

Archives of Aurgical Research

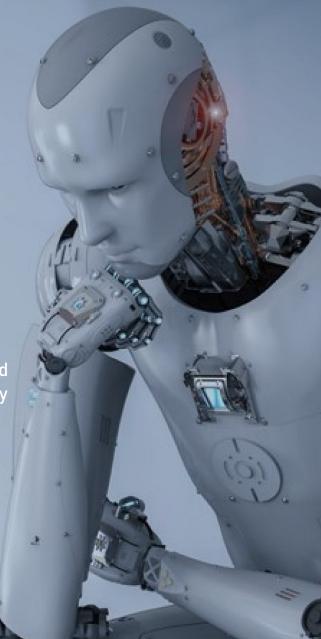
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Editor in Chief: Prof Khwaja M Azim FRCS

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.

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.



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Archives of Surgical Research

A Peer Reviewed Journal of Surgical Research & Education

Editor in Chief: Prof Khwaja M Azim FRCS

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

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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).

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.

The journal would cover endocrine, breast and surgical oncology



Prof. Khwaja M Azim FRCS President PETSA

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Archives of Surgical Research | Editorial

Knowledge Management in Modern Era: A Food for Thought for Surgeons

Muhammad Farooq Afzal

IMPORTANCE The modern digital world has changed the definition of knowledge. As bricks form a wall, so does the data to the basis of knowledge. The raw observation (data) when becomes meaningful, is called information and the use of this organized information is called knowledge. Hence knowledge is different from knowing which is merely a state of being informed. The present scientific advancements have largely been based on knowledge acquired and applied by individuals and organizations. It is becoming increasingly important to differentiate between information and "valuable knowledge" for all medical disciplines and so is in surgery.

KEY WORDS Knowledge Management, surgeon, surgery

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Editorial

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hat is knowledge? Is it the same as knowing? How is it different from information? How can we manage the information over load in modern digital world? These are the few questions perplexing the mind of all surgeons especially when there seems to be an overload of information in present world. Let's discuss these questions one by one.

What is knowledge? Traditionally, it is defined as 'Justified true belief". Though Gettier has pointed out few weaknesses in this definition but it served the purpose of defining knowledge for centuries. Let's understand this definition by quoting an example of two apples, one is a plastic replica of an apple and another is a real apple. The plastic apple is also same as the other apple but by definition, this is not a real apple because It lacks the texture and one cannot bite it though it looks and appear as apple. Hence for me to take it as an apple (a belief), I have to have justification that has to be true. That justification comes from experience gained through our senses or developed by logic. So, there are two types of knowledge, empirical that comes from observation and experience through our senses and rational that is based on logic like the formulae of mathematics.

The modern digital world has changed the definition of knowledge. As bricks form a wall, so does the data form the basis of knowledge. The raw observation (data) when becomes meaningful, is called information and the use of this organized information is called knowledge. Hence knowledge is different from knowing which is merely a state of being informed. The present scientific advancements have largely been based on knowledge acquired and applied by individuals and organizations.

Learning is a life long journey. To keep up with the complex surgical problems like cancers and trauma, and to learn the modern techniques of laparoscopy, robotics and artificial intelligence, surgeons need new knowledge and skills.

Currently, we have many sources of information, like websites, social media applications, webinars and print media like journals and textbooks. One big source of such knowledge comes from research published in the journals. There are more than 4000 surgical journals published monthly. So, poor surgeons are bombarded with lot of information and it is difficult for them to differentiate which one is the most valid and reliable.

The ability to differentiate wheat from chaff comes from learning the skills of critical appraisal of literature. The McMaster University has developed the critical appraisal tools like EBM (Evidence Based Medicine) and the GRADE (Grading of Recommendation, Assessment, Development and Evaluation) which should be in the toolbox of all academic surgeons. Knowing the quality of evidence helps its efficient use in solving the local problems which might be very different from the one mentioned in the studies or population-based guidelines.

There is also a role of journals to help the readers by selecting, editing and publishing high quality research. One way of ranking the journal is the impact factor of the journal which is a measure of the frequency with which an average article in the journal has been cited in a particular year. Similarly, there are many video-based sources of information and knowledge which can be used by surgeons to learn and then practice operative skills by observing the

experts operating. However, the down side of the video-based resources is the learning of wrong or unsafe procedures. Hence, careful selection of the source is desired. Online resources like WebSurg, AIS channel and YouTube, are few great resources for learning the operative procedures.

So, if you want to keep yourself current but at the same time, manage the knowledge overload, develop the critical appraisal skills for reading surgical literature, consult the sources of evidence-based reviews like Cochrane and read journals that have high impact factor. This is the only way you can keep your toolbox updated to solve the clinical problems in surgery in more efficient and evidence-based way^{1–4}.

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2

Archives of Surgical Research | How | Do | It?

Thyroidectomy: How I do it

My Romance with The Thyroid and The White Lady: A Tale Of 43 Years

Khawaja Muhammad Azim

(Narrated by Zaitoon Zafar & Mr Talat Waseem FRCS England)

IMPORTANCE Thyroidectomy still remains a highly technical procedure if not done properly can lead to multiple complications. The art involved in learning thyroidectomy involves many important factors. Learning thyroid surgery starts with higher level of conviction, nourishes with delicate tissue handling, art of compulsive hemostasis, knowledge of anatomy and skill to dissect within planes and manifests into success with a belief in perfection.

KEY WORDS Techniques, Thyroidectomy, recurrent laryngeal nerve

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How I Do It

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was not born to be a surgeon, in fact I was afraid to be a surgeon, and even more afraid to be trained by the great Prof Syed Zafar Haider— like many others. Prof Zafar Haider was on a mission run and very few could run along! I think destiny has its own plans and the things planned in the heavens are probably better suited to a man's needs provided he has the courage to work hard and be patient. In short, I was the one made to serve him, to walk along and run along! My thyroid skill is a small byproduct of this kindred.

To train and to get trained in head and neck surgery, both require patience and hard work. I cannot emphasize enough on the role of mentorship, and the mentee's obedience and conviction to learn this type of surgery. The quality of dissection within planes and mastery over hemostasis are the basic prerequisites. My compulsive personality and love for perfection are my own two quality assurance measures that have helped me gain and maintain the quality of care that I have provided over the years. To play within the neck safely all above remain instrumental. I have loved the white lady (recurrent laryngeal nerve) and preserved it well!

To understand thyroid surgery, it would probably be prudent to know its history a bit! I would recommend another fine article about history of thyroid surgery written elsewhere¹.

A Moor physician named Albucasis performed the first successful thyroidectomy in 952. Unfortunately, he was pushed aside in the books of history and for hundreds of years there was almost no progress in thyroid surgery. In 1850, the mortality rate for thyroid surgery was incomprehensibly high (50%), patients usually died from hemorrhage. It wasn't until Professor Emil Theodor Kocher arrived onto the scene that progress started up again. Iodine deficient goiter was a common disease in his native mountainous region of Switzerland, and Kocher performed over 5000 thyroidectomies for goiter. Kocher

advocated precise, gentle, meticulous surgery that preserved the parathyroid glands and the recurrent laryngeal nerve^{1–3}.

A complete thyroidectomy was considered a risky procedure when Kocher started his work, estimates put the mortality of thyroidectomy as high as 75% in 1872. He advocated subtotal thyroidectomy for the treatment of goiter, an operation that is still practiced today. For his work in the physiology, pathology and surgery of the thyroid he received the Nobel Prize in 1909 in Physiology or Medicine².

Now, thyroid surgery has become quite safe. Techniques, equipment and understanding of the disease pattern have all helped in this regard. In Pakistan, this is in large part due to Prof Syed Zafar Haider, from whom I learnt this all.

A few days ago, I went through "Surgery of the Thyroid & Parathyroid Glands" by Gregory Randolph⁴. It is a beautiful book and I would recommend for an Endocrine Surgery Fellowship Curriculum. In another book, Daniel Oertli has described the technique of thyroidectomy most of the thyroid surgeons are pursuing⁵. I would narrate few of the steps:

- 1. Kocher's incision; a transverse, slightly curved incision about 2 cm above the suprasternal notch, a 4- to 5-cm incision allows safe thyroidectomy in most cases and results in excellent cosmesis
- 2. Splitting of the strap muscles in the midline. Small crossing vessels are treated with bipolar coagulation. For a bilateral approach, the left thyroid lobe is first dissected.
- 3. Using Kocher's forceps, lateral retraction of the upper pole of the thyroid lobe is applied in order to open up the avascular space between the lobe and the cricothyroid muscle, thus exposing the external branch of the superior laryngeal nerve

- 4. By blunt dissection of the isthmus, it is freed from the underlying trachea and divided between transfixing ligatures.
- 5. Capsular dissection of the Hilum of the thyroid gland
- 6. Preservation of the parathyroid tissue
- 7. The transection of the vessels running to the lower pole is usually done after proper exposition of the RLN
- 8. During the final steps of the thyroidectomy, the lobe is dissected away from the trachea under constant exposure and preservation of the RLN
- 9. The strap muscles are sutured continuously with a 3-0 absorbable thread, the platysma with a 4-0 thread, and the skin is closed by an intradermal running suture using 5-0 absorbable thread.
- 10. Postoperatively, a smooth collar may be used for the first 24 hours and the patient should be advised to keep a head up position of about 30° in order to minimize venous congestion and swelling of the soft tissues around the wound.

This technique is superb and reproducible; however, I have few cents to share.

I follow Lahey's technique, which Prof Syed Zafar Haider learnt from Lahey Clinic and later inculcated in me. Dr Frank Lahey was founder of the Lahey Clinic, a physician-led nonprofit teaching hospital of Tufts University School of Medicine based in Burlington, Massachusetts. He is regarded as one of America's greatest teachers of surgery. He was a huge proponent of adequate exposure for the thyroid surgery¹.

In the mid to late 1930s, Frank Lahey proposed the division (as opposed to the splitting mentioned in Step2) of the strap muscles, full exposure of superior poles and visualization of the Recurrent Laryngeal Nerve (RLN) and parathyroid glands. He showed that the RLN could be dissected along its course and that this could be a safer way of operating on the thyroid⁶. At the time, the rates of nerve injury stood at 3% while in Lahey's clinic the nerve injury rates were 1.5%^{1,6}. He operated on 3000 nerves at risk and followed up with the patients. As a result of this endeavor, the nerve injury rate come down to 0.6%. In conclusion he says; "As the result of exposing at least 3,000 recurrent laryngeal nerves in a period sufficiently long (three years) to permit late complications to occur if they were to occur, it may be said that the routine exposure of recurrent laryngeal

nerves in thyroid surgery is a safe and justifiable procedure and will diminish, if not largely eliminate, injuries to that nerve".

I believe in generous exposure and can attest that, with adequate exposure and proper dissection within planes all this is reproducible. Hence, I still believe, despite living in the era of IONM (intraoperative nerve monitoring), the surgeons still can be trained on visual ques and can reproduce high quality outcomes in terms of nerve safety and parathyroid preservation.

Lahey operated until the weeks before his death. He himself performed over 10,000 thyroidectomies, and his clinic exceeded over 40,000 during his reign, with the overall mortality of 0.1%¹. This is phenomenal in terms of quality outcomes.

In agreement with Dr Lahey, we routinely identify and visualize RLN and its branches in all cases and we understand that without visualization everything is blind and at stake. Extracapsular dissection can be quite helpful in this regard. The problem lies when we are dissecting at the level of the ligament of Berry and here many factors play which can be related to anatomy, mobility of gland, presence of malignancy in upper pole and fibrotic texture of tissue mostly. These factors can influence plane of dissection and essentially if we stay along the capsule here and try to minimize handling of nerve, the chances of neuropraxia can be as low as 1-2%. Here the dissection along the branches or RLN itself becomes riskier and can lead to higher rate of neuropraxia ranging up to 11%. This when observed in overall practice dilutes to around 5-6% and remains largely under-reported. We believe that when compared in terms of plane of dissection here at the ligament of Berry, dissection towards gland is safer. Unfortunately, in many cases because of anatomical reasons or tissue pathology we still have to get along RLN. In difficult cases IONM can be helpful in preventing permanent RLN compromise, but closer handling of nerve especially when it splits into smaller branches can be quite difficult scenario.

Learning thyroid surgery starts with higher level of conviction, nourishes with delicate tissue handling, art of compulsive hemostasis, knowledge of anatomy and skill to dissect within planes and manifests into success with a belief in perfection.

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Archives of Surgical Research | Meta-analysis

Impact of Branch vs. Truncal Ligation of Inferior Thyroid Arteries on Post-Thyroidectomy Hypocalcaemia: A Meta-Analysis of Controlled Trials

Safia Zahir Ahmad¹, Talat Waseem², Zaitoon Zafar², Maham Abid²

IMPORTANCE Hypoparathyroidism following a thyroidectomy remains a significant clinical challenge for an endocrine surgeon. Recently, it has been proposed by some endocrine surgeons that truncal ligation may lead to a higher incidence of postoperative hypocalcemia, while others have refuted this notion by citing no long-term impact on incidence of hypoparathyroidism.

OBJECTIVE This study aims to compare the effect of truncal versus branch ligation of inferior thyroid arteries on postoperative hypocalcaemia.

DESIGN This is a meta-analysis.

DATA SOURCES Articles were identified using the MeSH, and Free Keyword searches "Thyroid", "Truncal Ligation" and "Hypocalcaemia" in PubMed, Embase, PubMed Central, Cochrane library, Latin American and Caribbean Health Sciences Literature database and Google Scholar.

METHODS Randomized and nonrandomized controlled trials of patients who underwent subtotal/total thyroidectomy, completion thyroidectomy and thyroidectomy with neck dissection were searched, and outcomes of truncal ligation versus branch ligation of inferior thyroid arteries were compared. Quality of methods of randomized controlled trials were reviewed in accordance with Cochrane Collaboration Guidelines on RevMan and non-randomized controlled trials were assessed with Newcastle-Ottawa Quality Scale. Meta-analysis was performed using a random effects model, and pooled results shown as risk differences. The primary outcome was transient postoperative and definite hypocalcaemia.

RESULTS We found 13 randomized controlled trials (RCT) and 11 nonrandomized controlled trials (non-RCT) with 2580 patients: 1267 patients belonged to trunk ligation group and 1261 to the branch ligation group. The risk difference of symptomatic hypocalcaemia was 8% (95% CI :3% to 12%), for biochemical hypocalcaemia; 8% (95%CI: 4% to 13%), and for definite hypocalcaemia was 0% (95% CI: -1% to 1%).

CONCLUSION An increase in the risk of transient postoperative hypocalcaemia is observed following truncal ligation, compared to branch ligation of the inferior thyroid arteries, with no significant risk difference in definite hypoparathyroidism.

KEYWORDS Thyroidectomy, Trunk Ligation, Hypocalcaemia, Inferior thyroid artery, Hypoparathyroidism

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Meta-Analysis

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ostoperative hypocalcaemia is a well-established entity following a total thyroidectomy procedure¹. Most studies have estimated that the incidence of transient hypocalcaemia ranges from 6% to 55%^{2,3}, while some have even reported up to a 50-68%⁴ incidence rate. Moreover, the risk for development of definite hypoparathyroidism has been estimated to be 1-3%⁵. Existing literature states that various patient factors contribute to the development of postoperative hypocalcaemia; such as preoperative calcium and vitamin D levels, the presenting indication for surgery, disease severity and type and size of the gland in addition to surgeon related factors such as surgical techniques, and the respective surgeon's experience^{6,7}. However, compromise of the blood

vessels to the parathyroid gland or direct trauma to the glands is considered the most important risk factor in the development of postoperative hypocalcaemia⁸.

Different surgical strategies and innovations have been brought into practice to prevent the postoperative complication of hypocalcaemia. Some studies have used localization tools to localize the parathyroid gland, and others have used autotransplantation to prevent postoperative hypocalcaemia⁹. Endocrine Surgeons have revised and refined surgical techniques multiple times in order to avoid inadvertent damage to the vasculature of the parathyroid gland. Such revision of techniques includes utilizing vessel sealing devices, staying in the capsular plane for dissection, and ligating the more delicate branches of inferior thyroid artery near the capsule¹⁰. As the

parathyroid gland is in close relation with the inferior thyroid lobe, and is supplied by the inferior thyroid arteries, experts have proposed that the traditional approach toward ligating the trunk of inferior thyroid artery can lead to hypocalcaemia¹¹, hence, a more conservative approach towards ligating the branches of inferior thyroid artery has been adopted⁸. However, others like Romano¹² and Dolapci¹³ et al. have refuted this notion citing no long-term difference in the incidence of postoperative hypocalcaemia using the branch ligation technique.

Patient related factors
Disease severity
Indication for surgery
Preoperative calcium levels
Preoperative vitamin D levels
Size of gland
Type of gland
Surgery related factors
Surgical technique
Surgeon's experience
Injury to blood vessels
Table 1: Risk factors for the development of postoperative

The role of ligation of inferior thyroid arteries either at truncal or branch level and its effect on incidence in post-thyroidectomy hypocalcaemia remains a matter of significant scientific debate. Sanabria et al. did a meta-analysis on 9 RCT and 11 non-RCT to demonstrate that the ligation of the inferior thyroid artery increases the risk of temporary hypocalcaemia and that the patient develops symptomatic hypocalcaemia, but the meta-analysis could not establish a risk of definite hypocalcaemia¹⁴. The meta-analysis had a few methodological compromises; it relied on small individual sample size studies available, and excluded the timing of measuring the outcomes of hypocalcaemia, in addition to excluding cases of malignancy. Recently, a few large sample sized studies have been published which might provide a more credible analysis and compensate for the methodological shortcomings of previous studies.

The objective of this meta-analysis study was to compare the outcomes of truncal ligation of inferior thyroid artery versus branch ligation in postoperative patients of thyroidectomy with additional high quality RCT literature available compared to the last meta-analysis conducted and review the effect of these techniques on postoperative hypocalcaemia.

