrospective Chart Review	Administration of tranexamic acid effectively reduces the need for blood transfusion.	
2021	Pinsornsak et al.	Thailand	RCT	Peri-articular injection of tranexamic acid in total knee arthroplasty is better for high risk patients in terms of adverse effects as compared to intravenous injection.	
2021	Xie (Xie et al., 2021)	People's Republic of China	Case Report	Perioperative tranexamic acid transfusion may increase the risk of thromboembolism.	
2021	Wei et al.	China	Systematic review and meta- analysis	Prophylactic tranexamic acid administration reduces blood loss during primary shoulder paediatric surgery.	
2020	Kang et al.	China	RCT	Perioperative use of tranexamic acid in three doses during total knee arthroplasty reduces fibrinolytic response and inflammation safely.	
2020	Monaco et al.	Italy	RCT	Infusion of tranexamic acid prophylactically in abdominal aorta aneurysm repair does not reduce intraoperative blood loss.	
2020	Gao et al.	China	Clinical Study	Topical use of tranexamic acid during arthroscopic shoulder surgery reduces tissue swelling safely.	
2020	Yoon et al.	Republic of Korea	RCT	Haemorrhage does not differ among different routes of tranexamic acid administration during reverse total shoulder arthroplasty. Topical administration has a better safety profile and should be preferred.	
2020	Hurley	Ireland	RCT	Perioperative use of tranexamic acid during Latarjet procedure decreases post-operative bleeding, pain, swelling, hematoma formation and opioid use.	

2020	Meissner et al.	Germany	Cohort Study	Perioperative use of tranexamic acid does not reduce haemorrhage after open –heart surgery. Its use should be confined to patients at	
				risk of massive blood loss and hyperfibrinolysis.	
2020	Khadanga et al.	India	Cohort Study	Tranexamic acid administration reduces blood loss during Off Pump Coronary Artery Bypass Grafting.	
2019	Abdul et al	Nigeria	RCT	Adjunctive use of tranexamic acid with tourniquet during myomectomy reduces haemorrhage.	
2019	Zhang et al.	People's Republic of China	RCT	Both peri and intra articular injections of tranexamic acid safely reduce bleeding in total knee arthroplasty.	
2019	Liu et al.	Taiwan	RCT	Parenteral tranexamic acid administration reduces perioperative haemorrhage, pain and analgesia requirement during and after arthroscopic shoulder surgery	
2019	Hirose et al.	Japan	Case series	Tranexamic acid is effective in improving range of motion after total knee arthroplasty.	
2019	Fenger-Eriksen et al.	Denmark	RCT	Intraoperative and postoperative tranexamic acid administration reduces bleeding and need for blood transfusion.	
2018	Kim et al.	Republic of Korea	Clinical Trial	Prophylactic tranexamic acid administration safely reduces blood loss during craniosynostosis surgery.	
2018	Saleh et al.	Egypt	RCT	Perioperative use of tranexamic acid during posterior spinal fusion surgery increases the need analgesia, indicating increased nociception.	
2018	Sallam and Shady	Egypt	RCT	Parenteral and topical tranexamic acid administration safely reduces blood loss during abdominal hysterectomy.	
2018	Prasad et al.	India	RCT	In abdominal tumour resection surgery, tranexamic acid bolus followed by infusion is superior to a single bolus in reducing haemorrhage.	
2018	Shady et al	Egypt	RCT	Parenteral and topical tranexamic acid administration safely reduces blood loss during abdominal myomectomy	
2018	Yozawa et al.	Japan	Observational study	Peri-articular injection of tranexamic acid in total knee arthroplasty is better for high risk patients in terms of adverse effects as compared to intravenous injection.	
2018	Abbas et al.	Egypt	RCT	Perioperative use of tranexamic acid results in decreased haemorrhage during cesarean section for placenta accreta.	
2018	Cvetanovich et al.	USA	RCT	Prophylactic tranexamic acid administration reduces blood loss during primary shoulder arthroplasty.	
2017	Vara et al.	USA	RCT	Tranexamic acid administration in reverse total shoulder arthroplasty reduces bleeding and reduction in haemoglobin.	
2017	Pauzenberger et al.	Austria	RCT	Intraoperative transaumic acid administration reduces bleeding and need for blood transfusion, pain and hematoma formation in total shoulder arthroplasty.	
2016	Sujata et al.	India	RCT	Preoperative intravenous tranexamic acid administration reduces the need for additional uterotonics in women at risk for post-partum haemorrhage.	
2016	Topsoee et al.	Denmark	RCT	Prophylactic tranexamic acid administration safely reduces blood loss during elective benign hysterectomy.	
2016	Mao et al.	People's Republic of China	Comparative Study	Both peri and intra articular injections of tranexamic acid reduce bleeding in total knee arthroplasty. However, peri-articular injection shows superiority in reducing haemorrhage.	
2016	Alhomoud	Kuwait	Prospective randomized study	Tranexamic acid administration before laparoscopic sleeve gastrectomy reduces intraoperative bleeding without any side effects.	
2015	Gillespie et al.	USA	RCT	Tranexamic acid reduces haemorrhage in total shoulder arthroplasty.	
2014	Lundin et al.	Sweden	RCT	Prophylactic tranexamic acid bolus reduces blood loss during advanced ovarian cancer surgery	
2013	Goswami et al.	India	RCT	Perioperative use of tranexamic acid during lower section caesarean secton reduces the need for blood transfusions, especially in anaemic patients.	
2013	Sentürk et al.	Turkey	RCT	Prophylactic administration of tranexamic acid before caesarean section safely helps reduce haemorrhage.	

2013	Shahid and Khan	Pakistan	RCT	Perioperative use of tranexamic acid during lower section caesarean secton reduces bleeding during surgery, but not after it.	
2013	Xu et al.	China	RCT	Perioperative use of tranexamic acid safely results in decreased haemorrhage during cesarean section.	
2013	Eldaba et al.	Egypt	RCT	Adjunctive use of single bolus tranexamic acid during functional endoscopic sinus surgery reduces haemorrhage and duration of surgery.	
2012	Pfizer	India	Interventional Clinical Trial	Administration of tranexamic acid reduces blood loss during surgery.	
2012	Aggarwal et al.	India	RCT	Sonoclot analysis is a safe and useful tool to monitor fibrinolysis and clotting in patients going intra-cardiac repair for tetralogy of Falot.	
2012	Kumar et al.	India	RCT	Parenteral tranexamic acid administration safely reduces perioperative haemorrhage in percutaneous nephrolithotomy.	
2012	Brum et al.	Brazil	RCT	Parenteral tranexamic acid administration does not reduce perioperative haemorrhage.	
2011	Goobie et al.	USA	RCT	Perioperative use of tranexamic acid in surgical correction of craniosynostosis results in decreased haemorrhage and need for blood transfusion.	
2011	Dadure et al.	France	RCT	Perioperative use of tranexamic acid in surgical correction of craniosynostosis results in decreased haemorrhage and need for blood transfusion in children pre-treated with erythropoietin.	
2011	Shimizu et al.	Japan	RCT	In paediatric cardiac surgery, tranexamic acid reduces haemorrhage but not transfusion rate.	
2008	Allanki et al.	India	RCT	Perioperative use of aprotinin and tranexamic acid during orthotopic liver transplant may reduce the need for blood transfusions.	
2006	Wu et al.	China	RCT	Parenteral tranexamic acid administration reduces perioperative haemorrhage.	
2005	Bulutcu et al.	Turkey	RCT	Perioperative use of aprotinin and tranexamic acid during cardiopulmonary bypass reduces the need for blood transfusions.	
2005	Sethna et al.	USA	Clinical trial	Tranexamic acid administration safely reduces blood loss during surgery for scoliosis.	
2004	Chauhan et al.	India	Clinical Trial	Tranexamic acid bolus administration before skin incision, on bypass, and after giving protamine gives the best results to reduce bleeding during paediatric cardiac surgery.	
2004	Chauhan et al.	India	Clinical Trial	Infusion of tranexamic acid and/or Epsilon Aminocaproic Acid prophylactically in surgery for cyanotic heart disease equally reduces intraoperative blood loss and need for transfusion.	
2000	Dalmau et al.	Spain	RCT	Prophylactic administration of tranexamic acid before liver transplant helps reduce haemorrhage within the first 24 hours. However, adverse effects such as arterial thomboses need to be kept in mind.	
1997	Kaspar et al.	USA	RCT	Small dose tranexamic acid infusion reduces fibrinolysis but not the need for blood transfusion in orthotopic liver transplant surgery.	
1996	Boylan et al.	Canada	RCT	High dose tranexamic acid infusion during orthotopic liver transplant may reduce the need for blood products transfusions.	
1996	Zonis et al.	Canada	Clinical trial	Tranexamic acid administration in children undergoing cardiac surgery reduces bleeding only in the first 6 hours of the surgery.	
1993	Yassen et al.	UK	RCT	Perioperative tranexamic acid administration may result in serious adverse effects, blood loss, and transfusion requirements.	

