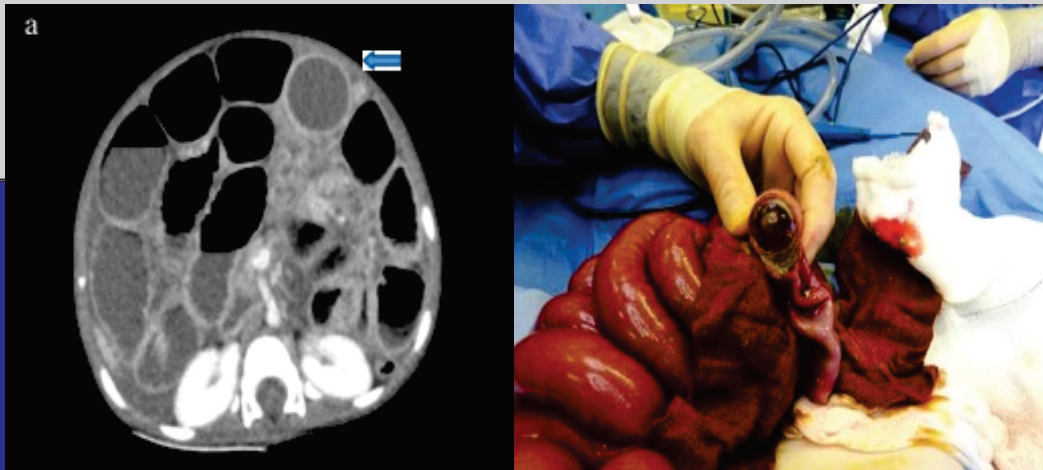




# THE SRI LANKA JOURNAL OF SURGERY

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## In this issue

- Epidemiology and care of surgical cancers in Sri Lanka
- Colorectal cancer care and homegrown data
- Neurovascular structures related to the submandibular gland
- Ureteral stent placement and post-ureteroscopy complications
- Identification of facial nerve in parotid gland dissection

**The College of Surgeons of Sri Lanka**

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**Contents**

Scientific Articles	Pages
<b>Epidemiology and care of surgical cancers in Sri Lanka</b> U. Jayarajah	01-06
<b>Quality improvement in colorectal cancer care; marching towards homegrown data</b> C. Chandrasinghe	7-14
<b>Surgically important neurovascular structures related to the submandibular gland.</b> V. Abeysuriya, C. Gunathilaka	15-18
<b>The effect of routine ureteral stent placement on post-ureteroscopy complications: A prospective study from a resource limited setting.</b> B. Balasingam, R. Sripandurangana, M. Sivashankar, S. Varothayan, K. Dinoshiga, K. Heerthikan, K. Priyatharsan, T. Vaishnavi, G. M. Suresh k	19-23
<b>Usefulness of simultaneous use of anatomical landmarks in identification of facial nerve in parotid gland dissection.</b> V. Abeysuriya, H. Modaragama	24-27
<b>Anatomical relations of the recurrent laryngeal nerve in thyroid dissection.</b> V. Abeysuriya, S.A.P.D. Anjula	28-31
<b>Review Articles</b>	
<b>Conquering immunological barrier in kidney transplantation: ABO incompatible transplantation</b> D. U. S. Ratnapala , P. Phelan	31-36
<b>Understanding HLA, non HLA, DSA and PRA: Transplant essentials</b> D. U. S. Ratnapala , P. Phelan , D. Tunrner	37-42
<b>The lateral stability of the knee, A review of the clinical Anatomy of the Popliteal hiatus and its clinical pathologies</b> C. Karunathilaka	43-50
<b>Radiological investigations in nephrolithiasis and: a narrative review</b> S. Siriwardana, V. Abeysuriya	51-57



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## Contents

Perspectives	Pages
<b>We report you decide</b> R. C. Siriwardana	58-59
<b>Case Reports</b>	
<b>Leiomyosarcoma of the Inferior Vena Cava and its tributaries, a case series and review of the literature</b> J. Arudchelvam , A. A. Pathirana, M. Nandasena, H. Udayakumara, A. S. K. Banagala	60-63
<b>Recurrent Ureteric Obstruction due to an intraluminal hematoma following live donor renal transplant</b> V. R. Gunasena, A. Weerasuriya, S. Godahewa	64-66
<b>Acute abdominal distension in an one year old due to ingestion of unknown foreign body</b> M. Ranjithatharsini, O. Jackson	67-69
<b>A case of Castlemans disease presenting as left axillary tumor</b> S.Sivakumar , V. Rangarajan, M. Manikesi, A. Akeel , S. G. Krishnan	70-72
<b>Spontaneous cholecystocutaneous fistula: a rare complication of gallbladder disease</b> A.R.M. Isthiyak, A.S.K. Banagala	73-75

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## Epidemiology and care of surgical cancers in Sri Lanka.

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**Keywords:** Cancer, Cancer care

### Introduction

Rising burden of cancer is a major challenge in the developing world. Cancer burden is estimated mainly by the incidence of cancer within a defined population while considering economic, social and emotional impact it causes. In Sri Lanka, the newly diagnosed cancer cases has increased by two fold over the last 3 decades with a concomitant rise in deaths related to cancer. Breast cancer is the commonest cancer in Sri Lanka. Other commonly prevalent cancers such as oropharyngeal, laryngeal, lung, oesophageal, gastric and colorectal malignancies also demonstrate a rising trend in incidence.

Due to the effective public health network and universal health care across the country, Sri Lanka is known for its commendable achievements in health outcomes compared to other neighbouring low middle income countries. While this success is laudable, Sri Lanka should enhance the existing health resources to cater the cancer epidemiological transitions. Quantification of the trends of the incidence of cancers is essential for the policy makers for the distribution of resources. Therefore, this oration is aimed to describe the trends and patterns of the incidence of common surgical cancers in Sri Lanka supported by additional data from cohort studies regarding the clinical patterns and outcomes.

### Methods

The analysis was conducted among selected common surgical cancers in Sri Lanka with high incidence. Specifically, cancers of the breast, thyroid, oropharynx, gastrointestinal tract (oesophagus, stomach and colorectum), hepatopancreaticobiliary system (liver, pancreas and biliary), urological system (prostate, bladder and kidney) were analysed. Details of specific cancers between 2001-2019 were extracted from the Sri Lanka Cancer Registry. The specific ICD-10 coding system was used to define the

anatomical regions of cancer. The data on age, sex and histology type were analysed and WHO age standardized rates of specific cancers per 100,000 population were calculated for each year by sex, using the WHO age standardized populations.

The trends and patterns in the incidence of specific cancers were analysed and quantified by Joinpoint regression software version 4.3 which discerns points where a statistically significant change in the trend has occurred. The estimated annual percentage change (EAPC) was quantified for each curves.

Additional findings from cohort studies including individual cancer patients from National Hospital of Sri Lanka (bladder cancer) and Apeksha Hospital (National Cancer Institute) (breast and colorectal cancers) was used to back arguments and support recommendations. Ethical clearance was obtained from the Ethics Review Committee of the Faculty of Medicine, University of Colombo and the relevant institutions.

### Results

Incidence and trends of common surgical cancers in Sri Lanka

#### Breast cancer

Out of 53000 patients with newly diagnosed primary invasive

**Table 1:** Incidence and trends of common surgical cancers in Sri Lanka (\* implies  $p < 0.05$ )

Cancer type	Incidence 2019	EAPC (Male/Female)	Average age male	Average age female	Highest incidence (Male/ Female)
Breast	19.8	4.7* (2.7*/6.9*)	59	54.5	75+/60-64
Thyroid	11.7	6.5* (10.7*/4.5*)	47	43	35-39
Oral	12.2	4.3* (6.7*/2.3)	62.6	60.4	70-74
Pharyngeal	3.5	8.4* (9.7*/2.4)	60.3	59.2	70-74
Oesophagus	8.5	1.5* (4.6*/1.9)	62.2	63.5	70-74
Gastric	2.9	8.3* (8.2*/9.9*)	60.9	60.5	70-74
Colorectal	11.2	9.1* (8.5*/10*)	60.7	59.6	70-74
Liver	2.4	7.6* (8.0*/7.4*)	61.4	56.7	70-74
Biliary	1.1	6.5* (7.5*/5.8*)	59.9	59.8	70-74
Pancreas	1.0	5.3* (5.2*/5.6*)	58.6	57.1	70-74
Bladder	3.0	12.1* (13.5*/11.5*)	64.6	63.0	70-74
Kidney	2.8	8.1* (8.4*/11.7*)	55.1	49.4	70-74
Prostate	10.8	11.4*	69.3	-	75+

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breast cancer, around 97.2% were females. The WHO age standardized incidence in Sri Lanka has increased from 9.2 to 19.8 per 100,000 from 2001-2019 with an estimated annual percentage change (EAPC) of 4.7 ( $p < 0.05$ ).

Analysis of data from 2001-2010 showed only a modest rise in incidence among the younger (< 50 years) women with breast cancer (EAPC=2.3), while the rise was considerable among older women (50 years and older) (EAPC=5.5). However, analysis up to 2019 revealed that the incidence among younger women is also increasing at a greater rate (EAPC=3.0 compared with 4.7 among older women).

#### *Analysis from a cohort study*

Analysis of 5181 women with newly diagnosed breast cancer with a mean age of 56 years from Apeksha Hospital, Maharagama was conducted during the 5-year period from 2016 to 2020. Around two thirds of the breast cancers were diagnosed at an early stage (stage I & II). The ER / PR and HER-2 positivity rates were 72% and 22% respectively. Two thirds underwent mastectomy. Around 90% of females with node positive disease received chemotherapy while 77% of those indicated had received adjuvant radiotherapy. The rate of endocrine therapy was 88% among the eligible, while the rate of administration of trastuzumab was around 60% among eligible patients with HER2 positivity.

#### *Thyroid cancer*

Analysis of 25571 thyroid cancers over the 19-year study period (2001-2019) showed that majority were females (81%). The WHO age standardized incidence of thyroid cancer in Sri Lanka surged significantly from 2.44 to 11.7 per 100,000 from 2001-2019 ( $p < 0.05$  for trend). Although the increase was gradual over 2001-2012, thereafter it was variable with an overall increasing trend. The EAPC during the rise was 6.5 (95% CI 4-9.1).

#### *Oropharyngeal cancers*

##### *Oral cancer*

Over the 19-year study period, a total of 36,880 oral cancers were recorded. There were 77.8% males diagnosed (male: female = 3.5:1). The WHO age standardized incidence of oral cancer increased from 7.5 to 12.2 per 100,000 from 2001-2019 ( $p < 0.05$  for trend), with an EAPC of 4.3 (95% CI 3.5-5.1). Oral cancer in males showed an initial non-significant decreasing trend till 2003 and a significant increasing trend up to 2016 (EAPC: 6.7) followed by another non-significant decreasing trend.

##### *Pharyngeal cancer*

In the 19-year study period, 11,451 patients were diagnosed.

There were 82.7% males (male: female ratio = 4.8:1). The WHO age standardized incidence increased significantly from 1.98 to 4.43 per 100,000 from 2001-2016 followed by a decreasing trend (3.5 per 100,000 in 2019). Males had a greater proportional increase in incidence.

#### *Common cancers of the gastrointestinal tract*

##### *Oesophageal cancer*

From 2001-2019, 26 459 oesophageal cancers were diagnosed with a male predominance of 53%. The WHO age standardized incidence of oesophageal cancer has risen significantly from 5.78 to 8.46 per 100,000 from 2001 to 2019. This increase was prominent till 2016 and thereafter, showed a decreasing trend till 2019. During the rising period, the EAPC was 1.5. The magnitude of the rise in incidence was considerably higher for males.

##### *Gastric cancer*

From 2001-2019, 7914 gastric cancers were diagnosed with a male preponderance of 71%.

The WHO age standardized incidence of gastric cancer in Sri Lanka has increased from 1.06 to 3.3 per 100,000 from 2001-2016, followed by a decreasing trend to 2.9 per 100,000 in 2019. Females showed a higher proportional increase in incidence (EAPC of 9.9 vs. 8.2).

##### *Colorectal cancer*

A total of 26 316 colorectal cancer (CRC) were diagnosed over the 19-year study period with an equal gender distribution (male: female: 1). The rectum was the commonest anatomical location (51.1%) and other common locations were sigmoid colon (12.1%) and recto sigmoid junction (4.8%). The WHO age standardized incidence of CRC was observed from 2.9 to 11.9 per 100,000 in from 2001-2017 ( $p < 0.05$  for trend) followed by a decreasing trend to 11.2 per 100,000 in 2019 with an EAPC of 9.1 for the rising trend.

#### *Analysis from a cohort study*

Analysis of 1578 colorectal cancer patients (colon: 53% (n = 830) and rectum: 47% (n = 748) aged over 18 years (mean age: 61 years) was conducted at the Apeksha Hospital Maharagama from 2016-2020. Stage I, II, III and IV was observed among 13%, 28%, 46%, and 12% respectively. Adjuvant chemotherapy was administered to 82% of stage III colon cancer patients. Neoadjuvant chemoradiotherapy was delivered to only around 50% of patients with stage III rectal cancer.

#### *Common cancers of the hepatopancreatobiliary system*

##### *Liver cancer*

From 2001-2019, 5019 primary liver cancers were diagnosed with a male predominance of 72.7%. The WHO age standardised incidence rates of liver cancer has risen from 0.6 to 2.44 per 100,000 from 2001-2019 ( $p < 0.05$  for trend), with an EAPC of 7.6.

#### *Pancreatic cancer*

Analysis over the 19-year period included 2331 pancreatic cancers with a male predominance (52.8%). From 2001-2019, the WHO age standardized incidence rates rose from 0.44 to 0.97 per 100 000 from 2001-2019 with an EAPC of 5.3. Females showed a higher proportional rise than males (EAPC: 5.6 vs. 5.2).

#### *Biliary cancers*

Analysis was performed from 2006-2019. During the 14-year study period, 2144 biliary tract cancers were diagnosed with a female preponderance of 54.5%. The incidence of biliary cancer has risen from 0.53 to 1.06 per 100,000 from 2006-2019 ( $p < 0.05$  for trend), with an EAPC of 6.5. The steady increase in incidence was observed among both genders with a higher EAPC among males (7.5 vs. 5.8).