METHODS

hypocalcemia

Search strategy and inclusion:

A comprehensive search of controlled trials and analytical studies was conducted on PubMed, PubMed Central, Embase, Cochrane Library and Latin American and Caribbean Health Sciences Literature database and Google Scholars, and studies were time framed from July 1965 to July 2020. The Medical Subject Heading and following term used as Free Text in the search:" Thyroid" OR "Truncal Ligation" AND "Hypocalcaemia". Further expanded data was extracted from articles, and cited authors and references were explored. Language barriers were overcome to include relevant data.

All clinical trials which used the surgical technique of truncal ligation and branch ligation of inferior thyroid artery after bilateral subtotal/thyroidectomy were included. Studies mentioning the use of surgical method of ligation and outcome of hypocalcaemia were selected. Single arm studies/non-comparable studies, reviewers/ letters, abstract articles with no full articles were excluded. Trials and studies of unilateral lobectomies and isthmectomies, capsular dissections without definite artery ligation site, autotransplantations of parathyroid gland following inadvertent removal and studies with undefined methods of inferior thyroid artery point ligation and prophylactic preoperative calcium administration were also excluded.

Population selection and outcome:

Patients undergoing bilateral subtotal thyroidectomy (removal of one lobe and subtotal resection of the contralateral lobe), total thyroidectomy, completion thyroidectomy and thyroidectomy with neck dissection for benign and malignant diseases were the focus of the study. The primary outcome analyzed was postoperative hypocalcaemia. Postoperative transient and definite hypocalcaemia were included according to the author's definition. Hypocalcaemia was divided into biochemical hypocalcaemia with an asymptomatic picture, and symptomatic hypocalcaemia according to serum levels of calcium and ionized calcium. We recorded the serum calcium and parathyroid hormone levels and replacement regimen given.

Data Extraction:

Identified studies were reviewed and the Preferred Reporting Items for Systematic reviews and Meta-analysis (PRISMA) guidelines were followed 15. Two authors screened and identified studies after an extensive search. Any discrepancy in the studies was further reviewed. E-mails were sent to the author and the editor when full-text articles were not available. Duplicated publications were excluded, and a third author confirmed excluded studies.

Further full text articles were reviewed, and eligibility criteria were discussed in case of queries. All data after extraction was counterchecked before analysis. The quality of RCTs was assessed according to the Cochrane collaboration assessment tool16, selection bias was assessed with random sequence generation and allocation concealment, performance bias was assessed by blinding of participant and personnel, detection bias was assessed by blinding

outcome assessment, attrition bias and reporting bias. For non-RCTs, nine-point Newcastle-Ottawa assessment scale (NOS) 17criteria was used to assess the quality of the studies. The maximum star awarded for each item was 4 for selection,

3 for the outcome and 2 for comparability. Articles awarded six or more were considered as high-quality studies. The higher the number of scoring, the higher the quality was considered of the study.

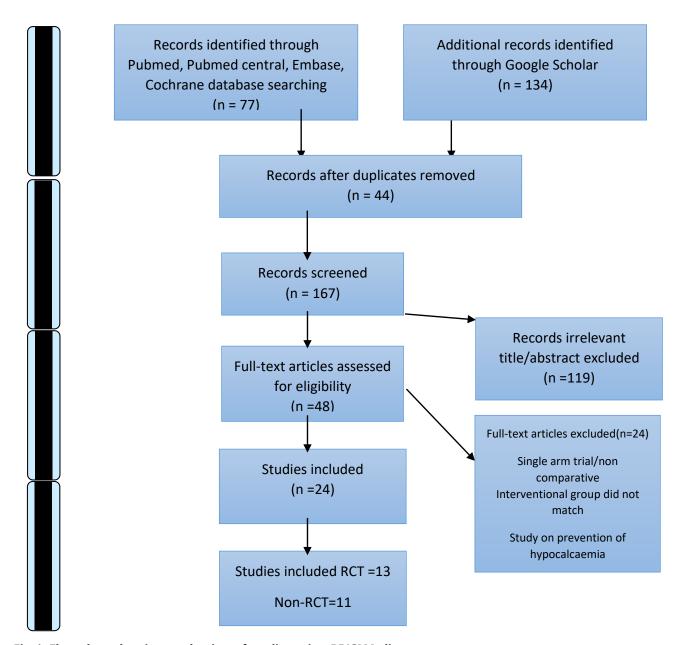


Fig 1. Flow chart showing a selection of studies using PRISMA diagram

Analysis:

The quality of the RCTs and non-RCTs was reported and weaknesses further discussed. A meta-analysis was performed with comparable studies, and variability of population was prevented by using Mantel-Haenszel random effect model. Data for the individual study was obtained for risk difference calculation with chi square test 2x2 table using Review Manager 5.4 software. The meta-analysis is presented as a risk difference (RD) with a

confidence interval (95% CI). Results of intervention effects were illustrated with Forrest plot and defined as subgroups of RCT and non-RCT.

Sensitive analysis was conducted by excluding each study in turn, in order to evaluate the influence on the pooled results. Cochran's Q test was used to assess the heterogeneity, I2 test was used for the statistical analysis of the degree of heterogeneity across the studies. The heterogeneity of the individual effect of the studies was assessed with Galbraith

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and L'Abbe graph, and a funnel plot was constructed for the extent of publication bias. The degree of heterogeneity of interpreting the statistics was as follows: 0-40% may not be significant, 30-60% moderate heterogeneity, 50-90% substantial heterogeneity and 75-100% as considerable heterogeneity.

RESULTS

After an extensive literature search, 211 articles were screened, and 48 studies were assessed for eligibility. 24 studies fulfilling the criteria of the selection process were chosen after a detailed review. Rest of the articles were excluded, as shown in Fig 1.

The study included 13 RCTs^{1,5,12,18,-27} and 11 non-RCTs²⁸ -³⁷ which were reviewed with the characteristics shown in Fig 2. All were prospective studies except for one, which was a retrospective study. Most of the studies included patients who underwent near/subtotal thyroidectomy in bilateral lobes and a total thyroidectomy. 9 studies worked solely on

patients undergoing a total thyroidectomy. 1 study included a total thyroidectomy with neck dissection. Malignancy and recurrent thyroid goiter were excluded in all the articles except a recent publication by Waseem et al., which included malignancy and neck dissection and completion thyroidectomy in their trial. All studies monitored serum calcium levels postoperatively, save for 5 studies which did not report their calcium levels. Ionized calcium was monitored in 4 articles. In addition, 10 studies also monitored the parathyroid hormone levels. 7 studies did not mention the symptomatic presentation of hypocalcaemia. Definite hypocalcaemia was not recorded in 9 studies, and 1 study was not clear about which group had definite hypocalcaemia. Serum calcium was mostly monitored on the first postoperative day, except in 4 studies, which monitored on the second day and 2 studies, which monitored on the third day. The follow up time was mostly not recorded in studies except in 3 studies, which followed patients for six months, and another 9 studies, which followed patients for more than six months, and Nies et al. lost 5 hypocalcaemic patients in their follow up period.

	Trunk Li	gation Of ITA			Branch Ligation of ITA					
Authors	No. of Pt	Biochemical hypocalcemia	Symptomatic hypocalcemia	Ionised Hypocalcemia	Definite hypocalcemia	No. Of Pt	Biochemical Hypocalcemia	Symptomatic hypocalcemia	Ionised Hypocalcemia	Definite Hypocalcemia
Non-RCT										
Azam 2013	20	7	NR	NR	3	23	5	NR	NR	2
Abou-Amra	20	2	2	NR	0	20	1	1	NR	0
2011										
Iqbal 2015	50	12	10	NR	0	50	10	9	NR	0
Chiad 2009	62	50	NR	NR	7	46	22	NR	NR	0
E Ahmed 2011	23	4	NR	NR	NR	27	7	NR	NR	NR
Cakmakli 1992	50	21	7	NR	0	30	13	3	NR	0
Khan 2008	50	11	NR	NR	NR	50	13	NR	NR	NR
Kalliomaki 1961	16	NR	0	NR	NR	17	NR	0	NR	NR
Maralcan 2010	104	15	15	NR	0	126	3	3	NR	0
Salamatullah	30	4	2	NR	NR	30	3	0	NR	NR
2012										
Pelizzo 1995	10	3	0	NR	NR	10	5	1	NR	NR
RCT										
Romano 2015	92	51	NR	NR	1	92	39	NR	NR	2
Araujo-Filho	24	5	4	NR	1	24	2	2	NR	0
2000										
Naseem 2015	50	NR	14	NR	NR	50	NR	2	NR	NR
Al-Kordy 2019	15	3	3	NR	NR	15	1	1	NR	NR
Cocchiara 2010	63	NR	8	21	2	63	NR	1	10	1
Kebsch 2015	42	12	1	NR	NR	39	22	0	NR	NR
Maralcan 2006	49	NR	1	14	0	49	0	NR	12	0
Nies 1994	50	38	10	15	1	50	37	12	16	1
Sapmaz 2020	68	38	22	NR	?1	71	25	11	NR	?1
Waseem 2020	157	36	36	NR	0	162	5	5	NR	0
Topal 2007	40	NR	4	NR	NR	52	NR	5	NR	NR
Chaudhary 2007	163	10	NR	NR	3	147	7	NR	NR	2
Nawrot 2000	19	8	NR	NR	0	18	7	NR	NR	0

Fig 2. Showing the studies characteristics of randomized control trial and nonrandomized control trial. NR=Not reported

The quality of non-RCTs was assessed using the Newcastle-Ottawa assessment scale and only those studies which scored seven and above, were chosen, as shown in Fig 3. Although there was mention of an adequate follow up of hypocalcaemic patients in the studies, it, unfortunately,

could not be applicable for definite hypocalcaemia. RCT studies were evaluated using the Cochrane collaboration assessment scheme, which showed most of the studies were unclear or low risk as shown in Fig 4.

NRCT	Representative	Selection	Ascertainment	Outcome of interest	Comparability	Assessment of Outcome	Length of follow up	Adequacy of follow up	Total
Azam et al 2013	1	1	1	1	2	1	1	1	9
Abou-Amra et al 2011	1	1	1	1	2	1	1	1	9
Iqbal M et al 2015	1	1	1	1	2	1	1	1	9
Chiad et al 2009	1	1	1	1	2	1	1	1	9
E Ahmed et al 2011	1	1	1	1	2	1	1	1	9
Cakmakli et al 1992	1	1	1	1	2	1	1	1	9
Khan et al 2008	1	1	1	1	2	1	1	1	9
Kalliomaki et al 1961	1	0	1	1	2	1	1	1	8
Maralcan et al 2011	1	1	1	1	1	1	1	1	8
Salamatullah et al	1	1	1	1	2	1	0	0	7
2012									
Pelizzo et al 1995	1	1	1	1	2	1	1	1	9

Fig 3. Nonrandomized comparative trials quality assessment using New Castle Ottawa Scale Criteria scale.

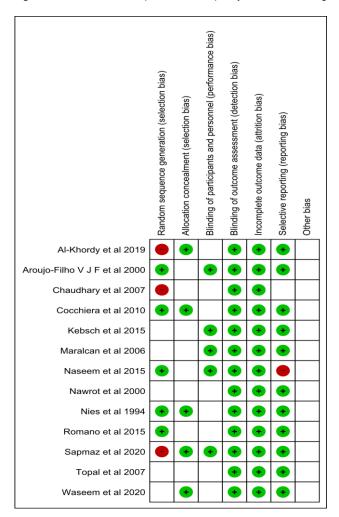


Fig 4. Risk of Bias summary using the Cochrane collaboration assessment tool for randomized control trials. + (Low Risk); - (High Risk); ? (Unclear); A total of 2580 patients were included, 1267 patients who had trunk ligation at inferior thyroid artery group and 1261 patients who had ligation of inferior thyroid artery at branch level

The number of RCT studies that reviewed postoperative biochemical hypocalcaemia were 11 and 10 were non-RCT. Pooled results of risk difference using Mantel Hansel random effect of biochemical hypocalcaemia was 10% in 1472 patients who were in the RCT group, and 6% in 831 patients in non-RCT group. Out of the 1142 patients in branch ligation group, 235 developed biochemical hypocalcaemia, while 360 patients developed hypocalcaemia out of a total of 1161 patients in truncal ligation group. This indicates a low risk of biochemical hypocalcaemia in branch ligation of inferior thyroid artery with the overall effect of P-value of 0.0005. (Fig 5). Heterogeneity of the study was further explored and by excluding Chiad et al., the heterogeneity decreased to 9% and upon further excluding Chaudhary et al., it resulted in 22% without a change in total RD level.

Symptomatic hypocalcaemia was reported in 10 RCT and 7 non-RCT studies. Risk difference reported in RCT Group was 10% (CI 95% 3-17%) while in non-RCT studies it was 7% (CI 95% 2-11%). In 1133 patients in the RCT group, 48 patients were reported to have symptoms of hypocalcaemia in branch ligation group and 116 were symptomatic in truncal group. In a total of 570 patients in the non-RCT group, 36 were identified to develop symptoms of hypocalcaemia in trunk ligation as compared to 17 patients with a P-value of 0.003. (Fig 6). Pooled results of RD were 8% in total 1703 patients with a higher risk of developing symptomatic

hypocalcaemia in ligating the trunk of the inferior thyroid artery.

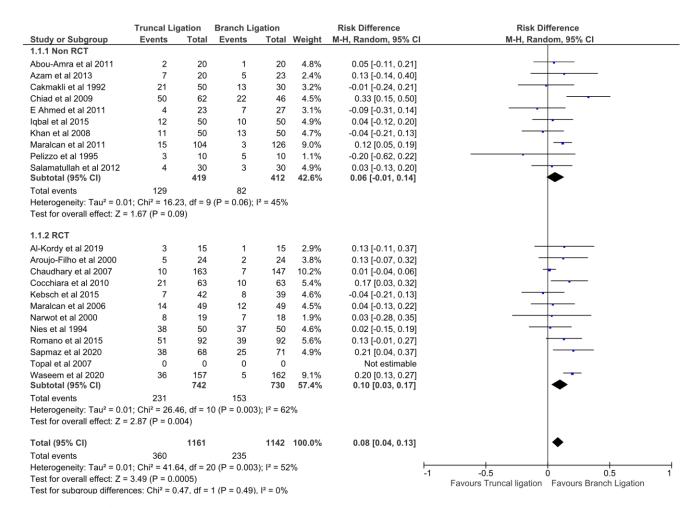


Fig 5. Forest plot for biochemical hypocalcaemia between trunk ligation and branch ligation showing 8% (95% CI 4% to 13%).

Definite hypocalcaemia was documented in 14 studies from both non-RCT and RCT groups, in which total 1962 patients were found. 19 cases developed permanent hypocalcaemia in the truncal group while 8 patients were found in branch ligation group with a pooled RD 0% (CI 95% -1%- +1%). Pooled RD results of non-RCT was 2% in 1703 patients while 0% in RCT group with 1361 patients showing no statistical significance as documented in the literature. Analysis of heterogeneity of the studies was further explored and excluding Chiad et al. reduced the result to 0% (CI 95% 1%-2%) with no global change in pooled results.

Further analysis done between total thyroidectomy and subtotal/total thyroidectomy studies and pooled results of biochemical hypocalcaemia shows 4% (CI 95% 2-9%, I^2 =28%) in subtotal thyroidectomy and 15% in total thyroidectomy (CI 95% 11-19%, P-value <0.00001, I^2 =0%). In symptomatic hypocalcaemia, 5% (CI 95% 0-9%, P value 0.03, I^2 =33%) in subtotal/total thyroidectomy and in total thyroidectomy 13% (CI 95% 7-19%, P value <0.0001,

 I^2 =38%). Analysis of total and subtotal/total thyroidectomy to evaluate the definite hypocalcaemia was 0% with no change in overall pool results.

Asymmetry of publication bias was not found in the funnel plot, as shown in fig 8.

DISCUSSION

Postoperative hypocalcaemia mainly results from an iatrogenic injury of the parathyroid gland during thyroid surgery and decreases the quality of life of the affected total/bilateral subtotal thyroidectomy patient. The incidence of temporary postoperative hypocalcaemia varies, and authors report an incidence range from 6-55% to 83% depending on the age of the patient, size of the gland, type of surgery, the extent of surgery, surgical technique used, the timing of calcium and PTH level checked postoperatively

and the outcome. However, definite hypocalcaemia has been reported as $1-2\%^{24}$ throughout all published and

analyzed literature with no change in its reported incidence rate.

	Truncal Lig		Branch Lig	_		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
2.1.1 Non RCT							
Abou-Amra et al 2011	2	20	1	20	4.5%	0.05 [-0.11, 0.21]	
Cakmakli et al 1992	7	50	3	59	6.5%	0.09 [-0.02, 0.20]	 • • • • • • • • • • • • • • • • • • •
lqbal et al 2015	10	50	9	50	4.8%	0.02 [-0.13, 0.17]	
Kalliomaki et al 1961	0	16	0	17	6.6%	0.00 [-0.11, 0.11]	
Maralcan et al 2011	15	104	3	104	8.4%	0.12 [0.04, 0.19]	-
Pelizzo et al 1995	0	10	1	10	2.7%	-0.10 [-0.34, 0.14]	
Salamatullah et al 2012	2	30	0	30	6.8%	0.07 [-0.04, 0.17]	 -
Subtotal (95% CI)		280		290	40.3%	0.07 [0.02, 0.11]	◆
Total events	36		17				
Heterogeneity: Tau ² = 0.0	0; Chi ² = 5.50	0, df = 6	$P = 0.48$; I^2	9 = 0%			
Test for overall effect: Z =	2.96 (P = 0.0	003)					
2.1.2 RCT							
Al-Kordy et al 2019	3	15	1	15	2.7%	0.13 [-0.11, 0.37]	
Aroujo-Filho et al 2000	4	24	2	24	3.8%	0.08 [-0.10, 0.27]	
Cocchiara et al 2010	21	63	10	63	5.0%	0.17 [0.03, 0.32]	
Kebsch et al 2015	1	42	0	39	8.9%	0.02 [-0.04, 0.09]	+
Maralcan et al 2006	1	49	0	49	9.4%	0.02 [-0.03, 0.08]	+
Naseem et al 2015	14	50	2	50	5.5%	0.24 [0.10, 0.38]	
Nies et al 1994	10	50	12	50	4.5%	-0.04 [-0.20, 0.12]	
Sapmaz et al 2020	22	68	11	71	5.3%	0.17 [0.03, 0.31]	_ -
Topal et al 2007	4	40	5	52	6.0%	0.00 [-0.12, 0.13]	
Waseem et al 2020	36	157	5	162	8.6%	0.20 [0.13, 0.27]	_ -
Subtotal (95% CI)		558		575	59.7%	0.10 [0.03, 0.17]	◆
Total events	116		48				
Heterogeneity: Tau ² = 0.0	1; Chi ² = 38.8	37, df = 9	(P < 0.0001	1); I ² = 77	7%		
Test for overall effect: Z =	2.67 (P = 0.0	(800					
Total (95% CI)		838		865	100.0%	0.08 [0.03, 0.12]	•
Total events	152		65				
Heterogeneity: Tau ² = 0.0	0; Chi ² = 42.1	19, df = 1	6 (P = 0.000)4); I ² = 6	62%		1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1
Test for overall effect: Z =			,	<i>'</i>			-1 -0.5 0 0.5
Test for subgroup differen	`	,	1 (P = 0.46)	$I^2 = 0\%$			Favours Truncal Ligation Favours Branch Ligation

Fig 6. Forest plot in symptomatic hypocalcaemia in Truncal ligation versus branch ligation showing 8% (CI 95% 3-12%) favoring branch ligation group.