DISCUSSION

Patented for the first time in 1957 and approved in the US in 1986, tranexamic acid is a synthetic lysine derivative used as an antifibrinolytic. Tranexamic acid is 10 times more potent than epsilon-aminocaproic acid.¹⁹ Tranexamic acid competitively inhibits the activation of plasminogen to

plasmin, hence, inhibiting the pathway of fibrinolysis. The recommended dosage of Tranexamic acid after cervical conisation is 1.5 g thrice daily for up to 14 days postoperatively¹⁹; though administration of Tranexamic acid is not recommended for mild gynecological interventions e.g. myomectomies.^{11, 20} It does so by blocking the lysine sites of plasminogen completely,²¹ to keep in check the extension of coagulation and clot formation beyond the

injury.²² At higher doses, it can directly inhibit plasmin function.²³ By inhibiting the binding of plasmin to fibrin, it prevents the dissolution of fibrin, thereby, stabilizing clot and preventing hemorrhage.

The therapeutic indications for IV, topical or oral tranexamic acid depend on the severity of the clinical condition and physicians' assessment. Major indications preoperative hemorrhagic prophylaxis and perioperative and postoperative hemorrhage management. It is especially useful in geriatric populations undergoing surgery who are more vulnerable to bleeding and other perioperative complications such as thrombosis mainly due to their comorbidities.⁷ Other indications include bleeding in gastrointestinal conditions, UTIs, menorrhagia, epistaxis, trauma, and coagulopathies. (Table 1) It is used perioperatively in cases where a decrease in hemoglobin drop, blood loss, drain output, and blood transfusion rate is highly desired without an increase in adverse effects such as DVT or infection.²⁴ Perioperative hemorrhage makes for problematic dissection, unclear surgical field, poor healing of surgical site, increased incidence of complications, and poor functional results.²⁵

It has been used and studied widely in orthopedic procedures with remarkable results^{26,27} Tranexamic acid has long been studied for its efficacy and safety. It has been used by clinicians due to its desired outcomes for years. It may be used intravenously or topically, both methods being remarkably advantageous.²² But its widespread and overthe-counter use deserves a safety and efficacy profile.

Intravenous administration

Prophylaxis and treatment of bleeding due to a local or systemic hyperfibrinolysis

Menorrhagia

Gastrointestinal bleeding

Bleeding in urinary tract infections, post-op bleeding following prostatectomy

Ear, nose, and throat surgery

Gynecological or obstetric hemorrhage

Abdominothoracic and cardiac surgery

Antidote in bleeding needing immediate treatment in patients on fibrinolytic treatment

Oral administration

Hypermenorrhoea (menorrhagia)

Prostatectomy

Epistaxis

Conisation of the cervix

Prophylaxis of recurrent traumatic bleeding

Mucosal bleeding in patients with coagulopathies

Hereditary angioneurotic edema

Table 1: Indications for tranexamic acid

The role of tranexamic acid specifically in elective surgeries is reviewed in this article. Many studies support the use of

tranexamic acid in pre, peri, and postoperative bleeding. It reduces the incidence of hemorrhage, hence, theoretically reducing the blood transfusion requirement. Practically this is not always the case.²⁸ Blood transfusions themselves pose the threat of early recurrence of various neoplasia, the transmission of viral infections, hypersensitivity reactions, circulatory overload, bacterial contamination, and reduced immunogenicity.²⁹ But the real question is does this desired outcome of hemorrhage prevention come with undesired incidence side effects? Does it increase the thromboembolism, ischemic damage, organ disseminated intravascular coagulation?

The S3 guidelines of the German Society of Accident Surgery³⁰, for Anaesthesiology, Austrian Society Resuscitation and Intensive Care, and European guidelines¹⁰, 11 recommend early administration of tranexamic acid whenever hyper-fibrinolysis is suspected in polytrauma patients.31 The CRASH-2 study shows that administration of tranexamic acid later than 3 hours is associated with increased mortality,15 suggesting it should be used as early as possible.¹⁹ The use of tranexamic acid is well-known in acute bleeding following severe trauma due to this study.17,32-34 However, in some literature, it is not more effective than other measures to control hemorrhage.35 Another systemic literature review demonstrates the advantage of using tranexamic acid for decreased bleeding risk in elective extrahepatic surgical operations.³⁶ This study also makes known no increased risk of thromboembolism.³² The WOMAN trial³⁷ also established that tranexamic acid should be administered as soon as possible after the initial onset of bleeding, and reported decreased incidence of deaths. The optimal timing and dosage of administration, however, remain debated.³⁸ It is to be extrapolated from the HALT-IT trial that bleeding from tranexamic acid has different effects on different populations and different pathophysiologies of hemorrhage.³⁶ Two important guidelines for anticoagulation management issued by the Society of Thoracic Surgeons (STS) and the European Association for Cardio-Thoracic Surgery (EACTS) deal with the intraoperative use of anti-fibrinolytic in cardiac surgeries: both Tranexamic acid and Epsilon-aminocaproic acid are consistently recommended to minimize hemorrhage and blood transfusion requirement.9, 39

Many contraindications have been reported for tranexamic acid but no study reported an increased risk of thromboembolism, hypoxic tissue injury, and disseminated intravascular coagulation even with a longer duration of administration and higher dosages.⁴⁰ Data available continue to support the use of tranexamic acid in medical and surgical cases due to its strong safety profile with

minimal side effects and no increased thromboembolic risk.⁴¹ Caution should be taken when dealing with patients having kidney dysfunction as tranexamic acid clearance is dependent on renal creatinine levels so dosage should be reduced but it does not increase the risk of renal failure (Table 2).⁴²

Hypersensitivity to TXA

Early pregnancy, in late pregnancy only when vitally indicated

Disturbances of color vision

Massive bleeding in the upper urinary tract (risk of ureter obstruction due to clot)

Acute venous or arterial thrombosis

Severe renal impairment

History of convulsions

Intrathecal and intraventricular injection, intracerebral administration (risk

of cerebral oedema and convulsions)

Disseminated intravascular coagulation (DIC)

Table 2: Contraindications of tranexamic acid

Dosing regimens sometimes vary owing to the practitioner's clinical assessment, deciding whether re-dosing is necessary. The prescribed regimen is 1 to 1.5 gm or 15 to 25 mg/kg up to four times daily⁴³, and 3g for topical use.⁴⁴ A dose of 15mg/kg was more efficacious as compared to 10mg/kg in one study.45 Repeated doses have the disadvantage of nonuniform levels of tranexamic acid in the blood, which leads to unpredictable coagulopathic behavior in blood.46 Nonetheless, the outcome supports its utility in preventing life-threatening blood loss with negligible adverse effects perioperatively.³ Since, tranexamic acid prevents the lysis of already formed fibrin deposits, it should increase the thromboembolic risk. However, the literature did not report any statistically significant incidence of thromboembolism with the use of tranexamic acid in major surgeries.^{37,47} Tranexamic acid has a well-known safety profile with no increase in the risk of thromboembolism, irrespective of its dosage. (Table 3)