#### *Common cancers of the urological system*

##### *Bladder cancer*

A total of 7,349 newly diagnosed bladder cancers were documented (males = 80.9%, male: female = 4.24: 1) from 2001-2019. The Joinpoint analysis showed that the incidence of bladder malignancies has surged from 0.88 to 3.9 per 100,000 population from 2001 to 2017; with an EAPC of 12.1 ( $p < 0.05$  for trend) with a subsequent decline in incidence (2.97 per 100,000 in 2019).

##### *Analysis from a cohort study*

A retrospective analysis of 314 newly diagnosed primary bladder malignancies (mean age = 65.4; males=245, 84.8%) from 2007-2017 at a Urology Unit and National Hospital of Sri Lanka was performed. Of the 289 (92%) urothelial cancers, around 64% had non-muscle invasive cancers (pTa: 30.1%; pT1: 34.3%) and the rest (36%) were muscle invasive. The majority were high grade tumours (n=156, 54%). Around 17.5% had pT1 high grade (pT1-HG) tumours. Of the 55(17.5%) women with bladder cancer, 80% had urothelial cancers. Women had a disproportionately higher proportion of non-urothelial cancers (20% vs. 5.4%,  $p < 0.001$ ) and muscle invasiveness (45.5% vs. 33.5% (82/245) than in men.

##### *Prostate cancer*

Analysis was performed from 2006 to 2019. A total of 9695

prostate cancers were diagnosed over the 14-year study period. The WHO age standardized incidence observed for prostate cancer has been increasing from 2006 to 2016 from 4.4 to 12.3 per 100,000 population with an EAPC of 11.4 ( $p < 0.05$ ). Thereafter, the rate was static till 2019 to 10.8 per 100,000 with an EAPC of -1 ( $p > 0.05$ ).

##### *Renal cancer*

Analysis was performed from 2006-2019. During the 14-year study period, 3833 renal cancers were diagnosed with a male preponderance of 70.4%. The incidence of renal cancer in Sri Lanka has increased from 0.8 to 2.8 per 100,000 from 2006-2019 ( $p < 0.05$  for trend), with an EAPC of 8.1. The steady increase in incidence was observed among males (EAPC: 8.1), whereas females showed a varying trend.

## **Discussion**

### *Summary of findings*

Analysis of data from 2001-2019, revealed a steadily rising trend in the incidence among breast, liver, biliary, oral and renal cancers and variable trends in other cancers. These trends are likely due to the combination of better reporting and diagnosis and true increase in incidence. Analysis of a cohort of breast, colon and bladder cancer patients showed that the diagnosis of malignancy was at a more advanced stage. Furthermore, the concordance with the treatment guidelines was suboptimal.

### *Primary prevention for common surgical cancers*

Tobacco use, chewing of betel quid, alcohol and obesity as a result of unhealthy diet and physical inactivity are some of the major preventable causes. It is commendable that tobacco smoking in public places and advertisements were banned. However, smokeless tobacco and betel chewing is a major predisposing factor for oropharyngeal and upper gastrointestinal cancers in Sri Lanka and there are cultural barriers in banning it completely. Measures should be taken to ban smokeless tobacco to prevent upper aerodigestive cancers.

Minimising exposure to carcinogens is given priority in prevention. However, much greater importance is essential to manage metabolic risk factors that include dietary factors, physical inactivity and obesity. Encouraging a healthy life style by mass education using various media is therefore imperative.

### *Screening*

The NCCP delivers screening programmes for selected malignancies such as breast and oral cancers. Sri Lanka lacks

enough mammography machines to offer nationwide community based mammographic screening for breast cancer. Although clinical breast examination is readily offered in well-women clinics, such facilities are underutilised. Based on age distribution of incidence, women over 40 years may be advised to undergo at least a clinical screening for breast cancer annually.

Similarly, community based screening centres for oropharyngeal cancers are conducted islandwide. However, the compliance and adherence to screening seems suboptimal. Screening should be offered to older individuals with exposure to carcinogenic risk factors including areas where smokeless tobacco consumption is prevalent.

Establishment of endoscopic screening has been established in high-income countries with a high prevalence of cancers of the upper and lower gastrointestinal tract. Currently, similar screening programmes are not established in Sri Lanka due to resource constraints. Owing to rising incidence of colorectal oesophageal and gastric cancers, opportunistic screening via endoscopy/ faecal testing should be offered to symptomatic individuals aged over 40 years based on the incidence patterns. As the majority of cancers are found in the left colon (approximately 70%), screening with sigmoidoscopy can be considered as an alternative for colonoscopy in the context of limited resources.

Prostate cancer showed a rising trend in the incidence and has become the fifth commonest cancer among Sri Lankan males. Although there is no established screening program, prostate specific antigen (PSA) based opportunistic screening should be encouraged among older men with lower urinary tract symptoms.

#### *Diagnosis and Treatment*

Although, facilities for medical oncology has been established in every district general hospital in Sri Lanka, there is a lack of radiation oncology facilities in the country. Restriction of radiation oncology facilities to a few hospitals leads to increased waiting time, and default rate. As most of above cancers need radiotherapy in the form of adjuvant or neoadjuvant therapy, increasing the radiation oncology facilities is an urgent need.

Cancer care with a multidisciplinary approach is less commonly practised in Sri Lanka. Currently, there are no dedicated breast and endocrine cancer centres despite these being the top two cancers in Sri Lanka. Currently, there are no centralised and dedicated cancer centres for hepatopancreaticobiliary and urological cancers which need

specialised expertise and resources. Thus establishing specialised dedicated centres with formal referral pathways is a timely need.

Due to the rising incidence, enhancing the resources for ancillary services such as minimally invasive radiology, immunohistochemistry and molecular diagnostics is an urgent need.

Most cancers in Sri Lanka are treated based on globally accepted guidelines formulated by developed nations. More evidence should be generated to enrich the local guidelines to suit the local setting. The cohort analyses of breast and colorectal cancers revealed considerable lapse in the concordance with the guidelines in terms of administration of neoadjuvant and adjuvant chemoradiotherapy. Establishing nationally accepted local guidelines may reduce such discrepancy.

#### *Cancer research and improvement of cancer registry*

In Sri Lanka, the National Cancer Registry is the most extensive database for cancer incidence. However, there are challenges of obtaining data related to mortality. Obtaining nationwide cancer mortality data will give important insight to mitigate the increasing burden of cancer in Sri Lanka.

It is documented that characteristics of cancers in this region of the world may be dissimilar to established literature from the developed world. Furthermore, the effects on quality of life and psychological impact are different due to the sociocultural variations. Thus original studies from Sri Lanka in these aspects are a timely necessity.

#### *Palliative care*

In Sri Lanka, palliative services are established only in selected tertiary care hospitals and community based palliative care is lacking. According to the analysis of incidence most patients with cancer are diagnosed at an age above 70 years. Such patients with comorbidities may not be suitable for major resections despite resectability and will need palliative care. With the increasing population of the elderly in Sri Lanka, the number of patients needing palliative care is expected to rise exponentially. Thus establishment of both tertiary care and community based palliative cancer services is an urgent need in Sri Lanka.

#### *Health literacy and public education of cancer*

Education of the public and health literacy is imperative for primary prevention, participation in screening and compliance to treatment. Credible information should be



provided by the experts without inducing unnecessary anxiety among the healthy public. In this era, the public seek information from the internet which may be of suboptimal quality and lack updated information. Furthermore, due to issues in readability, the information may be difficult to comprehend or may be misinterpreted. Publishing online information for common cancers is a welcome initiative by the NCCP. However, more focussed information on common malignancies compiled by local experts based local practices in relation to treatment will be useful.

### Limitations

The technological advancements over the years would have caused an increase in the diagnosis and data collection which might have contributed to reported increase of cancers. Incomplete and missing data was noted in the treatment modalities and adjuvant therapy among breast and colorectal cancer cohort and considerable lost to follow up among bladder cancers. However, such limitations would have negligible influence on the reporting of disease characteristics and staging which is more relevant to this analysis.

### Conclusions

An overall rising incidence of surgical cancers has been observed. These trends are likely due to the combination of better reporting and true increase in incidence. Regardless, more robust community based screening programmes for selected cancers should be considered. Expansion of the coverage of Sri Lanka Cancer Registry is needed in terms of cancer related mortality. With the rise in surgical cancers, more facilities for curative surgical services, radiation oncology and ancillary services are needed. Establishing nationally accepted local guidelines may reduce the discordance with guidelines however, further studies are needed to study other factors that may have led to this observation. A lack of tertiary care and community based palliative care facilities is a major concern in Sri Lanka and should be addressed urgently.

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## Quality improvement in colorectal cancer care; marching towards homegrown data.

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**Keywords:** colorectal cancer, South Asia, Sri Lanka, quality improvement, data collection, survival.

### Background

Colorectal cancer (CRC) is currently the 3rd commonest cancer and the 2nd commonest cause of cancer deaths globally (1). Low and middle-income earning countries have experienced a recent surge in the incidence of CRC while there is a drop in incidence in the west (2)(3)(4). Sri Lanka has seen a steady increase in the incidence of CRC over the last two decades and it is currently the 3rd commonest cancer amongst Sri Lankans of both sexes (5). Currently 1.9 million new CRCs are diagnosed annually worldwide which is expected to increase up to 3.2 million new cases and 1.6 million deaths per year (6). The management of CRC has evolved significantly during the last century from a disease with almost 100% mortality in the early 20th century to a disease treated with curative intent for stage IV in the 21st century.

There is ample data on survival predictors and surgical quality parameters in colorectal cancer that were generated in the western populations (7–9). The human developmental index, genetics, social and environmental factors play a significant role in survival and the quality of surgical care (10–13). Therefore, direct application of available evidence on local populations is debatable. Hence there is a need for locally adopted data. Data on survival from CRC in Sri Lanka is scarce owing to the absence of a national programme for prospective data collection (14). Several authors have highlighted the lack of survival data and the possible inaccuracies of the existing incidence data in the Sri Lankan cancer registry (15). (14)

The North Colombo CRC database was established in the year 1995. Prospective data collection was done on all patients undergoing curative resections for CRC. The prospective data collection was initiated with printed pro-

forma and has currently developed to a point of care real time data entry into a cloud based data storage using the RedCap platform.

This oration presents the attempts of the North Colombo University Unit to develop locally applicable evidence in the improvement of patient care. Whilst each of the studies is presented and analysed separately, the discussion will focus on the value of data from Sri Lankan patients, including the ability to compare our results with international studies and will focus on the value of scientifically informed adoption of clinical treatment pathways for CRC in Sri Lankan patients.

### Methodology

Data is extracted from the North Colombo CRC database, from patients who underwent surgery with curative intent for CRC. Preoperative work up and management was standardized by protocol described in detail elsewhere (16). Neoadjuvant chemoradiotherapy (NCRT) was adopted for rectal cancers from the early 2000s and principles of enhanced recovery have been gradually incorporated to be a standard protocol. The same team at the university units performed surgery and histopathological assessment of the specimens. All postoperative complications were recorded and updated up to 30 days and at subsequent clinic visits. Anastomotic leakage was diagnosed with clinical evidence of intra-abdominal sepsis and ultrasound or CT evidence of intra peritoneal fluid.

Post operative surveillance is carried out with clinical examination coupled with carcino-embryonic antigen (CEA) levels three monthly for the first 2 years and biannually for 3 years. A colonoscopy and computer tomographic evaluation of the abdomen and pelvis at 1, 3 and 5 years post operative is undertaken.

Four areas pertaining to CRC management were assessed throughout this period. Namely, development of a locally feasible prognostic marker, response of the local population to NCRT, optimal nodal harvest in the local population with a survival advantage and improvement in patient outcomes over time.

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The ethics review committee at the University of Kelaniya medical school, Sri Lanka, approved the data base maintenance.

In selecting a cut-off value for serum preoperative albumin and optimum nodal harvest, serial increments were used instead of arbitrary values. Serially ascending values of 5 g/L of serum albumin were compared to define a finite cut-off value while serially ascending values of lymph nodes starting from a minimum of 5 were used. (17,18). Survival analysis was performed using Kaplan Meier curves while Kaplan-Meier analysis and Cox proportional hazard model were used for univariable analysis of confounding factors. For the significant confounders identified in the cohort for serum albumin, a type III analysis with a Weibull hazard model and

**Table 1.** Survival comparison using Kaplan-Meier method for serially ascending serum albumin levels. Reproduced from Chandrasinghe et al. 2013 (17)

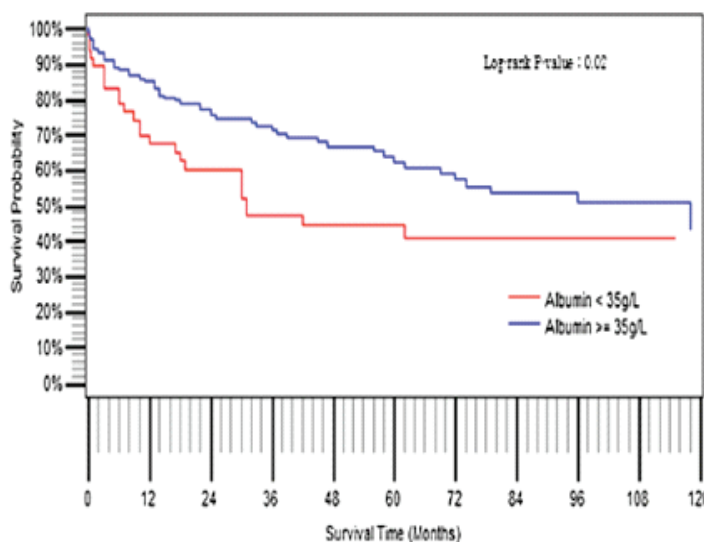
Serum albumin level	5 year survival rates	P value
<20 g/L VS. ≥20 g/L	90% VS. 60%	0.44
<25 g/L VS. ≥25 g/L	90% VS. 59%	0.10
<30 g/L VS. ≥30 g/L	43% VS. 63%	0.04*
<35 g/L VS. ≥35 g/L	49% VS. 69%	0.02*
<40 g/L VS. ≥40 g/L	58% VS. 62%	0.48
<45 g/L VS. ≥45 g/L	58% VS. 73%	0.17

\* - significant value.

two-way interaction terms were used for multifactorial analysis while Cox-proportional hazard model was used for the group for optimum nodal harvest. Patients with both stage II and III with a minimum of 3 year follow up were included in the lymph node harvest analysis to minimize biases.