Causes of postoperative hypocalcaemia in a previous normocalcaemic patient have been scrutinized at multiple occasions, and literature found that devascularization of the parathyroid gland due to vascular spasm during manipulation or direct injury can result in hypocalcaemia³⁸. It was first suggested by Wade et al. in 1965 that infarction of parathyroid gland is due to vascular damage. Postoperative hypocalcemia can result from direct or indirect injury to an artery supplying the parathyroid gland during dissection of thyroid gland. Devascularization has been suggested as an important cause, but vascular spasm and iatrogenic damage to parathyroid gland also causes hypocalcemia. Biochemical hypocalcemia can be explained by manipulation of the gland, with a clear tendency to recover in long term due to redundant vascularization of gland. Different endocrine surgeons in the last decade have tried to find a solution to prevent or minimize this wellknown complication by using different techniques.

To overcome this obstacle, it has been suggested to ligate the inferior thyroid artery close to the capsule of the thyroid gland, therefore sparing the main trunk and the preserving the vessel supplying to the parathyroid gland³⁹. However, multiple authors cited in this study did not find any major

discrepancy of outcome using differing surgical techniques, and their patients recovered similarly to comparative groups of patients who had their inferior thyroid artery ligated near the origin of the vessel⁴⁰.

Literature which compares surgical techniques in order to deduce each technique's effect on postoperative, symptomatic biochemical and definitive hypocalcaemia and subsequent use of long-term calcium and replacement regimen, is sparse. Antakia et al⁴¹. did a systematic review and a meta-analysis to evaluate the role of prevention and other surgical techniques on hypocalcaemia. One of the outcomes reviewed was ligation of trunk of the inferior thyroid artery and they found no impact on temporary or permanent hypocalcaemia. However, the study population reviewed included just 3 RCTs and a single cohort study. The quality of the included studies was also questionable.

In 2017, an up-to standard meta-analysis was conducted by Sanabria et al.¹⁴, focusing on the role of ligation of inferior thyroid arteries on hypocalcaemia after thyroidectomy. The authors found that ligating the trunk of inferior thyroid artery increased chances of the development transient hypocalcaemia, but had no long-term impact on definite hypocalcaemia. Their study, however, was based mostly on

low powered studies. Moreover, all selected studies excluded patients who had malignancy, which may

confound the outcomes of transient or permanent hypocalcaemia.

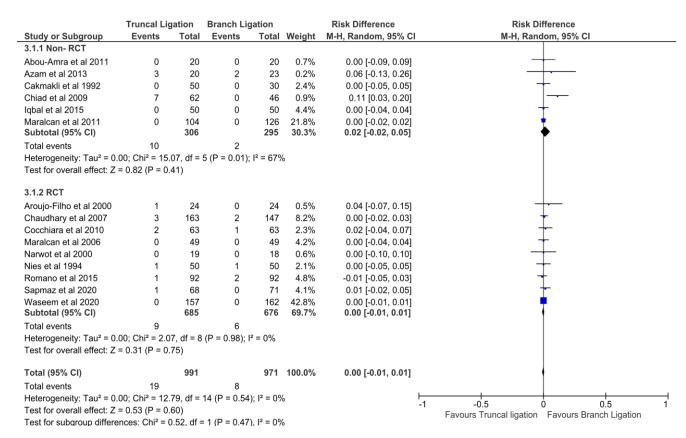


Fig 7. Definite Hypocalcaemia in Truncal ligation compared to Branch ligation with pooled RD of 0%.

One of the authors of this meta-analysis conducted a study on 319 patients and included patients with malignancy and undergoing neck dissection in addition to total thyroidectomy to review the impact of truncal ligation of inferior thyroid arteries on hypocalcaemia²⁷. With this largest sample size and robust inclusion criteria, we concur the findings of Sanabria et al. Here we have conducted a new meta-analysis including this large sample sized study using the Cochrane Collaboration Assessment Scheme and PRISMA guidelines.

The quality of the studies was explored in 13 RCTs using Cochrane collaboration assessment tool and found mostly 4 points of low risk of bias with unclear bias and in 11 Cohort studies using the Newcastle-Ottawa scale criteria found to have seven or above stars indicating the good quality studies or acceptable risk of bias making it a reliable to the overall results. Though the quality of these studies was taken into consideration in terms of biochemical and symptomatic hypocalcaemia, but the adequacy of follow up and long-term follow up for definite hypocalcaemia was defined by individual studies varies. Most of the studies followed-up their patients to the extent of the patient remaining asymptomatic or recovering from transient hypocalcaemia.

We used risk difference to estimate the pooled results and random effect due to the large variation of population and heterogeneity to conclude a good reliable outcome result.

Our analysis shows a lower incidence of temporary hypocalcaemia in patients who had branch ligation of inferior thyroid artery with a statistical significance of 8% in biochemical hypocalcaemia with a p value of 0.003 and 8% in symptomatic hypocalcaemia with a P value of 0.0004. For biochemical hypocalcaemia, heterogeneity of the studies decreased to 9% after excluding Chiad et al. and 22% when excluding Chaudhary et al., but the pooled result was consistent with no marked change. Although there was no change in the heterogeneity in symptomatic hypocalcaemia when individual studies were reviewed and excluded. In definite hypocalcaemia, there was no significant difference in the incidence rate in both of the groups with 0% result in agreement with the literature.

Traditionally, it is thought that postoperative hypocalcaemia is multifactorial and is caused by a disturbance in functional levels and removal or manipulation of parathyroid gland which can result in vasospasm⁴² or ischemia secondary to ligation of inferior thyroid arteries. Many authors suggest

that ligating the main trunk of inferior thyroid arteries is beneficial in terms of preventing on table bleeding and cite no impact on the long-term hypoparathyroidism, hence, they conclude that the benefits of ligating trunk of inferior thyroid arteries outweighs the risk of hypoparathyroidism²¹. In contrast to this notion, this meta-analysis favors ligating the inferior thyroid arteries at their branch level to prevent injury to the main supply of parathyroid gland, which originates 80% of the time from the ITA38. Furthermore, studies have shown that during surgical manipulation, the blood flow to the parathyroid gland is compromised, and derangement is seen in serum calcium and serum PTH, with the patient being asymptomatic¹². This explains the reason for biochemical hypocalcaemia and patient recovery in the postoperative period with no long-term morbidity and dependency of calcium supplements^{43,14}. Moreover, patients with malignancy who undergo neck dissection have results similar to patients of non-toxic goitre in terms of temporary hypocalcaemia^{44,27}.

Limitations

There were a few limitations we encountered during our research; a major limitation was the timing of the serum and ionized calcium levels checked postoperatively. Even though the pooled result did not show any difference, the authors believe it could prove a bias in the results. Similarly, the definition of permanent hypocalcaemia varied in each study

and follow up period with calcium replacement regimen was not clearly defined in individual studies to recognize the effects of hypocalcaemia. Moreover, it is not clear whether asymptomatic hypocalcaemia was treated with replacement regimen or not and needs further scrutiny. The extent of surgery performed in bilateral subtotal or a near total thyroidectomy is another factor that can be a cause of heterogeneity with no clear surgical definition. Surgeon's experience and technique on preserving the thyroid tissue can also influence the overall outcome.

CONCLUSION:

In conclusion, branch ligation of inferior thyroid arteries close to its capsule can result in a decrease in the outcome of transient hypocalcaemia and early recovery of biochemical and symptomatic hypocalcaemia but not the risk of the long-term effect on permanent hypocalcaemia. Furthermore, role of truncal ligation of inferior thyroid arteries and its impact on definite hypocalcaemia in long-term follow up requires further research.

ARTICLE INFORMATION

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Archives of Surgical Research | Invited Review

Pancreaticojejunostomy vs. Pancreaticogastrostomy in Whipple's Operation: A Literature Review

Muhammad Haroon, Faisal Hanif, Muhammad Imran Khan, Ijaz Ashraf, Adeel Aslam

IMPORTANCE Pancreatic malignancy is one of the leading causes of morbidity and mortality. The definitive surgical treatment for resectable pancreatic cancer includes pancreaticoduodenectomy (Whipple's Operation). Operative morbidity and mortality following pancreaticoduodenectomy (PD) is mainly associated with leakage of pancreatic enzymes leading to formation of either pancreatic fistulas or intraabdominal collections. Various types of pancreatico-enteric anastomosis have been proposed to prevent these complications. Different studies have been performed to compare the outcomes of Pancreaticogastrostomy (PG) verses Pancreaticojejunostomy (PJ) in terms of incidence of post-operative pancreatic fistulas (POPF). Although it is widely accepted that no one technique is superior to the other but one of the underlying facts is that there are various ways of doing pancreatic anastomosis and moreover individual surgeon's comfort and practice also matters. A review of literature was carried out to address the techniques of doing PJ and PG and comparison of postoperative complication rate in Pancreaticogastrostomy (PG) verses Pancreaticojejunostomy (PJ). We concluded that techniques of doing PJ and PG are surgeon dependent according to the characteristics of pancreatic remnant stump and there is no significant difference in the rate of clinical POPF between PG and PJ.

KEY WORDS Knowledge Management, surgeon, surgery

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Invited Review

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ancreaticoduodenectomy (PD) is the best surgical treatment option for benign and malignant tumors of the pancreatic head, distal bile duct, and ampulla. Despite improvements in post-operative care and advancement in surgical techniques, morbidity related to this operation remains very high. Since the establishment of PD, pancreatico-enteric reconstruction has been a highly valued research area, which is considered to be closely related to the success or failure of the surgery ¹. In general, pancreatico-digestive tract reconstruction includes Pancreaticojejunostomy (PJ) Unlike Pancreaticogastrostomy (PG). gastrointestinal anastomosis, these two types of reconstruction after pancreatic surgery are diverse, with different results and evaluations. Therefore, there is still room for improvement in PJ and PG and these procedures are still the focus of future research in PD. The incidence of complications after PD is significant, with some large pancreatic centers reporting an incidence of approximately 10-45% ²⁻⁷. The incidence of post-operative pancreatic fistula (POPF), delayed gastric emptying (DGE) and gastrointestinal or abdominal hemorrhage has been reported to be 3%-45% 8 , 5%-61% $^{9-10}$ and 1%-8% 11 respectively. Other complications include abdominal empyema, wound infection,

and pulmonary infection ¹². This review will provide an overview of the evolution of the pancreatico-enteric anastomosis following PD, the spectrum of anastomosis performed around the world, and finally present the current evidence in support of each anastomosis.

HISTORICAL BACKGROUND OF PANCREATICODUODENECTOMY

Codivilla performed the first *en bloc* excision of the head of the pancreas for pancreatic cancer ¹³. However, he did not perform a pancreatico-enteric anastomosis as part of the reconstruction. In fact, the first person to attempt a pancreatico-enteric anastomosis following a transduodenal partial PD was William Halsted ¹⁴. In 1898, he implanted the pancreatic duct into the repaired line of incision of the duodenum. He reported no POPF, an outcome that was also noted by other surgeons such as Koerte, Navarro, Kerr, Bohm, Schussler and Slaymer following transduodenal ampullary excision ¹⁵. By 1941, Allen Whipple began to appreciate that two important contributors to PD-related morbidity were pancreatic fistulae from the over sewed ducts, in the short-term, and fat indigestion necessitating pancreatic extracts in the long-term ¹⁶. By 1945, he reported the

success of his single staged procedure with the implantation of the pancreatic duct into the jejunum (PJ) below the choledochojejunostomy ¹⁷. The first to successfully perform a PG were Waugh and Clagett in a cohort of 30 patients ¹⁸. The rationale provided for PG being an improved alternative to PJ includes the suggestion that the anastomosis is tension-free since the body of the pancreas forms bed of the stomach and the weight of biliary and pancreatic secretions pooling up in the jejunum exerting a traction effect on the anastomosis is obviated, well vascularized (considering the robust gastric blood supply), without risk of activation of pancreatic enzymes or mixing of the pancreatic and biliary secretions ¹⁹⁻²⁰.

PANCREATICOJEJUNOSTOMY (PJ)

Conventionally Pancreaticojejunostomy is performed as end to side, double layer, duct to mucosa anastomosis in which inner layer incorporates full thickness jejunal wall to pancreatic duct and outer layer as seromuscular jejunal stitch to pancreatic tissue. Reported leak rate after conventional technique is 6-22% ²¹. Invagination of pancreatic tissue with or without duct to mucosa stitches has been studied with promising results. Invagination with duct to mucosa stitches is reported to have rate of POPF as low as 3.3% ²². The only major difference in the inversion or invaginating end-to-side anastomosis and the duct-to-mucosa end-to-side anastomosis is in the size of the jejunal opening, a wide jejunal opening matching the diameter of the cut surface of the pancreas in the former and a 'pin-hole' opening in the jejunum in the latter ^{23,24}.

PANCREATICOGASTROSTOMY (PG)

Conventionally Pancreaticogastrostomy is performed as invaginated double layer anastomosis to posterior wall of stomach with or without pancreatic duct stenting. Fernandez et al., reported doing pancreaticogastrostomy with gastric partition in which they made pancreaticogastric anastomosis to partitioned part of stomach. They compared it with conventional Pancreaticojejunostomy in a randomized controlled trial and demonstrated that this technique was significantly superior to Pancreaticojejunostomy in reducing pancreatic fistula risk 25. It has been proposed that lack of enterokinase and acidic environment in stomach inactivates pancreatic enzymes, which along with good blood supply of stomach may have role to play in reducing risk of anastomotic leak ²⁶. While potential of anastomotic leak is reduced by pancreaticogastrostomy, long term exocrine and endocrine functions are compromised more in these patients as compared to those who underwent Pancreaticojejunostomy Furthermore, risk of digestive tract bleeding is also more after pancreaticogastrostomy, though management of GI bleed is easy via upper gastrointestinal endoscopy should bleeding occur 28.

OTHER FACTORS FOR POPF:

In addition to postoperative care and surgical technique, certain patient and disease related factors predispose patients to high risk of POPF development ²⁹. Soft texture of pancreas is an established risk factor for POPF ³⁰. There are only a few randomized controlled trials that have been conducted on or have reported separate subgroup analysis for this select

subgroup of patients. Bassi et al., reported on difference in fistula rate after pancreaticogastrostomy versus pancreaticojejunostomy for patients with soft pancreas ³¹. Contrary to that, subgroup of patients with soft pancreas in randomized controlled trial by Topal et al., demonstrated that Pancreaticogastrostomy was superior to pancreaticojejunostomy for postoperative pancreatic fistula ³². There has been no meta-analysis to date to compare pancreaticogastrostomy versus pancreaticojejunostomy in patients with intra-operative soft texture of pancreas which needs to be addressed via pooled data analysis.

INDIVIDUAL VARIATIONS

There are many ways of performing pancreatic anastomosis and adopting one way of doing anastomosis as compared to the other depends upon comfort and training of operating surgeon in addition to other factors. Adopting and mastering another way of doing the same task when surgeon is comfortable with one way is not always easy and may not reproduce the same results as proposed by other surgeons. This is why same technique has different rates of pancreatic fistula reported from different centers ³³.

DISCUSSION

There are multiple randomized controlled trials conducted to compare Pancreaticogastrostomy versus Pancreaticojejunostomy. Three trials found that rate of pancreatic fistula significantly lower in Pancreaticogastrostomy group 34, 35, 36 and these trials had used definition proposed by International Study Group of Pancreatic Fistula (ISGPF) to define pancreatic fistula (PF). There are few trials which were conducted before 2005 and they used definitions of PF according to their individual centers. Metaanalysis conducted on these trials have reached at different results. Another meta-analysis conducted in 2016 by Qin et al., found statistically significantly less POPF in PG group as compared to PJ group ³⁷. This meta- analysis included all studies irrespective of their definition of pancreatic fistula. Another meta-analysis by Crippa et al., failed to detect any difference in the two groups 38 but random effect model was used to analyze the results as opposed to former meta-analysis.

A study conducted by the senior author (FH) of his own results of 101 patients undergoing PD, 87 % with PG and 13 % with PJ showed biochemical subclinical leak (Type A) in 13.9% whereas POPF Type B was 7.9% and Type C in 5%. Although a comparison of PG and PJ was not done but the study showed PG as a safe option in PD especially for soft pancreas with short pancreatic duct ³⁹.

A very recent meta-analysis published in 2019 included 11 randomized controlled trials and concluded that overall PF morbidity is significantly lower in the PG group than in the PJ group. Grade A PF did not affect the disease outcome; therefore, they further analyzed the incidence of grade B and C PF. Grades B and C PF was not significantly different between the two groups ⁴⁰.

According to recent Cochrane Review ⁴¹, PJ and PG reconstruction were similar in postoperative pancreatic fistula

rate, mortality, length of hospital stay, surgical re-intervention rate, and risk of any surgical complications. The overall postoperative pancreatic fistula rate was 24.3% (181/746) in the PJ group and 21.4% (164/767) in the PG group but they downgraded the quality of evidence to low due to high risk of bias⁴¹.