Events	RR	95% CI
Myocardial infarction	0.96	0.48-1.90
Stroke	1.25	0.47-3.31
Deep venous thrombosis	0.77	0.37-1.61
Renal failure	0.73	0.16-3.32

Table 3 Side effects of Tranexamic acid

There is a growing literature body advocating for perioperative use of tranexamic acid for a remarkable reduction in hemorrhage with negligible adverse effects in different fields, especially in orthopedic surgery as suggested by SJ et al.7, Zha et al.47, Liu et al.,24 Ek et al.48, Compton et al.³⁸, and Huynh et al.⁴⁹, with peri-articular injections having more potential benefits^{50–52} Similar results have been observed in pelvic^{53,54}, extrahepatic, cardiac^{55,56} and liver57,58 surgery.^{4,36} It is also proven to be efficacious in the pediatric population.^{59,60} It is postulated that a blood transfusion-free hepatectomy may be possible with the adjunctive use of tranexamic acid. 61 Tranexamic acid is found to be superior to ε-aminocaproic acid and other such antifibrinolytics in this regard in one study.⁶² Another study contradicts this finding and has found epsilon-amino caproic acid and tranexamic acid to be equally effective.⁶³

There may be multiple factors for explosive hemorrhage after liver transplant, some of which include mixing of tissue plasminogen activator, hypothermia, and residual heparin from the donor's liver.⁶⁴ Tissue plasminogen activators arise about 30 minutes after the start of surgery, which theoretically poses to be the best time for the administration. 65 Even topical irrigation with tranexamic acid in benign hysterectomy significantly reduces hemorrhage and postoperative hemoglobin decrease,65 with the advantage of reduced postoperative complications, and comparable effect to intravenous injection on reduction in hemorrhage^{66,67} In one study, tranexamic acid did not reduce the transfusion rate, but it is thought to be due to the already minimal need of blood transfusion in benign hysterectomy.⁶⁸ However in gynecological malignancy cases, tranexamic acid reduced the rate of transfusion by almost 12% in another study.⁶⁹ It is associated with a safe reduction in perioperative bleeding.⁷⁰ The antifibrinolytic action can be deduced by measurement of blood loss, D-dimers, clot lysis assay, thromboelastometry, and Sonoclot assay. 71,72 It is also found to be useful in cardiac surgery in the pediatric population, although the calculation of the dosing regimen in such patients is complicated.⁷³ Chauhan et al.⁷⁴ have put forward a regimen of dose of 10mg/kg thrice (at the time of induction, on cardiopulmonary bypass, and administration of protamine sulfate) during pediatric cardiac surgery, with good results.⁷⁵ A similar three-dose regimen showed good results in total knee arthroplasty. 76 Tranexamic acid use is also associated with a decrease in operative time, post-operative respiratory complications⁷⁷, pain, hematoma formation, blood volume loss in drainage, 78 anemia induced infarction, blood or blood products transfusions⁷⁹, recovery time⁸⁰ and hospital stay.⁸¹ which in turn reduces blood loss and morbidity.82 It however does not show a decrease in postoperative blood loss either after discontinuation⁸³ or additional dosing⁸⁴. In some studies it has only shown to reduce intra-operative bleeding, more often only during the first 6 hours.85 In other cases, it has not shown a benefit at all.⁸⁶ Some literature suggests that tranexamic acid is useful in only some cases, and in cases where it is not, it may cause ominous side effects such as fibrinolytic shutdown and thromboembolism⁸⁷, resulting in mortality.^{22,88} It is also postulated to increase nociception and hence, analgesia requirement and opioid use post surgery.⁸⁹ Some studies contradict this as there is of decreased hematoma formation and pain after using tranexamic acid ^{90,91}

Tranexamic acid can be used safely as an anti-fibrinolytic with minimal side effects in surgical patients prophylactically as well as postoperatively. It has significantly reduced morbidity and mortality rates associated with hemorrhage. It has particular significance in developing countries where it is conveniently available and cost-efficient as opposed to other means to control bleeding. 93,94

CONCLUSION

Hemorrhage is one of the most serious complications and the leading cause of high mortality rate in postoperative patients. Hemorrhages following abdominopelvic, gynecological, and trauma surgeries are unwanted and lifethreatening complications. To avert or manage this outcome without considering reoperation would be a significant advancement in surgical fields. Antifibrinolytic drugs such as tranexamic acid and aminocaproic acid have proven to be a life-saving miracle.

In multiple clinical situations, tranexamic acid has proven to prevent bleeding without increasing thromboembolic risk and has broad-spectrum clinical indications. Dosing regimens occasionally depend on the practitioner, but outcomes support their utility in preventing life-threatening blood loss with minimal side effects intraoperatively as well as postoperatively. However, the side effects should be kept in mind, which although rare, can be disastrous. The data reviewed in this literature study have shown that tranexamic acid is very effective in preventing hemorrhage-related deaths when timely administered.

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Archives of Surgical Research | Commentary

Artificial Intelligence in Surgery: Dawn of New Era

Minhaj Rafi, Haadia Ali, M Waqas Arshad

IMPORTANCE Artificial intelligence is rapidly reshaping science and healthcare. Approximately 37% of organizations have implemented some sub-entity of Al in their daily workings which include social networking, airplanes, robots, and deep learning computers and surgical science is no exclusion. This article aims to review and summarize major aspects of artificial intelligence (Al), along with its practical implementation, limitation, and potential in the field of surgery.

METHODS Published multidisciplinary literature search was conducted on artificial intelligence in medical science to recognize different techniques and prime concepts that are bringing about innovation across multiple industries, including surgery. Barriers and challenges of working with Al were also scrutinized.

RESULTS & DISCUSSION The major dimensions of AI include: (1) Machine learning, (2) reasoning, (3) problem solving, (4) perception, and (5) language. Their current role and future implementation in surgical practice were introduced including big data sets and systems that aid in medical decisions. Besides this, the duty of surgeons in promoting and facilitating this technology to optimize clinical effectiveness was also brought into consideration.

CONCLUSION Al carries the potential and aptitude to revolutionize the way surgery is being taught and practiced over the past years. The surgeons themselves are eager and well-positioned in integrating Al into modern practice, however, in order to attain this, they require the expertise of data scientists.

Keywords: artificial intelligence, surgeons, machine learning, reasoning, problem solving, perception, language, computer, machine, analysis, integration.

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y definition, "Al is the ability of a digital computer or computer-controlled robot to perform tasks commonly associated with intelligent beings4." It aims to develop a system endowed with the intellectual characteristics of humans such as reasoning, generalization, discovering meaning, or simply to learn from past experiences⁵. Al is significant mainly not only because it can give enterprises insights into their operation that they might have not known earlier, but also can complete the assigned task efficiently, with relatively few errors along with its ability to perform and analyze certain detailed tasks better than humans. We can practically see this with the help of a few examples like iRobot which uses AI to analyze, identify and remember efficient routes to keep the room clean, Hanson robot i.e Sophia an advanced robot that while using AI can communicate in natural language and human-like emotions through facial can convey expressions⁶. Another example can be seen in the form of a virtual nursing assistant which quarantees its availability

throughout the day, guides patients about their problems and directs them to the best healthcare setting with which they can save a huge amount of money annually. These advancements demonstrate that although machines are notorious yet are not only accepted but are also in high demand. From incorporating machines into our day-to-day work to the consequent industrial revolution, machines and Al have played a massive role in improving the quality of life². Therefore, surgeons should know the basics and impact of Al on the healthcare system and should consider possible ways in which they can interact with this technology.

DIMENSIONS IN AI

Al is a part of a lot of disciplines including philosophy, psychology, linguistics, statistics, robotics, maps, etc. Major advancements in computer science such as better speed and power led to the advent of Al and also contributed to

the growing popularity that helped it in venturing a capital investment worth \$ 5 billion dollars in 2016⁷.