Only patients with mid and lower rectal cancer receiving NCRT were analysed to assess tumour response and its implications for survival (16). NCRT regime comprised radiotherapy (5040 cGy) to the true pelvis, which was delivered in 25 fractions combined with cyclical 5-fluorouracil. Patients underwent low or extended low anterior resection with TME of rectal cancer, abdomino perineal excision (APR), transanal resection of residual tumour at a median of 10 weeks (range 8–11 weeks) post NCR. Tumour regression grading (TRG) was done as described by Mandard et al. TRG 1 was a complete response with the absence of residual cancer and fibrosis extending through the wall; TRG 2 was the presence of residual tumour cells scattered through the fibrosis; TRG 3 was an increase in the number of residual cancer cells compared with TRG 1, in which fibrosis was predominant; TRG 4 was residual cancer outgrowing fibrosis and TRG 5 was the absence of regressive changes. Degree of TRG was grouped into subgroups; good regression – TRG 1 + 2; moderate regression – TRG 3; no regression – TRG 4 + 5, for the ease of analysis.

For survival assessment across time periods, Kaplan-Meier survival curves were used to compare survival pre and post 2010. The year 2010 was considered as a half-way point for the survival analysis as the authors believe it is an appropriate time point to mark the improvement in technical and adjunct treatment in the management of CRC. Also this enabled sufficient patient numbers for comparison in each group with



**Figure 1.** Kaplan-Meier survival curves for rectal cancer based on serum albumin level. . Reproduced from Chandrasinghe et al. 2013 (17)



**Table 2.** Percentage of each category of regression grade in rectal cancers receiving NCRT. Reproduced from Deen et al. 2023 (16)

Regression grade	Percentage
TRG 1	43.1% (Good)
TRG 2	12.7% (Good)
TRG 3	22.6% (Moderate)
TRG 4+5	21.6% (Poor)

Good vs. Moderate vs. Poor - Chi-Square=2.58; DF=2; P=0.28

an adequate follow-up period to evaluate long-term survival.

## Results

### *Preoperative albumin as a prognostic marker*

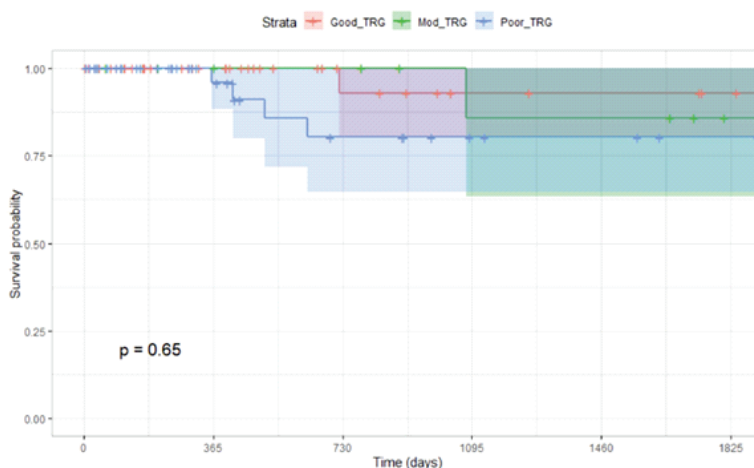
A total of 226 (male - 123 (54%) and female – 103) patients were studied (median age – 59 years; range 19-88, median follow up 36; range 10-160). 35 g/L was the cut-off serum albumin value at which most significant differences in survival emerged (Table 1). Forty-five patients (20%) of this cohort had hypoalbuminaemia (serum albumin < 3.5 g/L) according to this cutoff. Preoperative serum albumin of less than 35 g/L was associated with a significantly poor overall survivals following surgery for rectal cancer. (P=0.02; Figure 1).

Five-year overall survival rates between normo and hypoalbuminaemia groups were 69% versus 47%. The five-year disease free survival rate in the hypoalbuminaemia group was 69.7% compared to 83% in the normoalbuminaemia group (P = 0.02). Age, positive circumferential margin, perineural invasion, angio-invasion, lympho-vascular invasion, and advanced AJCC stage emerged as confounders in a univariable analysis while multi factorial model type III analysis of effects revealed that hypoalbuminaemia (P = 0.002), a positive circumferential margin (P = 0.002), and

AJCC stages III and IV compared with I and II (P = 0.003), were significant. Two-way interaction terms between the said factors using Weibull hazard model confirmed those factors to be independent risk factors for poor survival in rectal cancer.

Tumour response to neoadjuvant chemoradiotherapy and its effect on survival patterns in rectal cancer

Studying 153 patients with low or mid rectal cancer who received NCRT for locally advanced rectal carcinoma TRG 1 or TRG 2 was reported in 58.5% of the specimens. In total, 78.4% of patients showed tumour regression (TRG 1 - TRG 3) compared to 21.6% with either minimal or no tumour regression (TRG 4 + 5) (16). A median pathological tumour stage (T) of 2 was observed in good TRG, whereas poor TRG was associated with a median pathological T stage of 3 (Chi-square 16.6; DF = 2; P = 0.0002). Percentage response to NCRT was comparable between good (TRG 1 + 2), moderate (TRG 3) and poor (TRG 4 + 5) - (Chi-Square = 2.58; DF = 2; P = 0.28, Table 2). In all, 131 (79 male, 52 female; median age 57, interquartile range 47–62 years) patients who underwent low or ultra-low anterior resection of the rectum post-NCRT; 4 (3%) developed anastomotic leaks. Median follow-up at the time of analysis was 15 months (interquartile range 6–45 months).



**Figure 2.** Local recurrence free survival of rectal cancers based on tumour regression. Reproduced from Deen et al 2023 (16)

Local recurrence rate was 6.8% (9 of 131) and there was no significant difference in overall survival (Figure 2) or disease-free survival related to TRG. The 5-year disease-free survival rates for good, moderate and poor TRG did not differ significantly either (65%, 83% and 67% ; Chi-square = 0.01; DF = 2; P = 0.99).

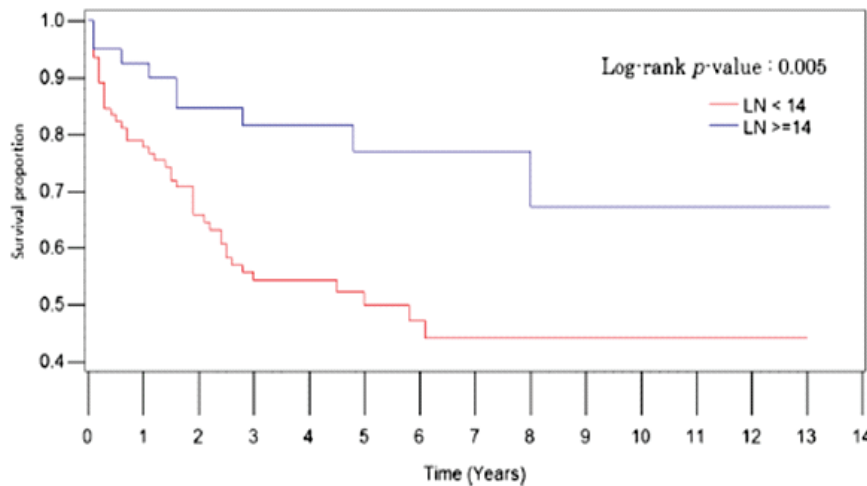
**Optimum lymph node harvest from colorectal cancer specimens based on survival advantage**

Out of a total of 131 patients ( male – 56%, colon-55, rectal – 76, mean follow-up - 4.1 years; SD- 3.4), 61 had stage II and 70 had stage III cancer. The most significant survival benefit was seen with 14 or more nodes for both colon and rectal cancers (Table 3). For the total population of stages II and III CRCs, the maximum survival benefit was observed with 14 or more nodes (Figure 3). When stages II and III cancers were

separately analysed, a similar observation was made (stage II, p= 0.07; stage III, p=0.03).

Lower risk of death (Hazard ratio - 0.37, 95 % CI, 0.18–0.77; p=0.007) was observed when more than 14 lymph nodes harvested. Advanced age, male sex, LVI, and preoperative CEA levels were the other significant factors associated with survival in an initial multivariable analysis. The lymph node yield remained significant with a hazard ratio of 0.19 (95 % CI, 0.066–0.593; p=0.004) after adjusting for the above mentioned factors using multiple regression analysis with stepwise selection

A significantly lower lymph node yield was observed in those who had NCRT (NCRT- 8; range, 5–20 vs. no-NCRT- 11; range, 5–45; p=0.0128) (Table 4). Analysing the patients



**Figure 3.** Kaplan-Meier curves for colorectal cancers based on lymph nodes harvested. Reproduced from Chandrasinghe et al 2014 (18)

**Table 3.** Overall survival comparison in colon and rectal cancers based on ascending numbers of lymph nodes harvested from specimens. Reproduced from Chandrasinghe et al 2014 (18)

Lymph node groups	Rectal cancer; mean survival (SE) in years	p-value	Colon cancer; mean survival (SE) in years	p-value
<6 vs. ≥6	4.0 (1.38) and 3.4 (0.28)	0.759	1.9 (0.35) and 6.5 (0.44)	0.356
<7 vs. ≥7	3.7 (0.77) and 3.4 (0.30)	0.729	1.4 (0.53) and 6.6 (0.44)	0.125
<8 vs. ≥8	3.2 (0.56) and 3.6 (0.32)	0.445	1.6 (0.33) and 6.5 (0.48)	0.580
<9 vs. ≥9	3.6 (0.48) and 3.5 (0.35)	0.988	1.6 (0.22) and 6.6 (0.47)	0.505
<10 vs. ≥10	3.4 (0.44) and 3.6 (0.37)	0.628	2.2 (0.27) and 6.9 (0.46)	0.103
<11 vs. ≥11	3.3 (0.40) and 3.8 (0.39)	0.295	2.3 (0.22) and 6.8 (0.51)	0.426
<12 vs. ≥12	3.1 (0.36) and 4.3 (0.43)	0.050	3.8 (0.43) and 7.2 (0.42)	0.091
<13 vs. ≥13	3.2 (0.35) and 3.7 (0.36)	0.033	4.0 (0.35) and 7.0 (0.60)	0.093
<14 vs. ≥14	3.2 (0.34) and 3.7 (0.38)	0.032	3.9 (0.33) and 7.5 (0.59)	0.085
<15 vs. ≥15	3.4 (0.32) and 3.6 (0.46)	0.230	3.9 (0.33) and 7.5 (0.59)	0.085
<16 vs. ≥16	3.5 (0.31) and 3.6 (0.52)	0.340	4.0 (0.31) and 7.4 (0.67)	0.128
<17 vs. ≥17	3.5 (0.32) and 3.5 (0.52)	0.340	4.1 (0.29) and 7.3 (0.85)	0.331
<18 vs. ≥18	3.6 (0.77) and 3.3 (0.30)	0.344	4.2 (0.26) and 6.9 (1.30)	0.856

receiving NCRT in the same patient population, the median number of lymph nodes harvested in patients with a good and moderate regression (TRG 1 + 2 + 3) was 6 compared to a median of 8 in the poor regression (TRG 4 + 5) group (16).

#### Change in survival patterns in patients with CRC over time

In the pre – 2010 time period, there were 276 (65%) rectal cancer and 149 (35%) colon cancer (right colon – 68, left colon – 81) compared with 165 (57%) rectal cancers and 124 (43%) colon cancer s(right colon – 49, left colon – 76) in the post-2010 group.

Post-2010 period demonstrated a significantly better overall survival compared to pre-2010 ( $X^2= 12.1$ ;  $DF=1$ ;  $P<0.001$ ). There is also a significantly better disease free survival (DFS) ( $X^2= 19$ ;  $DF=1$ ;  $P<0.0001$ ) and overall survival (OS) ( $X^2= 19.1$ ;  $DF=1$ ;  $P<0.001$ ) in patients with rectal cancer in the post 2010 period compared to pre-2010. Both DFS ( $X^2= 1.8$ ;  $DF=1$ ;  $P=0.2$ ) and OS ( $X^2= 0.1$ ;  $DF=1$ ;  $P=0.8$ ) were comparable for colon cancers in the two time periods (Table 5).

#### Discussion

CRC. This was the first study to report preoperative serum albumin level as a marker of long-term outcome in rectal cancer (19) and has been later supported by evidence from other investigators (20–22). Toyiyama and colleagues have shown that stage II CRC with a low albumin level or a higher CRP fared worse and suggest that stage II CRC with a low GPI to be considered for adjuvant chemotherapy despite of the TNM stage (23). The importance of albumin in the local setting is that it is easily accessible at an affordable cost. More complex inflammatory markers of prognosis may be available with the limitation of cost and accessibility in a resource poor setting.

Although NCRT for rectal cancers has a clear benefit in DFS the response of the tumors to such treatment varies depending on many factors. Pathologists have developed various grading systems to classify the tumour response (24) and there is conflicting data on the variability of long-term

outcome for different regression grades (25–27). The pattern of TRG has not been published previously for a Sri Lankan population and is important as a country with limited access to radiation treatment (28). Also the study reveals our local recurrence rates for low and mid rectal cancers to be 6.8%, which is comparable to global benchmarks (29–31). In an era where complete responders can be offered organ preservation, further studies on tumour regression patterns is of high importance.

The indirect benefit of nodal assessment on survival may be observed due to accurate staging of the disease. Nodal harvest from CRC specimens is a team work between the surgeon and the pathologist. Sound surgical technique to include maximal mesentery in the specimen coupled with dissection techniques to increase nodal harvest (24,25). A previous study by Siriwardene et al on the same patient population has demonstrated pro-forma based reporting to enhance the reporting standards (26). Description of a cutoff value for local population is important in developing local management guidelines in the future for CRC. Furthermore, this analysis elaborates on the effect of NCRT for a reduced nodal harvest. This effect was previously demonstrated for the first time in a local population by Wijesuriya et al (27). It will be necessary to adopt cost effective techniques such as pre-operative tattooing to increase the nodal harvest in this patient group (28,29).