In another study conducted by Savio George Barreto and et all, it has been concluded that there is no difference in POPF rates between PG and PJ, as well as individual variations, except in a high-risk anastomosis where performance of a PJ may be preferred ⁴².

Analysis of post-operative hemorrhage was done in nine trials with 788 PG and 734 PJ patients. Postoperative hemorrhage showed a significantly lower morbidity in the PJ group than in the PG group ⁴⁰ but DGE was not significantly different between the two groups. Similarly, the overall rate of postoperative bleeding was 9.3% (63/681) in the PJ group and 13.8% (97/705) in the PG group according to Cochrane review ⁴¹.

However, there is no trial or meta-analysis published as yet that reported superiority of Pancreaticojejunostomy over Pancreaticogastrostomy.

CONCLUSION

There is no difference in the incidence of clinically significant PF between the two groups. However, postoperative bleeding is higher in PG than in PJ. Surgeon's training and comfort and features of pancreatic remnant should be important consideration while selecting the type of pancreatic anastomosis.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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Archives of Surgical Research | Covid-19 Special Feature

Endocrine Surgery during COVID-19 Pandemic: A Collective Review of Guidelines

Muhmmad Imran Khokhar, Muhammad Farooq Afzal, Shabbir Ahmad, Suleman Asif, Muhammad Zubair

IMPORTANCE Coronavirus disease (Covid-19) took pandemic status after outbreak in Wuhan, China, in December 2019. In Pakistan, first case of Covid-19 was reported on February 26th 2020. After striking peak during last week of June, it started declining in Pakistan. During next three months it declined rapidly as compared to other countries. Our aim is to evaluate the current recommendations based on review of literature that can help plan the surgery and protect both patients and healthcare workers, during and after pandemic.

METHODS We reviewed several papers on endocrine surgery during Covid-19 pandemic, published in leading journals. Different search engines were used including Google, Yahoo and Bing. Recommendations about optimal timing for endocrine surgery during Covid-19 pandemic were evaluated.

RESULTS As in other countries, all elective and non-emergency surgeries were postponed in Pakistan in mid of March 2020. Most of the endocrine operations can be postponed for a certain period of time. During the process of covid-19 spread, guidelines for safe surgery were established by leading endocrine surgical societies. Like other countries, surgeries were started in three stages in Pakistan. During early days of pandemic life-threatening surgeries were performed (First stage). Cancer surgeries were started when outbreak was being controlled (Second stage). Elective surgeries have been started recently with suppression of outbreak, taking all precautionary measures during surgery (Third stage).

RESULTS & INTERPRETATION The endocrine procedures need to be triaged according to the level of urgency and priority. In the light of guidelines from various endocrine surgical societies we may recommend that most of endocrine cases can be postponed to the third stage of the epidemic.

KEYWORDS: Endocrine surgery, Pandemic, Coronavirus, Covid-19

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Covid-19 Special Feature

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uring Covid-19 pandemic, number of infected patients increased gradually as in other parts of the world. After striking peak during last week of June, it started declining in Pakistan. Total cases reported till the last week of September 2020 were 0.31million with 6484 deaths. At the same time, worldwide reported cases were 34 million with 1.01 million deaths¹.

Since early stages of pandemic, specific precautionary measures were recommended all over the world. This included hand sanitization, use of face mask and social distancing. Similarly, certain standard operating procedures (SOPs) were established for all surgical procedures including endocrine procedures. Various endocrine surgical societies have recommended specific SOPs for thyroid, parathyroid, pancreas, supra renal gland and neuroendocrine surgeries^{2–4}. These measures are taken to minimize mortality and morbidity in high risk patients.

Endocrine societies of America, United Kingdom, Europe and Asia have developed protocols with a common aim of

optimal patient care by prioritization and triage. The variation observed among these societies in terms of SOPs, reflect the needs and demands of the healthcare system and needs. Generally speaking, during early stages of pandemic, only the patients of endocrine pathologies having life threatening problems were planned for surgery. Endocrine cancer surgeries were started when pandemic started declining. Benign endocrine surgeries have been started recently while pandemic has settled in most parts of the world. All precautionary measures were taken during all stages of pandemic to prevent the patient as well as surgical teams⁵. In Pakistan, we had similar approach for endocrine surgery at almost all centers across the country.

Below are guidelines proposed by international societies of Endocrine surgery:

(A) AMERICAN COLLEGE OF SURGEONS (ACS)

American College of Surgeons established certain guidelines and proposed Triage is divided in three phases³.

Phase I

(Few COVID-19 patients, hospital resources not exhausted, institution still has ICU ventilator capacity and COVID-19 trajectory not in rapid escalation phase)

Surgery restricted to patients likely to have survivorship compromised if surgery not performed within next 3 months.

Surgical cases that need to be performed as soon as feasible:

- Thyroid cancer requiring acute airway management
- Resectable anaplastic or poorly differentiated thyroid cancer without BRAFV600E mutation*
- Progressive/clinically aggressive differentiated or medullary thyroid cancer
- 4. Large suspected thyroid malignancy with documented progression
- Large goiters with significant symptomatic airway compression**
- 6. Suspected parathyroid carcinoma with significant symptomatic hypercalcemia
- 7. Suspected adrenocortical carcinoma
- 8. Medically uncontrolled hyperfunctioning endocrine tumors

Surgical cases that can be safely deferred:

- 1. Differentiated thyroid cancer***
- 2. Medullary thyroid cancer***
- 3. Indeterminate thyroid nodules without documented progression
- 4. Thyroid goiters**
- 5. Primary hyperparathyroidism
- Medically controlled hyperfunctioning endocrine tumors
- 7. Incidental, nonfunctional adrenal lesions

*Patients with anaplastic thyroid cancer with BRAFV600E mutations should be offered BRAF/MEK inhibitor therapy initially, and surgery can be deferred.(6)

**Generally, mildly symptomatic airway compression from large goiters is subacute or chronic and does not require immediate intervention. Very rarely, a patient may present with significant and acute airway compromise, in which case surgery or airway intervention cannot be safely postponed.

***Most differentiated and medullary thyroid cancers are slowgrowing tumors that do not cause significant morbidity over the short term, although there is a subset of more biologically aggressive cancers that progress more rapidly. Therefore, clinical correlation with rate of progression (if known), size, invasiveness of surrounding structures, and proximity to critical structures is recommended.

Phase II

(Many COVID-19 patients, ICU and ventilator capacity limited, and/or operating room supplies limited)

Surgery restricted to patients likely to have survivorship compromised if surgery not performed within next few days.

Surgical cases that need to be performed as soon as feasible:

- Thyroid cancers requiring acute airway management
- Resectable anaplastic or rapidly progressive poorly differentiated thyroid cancer without BRAFV600E mutation*
- 3. Rapidly progressive/clinically aggressive differentiated or medullary thyroid cancers*
- 4. Rapidly progressive adrenocortical carcinoma
- Medically uncontrolled hyperfunctioning endocrine tumors
- Suspected parathyroid cancer with significant hypercalcemia refractory to medical management

All other endocrine diagnoses can generally be deferred.

*Some anaplastic, poorly differentiated, and advanced progressive differentiated and medullary cancers require major surgery such as laryngectomy, tracheal resection, and/or sternotomy. These more advanced and complex cases should be considered in alignment with available hospital resources.

Phase III

(Hospital resources are all routed to COVID 19 patients, no ventilator or ICU capacity, OR supplies exhausted)

Surgery restricted to patients likely to have survivorship compromised if surgery not performed within next few hours.

Surgical cases that need to be performed as soon as feasible:

- 1. Thyroid cancer requiring acute airway management
- 2. All other endocrine diagnoses are deferred.
- 3. Alternative treatment approaches for endocrine neoplasia for which surgical intervention is deferred due to COVID-19 pandemic:
- Most surgeries for thyroid nodules, thyroid goiters, differentiated thyroid cancers, and medullary thyroid cancers and adrenal nodules can be safely deferred without need for medical therapy
- Consider TSH suppression for differentiated thyroid cancers
- Anaplastic, poorly differentiated, or progressive/advanced differentiated and medullary

- thyroid cancers with targetable mutations may be candidates for targeted systemic therapy
- 7. Optimize medical management of hyperfunctioning endocrine tumors (thyroid, parathyroid, and adrenal)
- 8. Coordination of care with other health care providers/facilities according to resource availability and travel restrictions

(B) BRITISH ASSOCIATION OF ENDOCRINE AND THYROID SURGEONS (BAETS)

The risk of contamination to COVID-19 negative patients and healthcare workers, hospital facilities, especially the conditions regarding the operating room and postoperative care should be considered while planning for surgery during COVID-19 pandemic⁶. During pandemic period, the plans and recommendations made on this subject were based on expert opinions by considering factors, such as the course and biology of the disease, rather than being evidence-based. The proposal by the British Association of Endocrine and Thyroid Surgeons (BAETS) for the timing of the surgery, related to the urgency and priority of endocrine surgeries during the pandemic seems practical and feasible^{7,8}.

Endocrine surgeries are divided into following four priority levels by British Association of Endocrine and Thyroid Surgeons (BAETS);

Level 1a: Life-threatening situations that need to be operated within 24 hours to save the patient

Level 1b: Conditions that need to be operated between 24-72 hours for life-threatening conditions that may cause, such as obstruction, bleeding, local or regional infection, permanent injury/clinical harm from the progression of conditions, such as spinal cord compression

Level 2: Conditions requiring elective surgical intervention and where surgery can be postponed safely for up to four weeks before a negative condition develops

Level 3: Conditions in which elective surgical intervention can be postponed for up to three months without a predicted negative outcome

Level 4: Conditions in which elective surgical intervention can be postponed more than three months without a predicted negative outcome

Not only endocrine surgical interventions but also other elective surgeries had to be planned especially after the peak period of the COVID-19 pandemic. For this, all operations needed to be arranged in a certain order according to the hospital's facilities. So, it was recommended to classify and prioritize all postponed cases according to their specificities, such as cancer and transplantation, arranging all other surgeries according to an objective scoring system, and create an appointment plan according to this scoring^{2,9}.

(C) FRENCH-SPEAKING ASSOCIATION OF ENDOCRINE SURGERY (AFCE)

Specific guidelines have been proposed by the Frenchspeaking Association of Endocrine Surgery (Association Francophone de Chirurgie Endocrinienne- AFCE) for the surgical management of thyroid, parathyroid, endocrine pancreas and adrenal pathologies during the COVID-19 epidemic and afterwards¹⁰.

General principles for scheduling surgery during and after the COVID-19 pandemic

Endocrine surgery is prioritized as four scheduling levels:

- Urgent surgery that must be carried out as soon as possible because even a short deferral would be life-threatening;
- Semi-urgent surgery that can be deferred for a few weeks but not beyond 3 months without threat to life or adverse effects on cancer or functional prognosis;
- High-priority elective surgery that can wait for several months but must be given scheduling priority as soon as the epidemic is over;
- 4. **Distant elective surgery** that can be deferred until well after the epidemic is over, even more than 6 months, without compromising the indication.

The benefits versus risks must always be evaluated during emergency surgery planning keeping in mind that how both the national and local contexts are evolving, in particular the resources available: operating room, consumables and hospital capacities, particularly if intensive care may be needed. During epidemic setting, short hospital stays or outpatient care is recommended while prescribing surgery¹⁰. The surgery should be performed by one or more experienced surgeons to limit operating time and postoperative complications. To prevent unfavorable prognosis, the risk of infection should be assessed before surgery even if no symptoms of COVID-19 are apparent ^{11,12}. All surgeries on a patient infected or suspected of being infected must be performed according to the SOPs for the management of these patients ¹⁰.

Postoperative follow-up in the epidemic setting

Most of the teaching hospitals of country established telemedicine facilities for the optimal care of patients including endocrine surgery patients. Although, Outpatient departments started working in our country with all precautionary measures, telemedicine still has a role in preoperative and post-operative care of endocrine surgery patients. Following are few of the recommendations:

 Postoperative follow-up consultations need to be maintained during the epidemic. Tele-consultation is recommended to ensure continuity of care while limiting the risks of coronavirus spread in healthcare centers.

BAETS Prioritisation advice for Adult Endocrine Surgery during Covid-19 crisis

Priority level	1a	1b	2	3	4
Thyroid	Acute Airway Obstruction from Thyroid pathology		Tumour or goitre causing mild or moderate stridor Undifferentiated /poorly differentiated thyroid cancer amenable to surgical treatment Medullary thyroid cancer Thyroid cancer with metastatic nodal disease Uncontrolled thyrotoxicosis where medical treatment or radio iodine not suitable Uncontrolled Graves' in Pregnancy	Other thyroid cancers (including diagnostic lobectomy)	Surgery for uncomplicated benign thyroid disease
			Patients with sight threatening thyroid eye disease	Patients with recurrent and	Other perathus id
Parathyoid			Hyperparathyroidism associated with corrected calcium > 3.0 mmol/l who cannot be controlled with medical management Suspected parathyroid carcinoma. Repeated hospital admissions for medical management of hyperparathyroidism Pregnant women with significant hypercalcaemia (C.Ca> 2.85mmol/L) ideally in 2 nd trimester	symptomatic renal stones +- associated sepsis	Other parathyroid surgery
			Post Transplant hypercalcaemia with deteriorating renal function		
Adrenal			Adrenal Cancer or Highly Suspicious Masses – includes malignant phaeochromocytoma Indeterminate Masses > 6cm especially those that have been shown to be increasing in size or hot (and non-functional) on PT scan Adrenal pathology requiring urgent surgery for severe endocrine complications e.g. refractory Cushing's; Phaeochromocytoma with heart failure	Indeterminate Masses > 4cm, < 6cm with adrenal androgen excess or cortisol hypersecretion Adrenal Metastases -Rescan at 3 months and re-prioritise if progressing	Other adrenal surgery

Priority level 1a Emergency - operation needed within 24 hours to save life , Priority level 1b Urgent - operation needed with 72 hours

Based on: urgent / emergency surgery for life threatening conditions such as obstruction, bleeding and regional and / or localised infection permanent injury / clinical harm from progression of conditions such as spinal cord compression Priority level 2 Surgery can be safely deferred for up to 4 weeks - elective surgery with the expectation of cure

Based on: urgency of symptoms / complications such as local compressive symptoms / biological priority (expected growth rate) of individual cancers

Priority level 3 Surgery that can be delayed for up to 3 months with no predicted negative outcome

Priority level 4 Surgery that can be delayed for more than 3 months with no predicted negative outcome

Disclaimer: This document is intended to help BAETS members when planning services during the Covid-19 pandemic. It will be subject to change and updating over time. It is not comprehensive, and membehould take into account other healthcare resources when planning services. The legal responsibility for local decisions is through local governance structures and local healthcare organisations. No liability is accepted by BAETS, including the BAETS executive team, other contributors to this document, and those undertaking work on behalf of BAETS to distribute this document, for any errors or omissions in this document, or for any direct or indirect loss to third parties related to the advice given in the document.

- Video exchange is recommended in the conditions requiring diagnosis and detailed instructions regarding postoperative care of the patient.
- Most of the investigations must be performed outside hospitals.
- In a situation where medical drugs of major therapeutic importance may be in short supply, patients, who are dependent on a hormone

substitution treatment, should be reminded never to interrupt their treatment longer than 24 h for corticoids_13, longer than 48 h for calcium14, and longer than one week for thyroid hormones15.

CONFLICTS OF INTEREST:

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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Archives of Surgical Research Narrative Literature Review

Exploring Operating Room-Based Student Learning Experience: Perils & Pitfalls? A Narrative Literature Review

Talat Waseem; Hadia Munir Baig; Rahila Yasmeen; Rehan Ahmad Khan

IMPORTANCE Operating Room (OR) is a high-pressure setting where multiple complex surgical, educational, and administrative facets interplay. While considered an essential aspect of the undergraduate curriculum and a valuable tool for cultivating an unparalleled interest and enthusiasm in the young minds of medical students, the real-life experience of the operating theatre can pose a number of challenges to be dealt with. OR-based student learning has traditionally been suboptimal owing to many reasons. Exploring such perils and pitfalls remains a high research priority in order to design structured clinical encounters within the OR setting in future.

METHODS A literature search was done through PubMed, ERIC, and Google Scholar. Keywords used were "operating room", OR "operating theater", AND "student learning" OR "medical students". Following PRISMA guidelines, 1580 articles were identified, out of which 68 pertinent articles were initially selected for the literature review, and 52 articles were used for thematic analysis. The article evidence was thoroughly evaluated and analyzed, and various themes were identified.

DISCUSSION Operating theater-based student learning is influenced by a number of factors that likely include organizational, socio-environmental, and emotional factors and factors related to educational relevance and surgical educator. Conflicting roles of medical educators in this setting, their availability to students, confused learning objectives, the theatre environment, poor visibility of the procedure, and various emotional aspects of medical students are amongst other reasons. Although a number of studies have individually examined the role of various factors in 'OR' based student learning, their relative importance and influence remain partially explored. Moreover, the quality of evidence to substantiate these aspects still remains contextual with low external validity and generalizability.

CONCLUSION& RELEVANCE The reasons of suboptimal student learning within OR setting are multifactorial. In depth analysis of these factors influencing OR-based student learning remains a high research priority in order to design future structured clinical encounters within OR for a more meaningful and enriched learning experience.

KEYWORDS Learning experience; Operating Room; Operation Theater; Student Learning;

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Narrative Literature Review

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urgical training being the most important part of the medical school curriculum, has remained a traditional focus of attention 1-5. Operating room is the most versatile and unique learning environment that focuses almost all of the learning forms, such as spatial, aural, verbal, physical, logical, interpersonal, and intrapersonal⁷. The Operating Room (OR) offers students an opportunity to experience real-life cases that they once only used to read in textbooks. Most importantly, this setting enhances the learning experience, promotes independent thinking and learning, and facilitates retaining clinical knowledge for improved exam performance. Student learning in OR not only provides undergraduates with exposure to working with real patients but also enables them to adapt to the challenges and stressors related to OR6. Moreover, the surgeon's responsibility additionally transforms into an educator and leader in the OR, which requires significant organizational skills and professional expertise⁵.