The gist of AI, its subfields are discussed below:

- **A. Machine learning:** Amongst the different forms of learning the simplest and commonest is learning by trial and error². For instance, a computer tries a method, observes if it works in case it does not work, it tries a new method until a solution is reached. The program might then store the solution with the position so that the next time the computer encounters the same information it would recall the solution automatically. This basic act of memorizing individual items is known as "rote learning" which is relatively easier to implement on a computer⁸. With other Al applications machine learning has been enhanced to a supreme level that helps in solving major problems in no time.
- **B. Reasoning:** It simply is to draw inferences that are apt according to the situation. Inferences can either be deductive or inductive^{4,9}. An example of deductive reasoning is that "all spiders have eight legs. Since Tarantula is a spider, therefore, it has eight legs¹⁰." The example of inductive reasoning is "Mary and Jim are left-handed and use left-handed scissors since Bill is also lefthanded therefore he uses left-handed scissors as well¹¹. These examples show that in the deductive case, the truth of premises guarantees the truth of the conclusion and is used in mathematics and logic whereas, inductive reasoning is a general conclusion from a set of specific observations⁹. Therefore, inductive reasoning is more common in science where data is gathered, and tentative models are built⁴.

These inferences have been a success, especially deductive reasoning; however, true reasoning is more complex than this as it involves drawing inferences relevant to the solution of the problem, which is a challenge in itself⁴.

C. Problem-solving: Regarding AI, it systematically deals with a range of possible actions in order to reach a solution. It consists of two types a) special purpose and b) general purpose⁵. The special-purpose method deals with a distinct problem and frequently exploits specific features of the situation in which the problem is deep-rooted⁴ e.g., in UBER that gives the user the nearest link to its driver. In contrast to this, general-purpose uses a technique that is applicable to a wide range of problems on the basis of signal input for example a robot that has the ability to move forward or backward⁴.

D. Perception: In this, the environment is analyzed and interpreted with the help of various sensory organs, be it real or artificial. The analysis, however, is complicated by the fact that an object may appear differently depending on various factors like the angle from which it is viewed, and the intensity and direction of light present at the scene⁴. Machines in Al have different types of perception devices like cameras, mic etc. The camera assesses the object and a huge network of chipsets evaluates it and gives further commands according to the predefined dataset stored in its memory, for example, the self-driving mode in a car which assists in driving the car.

E. Language

It is a way of communication through vocals and signals both via which a person or robot can communicate with its surroundings. An important characteristic of human language is its productivity⁴. Similarly, a computer can communicate in innumerable ways like light signals, sound, written sentences, pictorials, etc. A developmental milestone in Al, SIRI can communicate with its user verbally on the basis of a vast datasheet and can fulfill the user's desires.

COLLABORATION OF AI WITH OTHER FIELDS

Al believes in combining its subfields with elements of computing such as database management and signal processing. The increasing popularity of AI in surgery due to synergy is parallel to that of other technological advancements for example mobile phones, fast computers, internet which have resulted from the use of hardware and software interchangeably⁷. BIXBY, a virtual assistant developed by Samsung electronics responds to its owner due to a combination of demesnes by means of various ways like pictures, songs, vocals, etc. Clinical application of this vast network led to the invention of various applications that helped dermatologists in diagnosing skin lesions with the help of memory stored in computers. Johns Hopkins University successfully developed STAR (smart tissue autonomous robot), which is programmed to perform bowel anastomosis in animal models⁷. Realistically, robotic surgery is out of scope for now, but with the progress and potential of AI, autonomous surgery is not far away from being practiced. Therefore, surgeons should engage in assessing the quality and applicability of Al advances to ensure minimal error in incorporating AI in the field of surgery.

Limitations of Al: As with any new technology, Al is subjected to unrealistic expectations from the media hype that can lead to utter disappointment and disillusionment

in the future⁷. As for now, Al depends upon the dataset stored in its program and cannot answer every query as expected by the media. Besides this, traditional procedures and methods can still outperform Al today in various ways as Al is not fully discovered and is a little too complicated to be understood¹². The main factors responsible for its limitations are enlisted below:

- 1. Limited data set
- 2. Poor algorithms
- 3. Limited sources
- 4. Fear of Al
- 5. Automated clinical interpretation².

IMPLICATION FOR SURGEONS

There are a lot of possibilities and ways with which a surgeon can utilize AI in their clinical practice. Sound knowledge of AI by surgeons can lead to good decisionmaking and better pre-operative, per-operative, and postoperative outcomes with more accuracy⁷. Surgeons can be trained to perform surgery for specific commands prior to actual surgery by 3D surgery trainer applications, where a surgeon can program different scenarios that he/she may encounter while performing actual surgery. Moreover, automated analysis of clinical data can provide more patient-specific risk score assessments that can have better post-operative results. Al applications can also monitor patients at their homes after surgery, which is better as it is with them and is in the surgeon's diary the entire day. Nowadays, scientists are gathering videos of various surgeries to store in a dataset of AI, so that it can perform autonomous surgeries in the future⁷. Such collection of datasets can lead to evidence-based practice and can create disruptive innovation in the field of surgery.

The role of surgeon: Surgeons are uniquely positioned and are talented enough to help drive these innovations further rather than just passively wait for the technology to become useful on its own4. Surgeons should seek opportunities in building partnerships with data scientists so that they can collect data that is required for AI, for the incorporation of AI into their field⁶. This, however, is only possible if the complete record of the patient is kept and is included in the dataset of Al. Surgeons hold immense importance in guiding scientists about different sets of questions that are required to examine the patient, as this can aid in better decision making, hence, better outcomes. A collection of huge data, advanced technology, and automated assessment can help surgeons in treating patients efficiently. The collected data can create 'collective surgical consciousness' that can lead to real-time technology augmented clinical decision support regarding pre-operative, intra-operative, postoperative complications.

CONCLUSION

The world is entering the dawn of AI, which is not only integrated into the business, telecom, and other fields but also assimilated into the fields of surgery and medicine. With expanding databases and sound knowledge, surgeons may have the power in the future to treat complicated cases that are currently untreatable. But, in order to reach such a stage surgeons should join hands with scientists to help them build a legacy that could be carried on in the future. This, however, is only possible with proper data recording and keeping along with encompassing AI into the server.

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Archives of Surgical Research | Perspective

PMC vs. PMDC Fiasco: A Legislative Chaos or an Effort for Quality Improvement?

Hira Ashraf¹, Hammad Naeem²

IMPORTANCE Rapid population growth and resulting economic crisis are posing challenges to maintaining and improving the quality of medical education in Pakistan. The health profession is governed and regulated by a single body in Pakistan since 1962, Pakistan Medical and Dental Council PMDC, which was transformed into Pakistan Medical Commission in 2020. Medical education and training are continuously evolving; several changes have to be incorporated at the undergraduate and postgraduate levels to keep pace with the world. PMC has introduced various changes in the running of the commission and educational regulation, which have been appreciated by some and criticized by others on the grounds of a non-inclusive change process. With recent political changes and the reversal of the PMDC act, there is enormous anxiety about the future of the body and its operational and policymaking processes. This is an opinion regarding this whole fiasco and how it would impact the future of the body and regulation of the healthcare system in Pakistan.

Keywords: Pakistan Medical Commission (PMC), Pakistan Medical and Dental Council (PMDC), National Licensing Examination (NLE), Medical and Dental Colleges Admissions Test (MDCAT)

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apid population growth and resulting economic crisis are posing challenges to maintaining and improving healthcare quality and education in this realm. The knowledge and clinical skills of Pakistani doctors are at stake if important steps are not taken to sustain this challenge in medical education and quality healthcare provision. The health profession is governed by a single body in Pakistan since 1962. Pakistan Medical and Dental Council (PMDC) was established as a legislative body in 1962 by Pakistan Medical Council Ordinance and since then three amendments were passed till 2020. Medical education and training are continuously evolving, and several changes were incorporated at an undergraduate and postgraduate level all over the world. However, PMDC could not keep pace with worldwide changes in healthcare education to incorporate these changes in curricula in the last few decades. Pakistan Medical Commission (PMC) was established on September 24th, 2020 for not only regulatory purposes but also to improve the standard and quality of medical and dental education and practice in Pakistan¹. PMC act incorporated a few changes and rules in existing curricula to raise the quality of medical and dental education and practice in Pakistan as per international standards.