Understanding the survival pattern of the local population is pertinent for deciding the future direction of the particular surgical service. A long term outcome analysis of the local CRC population with prospectively collected data allows us to assess the quality of the care provided and compare with standards. The overall survival in CRC for this local population is 68%, which is comparable to that of the United States according to the National Cancer Institute data (30). Further the study provides evidence to the improvement in survival in rectal cancer patients probably owing to the continuous improvement preoperative imaging, neo-adjuvant treatment and perioperative care as opposed to colon cancer. This phenomenon has been observed in other populations as well (31). Hemminki and colleagues analyzing data of 5

**Table 4.** Effect of NCRT on median nodal harvest in CRC. Reproduced from Chandrasinghe et al 2014 (18)

	No NCRT	NCRT	
LN<14 (n)	73	18	Total=91
LN>14 (n)	38	02	Total=40
Median nodal harvest (range)	11 (5-45)	8 (5-20)	$p=0.0128$

NCRT neoadjuvant chemoradiation

**Table 5.** The overall survival from rectal and colon cancers in the pre and post 2010 time periods

Time	CRC population		Rectal cancer		Colon cancer	
	<2010	>2010	<2010	>2010	<2010	>2010
5-year OS	59%	68%	54%	69%	70%	69%

decades from a Finnish population suggest that the improvement in survival in rectal cancers can be attributed to a large number of small improvements and not a single breakthrough (31).

#### *Future challenges and the way forward*

Sri Lanka will also face few challenges in managing CRC in the near future. Several of these aspects have been looked into at North Colombo using our cohort. The global pandemic of young and early onset colorectal cancers (EOCRC) may have been an established phenomenon in the local setting. A 20% EOCRC and a 16% young cancer rate is observed in the North Colombo cohort (32,33). An aging population is another challenge that the developing is faced with. Due to this an increasing number of CRC in the elderly population is seen with unique challenges in management. The north Colombo cohort has demonstrated that the chronological perse is not a predictor of poor outcome form surgery for CRC (34,35) Application of novel technologies is also challenging in this region die to the scarcity of resources and may need to be adapted to make them feasible in the local setting (35)

The most important perspective provided by these studies is the significance of maintaining prospective data. In a setting such as Sri Lanka where a centralized data collection and storage is lacking, the point of first contact is the best opportunity to capture individual patient data. While the national Cancer Control Programme maintained registries provides national data, the accuracy of the data collection sources is questionable. This is evident by the discrepancies in the CRC incidence by around 33% in the year 2017 provided by the same institute in the National Cancer registry and the Pathology based Cancer register (36,37). The North Colombo CRC database is now maintained as a cloud based electronic database. The infrastructure to manage online databases is present in Sri Lanka and several authors have demonstrated how prospective data could elaborate the landscape of patient care for better decision making (38,39). All units managing CRC should be encouraged to maintain updated data, which can be collaborated, in large multicenter studies to develop homegrown data. It is also an appropriate time to consider regional data hubs to collect data from the South Asian region which homes close to a 25% of the global population at present.

This is a synopsis of the SAARC oration 2023 delivered at the Sri Lanka Surgical congress 2023.

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# Surgically important neurovascular structures related to the submandibular gland.

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**Keywords:** facial artery, submandibular gland, facial nerve, Submandibulectomy, marginal mandibular nerve.

## Abstract

### Introduction

The pathologies and procedures of the submandibular gland are numerous. Comprehensive knowledge of the anatomy and its relations of the SMG will avoid iatrogenic injuries within the submandibular triangle. This study assesses the presence and frequency of neurovasculature related to the SMG with special interest on the facial artery and the marginal mandibular nerve of cranial nerve (CN) VII

### Methods

In twenty- five fresh cadavers, right and left side SMG (n=50) were dissected and observed in the department of Anatomy, faculty of Medicine, Ragama. Data were recorded on frequency of facial artery and postsynaptic sympathetic periarterial plexus and the marginal mandibular nerve of CN VII with relations to the SMG.

### Results

The majority 40/50 had the facial artery placed on the posterior surface of the SMG outside the capsule of the gland. Two of those specimens (2/10) had the e facial attires piercing through the parenchyma of the SMG. All facial artery anomalies were found to be present unilaterally, mostly on the right side and mainly among the females. 3/50 female cadaveric specimens had the marginal mandibular nerve of CN VII nerve traversing through the superficial part of the SMG. All of them were in the right side.

### Conclusions

The data indicate a higher rate of aberrant submandibular neurovasculature were on the right side with a female preponderance.

## Introduction

The submandibular triangle is demarcated by the inferior border of the mandible and the anterior and posterior bellies of the digastric muscle. The superficial and deep surfaces are formed by the platysma and the mylohyoid muscle, respectively [1]. The submandibular gland (SMG) is in the submandibular triangle. The pathologies and procedures of the SMG are varied and numerous [2-5] Comprehensive knowledge of the anatomy and its relations of the SMG will avoid iatrogenic injuries within the submandibular triangle.


Variation of the facial arterial pathway in relation to SMG has not been very well established. In majority, the facial artery is on the posterior surface of the gland and outside the capsule of the SMG. However, anomalies may divert the facial artery course within the parenchyma of the gland. This may result the facial artery and the postsynaptic sympathetic periarterial plexus that travers on its external surface at risk of iatrogenic injuries during surgical procedures. The other important structure related to the SMG is marginal mandibular branch of the facial nerve [6]. This is also at risk of an iatrogenic damage due to close relation to the SMG. This study assesses the presence and frequency of neurovasculature related to the SMG with special interest on the facial artery and the marginal mandibular nerve of CN VII.

**Table 1:** Anomalous facial artery and marginal mandibular branch

Category	Facial artery variants	CN VII - marginal mandibular branch variants
Male	3	0
Female	7	3
Left	2	0
Right	8	3
Total variants	10	3

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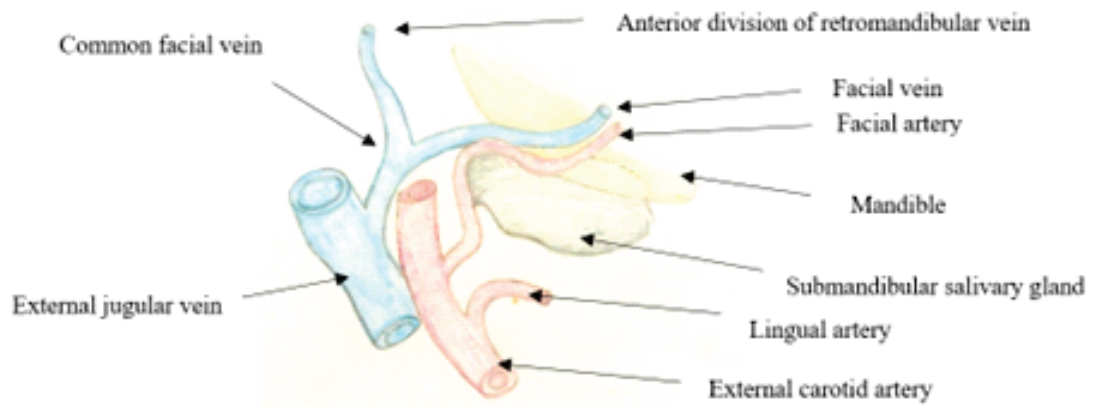
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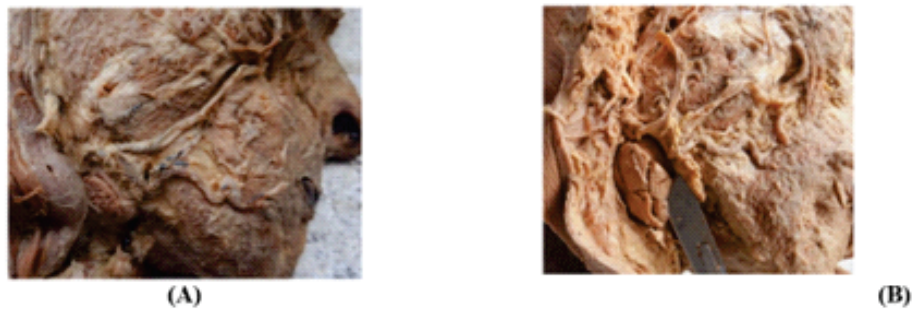
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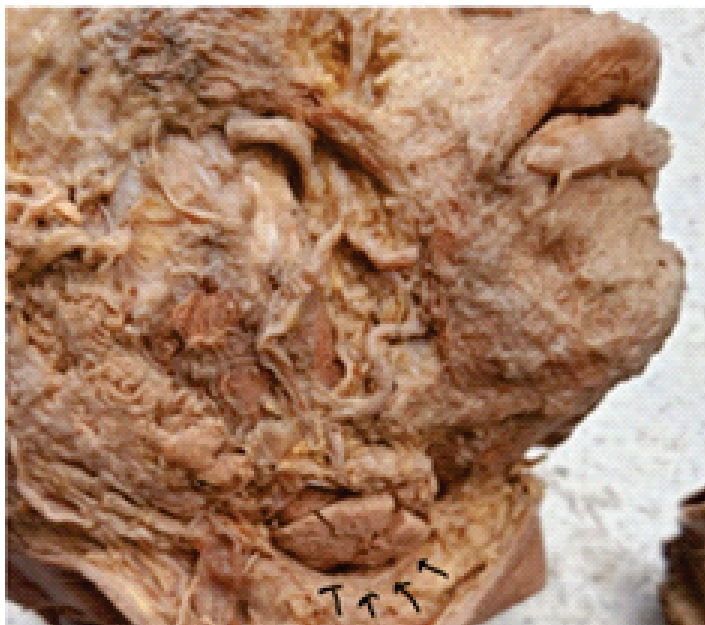


**Figure 1.** Normal anatomy of the Submandibular gland



**Figure 2.** Anatomical variants of the facial artery within the submandibular gland

(A) Lateral view of the Right-side SMG which has no facial artery anomaly; (B) Anatomical variant of the right SMG which facial artery piercing the SMG and dissected Right submandibular gland to visualize piercing facial artery.



**Figure 2.** Dissected and retracted downwards marginal mandibular nerve is marked in black arrows



## Method

In twenty-five fresh cadavers (13 M/ 12 F) right and left side SMG (n=50) were dissected and observed in the department of Anatomy, faculty of Medicine, Ragama. Data were recorded on frequency of facial artery and postsynaptic sympathetic periarterial plexus and the marginal mandibular nerve of CN VII with relations to the SMG. Nature of the study did not warrant any ethical clearance. No conflict of interest was declared.

## Statistical Analysis

Social Science Statistical Package (SPSS Inc., Chicago, IL, USA) computer software was used for the statistical analysis. The descriptive data were presented as mean, standard deviation and range.

## Results

Among the 50 dissected specimens, majority 40/50 had the facial artery placed on the posterior surface of the SMG outside the capsule of the gland. In 10/50 specimens' facial arteries were encapsulated by the SMG. Two of those specimens (2/10) had the facial arteries piercing through the parenchyma of the SMG. All facial artery anomalies were found to be present unilaterally and majority were in the right side (8/10 R/S, 2/10 L/S). It was further observed that 7/10 specimens that had anomalous facial arteries were of females.

With reference to the marginal mandibular nerve of CN VII with relations to the SMG, 3/50 female cadaveric specimens had the nerve traversing through the superficial part of the SMG. All of them were in the right side. Overall, it was observed that right side was more associated with anomalies with a female dominance. (Table 1) (Figure 01). Rest of the cases the nerve traversed below the angle of the mandible and inferior to the platysma. Initially it was superficial to the upper part of the digastric triangle and then turned towards the cephalic direction and ran across the body of the mandible to supply muscles of the lower lip.

## Discussion

Anatomical knowledge of the facial artery in relation to the SMG is vital in surgery. Clinical importance of the knowledge of facial artery and its anomalous pathways have been highlighted in relations to many surgical and interventional procedures related to the SMG [7], which includes significant concerns over the location of the facial artery and its penetrating branches, due to the interventions associated risks, such as formation of pseudoaneurysm with inaccurate needle placement following botulinum injection or from trauma to vessels of the neck and face [8]. Furthermore, the facial artery may be sacrificed in surgeries, for advancement, visualization, or mobilization [9]. Due to the amount of

collateral blood flow, removal of the facial artery has no clinical effect. However, knowledge of this piercing variant is important after trauma or locally invasive neoplasm as the facial artery may be used for facial flaps in reconstructive procedures. The previously accepted anatomical pattern of the submandibular triangle presumed that the facial artery courses via a posterior canal alongside the SMG. Our study showed that 20% specimens' facial arteries were encapsulated by the SMG. Two of those specimens 2/10 had the facial arteries piercing through the parenchyma of the SMG. All facial artery anomalies were found to be present unilaterally and majority were in the right side (8/10 R/S, 2/10 L/S). It was further observed that 7/10 specimens that had anomalous facial arteries were of females.

The marginal mandibular which supplies the muscles of the lower lip, is considered most at risk of iatrogenic injury during the surgical procedures involving the SMG [6]. In our study mostly, the nerve was below the angle of the mandible and deep to the platysma. Following its superficial course in the digastric triangle, the nerve ran upwards and crossed the body of the mandible to supply the lower lip muscles. In our study, in 3/50 female cadaveric specimens had the nerve traversing through the superficial part of the SMG. Therefore, in order to avoid and iatrogenic injury to the marginal mandibular nerve, placing an incision 2 cm or below from the lower margin of the mandible is safe. [6-8]

For SMG related surgical procedures, an understanding of the neurovascular anomalies would allow for appropriate planning and risk benefit consideration. To better understand the prevalence of aberrant anatomy related to the SMG, further studies are recommended especially on live subjects during SMG related procedures to assess rates of anatomical variance.