Operation theater-based student learning is influenced by a number of factors that likely include organizational, socio-environmental, and emotional factors apart from factors related to educational relevance and surgical educator⁸. Although a number of studies have individually examined the role of various factors in OR-based student learning, their relative importance and influence remain partially explored1. Moreover, the quality of evidence to substantiate these aspects still remains contextual with low external validity and generalizability⁹. Similarly, the students' and faculty's perspectives regarding these factors are still relatively unexplored.

Identification and analysis of the factors influencing ORbased student learning remains a high research priority in order to design future structured clinical encounters within the OR for a more meaningful and enriched learning experience⁴.

METHODS

In order to review the literature, a narrative approach was used to have a comprehensive, critical, and objective analysis of the data available related to the factors affecting student learning experience in the operating room.

2.1. Literature Search Process

Following PRISMA guidelines, literature search strategies were formulated for the databases (PubMed, ERIC, and Google Scholar) using search terms "operating room", 'operation theater", "medical students", "learning". A review of all search papers was conducted according to the selected search strategy from 1990-2020. Additionally, the reference research papers were also included for a comprehensive literature review.

2.2. Inclusion of Articles

1580 papers were identified in the literature search, 342 were excluded for duplication, and 1238 articles were assessed for pertinence. 68 articles were initially selected for review, of which 52 were included in the literature review. Only Full-text English language papers were selected. Studies that were not related to the topic were not included. The critical analysis of the searched literature was done using Harden's framework. The article selection process is presented in a flow diagram in Figure 1.

2.3. Data Synthesis and Analysis

The data was analyzed by thematic analysis of each paper's results. The outcomes of each paper were physically coded. Those codes were categorized as themes. The findings of all the papers were recorded according to categorized themes. The intermittent themes identified through data analysis are described in the table below.

DISCUSSION

Operating room learning is an important phase in medical students' training; however, it still remains unstructured^{4, 5, 10}. Students learn surgical skills, real case pathologies, and techniques to manage the patients. The medical students' learning in the OR is affected adversely by several factors in which organizational, educational, and emotional factors are included^{4,5}. Lack of clarity regarding learning objectives, lack of basic introductory sessions on OR etiquettes, syncope, a biased attitude of the faculty, poor teaching strategies, anxiety, fear, lack of motivation are some of the factors frequently reported by medical students⁴.

A total of 1580 articles were identified by the literature search strategy. 52 papers were included after the screening process by removing duplicates. These papers were analyzed thoroughly. The detailed analysis of the selected papers showed some recurrent themes affecting students learning in OR. These themes are described in Table 1. These themes were further divided into sub-themes to cover each theme in detail and make the literature analysis more comprehensive.

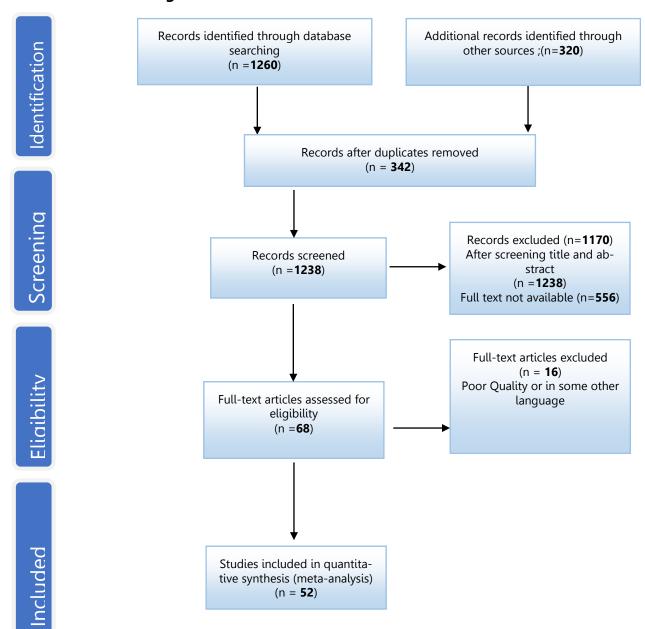
3.1. Educational relevance/Learning objectives

Clarity about learning objectives is very important for the students' OR learning ^{4,5}. When the learning objectives are not practical, they result in frustration, confusion, and hamper learning. It is also observed that students develop unrealistic goals when they are not educated about them⁴. For medical students to understand the purpose of their theatre placement, the senior faculty's active role in the mentorship and supervision of students cannot be overstated. This intervention can provide a sense of direction for students and is crucial for building a surgical competency and the ability

to sustain clinical knowledge. Previously, it has been identified that learning plans within the OR setting have remained suboptimal, and learning objectives for lesson plans have been unstructured and ill-defined⁵. Ravindra and colleagues found that almost 47% of the students were not clear about the learning objectives when they were asked about them.

The ratio of the students with planned learning objectives was as low as 13%¹¹. In order to achieve this goal, the importance of a comprehensive OR orientation session is pivotal. When the students were formally educated about learning objectives, it increased their confidence, and they performed better in the OR¹¹.

Figure 1: PRISMA Flow Chart for literature search



The other issue is the relevance of learning objectives about OR-based student learning and its place in the overall curricular picture⁵. There is frequently a disparity in what surgeons and medical students believe to be learning objectives. Faculty members have a tendency to suggest the student concentrate more on the disease process and cognitive portion of the operative procedure. The students, however, have a different perspective about OR learning, which does not correspond to the surgical teacher's thought process. The students want to learn more about the surgical procedure and surgical instruments and want to focus on the psychomotor component⁴. O'Neill and colleagues explored this issue further in their questionnaire-based study and found that 84% of students chose surgical skill acquisition to be their primary objective of the OR-based learning, to which only 11% of the surgeons agreed¹². Most of the surgeons in the same survey envisioned that learning disease processes, pathology and developing decision-making skills were far more important than learning surgical techniques.

It remains imperative to sort this dichotomy of thought with the ultimate objective to synchronize student and faculty vision about the OR-based learning process and content selection⁴. It remains of substantial importance that learning objectives are clear and comprehensive⁵. Pragmatism is another important element that should reflect in learning objectives.

3.2. Educator-related Factors

The surgeon, as an educator, plays an over-riding role in students' OR-based learning. The students perceived educators as the most influential factor in OR learning when they were asked to rate 27 different factors (unpublished evidence). The educator's positive attitude, interest, and competency are the factors that positively correlated with improved student learning and theater attendance⁴. But when the teacher is over critical and does not give feedback to students, it makes them feel burdened and not being welcomed4. It was observed that students found junior doctors to be more competent teachers within this setting and were able to come down to the level of students and address common queries they had. It is very crucial for the educator to prepare and educate the students for the OR session by preoperative teaching sessions and discussions and keeping them involved during a surgical procedure by live commentary and asking structured questions⁴. An established style of teaching is when surgical educators give a narration of the findings and make a constant commentary, which helps students gain an insight into procedures and cases in an unfamiliar setting. Often information that surgeons consider to be obvious is of immense importance for theatre-naïve students. It is found that when students are instructed to study up on topics and develop baseline knowledge on the anatomical regions that they are going to encounter, it can result in an improved quality of the theatre experience. Preoperative briefing and active participation in question-answer sessions can encourage undergraduate students to develop critical thinking skills and apply the information to new case scenarios¹³. The use of effective teaching strategies is as important as are pre and intraoperative teaching sessions in making teaching sessions productive. Students frequently associate the quality of their theatre experience with the effectiveness of the surgeon's teaching style. The teaching style of the educator has been considered to be an important factor influencing students' learning reported in various studies³.

Surgeons' formal training before working as educators can enable them to improve their teaching skills and as a result facilitates student learning¹⁴. There is also often a lack of communication within the surgical team as to who takes up the teaching role and a degree of confusion amongst students regarding who's in charge of teaching within the theatre. Rosters made to assign teaching roles to staff on a regular basis can help amend this issue¹⁵.

3.3. Organizational Factors

The institutes are required to provide all resources that students need to facilitate their OR-based learning. Previously, students have reported inadequate organizational support for OR-based learning¹⁶. When asked about attending OR orientation sessions, students denied any formal arrangement in this regard. This lack of orientation about the OR environment induces stress and confusion^{4, 17}. Besides conducting an orientation session, the institute can improve students' OR experience by fostering surgical skills in a simulated setting before exposing them to real-life scenarios^{18,} ¹⁹. Students who receive structured training in simulated settings prior to their OR rotation perform better than those who do not¹³. Simulations provide undergraduates a safe environment to practice in prior to their theatre placement. With adequate facilities, didactic lectures, web conferencing, online seminars, pre-theatre workshops, virtual training and simulated operation suites (SOS) can all significantly enhance the OR experience.

Another important limiting factor is the narrow surgical view as complained by many students previously²⁰. Poor visibility can be due to a confined working space, surgeries at a miniature scale, limited accommodation, or large batches of students. This problem can be managed through the use of head cameras worn by surgeons²⁰. This equipment allows the surgeon to teach students intraoperatively while highlighting regional anatomical structures. A new device called 'Video Glass' by Landry may improve visualization and enhance OR learning²⁰. Satisfactory organizational support has a substantial impact on the overall experience of the students and can improve theater-based learning.

Table 1- Qualitative thematic analysis of the literature evidence

Year	Author	Country	Research method	Themes identified	
1996	Hubbell 23	US	Questionnaire; Medical students = n-48 Response rate =98 %	Clarity of learning goals facilitates OR learning, Teaching styles; The effect of visual reinforcement	
1996	Hong ²⁴	Canada	Questionnaire; Medical students = n-8; Some other faculty members	Being welcomed; Being part of the team important to medical students; Feeling burden- some; Teaching strategies – advantages of surgical skills workshop; Importance of active interaction for students	
2002	Broderick ²⁵	US	Variety of medical background including medical students (n=11)	Cannot observe the surgical procedure affect students OR learning	
2003	Lyon ²⁶	Australia	Group interviews of medical students, detailed semi structured interviews. Questionnaire (n=197, response rate 87%); (surgeons=n 10, students = n15)	Fear affecting OR learning negatively; Ambiguity related to learning goals Embarrassment not being competent; Long OR sessions and their educational benefits	
2003	Stark ²⁷	UK	Semi- structured interview of consultants (n= 13) Focus groups of medical students (n=20)	Effect of teaching strategies on OR learning long OR sessions affecting student's attend- ance;Educational benefits of long learning sessions	
2004	Pettitt ²⁸	US	Questionnaire; n= 84; response rate =83 %	Fear affecting OR learning negatively; Medical students not treated well by the faculty	
2004	Lyon ²⁹	Australia	Questionnaire;(n = 197); Response rate = 83 % Detailed semi-structured interviews;Medical students (n=15); Surgeons (n=10); Group interview of medical students	Feeling being welcomed; Part of the team being important to the students Active interaction and participation; Teaching strategies affecting OR learning	
2004	Callcut ³⁰	US	Evaluation; Medical students (n= 70 +/- 7); Surgeons (n = 74)	Teaching strategies affecting students OR learning	
2005	Lee ³¹	Scotland	Questionnaire; (n=52); Response rate = 100 %	Ambiguity related to learning goals/ discordant; Lack of visualization	
2006	Thomas 32	UK	Personal reflection	Teaching strategies affecting OR learning; Benefits of orientation session; Humiliation	
2007	Fernando 33	Scotland	Questionnaire; Medical students (n=54); Response rate = 90 %	Feeling being welcomed; Ambiguity related to learning goals	
2007	Fernando ³⁴	Scotland	Questionnaire; Medical students (n=46); Response rate = 100 %; Consultants (n=42); Response rate 46	Ambiguity related to learning goals /discordant; Lack of visualization	
2008	Cloyd ³⁵	US	Questionnaire; (n=55); Response rate = 88.7%	Feeling being welcomed; Feeling being part of the team; Feeling burdensome Teaching styles – benefits of surgical skills workshop; Active participation	
2008	Berman ³⁶	US	Questionnaire; (n=116); Response rate= 89%structured mentorship program	Teaching strategies – benefits of preparatory course; Active participation Teaching strategies affecting OR learning	
2008	McIntyre ³⁷	US	Questionnaire (n=78)	Teaching strategies affecting students OR learning; Long OR sessions affecting student's attendance and their educational importance	
2010	Irani 38	US	Field observation; Satisfaction ratings; Medical students (n=11)	Learning objectives not clear/ discordant; Active participation	
2011	Hampton ³⁹	US	Focus groups; Medical student (n= 13); Faculty members (n=5)	Importance of learning objective to students and faculty; Feeling being welcomed; Feeling part of the team	
2012	Patel ⁴⁰	UK	Questionnaire; (n= 60)	Teaching styles – advantages of preparatory workshop	
2012	Martin ⁴¹	UK	Questionnaire; Medical students (n=36); Consultants (n=8)	Teaching style – advantages of preparatory workshop; Lack of confidence in students	
2013	Chapman 42	UK	Questionnaire; Medical students;(n=292); Response rate= 20.8%	Feeling being welcomed; Feeling being part of the team; Active participation	
2013	Coveney 43	Ireland	Free recall experimenting model	Effect of short-term free recall on students learning	
2013	Patel 44	US	Questionnaire; (n=33)	Teaching styles – advantages of preparatory workshop	
2013	Ravindra ¹¹	UK	Questionnaire; (n=209); Response rate 87%	Learning objective not clear; Victimization; Humiliation; Active participation Long OR sessions affecting students learning and their educational benefits	
2014	Flannery ⁴⁵	Northern Ire- land	Questionnaire; Medical students; (n=22); Response rate = 8%	Importance of learning objectives; Teaching strategies affecting students learning	
2014	Hampton ⁴⁶	US	Questionnaire; (n=68)	Advantages of setting learning objectives; Effective teaching strategies results in higher satisfaction	
2014	Bowrey ⁴⁷	UK	Semi-structured interview; (n=9 of 83 invited students)	Fear associated with OR; Intimidation; Feeling being welcomed; Feeling being part of the team	
2014	Drolet ⁴⁸	US	Questionnaire; (n=24); Response rate =100%	Teaching strategies – advantages of preparatory course; Lack of confidence in students	

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2014	Bauer ⁴⁹	Germany	Objective structured clinical examination; Written tests; Medical students (n=20)	Preoperative training for medical students; Teaching strategy affecting students learning; Students confidence
2015	Stone ⁵⁰	Canada	Questionnaire; (n=72); Response rate= 21%	Fear associated with OR; Intimidation; Teaching strategies – advantages of preparatory course
2015	Bakhshialibad ⁷	Iran	Medical students; (n=493)	Feeling being part of the team; Effective teaching strategy affecting students learning
2015	Piromchai ⁵¹	Australia	(n=210)	Teaching strategy affecting students learning
2015	Rothenberger ⁵²	Switzerland	Questionnaire; Medical students; (n=15)	Importance of preoperative training
2015	Zundel ¹⁶	Germany	Series of focus groups; Medical students(n=17); Surgeons (n=10)	Importance of learning objectives; Fear associated with OR; teaching strategies affecting students learning
2016	Flinn ⁶	US	Medical students; (n=40)	Stress; Criticism by surgeons
2016	Miandob	Iran	Questionnaire; (n=62)	Feeling being part of the team; Feeling being welcomed
2016	Morzycki ⁵³	Canada	Questionnaire; (n=180); Response rate =40%	Fear associated with OR; Intimidation; Feeling being welcomed; Feeling being part of the team
2017	O'Neill ⁵⁴	US	Questionnaire; Medical students(n=39); Surgical residents(n=9); Surgeons (n=9)	Importance of learning objectives; Feeling burdensome
2017	Butler 55	US	Multiple choice questions; Medical students; (n=21)	Teaching strategy affecting students learning
2017	Labadie ⁵⁶	US	Questionnaire; Medical students; (n=119)	Clarity of learning objectives; Students confidence; Preoperative surgical training affecting students learning
2017	Knight ⁵⁷	UK	Questionnaire; (n=201); Response rate= 81.4%	Feeling being part of the team; Feeling being welcomed; Considering OR learning useful
2018	Shipper ⁵⁸	US	Semi- structured interviews; Medical students(n=8) Instructors (n=5)	Teaching strategies – advantages of preparatory course; Fear associated with OR Intimidation
2018	Jensen ⁵⁹	Denmark	Ethnographic observation; (n=7); 70 hours of observation	Importance of learning objectives; Lack of confidence in students; Teaching strategies; Importance of intra-operative teaching; Teaching strategies affecting students learning
2018	Pilieci ⁶⁰	Canada	Questionnaire; Multiple choice questions; Medical students;(n=29)	Preparedness; Teaching strategy affecting students learning; Confidence
2018	Lee ⁴²	US	Objective structured clinical examination; Medical students ;(n=34)	Effective teaching strategy; Preparedness; Orientation session
2018	Leithead ²	US	Questionnaire Response rate = 80%	Effective Teaching strategy; affecting student learning
2018	Torbjörnsson ⁶¹	Sweden	Questionnaire; Medical students;(n=42); Nurses (n=4); Response rate=59%	Preparedness; Time pressure; Surgeon's behavior; Interprofessional learning
2019	Gallagher ⁶²	US	Peer assisted learning; Medical students; (n=100)	Teaching strategy affecting students learning; Satisfaction; helpfulness
2019	Rosen ⁶³	US	Questionnaire; (n=28)	Teaching strategy affecting students learning
2019	Z. Chaudhry ⁶⁴	Canada	Questionnaire (n=143)	Lack of confidence; Learning objectives not clear; Importance of preoperative teaching; Positive environment; Role of feedback
2019	Landry ²⁰	Canada	Questionnaire;(n=23)	Effective teaching strategy improved visualization
2019	Shore 65	Canada	Questionnaire; Medical students;(n=88)	Effective teaching strategy affecting students learning
2019	Ng ⁶⁶	Canada		Fatigue, stress, surgeon's attitude affecting students learning

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3.4. Emotional / Psychological Factors

Emotional or psychological factors also affect student learning in the OR setting. Various educational, organizational, and educator-related factors may trigger certain emotional responses in students in the challenging theater environment. Students have previously reported that being in an unfamiliar environment was fearsome, and they felt intimidated4. The OR setting greets students with an unspoken code of conduct that is expected to be adhered to strictly. A common sentiment amongst students is fear of not acting in accordance with the rules, looking like a fool in front of the staff, and not being able to live up to their teachers' expectations. Students report that trainees and residents often had a hostile attitude towards them which created feelings of anxiety and stress. It has been demonstrated that stress levels, beyond a certain extent, proved to be detrimental to student learning and performance and made retaining information difficult. Students also report that they felt their presence was undesired, constantly fearing of getting in the way or being told off for not maintaining a distance from the sterile field. Fear of syncope is also very common among the students as they try not to make any mistake and feel embarrassed²¹. Chapman and colleagues found that students were victimized by the faculty and seniors and received negative put-downs, which is quite stressful for students. Negative ethical environment results in low motivation, lack of confidence and poor selfesteem^{5, 22}. Not addressing these factors can lead to students being unnecessarily mentally drained, not being able to show their true potential, reducing their attention span and learning capacity.