PMC was a triumvirate, the Medical and Dental Council (MDC) was the apex body with National Medical & Dental Academic Board (NMDAB) and National Health Authority (NHA) working under its supervision. MDC of PMC consisted of nine members. Of these nine members, three were members of civil society including a philanthropist, a legal professional, and an accountant. Lay members were introduced in the council in conformity with other countries to protect public rights. The council meetings to be held every three months had the criteria of a minimum of six members forming a quorum². The majority of health professionals expressed their concerns regarding the addition of non-medical professionals to the council. They feared the authority that MDC had over NMDAB and NHA was in hands of irrelevant people. However, the addition of non-medical professionals to the council was deemed in conformity with other countries to protect public rights and monitor progress.

With an objective to standardize medical graduate entry, PMC announced to conduct a single medical and dental colleges admissions test (MDCAT) annually for admission in undergraduate programs in all provinces of Pakistan. The passing percentage of MDCAT was increased to 65%^{2,3}. Private colleges were authorized to postulate their criteria

of admission one year prior to admission. All public and private institutes recognized by PMC were responsible for providing paid internships to all graduates having provisional licenses for a period of 1 year. Conducting a single admission test was a step required for the standardization and centralization of health education. PMC raised eligibility criteria for medical and dental college entry tests. However, this change in criteria was introduced abruptly in a dictatorial fashion without taking the stakeholders on board effectively. Several students had to take a gap year to improve their marks. The health department of Sindh province and many private institutes had significant concerns over this change management.

PMC also introduced the National licensing examination (NLE) as a mandatory requirement for obtaining a full license. All local and foreign graduates were required to pass NLE after completing their internship to acquire the full license. All GPs were required to pass NLE at the time of license renewal every five years. NLE was announced to be held twice a year with no limit on the number of attempts ^{2,4}. NLE had a theory and a skill assessment portion; both of these portions are already part of the final year assessment. Hence, it was proposed by the majority of health professionals that improving existing assessment standards can reduce the hustle of giving an additional exam. Moreover, the pattern of exams was not consistent with the existing 5 year-long curriculum and their modes of assessment. Many argued that significant changes within the curriculum were necessary for the alignment of taught curriculum and modes of assessment at institutions, universities, and national levels.

NLE may have reduced quackery over the years, which has plaqued the reputation of the medical profession in Pakistan. It could have encouraged doctors to keep themselves up to date regarding current medical issues and technological advancements. Each year 20 to 30 thousand students apply to foreign medical colleges. Foreign students usually receive their degrees internships without adequate practical skill training due to limited resources. PMC conducted NLE for foreign students to evaluate their academic and practical skills. Approximately 2,344 students appeared in NLE and only 424 cleared the exam. This low passing percentage clearly indicated the low quality of teaching and clinical training of foreign graduates. In Pakistan, the health system is already burdened by quackery and the addition of incompetent foreign graduates necessitates strict scrutiny.

PMC implemented a digital system that expedites all the processes, thereby, benefiting doctors and stakeholders. PMC empowered MDC to inquire about cases of medical negligence and malpractice.

New ideas were suddenly introduced and implemented. The biggest issue was rapid legislation and regulation of the body processes without taking the stakeholders on board. Following the establishment of PMC, the first step taken by the Ministry of National Health Services (NHS) was sealing off PMDC and taking custody of all records. Fresh recruitment of PMC included new appointees and some former PMDC staff members. This resulted in backlash from political and professional stakeholders.

With a change in Govt, the system is again in limbo and chaos. National Assembly passed the PMDC bill on 8th June 2022. PMDC bill is passed taking into view the long-standing demand of doctors to improve PMDC performance and abolish NLE. In contrary to the policies and governance of PMC certain amendments can be seen in the PMDC bill. The Council of PMDC will have a majority of health professionals. The council meetings to be held every three months have the criterion of a minimum of twenty-four members forming a quorum. In this bill, doctors are given representation for monitoring and giving feedback regarding the performance of PMDC. A periodic review will be done to address concerns regarding its performance⁵. In the new PMDC bill, doctors are given a majority in the council.

PMDC has announced to annually conduct a separate MDCAT in each province for admission in both public and private undergraduate programs. MDCAT of each province will be valid all over the country for three years. However, a standardized and centralized assessment at the country level is a dire need for improvement in medical education. Criteria of admission to both public and private undergraduate programs will be regulated by PMDC. It will be mandatory for all foreign graduates to pass National Registration Examination (NRE) for acquiring full registration, while local graduates will be granted full registration following completion of their internship without passing NRE⁵.

The change in the name of the commission or council does not benefit the overall objectives of the body. An abrupt change in legislation and policies doesn't benefit the health profession. This political trend should be discouraged and all of the changes should be made rationally taking all stakeholders on board to avoid future problems. The

change management in PMC or PMDC should be well-thought and should be executed in such a way that it does produce confusion anxiety and chaos among the stakeholders. Regular quality assurance of governing body and incorporation of changes in curricula according to global standards can help advance towards betterment and

progress of the health professionals in Pakistan. Changes in the regulatory body should be solely based on quality improvement and politics must not influence the change process.

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Archives of Surgical Research | Case Report

Nonfunctioning Pancreatic Neuroendocrine Tumour (NF-PNET) Presenting as Pancreatitis: A Rare Clinical Association

Haseeb Arif, Hamza Azhar, Talat Waseem

IMPORTANCE Pancreatic neuroendocrine tumors are relatively rare tumors. They make up to 2-5% of all the pancreatic tumors. It is important to diagnose them in early stage. They are found incidentally or if malignant with either epigastric pain or distant metastasis. Very rarely PNETs may present with pancreatitis. Only 30 such cases have been reported previously which did present with focal pancreatitis. Here we present such a rare case.

CASE PRESENTATION A 51-year old female presented with history of recurrent epigastric pain for past 4 years. On Ultrasound and CT scan, a 2x2cm well defined mass in the head of pancreas was observed. The findings were confirmed with CT scan. Modified Whipple procedure was done and histopathological report showed WHO grade – I neuroendocrine tumor with chromogramin positive tumor cells.

DISCUSSION & CONCLUSION The association between neuroendocrine tumor and pancreatitis is very rare hence neuroendocrine tumors should be considered as a differential diagnosis while dealing with such cases.

KEYWORDS Nonfunctioning Pancreatic Neuroendocrine Tumour; NF-PNET; Pancreatitis; Whipple procedure; pancreaticoduodenectomy; Modified Whipple procedure

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Case Report

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ancreatic neuroendocrine tumours are a class of rare neuroendocrine tumours arising from the pancreas. The official WHO (2000) denomination for these tumours is gastroenteropancreatic neuroendocrine tumours¹. Pancreatic neuroendocrine tumours (PNET) may be functional; producing hormones such as insulin, gastrin, glucagon or somatostatin, or non-functional; which do not produce any hormones. Most Functional tumours tend to be symptomatic whereas non-functional tumours usually get discovered in the later stages when the tumour has greatly increased in size or has metastasised. Nonfunctional neuroendocrine tumours of the pancreas are more common, making up to 60-90% of all NETs^{2,3}. Pancreatic neuroendocrine tumours are rare entities, making up only 2% of all pancreatic tumours^{4,5}. Pancreatitis however is an ever rarer manifestation of PNET's. Only 30 cases of this nature had been reported by 20126. Though an uncommon manifestation, recurrent acute pancreatitis could be an early sign of an underlying pancreatic neuroendocrine tumour. This report presents one such case of a patient with recurrent attacks of acute pancreatitis found to have a PNET.