## Conclusions

This study revealed a high frequency of anomalous facial artery patterns. The data also indicate a higher rate of aberrant submandibular neurovasculature were on the right side with a female preponderance.

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## The effect of routine ureteral stent placement on post-ureteroscopy complications: A prospective study from a resource limited setting.

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**Keywords:** DJ stent, Stone management, Ureterorenoscopy, Limited resource setting

### Abstract

#### Background

Rigid ureterorenoscopy (URS) stands as a highly successful treatment for ureteral stones. The current guidelines from the European Association of Urology (EAU) recommends selective double J (DJ) stent placement post-URS to mitigate major complications. However, in resource-limited hospital setups, executing selective stent placement poses substantial risks in preventing complications and reducing readmission rates. This study aims to unveil the ramifications of our routine stent replacement approach after ureteric stone surgery on surgical outcomes in a resource-constrained setting.

#### Materials and Methods

This prospective study was conducted at a urological unit within a tertiary care center in Sri Lanka, over a one-year period, involving 112 diagnosed patients. Patients underwent routine DJ stenting following rigid URS for ureteral stone management, without additional intervention. Data collected from clinical records encompassed demographics, stone characteristics, and complications. Postoperative complications linked to routine DJ stenting were assessed using the Clavien-Dindo classification system. Descriptive statistics were employed for data summary using SPSS version 23.0.

#### Results

The mean age of patients was 47.3±14.9 years (range: 13-76 years), with 67.9% being males. The mean stone size was 15.35±6.58 mm (range: 4.5-35 mm), distributed across right (48.2%), left (44.6%), and bilateral (7.1%) ureters, of which 52.7% were proximal, 30.4% distal, and 17% mid ureteric

stones. Postoperative evaluation revealed 26.8% of patients experiencing Clavien-Dindo grade I complications (e.g., dysuria, haematuria, loin pain, and lower urinary tract symptoms), managed conservatively. Moreover, 4.5% encountered Clavien-Dindo grade II complications, predominantly postoperative fever, necessitating hospital readmission specifically for intravenous antibiotic administration.

#### Conclusion

Despite guidelines advocating selective stent placement, this study underscores the safety and efficacy of routine DJ stent implementation after the URS laser procedure. The findings showcase a notable reduction in postoperative complications alongside decreased hospital readmission rates in resource-limited environments. Embracing routine DJ stenting post-URS in such settings could serve as a pragmatic approach, potentially enhancing patient outcomes and minimizing healthcare burdens.


#### Introduction

Rigid ureterorenoscopy (URS) is the most common treatment modality with a high success rate in managing ureteral stones. It is commonly performed as a minimally invasive procedure in urological practice. URS involves the use of a rigid URS to visualize and manage stones located in the ureter or kidney [1]. According to the current European Association of Urology (EAU) guidelines, selective placement of a double-J (DJ) stent after URS is recommended to prevent major complications [2]. Although URS is highly effective, occasionally it leads to potential complications, including ureteral injury, ureteral stricture and postoperative urosepsis. The reported range for complications is 9 to 25%. The major complications of rigid URS are ureteric perforation (2-4%) and ureteric avulsion (0.5-2%) [3].

The routine placement of a DJ stent after URS has been considered by many urologists based on surgeons' techniques and experience to prevent or reduce major complications to mitigate these risks [4]. However, the necessity and benefits of routine DJ stenting after URS remain a subject of debate,

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due to disturbing stent-related symptoms such as dysuria, haematuria, storage urinary symptoms and loin pain and need for second procedure under local anesthesia for stent removal [5,6,7].

The infrastructure setting includes human resource and operating theatre facility play a crucial role in the surgical management of urolithiasis. Limited resource settings often encounter challenges such as restricted access to emergency healthcare facilities, financial constraints, and scarcity of medical resources. In such settings, where resources need to be allocated wisely, it becomes crucial to determine necessity and potential benefits of routine DJ stenting after rigid URS. This evaluation is essential to enhance patient safety by reducing major complications such as post-operative obstructed infected kidney with urosepsis which can lead to significant morbidity and mortality.

Routine DJ stenting after the URS procedure is the most reasonable approach and is typically placed for 3 to 6 weeks. This practice can potentially reduce the likelihood of unplanned emergency healthcare encounters and hospitalization while also enhancing patient satisfaction with the healthcare system and overall quality of life. In most cases, complications in post-URS patients with stent can be managed with minimal pharmacological management such as anticholinergics and analgesics rather than resorting to surgical intervention like emergency DJ stenting and percutaneous nephrostomy. The aim of the study was to investigate whether routine DJ stenting following ureteric stone surgery improve surgical outcome in a limited resource setting.

## Materials and method

This prospective study was conducted in a limited resource setting, in a urological unit of a tertiary care center, in Sri Lanka for one-year period. This study included 112 diagnosed patients, who underwent routine DJ stenting following rigid URS for the management of ureteral stones without any other intervention. All new patients with a ureteric stone confirmed through a non-contrast computerized tomography (NCCT) KUB and meeting the criteria outlined in the EAU guidelines were included in this study using a convenience sample technique and pre-stented patients were excluded from the study. A 5/6 Fr, 24/26 cm DJ ureteral stent was placed in each patient for 3-6 weeks. Patients were discharged from the hospital within 24-48 hours after the URS procedure.

Approval for the study was obtained from the Institutional Ethical Review Committee. Informed written consent was obtained from all the study participants before enrollment. Data collection was performed prospectively using a validated data collection form which included patient demographics, stone characteristics, and postoperative complications. Postoperative complications with routine DJ stenting were evaluated for 3 months based on the Clavien-Dindo classification system [8]. Pain perception was assessed by Visual Analogue Scale (VAS) after the procedure.

Collected data were summarized using descriptive statistics. Continuous variables were presented as either mean  $\pm$  standard deviation or median (interquartile range) based on their distribution. Categorical variables were presented as frequencies and percentages. The study aimed to observe and report the safety outcomes associated with routine DJ stenting following a rigid URS procedure.

Characteristic	Count	Percentage
No of patients	112	100%
Age		47.30 $\pm$ 14.97 (13-76 years)
Gender		
Male	76	67.9%
Female	36	32.1%
Stone size		15.35 $\pm$ 6.58 (4.5-35mm)
Stone location		
Right	54	48.2%
Left	50	44.6%
Bilateral	08	7.1%
Stone site		
Proximal ureter	59	52.7%
Mid ureter	19	17%
Distal ureter	34	30.3%
Hospitalization		1.38 $\pm$ 0.5 (1-2) days
Readmission hospital stay	5	3.78 $\pm$ 1.12 (3-5) days



## Results

Among the 112 patients, 67.9% were males and 32.1% were females, with a male-to-female ratio of 2.38:1. The mean age was 47.30±14.97 years (range, 13-76 years). The mean size of the stone was 15.35± 6.58 mm (range, 4.5- 35 mm). Stones were located in the right (48.2%), left (44.6%) and bilateral (7.1%) ureter, in which 52.7% were proximal, 30.3% were distal and 17% were mid ureteric stones.

All patients were discharged from the hospital within 24-48 hours and only 4.5% of patients were readmitted due to fever. The mean hospital stay during re-admission was 3.78±1.12 (3-5) days.

In post-operative analysis, 26.8 % of patients had stent-related Clavien-Dindo grade I complications such as dysuria, haematuria, loin pain, and lower urinary tract symptoms. Loin pain was a common symptom seen in 10.7% (12) patients while 7.1% (8), 6.3% (7) and 5.4% (6) of patients experienced haematuria, dysuria and LUTS respectively. Moreover, 4.5% of patients experienced Clavien-Dindo grade II complications, mainly post-operative fever which was successfully treated with intravenous antibiotics. There were no Clavien-Dindo III, IV, and V complications were noted during the follow-up period. When assessing pain perception in patients with a DJ stent, those who had a DJ stent experienced significantly lower pain scores, with a median VAS score of 2.68 (SD±0.90).

## Discussion

Selective placement of DJ stent after the URS procedure is a common practice in urology and stents are typically retained for 3-6 weeks. Stents facilitate the direct drainage of urine from the kidney to the bladder [5,9]. This study aimed to

investigate whether routine DJ stenting following ureteric stone surgery improve surgical outcome in a limited resource setting. The current study revealed that postoperative complications were not uncommon following rigid URS and routine DJ stenting. However, the most frequently reported complication was Clavien-Dindo 1 stent-related symptoms. According to a global survey, patients with renal stones (80%) and ureteral stones (60%) were more likely to receive a post-operative DJ stent which has demonstrated a substantial decrease in readmissions and hospital stays [5]. Another study reported that, although stent placement was associated with a 1.25 higher odds of emergency department visits (p=0.043), it did not result in hospitalization (p=0.12) [10]. This study also revealed that DJ stent placement had reduced both hospitalization (1.38±0.5 days) and readmission (3.78±1.12 days), when compare to the standard figures of complications given in most of the other studies including metanalysis of Makarov et al [20].

Stent placement promotes ureteric healing and prevents complications by maintaining the integrity of the ureteric wall, reducing inflammation and urine extravasation, and directing epithelial regrowth. It is also used as a method of drainage in acute presentation [11]. Thus, post-operative stent placement is recommended after URS in higher-risk cases such as solitary kidney, impacted stone, older age and higher stone burden, to reduce complications and facilitate the passage of residual stone fragments [5]. In the present study, DJ stenting was performed on all the patients who underwent elective URS and laser lithotripsy. Although minor complications were reported due to the DJ stent, it showed a decrease in both hospitalization and readmission.

Postoperative complication	No	%
Clavien Dindo 1	33	26.8%
Dysuria	7	6.3%
Haematuria	8	7.1%
Loin pain	12	10.7%
LUTS	6	5.4%
Clavien Dindo 2		
Fever	5	4.5%
VAS Score		2.68 ±0.90

A recent meta-analysis revealed that pain, dysuria, hematuria, irritative urinary symptoms, and urinary tract infections (UTI) were significantly more common in patients with postoperative DJ stent placement. But, the risk of unplanned readmissions was significantly higher in the unstented group ( $p < 0.01$ ) compared to the stented group according to Wang et al [12]. Joshi et al demonstrated nearly 80% of the patients experienced stent-related urinary symptoms [13]. However, the current study revealed that only 26.79 % of patients had stent-related symptoms such as dysuria, haematuria, loin pain, and lower urinary tract symptoms which were comparatively lower than the studies conducted in the developed countries.

A European study revealed a mean visual analogue score (VAS) of  $3.21 \pm 2.32$  [14]. However, the mean VAS in our cohort was  $2.68 \pm 0.9$ . This difference may be attributed to potentially better pain tolerance in our South Asian population and other explanation may be those with higher standards of living tend to complain more regarding minor issues.

Some studies have reported major complications such as ureteric avulsion, perforation, ureteric edema, urosepsis during and after rigid URS, and as well as ureteric stricture on follow-up. [15,16]. However, there were no major complications reported in the per-operative or follow-up period in this study. This may be due to single consultant doing all the procedures with better technique and routine stenting of all cases.

In a setting with limited resources, which includes lack of human resources and logistical deficiencies, such as insufficient theatre space and equipment, shortage of medical facilities for antibiotics and anesthetic supplies, and a lack of specialist consultant surgeons and medical officers, patient outcomes may be affected. As a result, the patients may experience complications and readmissions. Despite the popular belief that stent symptoms may have psychological, social, and economic impacts, the present study demonstrated improved patients' safety with fewer stent-related symptoms [2].

In a limited resource setting, managing unplanned visits, emergency hospital admissions and hospital stays following URS procedures can be challenging. In USA, around 20% of unplanned visits or hospital readmissions were identified after the stone procedure [17,18]. However, in this study, interestingly only 4.5% of patients required hospital admission due to post-operative fever which was managed successfully with intravenous antibiotics, and no other major

complications were reported. However, further studies are necessary to determine the long-term complication associated with stent placement.

## Conclusion

In conclusion, the placement of routine DJ stenting post-Rigid URS for stone management showed reduced occurrence of major complications in comparison previous studies. This has significantly reduced major complications and heightened patient safety within our resource-limited setting. Patients exhibited good tolerance toward minor stent-related issues. Therefore, we suggest that routine application of DJ stenting following Rigid URS in similar settings, emphasizing its potential to enhance patient safety and substantially diminish major complications compared to adhering solely to selective stent placement guidelines

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## Usefulness of simultaneous use of anatomical landmarks in identification of facial nerve in parotid gland dissection.

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**Keywords:** parotid gland, facial nerve, Tragal pointer, digastric muscle, parotidectomy.

### Abstract

#### Introduction

Identification of Facial nerve trunk is important in parotid surgery to avoid an iatrogenic injury. The objective of our study was to assess consistent and reliable landmarks for identification of the main trunk of facial nerve during parotid surgery.

#### Methods

This prospective study was carried out in the department of Anatomy, faculty of Medicine, Ragama from 2022 to 2023. Our study included 35 fresh cadavers (70 parotid regions). The anatomical landmarks of tragal pointer (TP), tympanomastoid suture (TMS), and superior border of posterior belly of digastric (PBD) muscle to the facial nerve trunk was measured. The shortest distances were taken from the facial trunk by using a slide calliper.

#### Results

The age of subjects of the cadavers ranged from 42 to 64 years with a mean of 54.4 years. The mean distance between the TP and the facial nerve trunk was 9.15 mm (8.1–11.7 mm). The mean distance between PBD and the facial nerve trunk was 8.6 mm (7.2–9.8 mm). The mean distance between the TMS and the facial nerve trunk was 6.5 mm (5.2–7.5 mm).

#### Conclusion

Our study showed that the tympanomastoid suture line is the closest to the facial nerve trunk, followed by the posterior belly of digastric muscle and the tragal pointer respectively. Further clinical studies are needed to assess these landmarks through various parameters to determine their usefulness in surgical practice.

#### Introduction

Identification of Facial nerve trunk is paramount in parotid surgery to avoid an iatrogenic injury to the nerve leading to facial muscle paralysis which can result in difficulties in speech, swallowing, eye closure, facial expressions and quality of life.[1-3] There are many anatomical landmarks described in literature such as tragal pointer, posterior belly of digastric muscle, tympanomastoid suture, stylomastoid artery, styloid process, ramus of mandible and transverse process of axis.[1-6] This implies that the use of multiple landmarks to identify the facial nerve trunk that there is less evidence on the consistence and safety of these landmarks in respect of avoiding an iatrogenic facial nerve injury during parotid surgery. The objective of this study is to assess consistent landmarks for identification of the main trunk of facial nerve during parotid surgery.