3.5. Limitations of the Study

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

3.6. Recommendations

The in-depth literature analysis has identified various factors influencing OR-based student learning. Based on the collective wisdom attained through this data, the following steps may be incorporated in future structured clinical encounters within the OR- setting:

1. Operating Room-based learning process in its entirety should be structured with well-planned lessons, defined instructional and assessment strategies which encompass all

dimensions of learning e.g. cognitive, motor and affective skills.

- 2. Establishing and implementing structured learning process within the OR setting is an uphill task. Organizational commitment and support to enforce and improve quality of learning process within the OR setting remains pivotal.
- 3. A structured OR preparatory orientation session explaining various aspects of OR sections and clearly defined learning objectives can be of substantial importance. This would generate clarity and reduce frustration among the students.
- 4. Prior intimation about operative procedures to be done in the OR can add to students' clarity about learning objectives and may be instrumental for students' preparation for the expected lesson.
- 5. The provision of student-centered learning objectives for the OR-based sessions would reduce confusion among students and would reinforce student preparedness about the expected lesson.
- 6. Intraoperative lessons should be structured, well prepared, and comprehensive. Effective teaching strategies should be utilized. There should be an ongoing commentary about the surgical procedure with questions to keep students involved in the session.
- 7. Faculty training remains the central cornerstone for an effective learning process within the OR setting. The surgeons should also receive training sessions, attend preparatory workshops and courses to improve and enhance their teaching skills especially within the OR setting.
- 8. The positive attitude of the faculty would increase students' participation, OR attendance, interest, and motivation. This will improve their confidence and self-esteem, and students will no longer feel victimized and intimidated.
- 9. Peer-assisted learning can be very effective as students can learn in a non-threatening environment and this can lessen the surgeon's workload too.
- 10. The surgeons and students should fill feedback forms at the end of each OR rotation to evaluate the process and highlight the concerns.

CONCLUSION

In conclusion, OR learning trains students professionally. They learn skills, techniques and patients' management. During this process, they learn how to cope with stress and anxiety, how to handle time pressure and remain calm when situations become challenging. Different variables play an important role during the learning process that affect the

overall quality of learning in the OR. These issues can be managed by acknowledging them and making positive changes to resolve them.

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Archives of Surgical Research | Invited Review

Cushing's Syndrome: What an Endocrine Surgeon Needs to Know

Asif Hussain; Jawaria Avais; Muhammad Tariq Rahim; Shahid Hameed Bhatti; Salman Rafique Chatha

IMPORTANCE Cushing's syndrome (CS) is pathological hypercortisolism with significant morbidity and mortality due to its structural and metabolic complications, delays in establishing the diagnosis and etiology, and complexity of its lifelong management. Advancement in surgical techniques especially laparoscopy have helped in reducing the treatment related morbidities and has become treatment of choice for majority adrenal causes of Cushing's syndrome, except carcinoma where still laparotomy is often needed. Non-surgical options such as medical therapy and/or radiotherapy are second line options when surgery is awaited or inadequate to control the disease. Diagnosis and management of such complex cases needs a team work by endocrinologist and endocrine surgeon. Patient education is an essential component for the successful handling of the case. We aimed to simplify the management with recent updates.

KEYWORDS Cushing's Syndrome, Medical Adrenalectomy, Surgical Adrenalectomy, Adrenal Lesions, Pituitary Microadenoma

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Invited Review

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ushing's syndrome is endogenous hypercortisolism with significant complications including infection, immunosuppression, obesity, osteoporosis, diabetes, hypertension, cardiovascular complications and significant increase in mortality ¹. The syndrome is often complicated by late diagnosis due to its variable presentations, difficulty in establishing the diagnosis due to limitations of available tests and complexities of the management. Also, even after correction of hypercortisolism, the established complications of the syndrome may take longer to resolve or need additional treatment ².

CLINICAL PRESENTATION OF CUSHING'S SYNDROME:

Pathophysiological mechanism of most of the clinical manifestations due to high cortisol are: 1) proteolysis to release amino acids for gluconeogenesis, hence reducing proteins in the bones, muscles & subcutaneous collagen, but at the same time increasing glucose, 2) cortisol causes triglyceride breakdown in peripheral fat which lead to fat influx in blood and central body, 3) apoptosis of lymphocytes and eosinophil, demargination of neutrophils, and boosts erythropoiesis in bone marrow, 4) fluid retention by mineralocorticoid properties. Adrenal androgens produced by the adenoma or more likely by the carcinoma

produces many of the androgenic features of Cushing syndrome [Table.1].

DIAGNOSIS OF CUSHING'S SYNDROME

Screening for Cushing's syndrome:

First thing is to document that the patient with suggestive clinical symptoms has hypercortisolism and that high level is pathological. High cortisol can be physiological due to any stress (physical or psychological), obesity, alcoholism, sleep disturbance, diabetes, pain, exercise and pregnancy. Many patients have Cushing syndrome due to exogenous replacement. corticosteroid Screening tests hypercortisolism includes: 24-hour urinary free cortisol (UFC), mid night salivary cortisol or Dexamethasone suppression test (DST). Usually we need two of these tests to document pathological hypercortisolism as all of these tests have limitations ². UFC can be high if urine volume is high such as over drinking or can be falsely low if patient has low urine output such as those with reduced GFR (renal failure) 3. Also, improper 24-hour collection of urine will affect UFC level. Similarly, DST can be affected by the factor affecting dexamethasone metabolism (drugs affecting cytochrome P450, pituitary disease-causing slow dexamethasone metabolism) or high cortisol binding proteins such as high estrogen level and OCPs. There are two types of assays for cortisol immunoassay measurement, such radioimmunoassay (RIA) or structure-based assay such as mass spectrometry (MS), later is more specific for cortisol and has lower reference range. However, immunoassays are more useful to detect milder cases. Also, the reference range varies even within the same type of assay. Hence, these tests should always be interpreted according to the reference range used ⁴.

Obesity: moon face, buffalo hump, central obesity with thinning of limbs.

Skin: Stria, thinning of skin, easy bruising, pigmentation of skin creases & buccal mucosa (if ACTH dependent Cushing), facial flushing, delayed wound healing, hyperandrogenic skin changes (acne, hirsutism, male pattern baldness).

Musculoskeletal: Proximal myopathy with normal CK level, osteoporosis, pathological fractures

Cardiovascular: hypertension, increased cardiovascular mortality, edema, hypercoagulability, VTE and pulmonary embolisms.

Metabolic: insulin resistance, hyperglycemia, diabetes, hyperlipidemia, electrolyte imbalance (low K, high Na, low serum Calcium, increased urinary calcium), increased urea level. increased ammonia level.

Reproductive: infertility, decreased libido, hypogonadism, hyperandrogenism, delayed puberty and short stature (in pediatric cases)

Psychiatric: depression, psychosis. insomnia, labile mood.

Infections and immunosuppression.

Hematological: Lymphopenia, eosinopenia, thrombocytosis, polycythemia, and neutrophilia.

 Table 1: Common Signs & Symptoms of Cushing 's syndrome:

ACTH dependent pathological hypercortisolism:

These patients with pathological hypercortisolism have high or normal / unsuppressed ACTH despite high cortisol (1 1pm plasma ACTH > 20 pg./ml) and includes pituitary adenoma (almost 80% of adult cases of Cushing's syndrome or 85 % of pediatric cases above 7 years of age) or ectopic ACTH producing tumors (rare, 1-2% of total cases). Ectopic ACTH secreting tumor is not suppressible by high dose dexamethasone suppression test (high dose DST) whereas the pituitary adenoma is suppressible by high dose DST. High ACTH will also cause skin and mucosal pigmentation, so the patients are dark complexion with pigmentation affecting buccal mucosa and skin creases or scars. MRI of the

hypo-thalamic pituitary axis may show adenoma but sometimes adenoma is too small to be seen by MRI and hence will need inferior petrosal venous sampling to demonstrate pituitary source of high ACTH. Rarely we need Corticotropin stimulation test when obtaining samples from

inferior petrosal sinus ⁵. Ectopic ACTH is commonly produced by small cell lung cancer and hence CT chest is often needed if we fail to demonstrate pituitary source of high ACTH ⁶.

ACTH independent pathological hypercortisolism:

These patients have high cortisol and suppressed (low) ACTH level (plasma ACTH < 10 pg./ml). This is either due to exogenous corticosteroid replacement or adrenal source of high cortisol. The term Cushing's Syndrome is commonly used when its adrenal gland causing hypercortisolism and is not suppressible by high dose DST. Low ACTH causes less melanin in skin and patients are often pale or white. CT Adrenal glands or MRI are often diagnostic, however rarely adrenal venous sampling may be needed to differentiate unilateral vs bilateral lesions as decision is important for unilateral or bilateral adrenalectomy 6. Also, it's important to document that the lesion found on the CT /MRI adrenal is producing pathological amount of cortisol and is not just an incidentaloma as adults over 40 years of age have incidental findings of adrenal tumors (10%) or micronodular hyperplasia (36%) on autopsy 7.

Androgen production such as dehydroepiandrostenedione (DHEA) is predominantly seen in cases of adrenal carcinoma and is less common in benign lesions, hence androgenic issues such as hirsutism and virilization are sinister signs in patients having Cushing's syndrome. Cushing's syndrome is due to adrenal causes in 20% adults and 15% children above 7 years of age and almost 50% in children younger than 7 years of age. Most common adrenal lesions are isolated sporadic adenoma, whereas carcinoma and congenital adrenal hyperplasia (CAH) are rare. Adrenal adenoma is mostly unilateral and often due to abnormal cAMP signaling pathway, whereas hyperplasia is mostly bilateral and genetic. Hyperplasia has many sub varieties such as micronodular, pigmented nodular, macronodular varieties, ACTH independent macronodular or massive macronodular hyperplasia. Macronodular hyperplasia are less likely to be genetic and are rare in pediatric patients 8. Adrenal carcinoma is an aberrant defect of growth factors and germ line or somatic mutation in tumor suppressor gene, P53.. Using the most commonly accepted radiological criteria of size more 5cm, adrenal carcinoma can be found in 7% of the adrenal lesions 9.

Step 3: CS

Step 2:

ACTH level High Dose DST

MRI Pituitary / Petrosal venous Sampling /CRH Stimulation test/ CT Adrenal gland/Search for EASC Adrenal

Step 1:

Symptoms and signs of CS & Screening tests: use two of the three tests:

1: 24-hour urinary free cortisol 2: Low dose DST

3: Midnight salivary cortisol level

Fig.1: Stepwise approach to diagnose Cushing's Syndrome: CS: Cushing's Syndrome, DST: Dexamethasone Suppression Test, ACTH: Adrenocotropic Hormone, CRH: Corticotropin Releasing Hormone, EASC: Ectopic ACTH Secreting Cancers.

MANAGEMENT OF CUSHING'S SYNDROME

Surgical treatment for Cushing's syndrome is first choice:

Recommended treatment for Cushing's syndrome is normalizing cortisol level and/or its actions in all patients except those where there are only mild biochemical abnormalities due to pituitary diseases without any clinical manifestations. The gold standard treatment for such patients is surgical resection of the underlying lesions unless the patient is unfit for surgery or surgery is not possible for other reasons, failed resection or recurrence of the disease 10

Pre-operative adjuvant management includes optimizing treatment of Cushing's related complications such as hypertension, diabetes, infections, hyperlipidemia, osteoporosis and electrolyte abnormalities. Also, treatment should be provided by a multi-disciplinary team including an experienced endocrine physician and an endocrine surgeon. Patients and their families should be educated about surgery and possible outcomes and also about other treatment options. In addition, age appropriate vaccinations should be provided such as influenza, herpes zoster and pneumococcal vaccine as these patients are often Venous immunocompromised. thromboembolic prophylaxis should be used perioperatively to reduce such complications. Patients with severe complications of hypercortisolism such as psychosis, pulmonary embolism, infections or cardiovascular complications should be treated urgently as soon as they are stable for surgery. Preoperatively normalization of cortisol is important by using the drug therapy ⁹.

Surgical resection of adrenal adenoma (unilateral) or bilateral macronodular disease or surgically resectable adrenal tumor by an experienced adrenal surgeon should be first option for all adrenal lesions. If adrenal cancer is not resectable, then medical treatment is an option. Adenomas are usually resected laparoscopically but carcinoma may need laparotomy. Laparoscopic surgery has reduced morbidity especially for those who have complications of Cushing's syndrome such as diabetes or hypertension. Surgery is often not curative for carcinoma due to metastatic disease or locally advance disease and needs medical treatment and radiotherapy 11. For adrenal carcinoma patients, surgery is either curative (for limited disease) or debulking for locally advance or metastatic disease. Also, when possible, resection of metastasis helps improve the survival. Mitotane is used as adjuvant therapy or monotherapy in inoperable cases 12.

Ectopic ACTH secreting surgically resectable cancers should be removed along with the regional lymph nodes when possible. Occult or metastatic ACTH secreting tumor or medically resistant ectopic ACTH related Cushing's patients may benefit from bilateral adrenalectomy. Patients who undergo bilateral adrenalectomy should be monitored regularly with MRI pituitary-hypothalamic axis and ACTH for Nelson Syndrome (ACTH producing pituitary tumor). Similarly, resection of pituitary adenoma by transsphenoidal approach by an experienced pituitary surgeon is recommended as first line options. However, if the first resection was not successful, then either repeat resection or radiation therapy or medical treatment is an option 7. Recurrence rates are higher in patients with pituitary macroadenoma and remission rates are higher in patients who have microadenoma of the pituitary. Recurrence depends on size and aggressiveness of the tumor, experience of the surgeon and type of the hormonal assay used to assess the recurrence ^{10,13}. Remission after pituitary resection ranges from 70-85% but can be as high as above 90% in centers where the procedures are done more often ¹⁴. Those who fail the first TSS pituitary adenoma resection, repeat surgery is often preferred if feasible before recommending other options including radiotherapy, medical treatment &/or bilateral adrenalectomy 15.

Immediate life-threatening complication of surgery is acute Addison's disease which needs to be identified and treated with IV cortisol replacement unless oral replacement is possible. Unilateral adrenalectomy done for cases having adrenal adenoma may eventually recover from Addison's disease when contralateral adrenal gland gradually recovers from atrophic effect and it may take a few months to a year. Bilateral adrenalectomy cases will require lifelong cortisol replacement. Generally, patients with unilateral adrenalectomy needs glucocorticoid replacement for 6-12 months and those with bilateral adrenalectomies need lifelong replacement of both glucocorticoid

mineralocorticoid. Post operatively, monitoring for electrolytes especially Na, K, Calcium and blood glucose levels are important. For pituitary resection, monitoring for prolactin, thyroid hormones and sex hormone is also important and should be replaced if low. Post-operative MRI should be done within 1-3 months to assess the remaining pituitary gland. It's important to monitor for cortisol values as patients may still be having hypercortisolism which may need further medical treatment or patients may be hypocortisolism which will need cortisol replacement. Patient education about Addison's disease and stress dose adjustment for cortisol is prudent. Those who had pituitary surgery should be assessed for remaining adrenal reserve by ACTH-stimulation test and if its normal, they may not need cortisol replacement ¹⁶.

Medical Treatment for Cushing's Syndrome:

Medical treatment is often a second line choice when surgical cure is not possible such as patients who are unfit for surgery, who have failed / inadequate surgical resection or recurrence of the tumors, occult or metastatic ectopic ACTH producing tumor, or in adjuvant adrenal carcinoma patients where complete resection is often not possible. Pituitary causes of Cushing's requiring medical treatment are managed by using somatostatin or dopamine analogues to reduce ACTH production with or without radiotherapy.

Corticosteroid synthesis inhibition by adrenal enzymes blocking drugs such as metyrapone (11 Hydroxylase blocker) ketoconazole (17)Hydroxylase blocker) aminoglutethimide or mitotane (11 Hydroxylase inhibitor) are options. As a monotherapy they are effective controlling hypercortisolism in 65% cases 8. These drugs can also be used in combination for severe cases. In addition, corticosteroid receptor blockers such as mifepristone, RU 486 has been FDA approved treatment for hyperglycemia in Cushing's syndrome patients 13. Chemotherapy for nonresectable adrenal cancer or ectopic ACTH producing tumor is an additional option which may also help 2. Mitotane is adrenocytolytic chemotherapeutic agent which helps control the disease in half to two third patients, and control disease progression in a third of adrenal carcinoma cases ¹⁷.

Follow up Monitoring:

Lifelong monitoring for recurrence of hypercortisolism or underlying malignancy or Addison's disease should be done by hormone testing and imaging. Patients and families should be educated about cure, recurrence and hormonal deficiency / excess. Comorbidities such as diabetes, blood pressure, osteoporosis etc. should be treated adequately ⁹. Quality of life is closer to normal after adequate treatment of Cushing's syndrome with clinical and biochemical remission. 75-90% of patients improve with regards to complications such as diabetes, hypertension, psychiatric issues, proximal myopathy and other symptoms. However

chronic fatigue and psychiatric symptoms are often persistent ¹⁸.

DISCUSSION:

Cushing's syndrome has significant morbidity and mortality due to its complications, late detection due to variable presentations, complex diagnostic approach and need for multi-modality treatment with lifelong follow up issues. High degree of clinical suspicion for Cushing's syndrome, proper clinical assessment, careful selection and interpretation of the biochemical tests followed by appropriate radiological imaging is essential to minimize these delays and complications. Rarely interventional testing is also needed to confirm the diagnosis. Confirmation of the diagnosis and identification of the underlying cause is imperative for its treatment as each cause has different treatment quidelines.