CASE PRESENTATION

The patient was a 51 year old Pakistani female from Mughalpura, Lahore, presented with an episode of severe epigastric pain. She had been having similar episodes of epigastric pain for the past 4 years. The pain was gnawing in character, associated with nausea and vomiting, radiating to the back, relieved on leaning forward and aggravated by the consumption of fatty meals. She had been admitted to various hospitals for similar episodes of epigastric pain in the past. Each time the pain settled over the period of a few days and the patient was discharged without a definitive diagnosis. There was no association with elevated pancreatic enzymes (i.e. Serum Amylase, Serum Lipase) thus the primary diagnosis remained APD. The patient was diagnosed with diabetes Mellitus 1.5 years ago, but had no family history of DM. This was partially controlled with oral hypoglycemics. She was also diagnosed with hypertension 1 year before presentation, which was being controlled with Atenolol. She also complained of pain in the left hip which began 1.5 months ago which was associated with a limp when walking. At presentation, she had mild pallor on general examination and abdominal examination showed mild epigastric tenderness. Her left hip was painful with reduced range of motion. Several blood tests were ordered including CBC, Urine C/E, LFT's, RFT's, serum electrolytes, Serum amylase, serum Lipase, Hepatitis B and C screening tests and HBA1C. Abdominal ultrasound, CT scan and a chest X-ray were also done. The patient's Hb was low (10.7 gm/dL), urinalysis showed glucosuria and some RBC's were also found in the urine, serum amylase and lipase were raised and HBA1C was also raised (10.5).

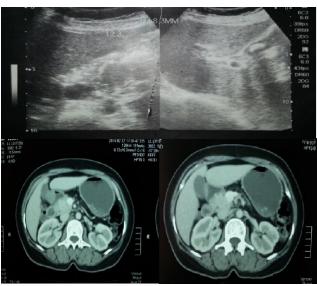


FIG 1: Patient's Abdominal USG (above) and abdominal CT scan (below)

The Ultrasound and CT scan showed a 2x2 well defined rounded growth in the head of pancreas with no vascular encasement and pancreatic atrophy attributed to chronic pancreatitis. An ultrasound guided FNAC was advised but was declined by the patient due to financial constraints. Surgical exploration was planned with curative intent to deal with a resectable symptomatic pancreatic neoplasm (Modified Whipple Procedure). The surgery was performed after; the pancreatitis was settled, adequate glycemic control was provided and cardiovascular disease was ruled out. Intraoperatively a small 2x2 cm mass confined to the head of pancreas was observed with an atrophic pancreas and no regional metastases. The resected tissues included; the pancreatic tumour and head of pancreas (4.2cm x 2.5cm), duodenum, CBD and the gallbladder. The histopathological report of the resected specimen showed a Neuroendocrine tumour WHO grade- I, 2cm in greatest dimension. Tumour cells were found to be chromogramin positive.

DISCUSSION

The association between acute pancreatitis and pancreatic neuroendocrine tumours is very rare. A 1996 study in the American Journal of surgery found only 21 such cases reported in literature 7 while another study in 2012 found only 30 reported cases of this nature as of 2012 6, with only 11 new cases reported between 1996 and 2012 over the span of 16 years. A Swedish population-based cohort study showed that out of 49,749 individuals with acute pancreatitis only 1% (536 individuals) developed pancreatic cancer8. With PNET's making up less than 2% of all pancreatic tumours 5 they are a truly rare entity. The tumour may cause pancreatitis through several different mechanisms though most commonly through the obstruction of the pancreatic duct, pancreatic enzymatic activation and ischemia due to vascular occlusion4. In a 2012 case report, S. Tejedor et.al presented 3 such cases of acute pancreatitis secondary to advanced neuroendocrine tumours⁶. Another 2018 study reported a case of an advanced stage pancreatic neuroendocrine tumour presenting as acute pancreatitis with metastases in the paratracheal, anterior cervical and mediastinal lymph nodes 9. In 2006 Jukemura J. reported the case of a 31y/o patient with weight loss and a history of acute pancreatitis that was diagnosed with a pancreatic neuroendocrine tumour. Jukemura J. concluded that the presence of a pancreatic endocrine tumour should be excluded in the presence of acute pancreatitis of undetermined etiology⁴.

Different types of PNET's are associated with different symptoms. Some well recognised forms of functional PNET's in order of incidence include; Gastrinomas, which may lead to Zollinger Ellison syndrome, Insulinomas leading to hypoglycaemic symptoms and glucagonoma which may present as a skin rash, new onset or worsening diabetes mellitus and weight loss. Some rarer types of functional PNET's may release: Erythropoietin; leading to polycythemia, Renin; leading to HTN, GLP-1/IGF-2; resulting in hypoglycaemia and Luteinizing hormone; leading to masculinisation and infertility¹⁰. Non-Functional PNET's do not release any hormones but their symptoms are related to their size and metastases. These symptoms may include abdominal pain, anorexia, nausea, obstructive jaundice and palpable mass/es11. Liver is the most common site of metastasis for these tumours. Yulong Tian et. al. reported a case of PNET's with metastasis in the liver leading to portal vein thrombosis5.

Neuroendocrine tumours (NETs) arise from neuroendocrine cells, mostly originating from the GI tract and pancreas. Pancreatic NET's may occur as a part of other disorders such as MEN-I, VHL and NF-1. It is generally assumed that the loss of a tumour suppressor gene or the gain of an Oncogene is the mechanism by which chromosomal alterations cause PNETs; for example abnormalities of the p53 tumour suppressor and the upregulation of the CCND1 (cyclin D1) gene are commonly found in PNET's. Diffuse endocrine cell hyperplasia, dysplasia or microadenomas found in the pancreatic tissue are considered to be precursor lesions for these tumours ¹². Over 1/3 of these tumours are located in the pancreatic head^{4,14}.

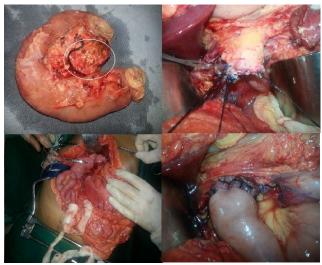


FIG 2: (clockwise) (1) the resected specimen: CBD, duodenum, jejunum, pancreas, (2), (3), (4) photos taken intraoperatively.

The diagnosis of PNET involves endocrine analysis, imaging and histological evaluation. Chromogranin A (CGA), neuron-specific enolase (NSE), and pancreastatin are the most useful PNET markers. Fasting levels of gastrin, proinsulin, insulin, glucagon and vasoactive intestinal peptide (VIP) may be useful for the detection of functional tumours. Imaging techniques such as CT scan and MRI can be useful in localising the tumour and any metastases. Advanced imaging techniques such as Gallium – DOTATOC can be effectively used to identify these tumours. DOTATOC is a somatostatin analogue and this can be radiolabelled with gallium to provide accurate diagnostic information for PNET's. Yulong Tian et .al. used 18F-FDG PET/CT examination to confirm pancreatic neuroendocrine tumour with multiple liver metastases in 2020⁵. The best predictor of PNET behaviour is the tumour grade. Obtaining a biopsy sample is therefore key, as it can be used to grade the tumour and hence predict the behaviour of the tumour¹². The malignant potential of pancreatic neuroendocrine tumours can be assessed by their size, Mitotic index, expression of the KI-67 protein, vascular invasion and perineural invasion¹³.

The only curative treatment of choice for localized pancreatic tumour is surgical resection. For non-functional NETs which are less than 2cm, an intense follow up with a non-surgical approach should be considered. Absolute indications for surgical intervention include: tumours that have metastasised, tumours more than 2cm in size and/or a yearly increase of more than 0.5cm in size. Decision regarding the type of surgery depends on the site of lesion. For pancreatic head lesions, pancreaticoduodenectomy or whipple procedure is done. In our case, a 2x2cm well defined rounded mass in the head of pancreas was found on ultrasound and CT scan. Due to its size and location modified whipple procedure for the resection of tumour was done.

Other treatment options for NETs includes locoregional ablative therapies like selective (chemo) embolization, radiofrequency ablation and radioembolization. Medical therapy has a role in management of advanced NETs. It include chemotherapy, biological targeted agents (like somatostatin analog IFN $-\alpha$), targeted molecular therapy (VEGF-R inhibitors, mTOR inhibitors) 15 . Hepatectomy should be done in patients with liver metastasis.