#### Methods

This prospective study was carried out to identify the main trunk of the facial nerve in the department of Anatomy, faculty of Medicine, Ragama from 2022 to 2023. Our study included 35 fresh cadavers (70 parotid regions). The tragal pointer, tympanomastoid suture, and superior border of posterior belly of digastric muscle were taken as anatomical landmarks. The shortest distance from the facial trunk to each landmark was measured. The ethical clearance was granted. No conflict of interest.

#### Dissection method

A Modified Blair's incision was used in our study. The skin flaps were elevated and, the dissection was carried out in between the pinna and the parotid gland and the tragal pointer. Following that, the sternocleidomastoid muscle and the posterior belly of digastric muscle was exposed by dissecting the lower part of the parotid. Once the above dissections were completed, the tympanomastoid suture was identified in between the tragal pointer and superior border of PBD. The facial nerve trunk was found adjacent to these landmarks and the measurements were taken accordingly.

#### Statistical Analysis

Social Science Statistical Package (SPSS Inc., Chicago, IL,

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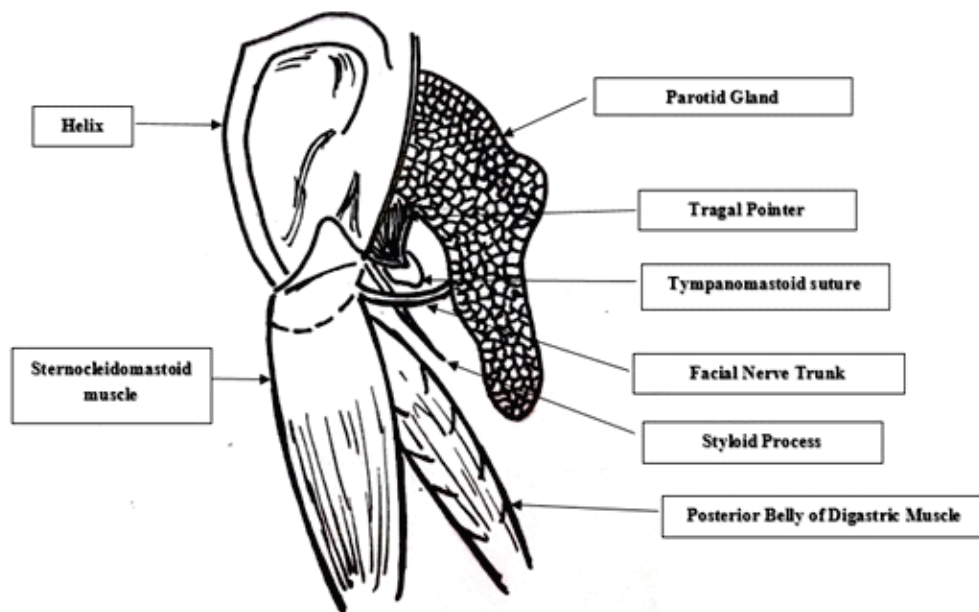
 <https://orcid.org/0000-0002-0986-7917>

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**Figure 1.** Diagrammatic representation of Facial Nerve Trunk

USA) computer software was used for the statistical analysis. The descriptive data were presented as mean, standard deviation and range.

### Results

We found that in 100% of cases we could identify the main trunk of facial nerve without much difficulty by using these three landmarks. The age of subjects of the cadavers ranged from 42 to 64 years with a mean of 54.4 years. The mean distance between the TP and the facial nerve trunk was 9.15 mm (8.1–11.7 mm). The mean distance between the PBD and the facial nerve trunk was 8.6 mm (7.2–9.8 mm). The mean distance between the tympanomastoid suture (TMS) and the facial nerve trunk was 6.5 mm (5.2–7.5 mm).

### Discussion

According to literature the tragal pointer is commonly used landmark for the identification of Facial nerve trunk during surgery. The literature revealed that the facial nerve lies around 1 cm deep and inferior to the pointer.[1] This was comparable with our study findings as well. However, it is possible that variable directions of the cartilaginous tip may give a false direction towards the main trunk of the facial nerve.

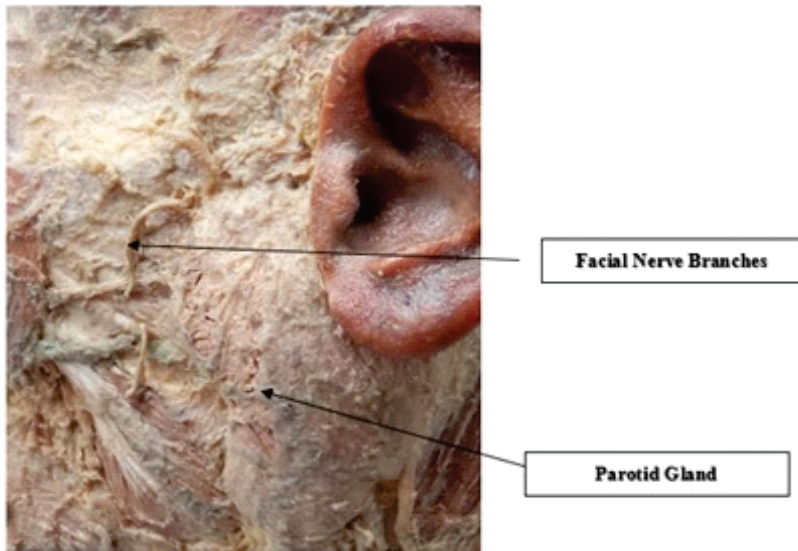
The available literature showed that the Facial nerve trunk was found to lie within 4.8–12.8 mm of posterior belly of digastric [4]. In our study, the range of distance of the facial nerve trunk from the PBD was like as it was in literature. Using a landmark, the PBD has advantages, such as it is being easily identifiable, and it lies superficial to the plane of facial nerve trunk. Furthermore, the tragal pointer and the PBD lie at

a same and superficial plane to the facial nerve trunk hence dissection at this plane is safe.

The literature revealed that the facial nerve trunk from TMS was in the range of  $3.79 \pm 2.92$  mm [1-4]. In our study, the distance of TMS to the main trunk of facial nerve was longer than the available literature. The advantage of TMS is due to the bony nature, it is less variable than the other landmarks. Because of the consistent position, the tragal pointer and tympanomastoid suture were taken mostly to locate the main trunk of the facial nerve in some literature [5,6].

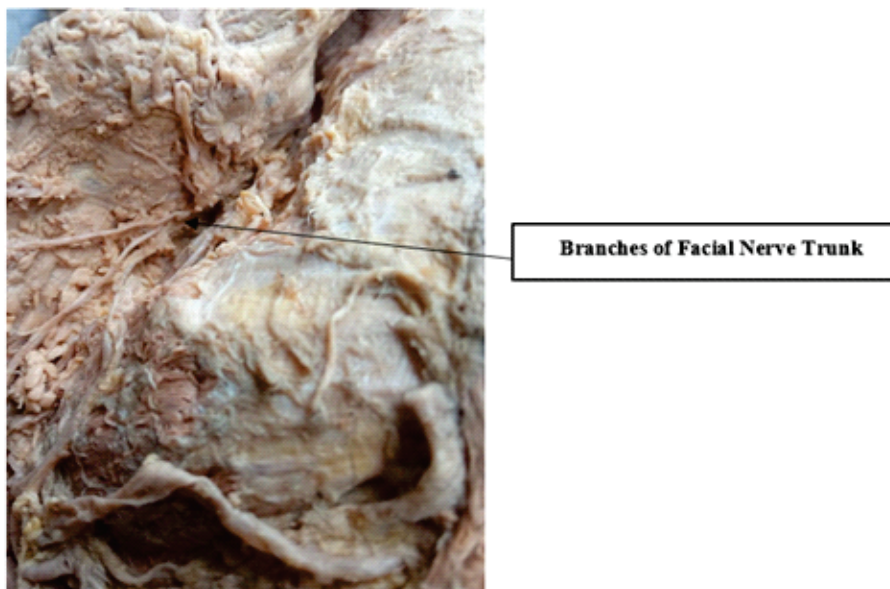
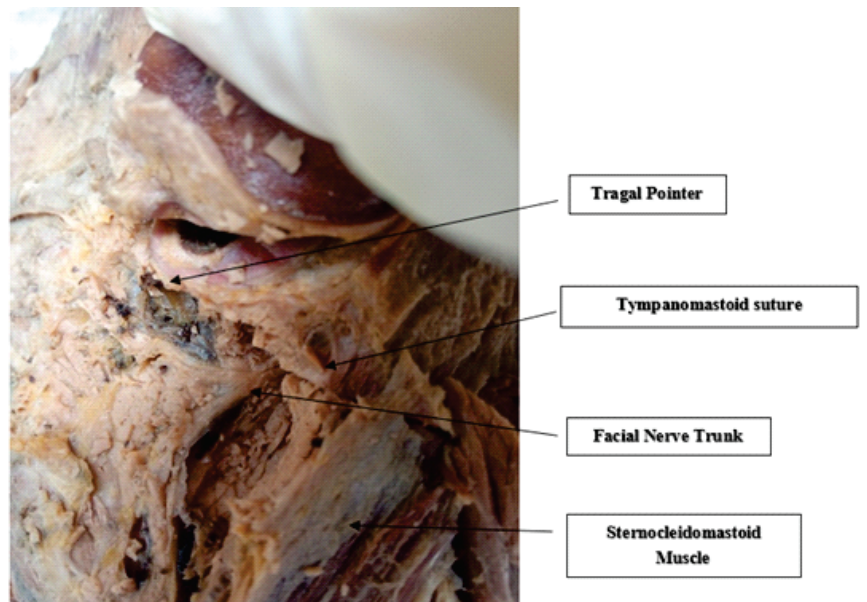
Even though some of the literature describes the use of stylomastoid artery as a landmark for the identification of the facial nerve trunk we did not make any attempts due to its inconsistent presence and anatomical variations and the possibility of artery spirals closely around the facial nerve trunk which could result in iatrogenic nerve injury during dissection. Similarly, the literature has described the styloid process as another landmark, but we felt that since it lies medial to the facial nerve trunk, the possibility of iatrogenic injury is more. [3-8]

In our study the simultaneous use of these three landmarks facilitates the identification of the main trunk of facial nerve. We observed that the tympanomastoid suture was the closest landmark, followed by the posterior belly of digastric muscle to the facial nerve trunk. This method may facilitate the dissection and reduce the total operating time. We would like to propose the simultaneous use of these landmarks for identification of facial nerve trunk easily.



**Figure 2.** Exposure of parotid gland in anatomical study

**Figure 3.** Exposure of Tragal pointer and tympanomastoid suture



**Figure 4.** Exposure of facial nerve branches in cadaver dissection

## Conclusion

Our study showed that the tympanomastoid suture line is the closest to the facial nerve trunk, followed by the posterior belly of digastric muscle and the tragal pointer respectively. Further clinical studies are needed to assess these landmarks through various parameters to determine their usefulness in surgical practice.

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## Anatomical relations of the recurrent laryngeal nerve in thyroid dissection.

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**Keywords:** recurrent laryngeal nerve, inferior thyroid artery, suspensory ligament of berry, inferior horn of the thyroid cartilage, Anatomical variants

### Abstract

#### Introduction

Recurrent laryngeal nerve (RLN) palsy is one of the major complications thyroidectomy. Visualization of the anatomical relations of the RLN with branches of the inferior thyroid artery (ITA) remains essential for preservation of RLNs. Suspensory ligament of Berry, inferior horn of the thyroid cartilage is considered as other important landmarks for safe thyroidectomy. The objective of this study was to describe the various anatomical relations of the RLN during thyroid dissection.

#### Methods

An observation cadaveric study was conducted by simple random sampling of 35 cadavers with a total of 70 RLNs over a one-year period, from June 2022 to June 2023. The cadavers that had thyroidotomies and goitres were excluded from the study

#### Results

The majority of RLNs in this series had a retrovascular course (with respect to the ITA or its branches): 57% on the right and 68.6% on the left. The course of 64/70 of the dissected nerves was posteromedial to the suspensory ligament of Berry, while the other 6 nerves passed between the fibres of this ligament. All RLNs penetrated the larynx by passing posteriorly to the inferior horn of the thyroid cartilage on both sides. No case of non-recurrent laryngeal nerve was observed.

#### Conclusion

This preliminary study illustrates the numerous anatomical variants of the RLN with respect to the ITA and its branches. The RLN mainly has a retrovascular course on both the right

and the left sides.

#### Introduction

Thyroidectomy is one of the most commonly performed surgeries in neck [1] One of the major complications of this surgery is recurrent laryngeal nerve (RLN) palsy.[2,3] A comprehensive knowledge of the anatomy of the thyroid region is essential to avoid iatrogenic RLN injuries. It has now been clearly established that visualization of the RLN remains the main factor of preservation of nerve and to reduce incidence of postoperative recurrent laryngeal nerve palsy.[4-6]

Visualization of the anatomical relations of the recurrent laryngeal nerve with branches of the inferior thyroid artery (ITA) is vital for preservation of recurrent laryngeal nerve. Suspensory ligament of berry and inferior horn of the thyroid cartilage are considered as other anatomical relations of recurrent laryngeal nerve. [1-6] The objective of this study was to describe the various anatomical relations of the RLN during thyroid dissection.

#### Methods


An observation cadaveric study was conducted by simple random sampling of 35 cadavers with a total of 70 RLNs over a one-year period, from June 2022 to June 2023. The cadavers that had thyroidotomies and goitres were excluded from the study

#### Dissection technique

Kocher neck incision made and the superior and inferior platysma skin flaps were created and the thyroid gland was exposed. Lateral surface of the lobe was dissected while observing the presence of middle thyroid vein. Dissection of the inferior pole was done, and the inferior thyroid veins were ligated. ligation of the superior vascular pedicle was done as close as possible to the superior pole. The method of identification of the RLN was lateral approach, the various anatomical relations of the recurrent laryngeal nerve especially with the ITA, variations of the course of the RLN, the presence of any extra laryngeal divisions and the presence of a non-recurrent laryngeal nerve were observed. The ethical

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clearance was obtained. No conflict of interest.