Once confirmed, patient needs to be assessed and stabilized for the surgical removal of the underlying lesion as it is first line treatment option in suitable candidates. Pre-operative treatment of comorbidities and complications, normalization of cortisol with medical therapy and patient education are essential. An experienced endocrine surgical team can have higher success rate. Immediate and long-term post op complications such as Addison's disease, recurrence of the underlying lesion, management of the ongoing complications of Cushing such as diabetes and hypertension, inadequacy/failure of surgical option make the post-operative course complex and laborious. Medical therapy is a second line option mainly for those where surgical therapy is not an option or inadequate. Lifelong follow up is essential.

CONCLUSIONS

Diagnosis and management of Cushing's syndrome is complex and needs a vigilant team approach including experienced endocrinologist and endocrine surgical team with efficient diagnostic approach, perioperative and postoperative care, and patient involvement is of utmost important. Surgical resection is first line treatment whereas medical / radiotherapy ae used when surgery is contraindicated or is inadequate.

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Archives of Surgical Research | Original Research Communication

Management of Wrist Ganglion by Aspiration and Triamcinolone Injection Versus Surgical Excision of the Cyst

Tariq Saeed; Asif Mahmood; Maleeha Hussain; Sarem Zarak Wali; Hira Ashraf

INTRODUCTION Ganglion cysts are commonly occurring lumps of the hand usually found on palmer or dorsal surface of wrist and palmer surface of the base of fingers. They are idiopathic in origin but can be caused by trauma. Ganglion cysts disappear spontaneously, hence, in most cases they are only observed. However, if they persist, become painful or limit activity several treatment options are available.

OBJECTIVE To assess recurrence rate of ganglion cyst following aspiration and injecting triamcinolone into the cyst and surgical excision of the cyst.

DESIGN This is a prospective comparative study

PLACE AND DURATION OF STUDY This study was carried out in Surgical Unit of Fauji Foundation Hospital Lahore and Mohsin Medical Complex Walton Lahore for a period of time from February 2018 to March 2020.

RESULTS This study was carried out in 50 patients, results were obtained and compared. Two groups were formed Group A and Group B, with 25 patients in each group. It showed that 21 patients (84%) of the Group A who were managed with aspiration and triamcinolone injection had recurrence of the ganglion cyst and patients expressed dissatisfaction. In Group B all 25 patients had surgical excision of the ganglion with only 3 patients (12%) having recurrence.

CONCLUSION It was concluded that aspiration and injecting triamcinolone into ganglion cyst is a simple procedure that can be performed inside the doctor's office. It gives quick relief without requiring patient preparation or post-surgical complications. However, it is an ineffective management of ganglion cyst. Whereas, surgical excision showed better results. Patients expressed satisfaction despite the surgical trauma and discomfort of 1-day hospital stay.

KEYWORDS Ganglion Cysts, Triamcinolone, Cystic, Excision

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anglion cysts are idiopathic in origin but most common cause is trauma. Minor trauma which is sometimes not even recalled by the patient can be a cause and can presumably reflect a variation in normal joint or tendon sheath function ¹. Ganglion cysts, also known as Bible cysts, ² are more common in women than men. 70% cysts are found in people between 20-40 years of age. Rarely, ganglion cysts occur in children younger than 10 years of age. Cysts near joints are connected to the joint and the leading theory is that a type of check valve forms that allows one-way flow of the fluid, only out of the joint 3. Ganglion is a sac-like swelling or cyst that arises from synovium lining a joint or a tendon. The cyst contains clear fluid, which is similar to but thicker than normal synovial fluid 4. They are most commonly found on the wrist joint, especially the scapho-lunate joint, which accounts for 80% of all ganglion cysts. Ganglion cysts are amongst common lumps of the hand and wrist that occur adjacent to joints or tendons 4. They are most commonly located on dorsal or palmer surfaces of the wrist and the palmer surface of the base of fingers ^{5,6}.

Ganglion cysts may change in size or even disappear completely. They may or may not be painful ³. These cysts are non-cancerous and do not metastasize. Diagnosis is usually based on location and appearance. Ganglion cysts are usually oval or round in shape and soft or firm in consistency. Cysts on palmer surface of the base of fingers are typically pea sized firm nodules that are tender to pressure ⁷. Ganglion cysts show positive trans-illumination test, which may be helpful in diagnosis. Clinician may request X ray to investigate adjacent joint. Cysts at the distal interphalangeal joint are frequently associated with arthritic bone spur ⁸.

Treatment can be non-surgical or surgical. In most cases, the cysts are only observed especially if they are painless, as they spontaneously disappear frequently. However, if the cyst becomes painful, limits activity, or is otherwise unacceptable for cosmetic reasons, several treatment options are available ⁹. The use of anti-inflammatory medication and splints can reduce pain associated with activity.

Aspiration of the cyst followed by injecting triamcinolone can remove fluid from the cyst and decompress it ^{7,10}. It is a

simple procedure and can be performed in most office settings. However, recurrence of the cyst is common and is seen in more than 50% of the cases. Cystic fluid is identical to the normal fluid found within a joint or a tendon sheath. However, the fluid can become gelatinous over time ¹¹. If nonsurgical management fails to provide relief or if recurrence occurs surgical management is availed ¹². Surgery involves removal of the cyst along with a segment of the joint capsule or tendon sheath. Even though surgical removal is the definitive treatment but recurrence is reported in a small number of cases ¹⁰. If ganglion cyst is present on the wrist combined use of traditional and arthroscopic technique yield good results ⁶.

It is important to have such lumps examined by the doctor. While most lumps around the wrist and hand are ganglion cysts (by far the most common), there are other conditions requiring different management such as lipoma, giant cell tumor, infections or carpal bossing (bone spur) ¹³. Sometimes ganglion cysts on wrists disappear spontaneously but most of the time they require management. Large ganglion cysts put pressure on surrounding structures especially underlying tendon which is painful.

An alternative traditional method is to smash the wrist ganglion cyst with a hard object ⁸. This rupture the lining of the cyst. Because the lining is disrupted the smashed ganglion cyst may not return quite as often as those drained by a needle. However, many patients are uncomfortable with this barbaric method of treatment ^{8,9}.

METHODS

We studied 50 patients who presented in the surgical outdoor patient department of Fauji Foundation Hospital, Lahore. All 50 patients had complaints of painful or painless swelling on the dorsum of the wrist joint. Patients were examined clinically and advised X- rays of the wrist joint. Patients were divided into two groups Group A and Group B with 25 patients in each group. Patients in Group A had aspiration of the ganglion cyst with 14 gauge I/V cannula followed by triamcinolone injection in the cyst wall. While patients in Group B were subjected to surgical excision of the ganglion cyst under general anesthesia. Patients were reassessed for any recurrent swelling after 6 months of the management.

Sample Collection: Patients were selected at random and their consent for inclusion in this study was taken. Patients were also divided in two groups at random. All patients reported to surgical outdoor patient department of Fauji Foundation Hospital Lahore and Mohsin Medical Complex Walton Lahore. Inclusion Criteria: Patients between age 10-60 years were selected. Gender limit was not used. All selected patients had no systemic illness.

Exclusion Criteria: Children less than 10 years of age and patients with systemic illness were excluded.

AGE GROUP	IN NUMBER OF MA	ALE NUMBER OF FEMALE
YEARS	PATIENTS	PATIENTS
10 to 15	0	03
16 to 25	03	26
26 to 60	03	15

Table 1: Of Sex Distribution

RESULTS

A total 50 patients were included in this comparative and analytical study. All of these patients presented in surgical outdoor patient department of Fauji Foundation Hospital Lahore and Mohsin Medical Complex Walton Lahore with ganglion cyst on the dorsum of the wrist joint. 44 out of 50 patients were females (88%), and 6 patients were males (12%). 60% of the patients were in their 2nd or 3rd decade of life with mean age of 24 years. 30% of the patients were in 4th decade of life. In Group A 21 patients (84%) showed recurrence and dissatisfaction with treatment. All patients were subjected to single attempt of aspiration followed by triamcinolone injection into the cyst. Patients in Group B were subjected to surgical excision of the ganglion cyst. Only 3 patients (12%) reported recurrence. Upon examination recurrence was seen in 2 patients (8%) while third patient (4%) had a fibrotic nodular swelling probably due to underlying fibrosis. Hence, it was concluded that surgical excision of the ganglion cyst should be the preferred method of management.

DISCUSSION

Ganglion cysts are idiopathic in origin. They presumably reflect a variation in joint or tendon sheath function. Occasionally, ganglion cyst formation is an early sign of arthritis. Dorsum of the hands and wrist joints are most commonly affected areas but ganglion cysts can sometimes be present on feet, knees or ankles. Ganglion cyst is the most commonly occurring lump of the hand, and tends to target women between the ages of 20 and 40 years, for unknown reason. Tendons anchor muscles to the bones but presence of a ganglion cyst on tendon may cause muscle weakness. Ganglion cysts may be present as just one large lump or a collection of many smaller ones attached to a single stalk deeper in the tissue ¹⁴.

One third to one half of ganglion cysts disappear spontaneously without the need for medical treatment ^{15,16}. However, it is always best to consult the doctor to rule out other possibilities. If the ganglion cyst is painful, limits activity, causes numbness or paresthesia doctor consultation becomes mandatory. Ganglion cysts can be diagnosed on medical history and physical examination. Furthermore, noninvasive investigations, such as ultrasonography and X-ray, and aspiration of cyst fluid aid in diagnosis ¹⁷.

Ganglion cysts can be managed using non-surgical and surgical approach. Needle aspiration and triamcinolone

injection in the cyst is one of the several ways to manage it ¹⁸. However, high recurrence rate is reported with this method of management. Some studies suggest that approximately half of the patients report recurrence following aspiration and triamcinolone injection. A ganglion cyst that is aspirated three times has more than 80% chance of complete cure ¹⁹. Another method is surgical excision of the ganglion cyst under general anesthesia. In this study it is seen that surgical excision of the cyst is far superior method of management with lesser rate of recurrence.

A splint is fitted whether ganglion cyst is aspirated or surgically removed. Complete recovery is seen in 2 to 8 weeks depending upon the site of excised ganglion cyst. Generally, early mobility of the joint is advised. Using splints for extended periods of time can hamper joint mobility and delay recovery.

CONCLUSION

Ganglion cysts are idiopathic in origin and have no definitive treatment with risk of recurrence. Depending upon size and location of the cyst and treatment preference of the patient several management options are available. In this study it is seen that surgical excision of ganglion cyst is far superior method of management in comparison with aspiration and subsequent triamcinolone injection.

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Archives of Surgical Research | Short Communication

Post-Mastectomy Implant Selection in Single-Stage Unilateral Immediate Breast Reconstruction

Muhammad Jibran Rabbani; Asif Zubair Bhatti; Sarah Rabbani

IMPORTANCE Incidence of implant based postmastectomy breast reconstruction is increasing as skin sparing mastectomies are proven oncologically safe. The choice of implant is multifactorial, including patients' factors, oncological factors and surgeons' preferences. Traditionally, anthropometric measurements have been used for implant selection, and volumetric measurements are least emphasized. Recently, more work is being done for calculation of breast volume and hence implant volume other than implant base width measurements. The present article discusses the recent studies for the calculation of breast implant volume in case of unilateral immediate breast reconstruction as it claims to have more aesthetic results and fewer surgical procedures.

KEYWORDS Breast Cancer, Mastectomy, Implant Based Reconstruction, Immediate Reconstruction

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Short Communication

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ost-mastectomy breast reconstruction can give more natural, feminine, attractive and balanced feel in terms of both looks and weight that appears normal in and out of cloths. This comes at the expense of long healing time, more time off from work and obviously, surgical scars. Furthermore, the chances of complications always remain there. Breast reconstruction can be done using autologous tissue or implants in a single stage or two stages. The primary goal of postmastectomy surgical management is to re-create symmetrical breast mounds. Implant based reconstruction can be one stage with the use of implant alone, or two-stage using tissue expander before replacement with a permanent implant. Many studies showed increasing trends of implant based reconstruction in comparison with autologous tissue reconstruction with a reported ratio of 2:1 to 9:1.1-3 According to a survey, the rate of breast reconstruction with autologous tissue remained same from 1998 to 2008 while that of prosthetic reconstruction increased by 11%.1 In 2016, 81% percent of breast reconstruction was by prosthetic method.4 Implant based reconstruction in the United States accounts for 65% of all breast reconstructions.5 The reason behind is multifactorial, including increased incidence of prophylactic mastectomy. contralateral Advantages of reconstruction with prosthetic technique include shorter operative time and hospital stay, fast recovery time and no need for donor tissue. Better symmetry and more attractive mound can be created with implant-based reconstruction and can help in patient's physio-psychological well-being. Nonetheless, there always remains risk of implant related complications like infection, implant migration or rupture

and capsular contracture. Also, prosthetic reconstruction lacks natural feel.⁶

Selecting a breast implant includes physical examination of the chest wall as this provides a foundation on which implant rests. Other measurements include breast base width, nipple to sternal notch distance on the normal side, nipple to inframammary fold distance on the contralateral side and internipple distance. Breast base width is measured from the medial breast footprint to the anterior axillary fold. Tissue quality that will be left after mastectomy should be assessed along with upper pole fullness. Lowering of the inframammary fold and recruiting skin from the abdominal wall may be warranted. Placement of mastectomy scar in favorable position is included in preoperative marking.⁷ Among all, breast base width measurement is the most significant parameter for selection of implant in immediate breast reconstruction. Base width should match the base of implant to eliminate the dead space and redundancy of skin.8 Subcutaneous layer of 1 cm thickness and well vascularized skin flaps are consistently viewed as basic to accomplish effective results.9 Assessment by operating surgeon is considered the single most important influencing factor.^{10,11} Asymmetry is seen in one third of patient when implant was selected on all above mentioned parameters. 12 Assessment and prediction of breast volume is an underrated parameter and is challenging in single stage breast reconstruction. Water displacement method and cast made from thermoplastic material or gypsum may be used in case of delayed reconstruction. 13,14 Weight of mastectomy tissue gives a wrong estimate of implant size and volume, due to weight and size of tumor itself.15

Different methods have been described in literature for assessment of breast volume, but still, no consensus has been made. 16 Yan et al., in 2018, published their study on 115 breast reconstructions using implants in immediate setting. They estimated breast volume and implant size by mammography pre-operatively. They proposed, implant size can be estimated pre-operatively by using a formula, calculated implant size (ml) = $\pi \times \text{height (cm)} \times \text{[base width]}$ (cm) - 3]. They found, retrospectively, the mean calculated implant size was 376.03 ml, and the mean actual implant size used was 324.49 ml. They found no difference in calculated and actual implant size (p=0.090). They also concluded that more accuracy of the formula was seen in cases where less than 350 ml breast implant size was needed while there was a tendency of overestimation in cases of larger implant sizes. They found this formula to be an easy and accurate preoperative tool for calculation of implant size.¹⁷ Anthropometric measurements are also used to calculate breast volume. Qiao et al. proposed a formula for estimation of breast volume by using anthropometric measurements i.e. breast volume = $\pi/3 \times MP2 \times (MR + LR + IR - MP)$ where MP-mammary projection, MR-medial breast radius, LRlateral breast radius, and IR-inferior breast radius. 18 Kayar et al., compared results of different methods and found mammography is more accurate in calculation of breast volume than anthropometric measurements.¹⁹ Stefanie et al. used 3D imaging with the Microsoft Kinect sensor for the estimation of breast implant size and volume preoperatively for unilateral breast reconstruction. They used Kinect II (Kinect for Xbox One, Microsoft) in ten patients to do so and found this technique to be fast, reliable and feasible though technically demanding.²⁰ Pawel et al. in 2014. compared preoperative anthropometric measurements, thermoplastic casting and optical method using 3D imaging by a 3D camera (analyzed by Antroposcan 3D program) for breast implant size selection in 50 patients of unilateral breast reconstruction. They found the highest accuracy in optical method for estimation of breast volume as compared to other two methods (p<0.0001). They concluded that the selection of breast implant using 3D scanning method is more precise than mostly used anthropometric and thermoplastic cast methods.²¹ Hyungsuk et al., in 2015, used magnetic resonance imaging (MRI), pre-operatively for assessment of implant volume and found mean implant volume was more close to the estimated volume of breast using MRI than measurement of mean weight of resected tissue intraoperatively (p=0.001).²²

Type of implant is also considered during selection. Different types of implants are available including saline vs silicone filled, smooth vs textured and round vs anatomical. Saline implants are easier to insert but have increased rates of rippling. Silicone implants have a better look and feel but have higher rates of capsular contracture and rupture, which is difficult to detect.²³ Higher patient satisfaction is seen with silicone implants.²⁴ Effort was made to reduce the capsular contracture by the introduction of textured implant in

replace of polyurethane coated prosthesis.²⁵ Macrotextureplus, macrotexture, micro texture and nanotexture (smooth) implants are commercially available.²⁶ Salt crystal addition to silicon in different concentrations gives texture to implant by producing small pores of different sizes which have potential to adhere to surrounding tissues.²⁷ In 85-90% of cases, textured implants are used as compared to smooth implants that is mainly due to their low capsular contracture rates.²⁶ Occurrence of capsular contracture can be lowered by placing the implant behind the muscle.²⁵ Concern has been raised for development of breast implant associated anaplastic large cell lymphoma (BIA-ALCL). The incidence of its occurrence is very low i.e. 0.1 to 0.3 per 100000 implantsbased breast surgery. Development of ALCL is more feared to develop with use of macro-textured implants.²⁸ Local inflammation due to texture of implant, silicon leak or formation of biofilm predispose patients to this condition.²⁹ In breast reconstruction, anatomical shaped implants are more preferred by surgeons as compared to round nonanatomical implants due to a better match for postmastectomy breast footprint. Furthermore, anatomical implants have better upper pole fullness and shape. Placement of shaped implants is technically demanding because it needs accurate pocket creation to prevent implant migration or rotation. Patients have reported firmer feel in comparison to round silicon-based implants.30

Recently, use of acellular dermal matrix (ADM) is advocated in prosthetic breast reconstruction as it is claimed to provide support to both soft tissues as well as implant by better utilization and definition of mastectomy pocket. ADM gives good definition to lateral breast border and inframammary fold, prevents implant rotation or migration and also improves projection of lower pole.³¹ Rate of capsular contracture has seen to decrease to 0 to 4% with use of ADM as compared to previously reported rate of 10 to 30%.^{31,32} However, high incidence of complications have been reported with the use of ADM including seroma formation, infection, mastectomy flap necrosis and failure of prosthetic reconstruction.^{33,34} It is generally accepted that the benefits of ADM use out-weigh its possible disadvantages.