CONCLUSION

Acute pancreatitis is an uncommon symptom of PNETs. 30 cases of acute pancreatitis secondary to neuroendocrine tumours have been reported in medical literature. Hence while dealing with a case of acute pancreatitis; neuroendocrine tumours should also be considered as a differential diagnosis.

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Archives of Surgical Research | Case Report

Fatal Anaphylaxis Due to Atracurium without Cutaneous Manifestations: A Case Report

Muhammad Naveed Azhar¹. Aamir Bashir²

IMPORTANCE Anaphylaxis or anaphylactic reaction is a medical emergency and it is a potentially life-threatening allergic reaction involving the various systems of the body, especially the cardiovascular and respiratory systems. It is usually triggered by an antigen with subsequent release of mediators from basophil and mast cells. Diagnosis is mainly clinical although laboratory investigations may help in further confirmation. Anaphylaxis during anesthesia is a rare event but could be life-threatening if not diagnosed and treated promptly. Among all the anesthetic agents, neuromuscular blockers are the most notorious to cause anaphylaxis. We are sharing a case of 44 years old female patient who underwent breast cancer surgery under general anesthesia and she developed anaphylaxis due to atracurium injection without cutaneous manifestations. She was managed actively with complete recovery and had her surgery done with the same general anesthesia.

KEYWORDS Anaphylaxis; atracurium; general anesthesia.

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Case Report

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ny drug administered during general anesthesia can cause an anaphylactic reaction and they are potentially life-threatening if not promptly managed. The incidence of anaphylaxis can vary from 1:10,000 to 1:20,000¹. Among the anesthetic medications, a higher incidence (69.1%) is reported by neuromuscular blocking agents especially the atracurium while this incidence was up to 12.1% with latex². The cardinal symptoms and signs of anaphylaxis are urticarial, urticaria, tachycardia, hypotension, and severe bronchospasm. Rarely, death may occur despite prompt recognition and management.

CASE PRESENTATION

A 44 years old female patient suffering from carcinoma right breast presented for modified radical mastectomy at Shaukat Khanum Memorial Cancer Hospital and Research Centre Lahore, Pakistan. She denied any other medical illness apart from high BMI (37kg/m2). Moreover, she was not allergic to any medication, had no previous general anesthesia and her clinical examination & laboratory investigation were essentially normal. After routine WHO safety checklist sign-in, monitoring was attached to get the baseline vitals followed by pre-oxygenation with 100% oxygen for 3 minutes. General anesthesia was induced with intravenous midazolam 2mg, fentanyl 100mcg followed by propofol 140mg. She had easy bag-mask ventilation, with

good EtCO2 trace on the cardiac monitor and stable vitals. After getting adequate depth of anesthesia, I-Gel # 4 was inserted and an EtCO2 trace was confirmed on the monitor. However, there was considerable leakage around the I-gel that didn't get better with all the maneuvers. Therefore, it was decided to intubate the patient after multiple attempts to adjust the I-gel. Intravenous atracurium 50mg was given and after 3 minutes of bag-mask ventilation, she was intubated with ETT # 7.5 mm with the help of a C-MAC video laryngoscope. She developed hypotension and tachycardia and her oxygen saturation started dropping. There was no EtCO2 trace on the monitor and it was almost impossible to ventilate the patient with the bag. Considering that the ETT may be blocked with secretion, ETT was changed immediately but that did not improve the situation. On auscultation, there was a silent chest and SpO2 continue dropping. Immediately call for help was summoned and adrenaline 20 mcg was given considering that anaphylaxis. The first dose of adrenaline slightly improved the situation, Capnograph trace came on the monitor. After 2 minutes, 2nd dose of Adrenaline 20 mcg was given followed by 3rd dose after another 2 minutes. Blood pressure surged and Capnograph traces still showed marked airway obstruction although SpO2 improved to 95% with FiO2 100%. There was marked wheezing all over the chest, a salbutamol inhaler was given through the ETT, chlorpheniramine 10mg IV, and hydrocortisone 100mg were given intravenously. An arterial line was placed in the left radial artery to get arterial blood gas analysis and for invasive monitoring. However, it took more than 20 minutes to stabilize the patient before we started the procedure. She underwent the surgical procedure and was extubated at the end of surgery with stable vitals. X-ray chest was done in the recovery room and it was normal with clear lung fields. After 4 hours of stay in PACU, she was sent to HDU for overnight oxygen support and monitoring. Surprisingly, there was absolutely no cutaneous manifestation of this allergic reaction and the patient had no previous history of an allergic reaction. The patient and her family were debriefed about the event and the flag was alerted in the hospital information system for future reference.

DISCUSSION

Perioperative anaphylaxis can happen due to any anesthetic medication. However, neuromuscular blocking drugs are one of the common causes of anaphylaxis during anaesthesia³. The pathogenesis of these serious and immediate hypersensitivity reactions may either be immunologic (immunoglobulin E mediated anaphylaxis) or related to direct stimulation of histamine release (anaphylactoid reactions)⁴. Although, both of these reactions are difficult to distinguish from each other as they present with similar symptoms and signs. Therefore, any suspected anaphylactic or anaphylactoid reaction should be thoroughly investigated to confirm the nature of the

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CONCLUSION

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agents is common, so all the muscle relaxants must be tested. A certain group of patients may experience more severe hemodynamic collapse and be difficult to treat, for example, patients who are taking β-adrenergic blocking drugs may be difficult to treat with conventional management⁵. Clinical features of anaphylaxis may vary from a mild allergic skin reaction to severe cardiovascular compromise and it is triggered by histamine medicated peripheral vasodilation leading to pooling of blood in peripheral areas of the body and decreased venous return followed by low cardiac output. The lack of circulatory volume may even lead to epinephrine-unresponsive shock⁶. The aforementioned clinical picture could also be due to other serious clinical conditions including tension pneumothorax. In our case, we also thought that ETT might be blocked so ETT was replaced but that didn't improve the situation. Acute cardiogenic pulmonary edema is another differential diagnosis but that was ruled out as there was no cardiac history with this patient. In spite of having severe hemodynamic collapse, our patient did not show any cutaneous manifestations or angioedema. This case was adequately managed as per standard recommendations of Resuscitation Council UK guidelines⁷.

Anaphylactic reaction can occur without skin manifestation.

reaction. Cross sensitivity among neuromuscular blocking

It needs prompt management and resuscitative measures to avoid catastrophic situation in perioperative settings.

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Archives of Surgical Research | Case Report

Laparoscopic Completion Cholecystectomy for Residual Gallbladder: A Case Report and Literature Review

Igra Imtiaz, Muhammad Touseef Asghar

IMPORTANCE Gallbladder infection can present with variable severity and in acute settings may compel surgeon to perform a relatively less complex, subtotal cholecystectomy in certain circumstances, which may lead to a residual portion of the gallbladder and associated complications in some cases. The reported incidence of such cases of subtotal cholecystectomy ranges from 0.4 to 3%, out of which 10% develop symptoms and present in healthcare centers with complications such as remnant cholecystitis and reoccurrence of cholecystolithiasis, or even gall bladder carcinoma. Here, we report a case of the residual gallbladder which was subsequently catered through a laparoscopic approach successfully

KEYWORDS residual gallbladder, postcholecystectomy syndrome, laparoscopic cholecystectomy, completion cholecystectomy, Magnetic Resonance Cholangiopancreatography, minimally invasive surgery

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Case Report

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commonly performed procedure across the globe that involves the removal of the gall bladder through an incision is called a cholecystectomy, which is the standard treatment for gall bladder stones. Inflammation resulting in adhesions that contribute to difficult dissection is commonly encountered in this surgery, which imposes a risk of bile duct injury.1 A residual gall bladder may be left intentionally to prevent such an injury or unintentionally due to unskilled or erroneous identification of the biliary system anatomy, often in such settings of adhesions². The reported incidence of such cases of subtotal cholecystectomy ranges from 0.4 to 3%, out of which 10% develop symptoms and present in healthcare centers with complications such as remnant cholecystitis reoccurance of cholecystolitiasis, or even gall bladder carcinoma^{1,3,4}.