### Statistical analysis

Data analysis was performed with Statistical Package for Social Sciences (SPSS) version 19.0. Data were expressed as frequencies.

### Results

A total of 35 cadavers were included in this study (28 F: 7 M). A total of 70 recurrent laryngeal nerves were identified. Seventeen right RLNs crossed the trunk of the ITA, mostly posteriorly;( 7 anteriorly and 10 posteriorly). The majority of left recurrent laryngeal nerves did not cross the trunk of the ITA (23/35). (Table 01)

Considering the anatomical relations of the right RLNs with branches of the ITA, 35 of the right RLNs dissected, the majority of nerves (17/35) crossed anterior to the branches of the ITA and 5/35 RLNs traversed between the branches of the ITA. (Table 01) On the left side, 18/35 traversed anterior to the branches of the ITA, 14 RLNs passed posterior to the branches of the ITA and 3 RLNs were between branches of the ITA. The majority of RLNs in our study had a posterior relation with the trunk or branches of the ITA, 57.14% on the right and 68.57% on the left. (Table 01)

**Table: 1:** Anatomical relations to the RLN

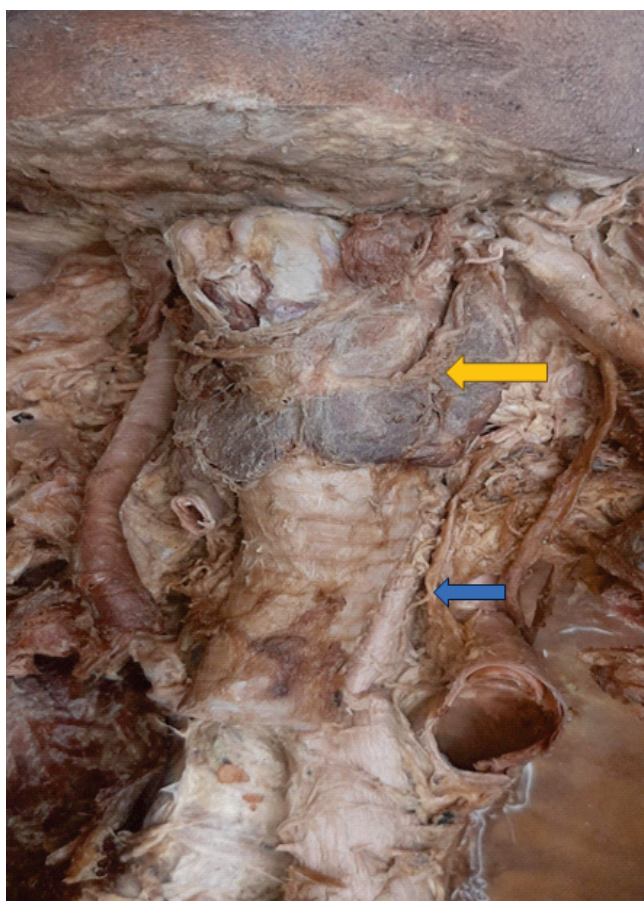
	Right side	Left side
Number of RLNs that cross the ITA trunk	17/35	12/35
Number of RLNs that cross the ITA trunk anteriorly	7/35	2/35
Number of RLNs that cross the ITA posteriorly	10/35	10/35
Number of RLNs that cross the branches of ITA anteriorly.	17/35	18/35
Number of RLNs that cross the branches of ITA posteriorly.	10/35	14/35
Number of RLNs that passes between the branches of ITA	5/35	3/35
Number of RLNs located posteromedial to the suspensory ligament of berry	32/35	32/35
Number of RLNs penetrated into the larynx by passing posteriorly to the inferior horn of the thyroid cartilage	35/35	35/35
Number of non RLNs identified	0/35	0/35

The course of 64/70 of the dissected nerves was posteromedial to the suspensory ligament of Berry, while the other 6 nerves passed between the fibres of this ligament. All RLNs penetrated into the larynx by passing posteriorly to the inferior horn of the thyroid cartilage on both sides.

No case of non-recurrent laryngeal nerve was observed in our series.

### Discussion

There are several approaches can be used to identify RLN. We lateral approach in our series. The anatomical relations between the RLN and ITA constitute a classical landmark for recurrent laryngeal nerve identification. Its main landmark is the inferior thyroid artery (ITA) at the middle or lower third of the posterolateral surface of the thyroid lobe and identification of the recurrent laryngeal nerve in the middle third of the lateral lobe.[7-15]



**Figure 1:** Thyroid gland (yellow arrow) and Left Recurrent laryngeal nerve (blue arrow).

In our study of 70 dissected nerves, the relations between the RLN and the ITA essentially concerned especially branches of the ITA), with a predominantly retrovascular course (57.14% on the right and 68.57% on the left). These results are like those of operative series reported [7,12,13,16]. However, the various relations of the RLN with the ITA observed in our series did not show any predominant differences according to the side. We observed a considerable percentage of RLNs passing between branches of the ITA (transvascular course, 14.28% on the right and 8.57% on the left). According to some literature, this transvascular pattern is predominant and would increase risk of intraoperative injury. [7,17,18] Even though numerous positions of the RLN in relation to the ITA have been described, [12,13,18] most literature stated that the classical location of the RLN would be anterior to the ITA on the right and posterior to the ITA on the left in more than 50% of cases [15,16]

The suspensory ligament of Berry is an important landmark of the course of the RLN before it enters the larynx. In our study, 91.43% of RLNs had a posteromedial course with respect to this ligament and 8.57% of nerves crossed the fibres of this ligament. These findings agree with the data of the literature. [14-19]

In this study, all recurrent laryngeal nerves penetrated the larynx by passing posteriorly to the inferior horn of the thyroid cartilage. The inferior horn of the thyroid cartilage, considered in the literature to be the most reliable landmark of the recurrent laryngeal nerve, indicates the point of entry of the nerve into the larynx. [8,10,20]. No case of non-recurrent laryngeal nerve was observed in our series. This anatomical anomaly remains rare, representing less than 1% of cases in many series [12,17,21] It is usually observed on the right, except in patients with situs inversus, with a retro-tracheo-oesophageal course of the left subclavian artery.[12,17,21] Even though, multiple extra laryngeal divisions are reported in the literature, with rates ranging between 24 and 70%. [12, 21] No multiple extra laryngeal divisions of the RLNs were observed in our study. This cadaveric study explores the anatomical relationship of the recurrent laryngeal nerve with the inferior thyroid artery and the ligament of Berry. The study shows that the course of both the right and left RLNs is primarily retrovascular, which differs slightly from what is published in the literature. [ 12,17,21] Thus, the results could be of interest to anatomists and surgeons.

## Conclusion

This study showed anatomical variants of the RLN with respect to the trunk of the ITA and its branches. The RLN

mainly has a retrovascular course on both the right and the left sides.

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# Conquering Immunological Barrier in Kidney Transplantation: ABO Incompatible Transplantation

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## Introduction

Chronic kidney disease is an ever growing global burden affecting nearly 10% of world population(1). Once a patient reaches end stage renal disease, kidney transplantation offers the best survival advantage and health related quality of life compared to other renal replacement modalities (2). Hence, the demand for organs continuously rises creating a gap between the organ availability and patients awaiting transplant.

Living donor kidney transplantation has demonstrated a significant patient and graft survival compared to deceased donation and is the most effective way to expand donor pool(3). However, immunological barriers such as ABO system antibodies and anti-Human Leukocyte Antigen antibodies pose restrictions to expansion. It's postulated that 30% of live donor kidney transplants are not feasible due these barriers(4). Hence, the ways to overcome this problem is to either transplant across the incompatibility upon immunomodulation or exchange the organs in one or more pairs with better compatibility.

ABO incompatible (ABOi) living donor kidney transplantation was long considered unfeasible, due the presence of isohemagglutinins, natural antibodies reacting with non-self ABO antigens(5). Nonetheless, utilization of pre conditional treatments to decrease isohaemagglutinins in recipient, commonly known as desensitization made ABOi kidney transplantation possible. Thenceforth, outcomes of ABOi kidney transplantation have markedly improved over the years(6).


The aim of this review is to summarize the principal aspects of ABOi kidney transplantation and its challenges ahead.

## ABO system and antibodies

The ABO antigen system consists of genetically determined expression of A,B or H oligosaccharide antigens predominantly found on red blood cells(7). Further, they are

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expressed on endothelial cells, glomeruli and tubuli making ABO antigen system in organ transplantation. Depending by the solitary expression of A or B antigen, A and B blood groups are determined respectively. AB Blood group is generated by co dominant expression of both A and B. In contrary blood group O has unmodified H antigen devoid of either A or B antigens. A blood group consists of two sub types, A1 and A2(8). A1 subtype is more common comprising 80% of A blood group. Compared to blood group A1 and B individuals, blood group A2 individuals depicts a low expression of blood group antigen molecules on surface of red blood cells, hence low immunogenicity(9,10)

The immunological barrier in ABOi transplant is due to preformed of anti- ABO antibodies (isohaemagglutinins) against non-self ABO antigens which emerge in early childhood(11). It's postulated that exposure of cell membrane antigens to gut commensal bacteria induces antibody production(12). Isohaemagglutinins show individual variations in class( IgM, IgG and IgA), titer, distribution hence pathogenic potential(6). Individuals with blood group O express higher antibody titers to both the A and B antigens. Hence, higher incidence of antibody-mediated rejection (ABMR) after transplantation is seen among blood type O recipients. (13)

## Immunomodulation and immunosuppression

Recipient desensitization is an integral part of ABOi transplantation to achieve a desirable isohaemagglutinin titer prior to transplant, yet here is no universally accepted desensitization protocol. The following strategies are routinely employed.

### 1. Apheresis

The key method for desensitization is currently based on apheresis techniques.

There are number of extracorporeal antibody removal techniques available. Plasma exchange removes all plasma proteins, while membrane separation can be used to remove certain plasma proteins like immunoglobulins. Immunoadsorption is another mechanism which could be selective or unselective.



### Plasma Exchange

Plasma exchange introduced by Alexandre et al is a non-selective apheresis method widely used for desensitization globally(14). It is less expensive and readily available(15). PEX has the important disadvantage of removal of coagulation factors, hormones, albumin, anti-bacterial and anti-viral immunoglobulins. Further, rebound of antibody is frequently observed. An alternative apheresis technique, the double-filtration plasmapheresis (DFPP), removes only the immunoglobulin fraction from the serum, therefore needing minimal fluid substitution. The utility of single or DFPP and the number of treatments vary between centres but mainly depends on the antibody titres.

### Immunoabsorption

Bannett et al. introduced this more selective apheresis technique, in which separated plasma pass through A and B antigen immobilized solid phase columns to remove anti ABO antibodies known as immunoabsorption(16). It is more efficient than conventional plasma exchange with fewer side effects although it's more expensive(17,18). Hence, as a cost saving strategy, Schiesser et al demonstrated that reuse after restoration of these columns does not reduce the antibody-depletion capability with similar safety and tolerability profile(6,19).

There are no randomized controlled trials comparing plasma exchange or immunoabsorption, hence the utilization of apheresis technique depends on centers experience(6).

### 2.Reduction of the B lymphocyte pool

Splenectomy was an integral part desensitization protocol prior to the introduction of anti B cell therapies. Rituximab, anti CD 20 antibody has substituted the protocols due to the surgical and infection risk associated with splenectomy. Rituximab has shown to reduce the risk of isoagglutinin rebound and the risk of ABMR as well as chronic rejection(20). Yet, Flint et al. reported 100% median graft and patient survival at 26 months after transplantation without Rituximab(21). In contrary, a higher of death-censored graft loss was observed in ABOi kidney transplants done after omitting Rituximab (22). Currently, most protocols do employ Rituximab usually using a dose of 375 mg/m<sup>2</sup> administering from 1 month before the transplantation(23).

### 3.Immunomodulation with intravenous immunoglobulins (IVIgs)

It is postulated that IVIG given pre-transplant prevents antiA/B antibody rebound seen immediate post-transplant. Further, it is believed that IVIG reduces post infectious complications by substituting depleted

immunoglobulins(24). In contrary, IVIG contains IgG antibodies against A/B antigens hence can increase antiA/B antibody titres upon administration(25).

### Maintenance immunosuppression

The maintenance immunosuppression in ABOi transplantation is same as in ABOc kidney transplantation apart from desensitization. The basal immunosuppression is initiated together with the desensitization. The suppression of B-cells by Tacrolimus, Mycophenolate mofetil, and steroids seems to be vital for antibody suppression and eventual suppression of acute ABMR in ABO-ILKT recipients(26).The augmented risk of acute rejection upon early or late steroid withdrawal is well documented(27,28). Overall, patients receiving transplant involving ABOi are not allowed to reduce immunosuppression.

### History of ABOi Transplantation and current outcomes

ABOi kidney transplantation has been considered a contraindication based on the adverse experiences from early transplant era(29–31). In 1974, transplantation of A2 renal allografts to O recipients with standard immunosuppression showed a partial success(9). Upon identification of this low antigenicity of A2 blood group, this strategy was soon adopted by multiple groups. Nelson et al. reported a 10-year experience with 50 A2 incompatible transplantations in 1998 with 1-month and 2-year graft survival rates of 94% and 94%, respectively(32).

Slapak et al. reported the first A1 incompatible kidney transplantation with selective immunoabsorption or plasmapheresis pretreatment in 1984 with overall 1-year graft survival rate of 87% (13/16)(33). Alexandre et al. from Belgium reported successful A1 incompatible kidney transplantation after using splenectomy and plasmapheresis for desensitization(14). Since then many countries adopted ABOi transplantation with advancements in immunomodulation and immunosuppression.