Other than breast footprint, soft tissue availability and type of implant, breast volume estimation is important in implant selection. Currently, work is being done on accurate volumetric measurement for breast implant selection preoperatively. None of the described methods has been universally acknowledged. Further studies are required to achieve global acceptance. Furthermore, accurate volumetric assessment does not obviate the need of symmetry procedure on the contralateral breast but may prevent gross asymmetry and help achieve good aesthetic results after symmetrizing procedures like fat grafting, mastopexy, reduction or augmentation mammoplasty.

Declaration of Interest: No conflict of interests. Submission Declaration and Verification:

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All types of research studies and clinical trials involving human participants should be preferably registered prior to submission, and proof of registration must be provided. Unregistered trials and studies may not be published.

Role of Funding Source

The funding source must be disclosed along with their degree of involvement with the research matter, if any, in the design, collection, analysis or interpretation of data; in the writing of the article, or in the decision to submit the article for publication. If the funding source had no involvement, then this should be stated. Any authors found guilty of scientific misconduct will be blacklisted from future publications.

4. PREPARATION

Reviewing Process

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

Reporting Guidelines

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

- Submit a completed checklist, indicating the page numbers where compliance to the guidelines was ensured.
- Mention in the 'Methods' section that the research is being reported in line with the relevant guideline, which should be named and cited.

Randomized Controlled Trials

All randomized controlled trials submitted for publication in Archives of Surgical Research must include a completed

Consolidated Standards of Reporting Trials (CONSORT) flow-chart and ensure that all features of the CONSORT checklist are present. A copy of the CONSORT checklist must be uploaded in supplemental material. Refer to the CONSORT statement website here.

Systematic Reviews

Systematic reviews are to be reported in accordance to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Guidelines and must include the flow-chart as a figure and the checklist as a supplemental material. Please download a PRISMA Flowchart and a PRISMA Checklist here. To aid and improve the methodological quality of your article, include an AMSTAR 2 checklist as well, which is available here.

Cohort, Case-control and Cross-sectional studies

Cohort, Case-control and Cross-sectional studies must be compliant with the STROCSS criteria (Strengthening the reporting of cohort studies in surgery), which is available here. Cite the following paper: Agha RA, Abdall-Razak A, Crossley E, Dowlut N, losifidis C, Mathew G, for the STROCSS Group. STROCSS 2019 Guideline: Strengthening The Reporting Of Cohort Studies in Surgery. Each study type has its own checklist which must be uploaded as supplemental material.

Diagnostic, Quality Improvement and Qualitative studies

Diagnostic studies should be reported according to the STARD statement criteria (Standards for the Reporting of Diagnostic Accuracy studies). The flow-chart should be a figure and checklist should be uploaded as supplementary material. Quality Improvement studies must comply with the Standards for Quality Improvement Reporting Excellence (SQUIRE) criteria, which is available here. Qualitative studies require the Consolidated criteria for Reporting Qualitative Research (COREQ) checklist, available here.

Health Economic Evaluation

Health Economic Evaluation studies should conform to the CHEERS statement, available here.

Tumour Marker Prognostic Study

Tumor Marker Prognostic studies should be reported according to the REMARK criteria.

Before and After Studies

Before and After studies measure specific characteristics of a population or group of individuals after an event or intervention, compare them with those characteristics before the event or intervention, then measure the effects of the event or intervention. These studies should conform to the STROCSS statement.

Experimental Animal Studies

Animal studies must be reported according to the ARRIVE guidelines (Animals in Research: Reporting In Vivo Experiments) and must include the checklist as supplemental material. An example of a completed checklist can be found here. The institutional protocol number must be included at the end of the abstract.

Qualitative Surveys

Qualitative Surveys should be reported according to the criteria detailed in the <u>SRQR Guidelines</u>. Guidelines for synthesis of qualitative research can be found <u>here</u>. Guidelines for interviews and focus groups are available <u>here</u>.

Case Series

Ensure that the case series is compliant with the PROCESS Guidelines and submit a completed PROCESS checklist. State that the work has been reported in line with the PROCESS criteria and cite the following paper: Riaz A. Agha, Mimi R.Borrelli, Reem Farwana, Kiron Koshy, Alex Fowler, Dennis P. Orgill, for the PROCESS Group. The PROCESS 2018 Statement: Updating Consensus Preferred Reporting Of CasE Series in Surgery (PROCESS) Guidelines.

Article Structure

Title Page

The title page should give the title in capital letters and a shorter running title. Avoid abbreviations and formulae if possible. In addition, the title page should also include:

- Correctly spelled names of all authors, and their affiliation addresses where the actual work was done. Include the e-mail address of each author.
- Signpost clearly the correspondence author who will maintain contact at all steps of reviewing and publication, and post-publication, and answer any questions about the research. All information must be updated in case of any changes.
- Present/permanent address of every author.
- The source of funding of the research.
- The number of figures and tables, the total word count and the total number of pages of the manuscript.
- A sample Title Page has been uploaded on this page above.

Abstract

All original articles must accompany a structured abstract of up to 250-350 words. It should state aims of the study, methodology and materials used, results obtained, and conclusions reached. Specify how the sample selection of study subjects or experimental animals was carried out, specify the observational and analytical methods, and give specific data and its statistical significance, where possible. Highlight novel and significant aspects of the study. Avoid references, but if necessary, cite the author(s) and year(s). Avoid non-standard or uncommon abbreviations, but if necessary they must be defined at their first mention in the abstract. This page should constitute of the abstract and keywords only.

Keywords

Right after the abstract, provide a maximum of 6 keywords, using British spelling. Avoid general and plural terms and

multiple concepts (avoid, for example, 'and', 'of'). Only abbreviations firmly established in the field may be appropriate. These keywords will be used to aid the indexing process of the journal.

Introduction

Outline the aims of the work and provide sufficient background information, avoiding a lengthy literature review or a summary of the results.

Methodology

Provide adequate details to allow the research to be reproduced by an independent researcher. If experimental apparatus is used, the manufacturer's name and address should be included in parentheses. Methods that have previously been published should be summarized, and signposted by a reference. If quoting directly from a previously published method, use quotation marks and cite the source. Any alterations to existing methods should also be described. If a drug is used, its common name, dose and route of administration must be included. For patients, age and sex with mean age ± standard deviation must be given where relevant to the data. Statistical methods employed for comparisons of data sets must be mentioned and any computer programs used for calculations must be specified.

Results

Results should be clear and succinct. They must be presented in the form of text, tables and illustrations. The content of the tables should not be repeated in the text; the tables should be numbered and identified and referenced to as their number. A conclusion that either supports or negates the hypothesis should be included. If the data is inconclusive, that should also be noted.

Discussions

This should emphasize present findings of the research, and the differences and similarities with prior work done in the field by other researchers. Data must not be repeated in the discussion, and lengthy citations and reviews must be avoided. Highlight the original and central aspects of the study and the conclusions that they lead to.

References

Please make sure that Mendley or some other software is used for referencing. The articles without compliance in this area would be sent back. American Medical Association (AMA Referencing Style) should be used. References should be typed in sequential numbers in superscript for intext citations, and numbered sequentially in the Reference List provided at the end. Maximum references for original article should not exceed 40; they should not exceed 10 for case reports, and 80 for reviews. Authors should ensure that locally published studies are given precedence. Add DOI number of documents where it is available.

References from books should include author, title, publisher, and year of publication. Example:

Das JC. Power System Harmonics and Passive Filter Designs. John Wiley & Sons, Inc; 2015.

For articles in journals, the authors, title of article, name of journal, year of publication, and an article identifier and page range (where available) must be included. See the following example:

Zhu Z, Hoffman JE. Condensed-matter physics: Catching relativistic electrons. *Nature*. 2014;513(7518):319-320.

Websites that are blogs and subject to changes by the author must be used as sparingly as possible, and when included, the author's name, the title, the name of website, date of publication, date on which the website was accessed, and a link to the website must all be included. Example:

Andrew E. After Years Of Conflict, Huge Project Could Help Scientists Decipher The Brain. IFLScience. Published June 18, 2015. Accessed October 30, 2018. https://www.iflscience.com/brain/after-years-conflict-huge-project-could-help-scientists-decipher-brain/

For government reports, technical reports, and scientific reports, if the report number is unavailable, then cite the report as a book. For reports it is usually not individual people that are credited as authors, but a governmental department or agency. Include the name of the agency, the title of the report, the publisher, and the year of publication. An example is as follows:

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

References to Ph.D. dissertations, Master's theses or Bachelor theses follow the format outlined below, and must include author, title, publication detail if applicable, and year of publication.

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

For newspaper articles, citation must include the author, title, name of newspaper, full date and page number. The example is as follows:

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.

Acknowledgements

All contributors who do not meet the criteria for authorship should be credited in this section. It should include persons who provided technical help, writing assistance and general support or supervision. Financial and material assistance must also be credited. Persons who have added to the material but do not justify authorship can be listed as "clinical investigators", "participating investigators", "scientific advisors", "reviewers', or "data collectors."

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.

Units, Abbreviations and Formulae

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

Artwork

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

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

Do not supply files that are optimized for screen use (e.g., GIF, BMP, PICT, WPG); these typically have a low number

of pixels and limited set of colors. Do not supply files that are too low in resolution. Ensure that each illustration has a separate caption that is not attached to the figure. A caption should comprise of a short title and a brief description of the illustration. Avoid text in the illustrations themselves but explain the symbols and abbreviations used.

Tables

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

Supplementary Material, Research Data, and Video

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

6. AFTER COMPLETION

Proofreading

Final version of the article is sent to corresponding author for proof reading before publication. In case of changes, corrections should be sent to the editor by email.

Processing & Publication Charges

This is open access journal and journal charges Article Processing Charges (APC) of Rs 5000/- for local manuscripts and \$US 100 for foreign manuscripts. Article Processing Charges are deposited at the time of submission and are non-refundable. Moreover, please also note that once accepted minimum publication charges for articles, manuscripts are Rs.4,000/- per page (in case of overseas US\$ 50/- per page; Overseas US\$ 50/- per page). Charges for photograph, films and illustrations are additional. Publication charges are payable in advance once the manuscript has been accepted for publication.

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.

Above-mentioned charges have been waived till further notice. A small amount may be charged at the time publication during this interim period.

Waiver Request

Those who cannot pay for processing and publication can apply for waiver at the time of the submission of their article.

Ethics Committee Approval

All manuscripts involving human subjects must be accompanied with certificate of approval by the relevant institutional review body or ethics committee.

Informed Consent

While the actual signed consent forms need not be sent to the journal, all manuscripts reporting the results of experiments involving human subjects should include a statement confirming that informed consent was obtained from each subject or subject's guardian, after the experimental protocol is approved by relevant institutional body or ethics committee.

Letter of Undertaking

Manuscripts must be accompanied by letter of undertaking signed by all the authors

Printed Copy

One printed copy will be sent to the correspondence author. Authors can order additional copies at the rate of *cost*. Payment for additional copies should be sent in with the publication charges.

Submission

All manuscripts must be Word documents.

Ombudsperson

The journal's managing Editor can be contacted by authors and other personnel in case any grievances should arise by e-mail.

7. PRIVACY POLICY

Archives of Surgical Research is committed to the protection of your personal information. The privacy policy outlined here applies only to information collected by Archives of Surgical Research through the http://www.archivessr.com/.

Information We Collect

We will request personal data from you to ascertain your individual user profile that may support all online activities allotted as an author, editorial member, or other connected role. Data like your name, postal address, e-mail address, telephone number and geographic locale are used as identifiers to permit access to certain content or to a secure

website. All personal information is treated by Archives of Surgical Research as strictly personal and confidential. Archives of Surgical Research won't disclose any personal information to third parties without your permission, unless required by law

Cookies

Cookies and log files are automatically recorded when you visit our site. These data includes some of the following information: IP address, host name, domain name, browser version and platform, date and time of requests, and downloaded or viewed files. This information is used to measure and analyze traffic and usage of the www.archivessr.com website and our digital products.

Making Changes to Your Information

When you have created an account on the http://archivessr.com, you can update your private information at any time through your account settings.

This statement may be periodically updated.

If you are concerned about how your information is stored, please contact us by email at editor@archivessr.com

8. PUBLISHING ETHICS

Archives of Surgical Research follows the <u>COPE Core Practices</u> and <u>ICMJE's Recommendations to conduct, report, edit and publish Scholarly Work in Medical Journals</u>, and expected an ethical behavior from authors, reviewers and editors to follow guidelines. We also follow the <u>Principles of Transparency</u> circulated through WAME.

Allegations of Misconduct

Archives of Surgical Research (ASR) defines research & publication misconduct as follows:

- Plagiarism: the practice of taking someone else's work or ideas and passing them off as one's own.
- Citation manipulation: a problem when references do not contribute to the scholarly content of the article, and are included solely to increase citations.
- Data falsification/fabrication : intentional misrepresentation of research results
- Conflict of interest: a conflict of interest exists when a manuscript's or journal's author, editor, reviewer have a financial or personal relationship that may influence their intentions or bias.
- Redundant publication: when a published work (or substantial sections from a published work) is/are published more than once (in the same or another language) without adequate acknowledgment of the source/cross-referencing/justification (https://publicationethics.org/category/keywords/redundant-publication)

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

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

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

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

In case of suspected data falsification/fabrication, respective authors will be asked to clarify and explain their methods. Failure to do so will 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

This is in accordance with **COPE** guidelines.

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

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

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

Disclosures

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

Authorship

Archives of Surgical Research (ASR) follows the <u>COPE flowchart to recognize potential authorship problems</u>. Ghost, guest, and gifted authorship will result in rejection of submitted manuscript, in accordance with <u>COPE guidelines</u>.

ASR implements <u>ICJME recommendations</u> for what constitutes authorship of a manuscript.

If a contributor does not fulfill the authorship criteria, ASR encourages listing them in the acknowledgements section. **All** authors are required to submit a Disclosure of Interest form, which can be found here: http://www.icmje.org/disclosure-of-interest/. In addition to submitting a disclosure of interest form, the manuscript must outline the specific contribution of each author. ASR Authors are also encouraged to link their ORCiD profiles.

Authorship disputes should be brought to light via email to relevant editors. They are handled through COPE Guidelines.

ICMIE Authorship Criteria

As per ICMJE guidelines the authorship should be based on the following criteria:

- Substantial contributions to conception & design, or acquisition of data, or analysis & interpretation of data.
- We do not allow ghost, guest and gift authorships and if found so we follow COPE guidelines to handle such
- Drafting the article or revising it critically for important intellectual content.
- Final approval of the version to be published. All those who meet the above three conditions are eligible to be included as Authors in the manuscript
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- 6. When a large multicenter group has conducted the work, the group should identify the individuals who accept direct responsibility for the manuscript. These individuals should fully meet the criteria for authorship defined above. Acquisition of funding, collection of data, general supervision of the research group does not qualify any one to be an author. All contributors who do not meet the criteria for authorship should be listed in the acknowledgment section. Those who provide technical support, writing assistance, or department chair who provided just general support should also be mentioned in acknowledgment. It is also important that all those whose names appear in acknowledgement must have given permission to be acknowledged.

ICMJE http://www.icmje.org

Complaints and Appeals

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

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

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

Data and reproducibility

Archives of Surgical Research (ASR) follows <u>ICMJE data sharing guidelines</u>.

In case of suspected data falsification/fabrication, respective authors will be asked to clarify and explain their methods.

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

This is in accordance with **COPE** guidelines.

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

Ethical Oversight

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

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

Post-publication Review and Audit

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

Conflict of Interest Policy

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

Articles would be published with statements or supporting documents declaring:

Authors' conflicts of interest

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

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

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

9. EDITORIAL POLICIES

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

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

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

10. PEER REVIEW POLICY

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

Initial manuscript evaluation

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

Type of Peer Review

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

How the Referee is selected

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

Referee Reports

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

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

How long does the review process take?

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

Final Report

A final decision to accept or reject the manuscript will be sent to the author along with any recommendations made

by the referees, and may include verbatim comments by the referees

Editor's Decision is Final

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

Conflict of Interest

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

Editorial and Peer Review Processes Generally Follow these Steps:

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

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

11. STATEMENT OF INFORMED CONSENT

We follow ICMJE and <u>COPE Guidelines</u> for appropriate consenting. Patient's privacy should not be breached without taking consent. In written descriptions there should not be any specifications regarding patients including names, hospital numbers, photographs or pedigrees unless the information is needed for scientific purposes and the patient

allows for publication with written informed consent. It should be disclosed by authors to the patients that any identifiable material could be available on the Internet or in printed form after publication. Patient consent ought to be written and archived with the journal, the authors, or both, as settled by local rules and regulations. Applicable laws vary from territory to territory, and journals should make their own policies with legal guidance. Since a journal that archives the consent will be aware of patient identity, some journals may decide that patient confidentiality is better guarded by having the author archive the consent and instead providing the journal with a written statement that attests that they have received and archived written patient consent.

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

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

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

12. GUIDELINE FOR REVIEWERS

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

Archives of Surgical Research follows <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 COPE Guidelines to manage the top hierarchy in terms of conflicts of interest and ethical considerations. We also following COPE Guidelines for maintaining relationship of journal management to the Pakistan Endocrine & Thyroid Surgeons Association to

ensure editorial independence. The journal editorial teams meets periodically at least biannually. The editorial team is independent of the society and is managed by a transparent process two yearly as per the ethical confines suggested by COPE, ICMJE and local guidelines.

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