CASE REPORT

A 34-year-old female presented to us on 24th December 2021 in the outpatient department with a history of right upper quadrant pain, nausea, and vomiting for 2 days. The pain radiated to her back and was sudden in onset. There were 3-4 episodes of vomiting associated with the pain, the vomitus being projectile in nature, yellow in color, and containing no blood. She also had loose green stools without the presence of blood, occurring intermittently.

She had seasonal allergies for which she had been taking Monteleukast for 10-12 years and had a surgical history of open cholecystectomy 10 years ago. Her family, personal and medical history were non-significant.

She was vitally stable, with no significant abnormal findings on general physical examination. There was no evidence of free fluid in the abdomen. Normal bowel sounds were heard. Lymphadenopathy was not present. The chest examination was unremarkable, and jaundice was not present.

Her baseline investigations showed a normal CBC, sugar profile, LFTs, RFTs as well as negative hepatitis and COVID-19 markers. Her ultrasound reported a small residual gall bladder stump occupied with an echogenic calculus. There was no notable intra or extrahepatic biliary dilatation.

A diagnosis of calculus in residual gall bladder stump was made based on the history, physical examination, and investigations of the patient. After anesthesia clearance for surgery, completion laparoscopic cholecystectomy was carried out. Under aseptic measures, four incisions were made, two trocars were inserted laterally in the right subcostal region, one in the subxiphisternum region, and one supra-umbilically. The abdomen was insufflated with carbon dioxide and pneumoperitoneum was created. The telescopic camera was inserted and identification of the

Calot's triangle was done. The gall bladder stump was retracted over the liver using long instruments for adequate exposure to the hepatocystic triangle. Cystic artery and duct were identified, clipped, and dissected. The gallbladder stump was identified and after careful dissection, the stone was removed. The stump was dissected and removed via the epigastric port. The incisions were closed and an aseptic dressing was done. Stitches were removed after 7 days, and the patient had an uneventful recovery. The histopathology report stated that the specimen shows chronic cholecystitis without any pathological evidence of granuloma or malignancy.



Figure 1: A laparoscopic image of a large stone retrieved from the gallbladder stump



Figure 2: Residual gall bladder stump

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CASE DISCUSSION

A residual gall bladder stump may be left during cholecystectomy because of a difficult gall bladder. It is relatively safe to do so. However, complications may arise in a fraction of post cholecystectomy cases, including postcholecystectomy syndrome and the development of a biliary fistula⁵. A residual gall bladder stump is more likely to lead to complications than a long cystic duct stump¹. There is an indication of subtotal cholecystectomy in 3 to 8% of the patients with gall bladder disease in case of unclear anatomy, intense inflammation and to avoid iatrogenic complications such as hemorrhage in the portal setting of hypertension². Laparoscopic cholecystectomy is the gold standard treatment of cholecystitis and it is recommended that a laparoscopic completion cholecystectomy be performed by a trained, expert and experienced team in case of complications of a gall bladder stump⁶. A residual gall bladder or cystic duct remnant can significantly increase morbidity. Stones in such cases should be removed surgically, to avoid further complications such as Mirizzi syndrome, carcinoma, gross dilation of the remnant, mucocele, and recurrent cholangitis. The chances of a residual gall bladder or cystic duct can be reduced by careful identification of the anatomy of the hepatobiliary system, milking of cystic duct before ligation or clipping, observation of the free flow of bile after removal of stone from the neck of the gall bladder or cystic duct, not leaving a cystic duct remnant of more than 0.5cm, transforation of cystic duct stump with absorbable sutures, routine intra-operative cholangiography in surgical candidates without extensive inflammation, as well as looking for a cystic duct with low insertion running parallel to the bile duct⁷.

To conclude, a subtotal cholecystectomy at times is the best approach in some surgeries and may lead to complications. A laparoscopic completion cholecystectomy by a surgeon with sufficient expertise is the way to go in the curative approach in such cases⁸.

Conflicts of Interest: There are no conflicts of interest

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Archives of Surgical Research | Letter to the Editor

Re: Utilities of Teaching EPAs: Expanding the Scope of EPAs beyond Clinical Context

Hadin Darain Khan

e read with interest a recently published article by Igbal et al. about the role of Entrustable Professional Activities (EPAs) in imparting skills in the medical field. This letter is a critical appraisal of the role of teaching EPAs in training in medicine and healthcare. The authors have detailed well about the utility of the EPAs and delineated the areas where teaching EPAs can be effective in not only training the clinical trainers but also endorsing their role as a trainer. The authors identified components of EPAs that are vital to the effectiveness of the teaching programs i.e., developing a framework of building teaching skills, reinforcing their personality development, and lastly credentialing the trainers. Teaching EPA frameworks can be used to design structured faculty development programs for specific teaching roles. Expanding the concept of EPAs beyond clinical practice is a unique concept that can revolutionize the clinical teaching modalities¹.

We as surgeons feel that the role of EPAs in surgical training is enormous and the outcomes that can be achieved through implementation can be significant. They can be an important addition to standardized surgical skill transfer². Moreover, they can be also used for faculty development, credentialing of the teachers, and help the administrative bodies with resource allocation and standardized skill transfer³. The important aspect that can be added to the topic under discussion is the addition of a program that can mitigate the barriers associated with the identity formation of the clinical teachers⁴. This can enhance their confidence to teach the trainees⁵.

Recently, the American Board of Surgery and Intercollegiate Board in Britain have initiated the exercise to incorporate these EPAs in the surgical training curriculum. We think that the College of Physicians and Surgeons should also take a lead and incorporate these EPAs in surgical training.

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Government Accountability Office. The Manager, the Government, and the Accounting Profession. U.S. Government Printing Office; 1968.

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Campbell AJ. History transformed: Sengoku Daimyo in lapanese popular media. Published online 2012.

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Kinsley M. Paid Leave Counts as Progress. New York Times. May 27, 2017:SR3

Avoid referencing personal communications and unpublished observations, but they must be presented in parentheses in the text if included, and not in the list of references in the appendix. A research article may not be cited as "Under Publication" or "In Press" unless it has been accepted for publication. In such a case, the name of the journal must be given.

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5. FURTHER CONSIDERATIONS

World Limits

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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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):

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

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- communication of the authors' misconduct will be made to relevant institutions and regulatory bodies
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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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To Improve transparency, we encourage use of and link to international standard reporting guidelines such as those listed in the EQUATOR Network. We encourage preregistration 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 <u>system of scruitiny</u> to find such data manipulations, if found may result in:

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

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Articles would be published with statements or supporting documents declaring:

Authors' conflicts of interest

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9. EDITORIAL POLICIES

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- 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.

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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:

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- 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.
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- Authors could not see reviewers' information.
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- Accepted articles are forwarded to publishing process.
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- 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

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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 <u>COPE Guidelines</u> 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 <u>COPE Guidelines</u> to manage the top hierarchy in terms of conflicts of interest and ethical considerations. We also following <u>COPE Guidelines</u> 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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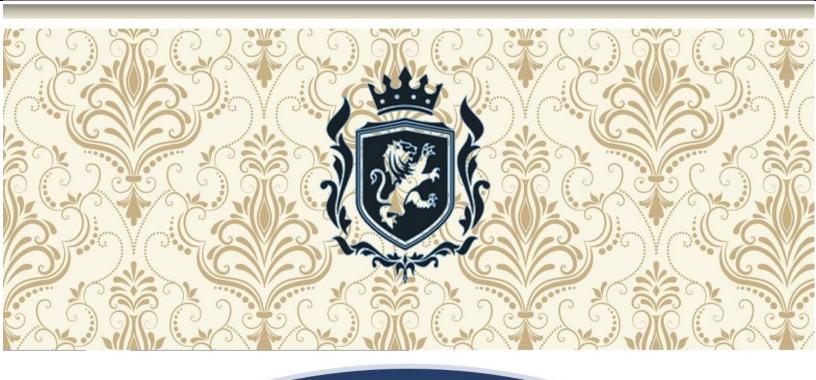
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