Successful substitution of splenectomy using rituximab, a chimeric anti-CD20 antibody, to suppress anti-blood group antibody production was first reported by Tyden and group from Sweden depicting excellent short-term outcomes for ABOi kidney transplantation(34). Later Studies at Johns Hopkins, Mayo Clinic and Japanese teams also reported that excellent short-term outcomes for ABOi transplantation were achieved with rituximab, hence agreeing on a consensus that splenectomy is no longer required for desensitization in ABOi kidney transplantation(35–37).

With increased number of successful ABOi transplants, the attempts were made to reduce costs and desensitization

associated complications (25,36). Barnett et al. adopted a individually tailored desensitization strategy for ABOi. The desensitization was escalated with rising antibody titers, which showed similar allograft and patient survival rates at 1 and 3 years or in the ABMR rates highlighting the place for personalized therapy (38).

ABOi kidney transplantation outcomes have significantly improved over the years. Graft survival and patients' survival is comparable with ABO-compatible kidney transplant(39–42). Additionally, several studies show even a less incidence of chronic ABMR and better renal function in patients with ABOi kidney transplant compared to ABO-compatible living transplant(20,43).

### **Controversies and Challenges in ABOi transplantation**

#### **Accommodation**

Following ABOi transplant upon exposure to a low ABO antibody titre, the allograft develops ability to resist complement-mediated damage. This phenomenon is known as accommodation where no evidence of clinical rejection occurs in the presence of circulating ABO antibodies (44,45). There will be C4d deposition in kidney biopsy suggesting ongoing complement activity yet it's not considered as a marker of ABMR in ABOi transplantation in contrary to HLAi transplantation. The pathogenesis of the accommodation is believed to be due to low titer of low affinity antibodies, with blockage of complement activation, leading endothelial cells to develop an acquired resistance to antibody damage(46,47). Accommodation is also responsible for kidney protection over a long period of time.

#### **Antibody mediated rejection**

ABMR is the leading cause of graft loss in ABOi transplantations which usually occurs early post transplant(48). The risk for ABMR is related to the isoagglutinin level at transplantation and to the presence of anti-HLA antibodies(49). The incidence of ABMR ranges between 10% and 30%(50). Lo et al, in his meta-analysis demonstrated an acute rejection rate of 32.9%, most of which were ABMR(51).

#### **Isoagglutinin quantification**

The isoagglutinin titer is vital to decide on the immunosuppression and more importantly the apheresis technique to be used. The best available method is flow cytometry. However, the less expensive methods such as tube and gel techniques for ABO antibody titration are also frequently used (52,53). Most centers aim an antibody titer of 1:8 before transplantation(54). Nonetheless, it has been depicted that both the antibody basal titer before

desensitization and the post-transplantation titer have a low predictive value for ABMR(28).

#### **Post-operative antibody monitoring**

There is contradictory evidence for post operative antibody monitoring and therapeutic plasma exchange avoiding ABMR. Tobian et al. from Johns Hopkins reported that the incidence of ABMR was markedly higher in recipients with high post-transplant titers for the anti-blood group antibody of more than 1:64(55). In contrary, Ishida et al. from Japan described that (56) postoperative anti-blood group antibody rebound was not associated with the incidence of acute rejection therefore not recommending plasma exchange (57).

#### **Infection**

There is conflicting evidence regarding infectious risk post kidney transplantation. It's probably due to varying immunosuppression in different centers. Habicht et al. reported higher frequency of viral infection such as cytomegalo virus, Herpes simplex virus, varicella zoster and polyoma virus to be higher in ABOi transplants(58). Shariff et al. reported higher incidence of BK virus nephropathy among ABOi compared to HLAi recipients(59). Lentine et al. reported that ABOi is associated with higher risk of pneumonia, urinary tract infection and wound infections(60).

#### **Malignancy**

Hall et al. reported that ABOi recipients carry no higher cancer risk matched ABO compatible controls(61). The same was seen in a similar large scale study involving 1,420 ABOi recipients(22).

#### **Bleeding risk**

An increased risk of early post-operative bleeding was observed in several studies(60,62). This was postulated to be due to clotting factor removal during apheresis. Confirming this assumption, Weerd et al. showed a significant correlation between the number of pre-transplant apheresis treatments and the peri- and post-transplant bleeding risk(63).

#### **Future perspectives**

Multiple novel strategies have been proposed to overcome immunological barriers of ABOi transplantation. A novel ex-vivo therapy, endo-beta-galactosidase is proposed to reduce blood group antigens in the allograft kidney(64). Another method is to utilize a monoclonal anti-A or B antibody Fab fragment or neutralizing antibody with an ABO blood group trisaccharide carbohydrate epitope to interference with the binding of anti-A/B antibodies to blood group antigens (65,66). There is novel evidence emerging for usage

anticomplement antibody, Eculizumab in ABOi transplant. It is a monoclonal antibody against C5, which prevents complement mediated injury upon binding of antibodies to allograft endothelium(67,68).

Nonetheless, it is crucial to be attentive regarding the risks related to the augmented cumulative immunosuppression used in ABOi kidney transplant. Better comprehension of immunologic mechanisms of anti-A/B immune responses and ABOi graft tolerance will provide the basis for evolving new and safer desensitization strategies.

Paired kidney exchange transplantation is a great alternative to ABOi transplantation. It needs less immunosuppression hence lower infective complications. Paired exchange effectively increases donor pool as well as reduces the waiting times on maintenance haemodialysis(69).

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## Understanding HLA, non HLA, DSA and PRA: Transplant Essentials.

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### Introduction

Transplantation of cells, tissues or organs reinstates physiological function and prolongs life being superior to any other alternative treatment. Immune compatibility between the donor organ and recipient is the major barrier for a successful transplant. Incompatibility can result in allograft rejection which can be T cell or antibody mediated. The Human Leucocyte Antigens (HLA), with genes located on chromosome 6 in humans are pivotal in immune recognition and hence allograft rejection.

In the last 50 years there have been major advancements in HLA antigen and antibody recognition assays leading to changes in modern practice. Hence, this review outlines the concepts of HLA antigens, antibodies, DSA (donor specific antibodies) and PRA (panel reactive antibodies) along with the progression and utilization of HLA antibody detection assays in the current transplantation era.

### What is HLA?


The Major Histocompatibility Complex (MHC) is the group of genes found in higher vertebrates that encode the cell surface molecules responsible for both antigen presentation and immunological identity. The human MHC is known as the HLA complex. Due to the huge variation exhibited by the HLA genes, HLA tend to vary between individuals and the response against them is instrumental in rejecting grafts expressing non-self HLA antigens. There are two broad classifications of HLA molecules known as class I (A,B,C) and II (DP,DQ,DR). Class I molecules are present on all nucleated cells, while class II are found expressed constitutively on antigen presenting cells such as B cells, macrophages, dendritic cells and Langerhans cells.

### What are HLA antibodies?

Antibodies against the above mentioned HLA antigens are known as anti-HLA antibodies. In relation to organ transplantation antibodies can be pre-formed or de-novo.

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HLA antibodies occur due to a sensitization event like pregnancy, blood transfusion or a previous transplant. The objective of screening transplant recipients for HLA antibodies prior to transplantation is to detect pre-existing anti-HLA antibodies, define their specificity (which HLA antigens they react against), and determine their relative strength.

### What are Donor Specific Antibodies (DSA)?

DSA are HLA antibodies directed against the HLA antigens expressed by the donor. Presence of HLA-DSA in a recipient is detrimental to the transplant outcome. Preformed DSA can cause early rejection, such as hyperacute rejection, accelerated antibody mediated acute rejection and graft loss. Further, de novo HLA DSA developed after transplant are associated with late acute antibody-mediated rejection, chronic antibody-mediated rejection, and transplant glomerulopathy. Nonetheless, "benign" DSAs exist that may not be clinically associated with ABMR or graft failure.

### HLA antibody detection

Since the introduction of the complement dependent cytotoxicity (CDC) technique as the initial crossmatch methodology between recipient and donor pairs, novel, more sensitive and reproducible assays have been introduced. Below we describe the assays used in HLA antibody detection.

#### 1. Complement-Dependent Cytotoxicity

Upon introduction of this test for crossmatching by Terasaki in 1964, it quickly became established as a crucial and non-negotiable pre-transplant test predicting hyperacute rejection, with a negative result enabling renal transplantation to proceed.

This test consists of incubating patient's serum with potential donor lymphocytes separated from peripheral blood or spleen with subsequent addition of rabbit serum as a source of complement. If recipient serum contains HLA-DSA, they will bind to antigens on lymphocytes resulting in cell lysis via the classical complement pathway. The percentage of dead cells can then be scored via two-colour fluorescence microscopy.

CDC is less expensive and effectively avoids hyperacute rejection upon transplantation. However, it lacks sensitivity compared to novel techniques for detecting HLA-DSA. Furthermore, viability of donor cells is vital for accurate CDC assay. However, optimal viability may not be achievable in case of deceased donors. As well as clinically relevant IgG antibodies, the test detects IgM, auto antibodies and non-HLA antibodies where corresponding antigens are expressed on donor cells. Due to these inherent disadvantages and its general lack of sensitivity to identify lower levels of HLA-DSA, CDC has gradually been replaced by novel assays.

Modifications were made to the assay to enhance the specificity by using 1,4-dithiothreitol (DTT), which breaks down IgM, although this can also result in some loss of IgG antibody. Addition of antihuman globulin (IgG) to enhance DSA binding, lengthening of incubation time and extra wash steps to remove anti-complement factors, which may give false negatives, can also be employed to increase sensitivity.

## 2. Flow cytometry

Garavoy et al introduced the flow cytometry crossmatch (FCXM) into modern clinical practice. During this test, donor cells are incubated with recipient serum followed by addition of a fluorescent -labeled second anti-human IgG immunoglobulin which fixes to recipient's antibodies bound to donor cells. Subsequently, the test is read on a flow cytometer with the degree of positivity being expressed as a channel shift.

FCXM is a more sensitive than CDC for detecting HLA-DSA. Further, FCXM detected antibodies have shown a predictive value regarding post-transplant rejection and graft loss. Positive FCXM with negative CDC is seen in approximately 15% of primary and 30% of second transplants correlated with a higher incidence of early graft loss (<3 months), rejection and poorer 1-year allograft survival for both primary, and second transplants.

The significance of a positive FCXM result with a negative CDC could be due to presence of low-level HLA-DSA, presence of non-complement fixing antibodies or presence of low level non-HLA antibodies. To confirm the presence and specificity of HLA antibodies a solid phase assay like Luminex testing is often used. Many studies show that, if no HLA-DSA is detected using Luminex, then a positive FCXM has no impact on allograft survival.

One important limitation in FCXM based crossmatching is that there is considerable inter-laboratory variability in methods and cut off values making results between

laboratories discordant.

With the introduction of solid phase assays, particularly single antigen bead (SAB) technology which detects low levels of HLA antibodies, FCXM is used in many centers to assist clinical decision making. For example, in the presence of a weak HLA-DSA detected by SAB, the decision to proceed transplant may be influenced by the FCXM result, depending on the degree of immunological risk warranted for a particular patient.

## 3. Solid Phase Antibody Detection Assays

### 3.1. Enzyme-Linked Immunosorbent Assay (ELISA)

In this assay, HLA antigens are immobilized in the wells of microtiter trays. Recipient serum is added followed by addition of an enzyme attached anti IgG antibody and a chromogenic substrate. Presence of HLA antibodies will result in a color change of the wells.

The ELISA technique is more sensitive than CDC or FCXM in detecting HLA antibodies. ELISA identifies HLA-specific antibodies and further differentiates between anti-HLA class I and II antibodies. Moreover, it allows retrospective crossmatch using frozen sample, especially in deceased donations.

The inability to differentiate between CB and non-CB antibodies is a potential shortcoming of this assay. Although, this technique was utilized effectively for detecting pre and post-transplantation antibodies, currently its mostly superseded by the SAB technology.

### 3.2. Luminex Bead Technology

In the late 1990s, a new solid phase assay using fluorescent labeled bead technology began to be introduced, transforming HLA antibody testing. Currently available commercial kits (One Lambda, Immucor) consist of beads impregnated with different ratios of two fluorochromes generating a unique signal for each set of beads. Depending on the kits used, beads have either a single or several types of HLA molecules attached.

In order to perform this bead based testing, firstly the recipient's serum is incubated with the beads. In case of presence of HLA antibodies, the serum will react with the bead expressing the corresponding HLA molecule. Upon washing of excess serum, the incubation of beads is done with a secondary antibody, usually a phycoerythrin-labeled anti-human IgG. Then, a Luminex fluorocytometer with dual laser beams is employed to identify either presence of HLA

antibody (positive/negative for HLA class I and II) if using 'screening' kits or to give the HLA specificity and a measure of the antibody level in the sample, if using single antigen bead kits. The degree of fluorescence is stated as mean fluorescence intensity (MFI), which is normalized based on the degree of fluorescence perceived with an antibody negative serum and beads with no HLA molecules attached.

The definitive Luminex assay utilizes SAB technology where beads bound with single HLA molecules are produced by recombinant technology which enable characterization of a patient's HLA antibody profile in a few hours. This technology is the most sensitive means of detecting HLA antibodies and currently regarded mandatory for the pre-transplant testing of sensitized patients.

In 2008, Billen et al. introduced beads for donor-specific cross-matching using Luminex assay. Yet, to date, the published literature doesn't support the Luminex cross match as a stand-alone method for organ allocation.

#### **Interpretation challenges of Luminex SAB**

Although, Luminex SAB is considered as the gold standard HLA antibody detection assay, there are many inherent challenges in interpretation of results.

First of all, with SAB assays being very sensitive, this raises problems in interpretation in the context of a negative FCXM. The clinical relevance of these HLA antibodies in rejection in organ transplantation is debated. Secondly, there is no consensus on "cut off" value for MFI positivity. Hence, it is obligatory for each laboratory to establish their own MFI "cut off" levels based on the experience gained over time. Thirdly, SAB express denatured molecules in addition to native molecules as a result of the assay manufacturing process which may confuse assay interpretation. The denatured molecules could express cryptic epitopes which are not typically accessed by antibody molecules. Antibodies reacting with these exposed cryptic epitopes on denatured molecules have been spotted in individuals inclusive of non-sensitized males. It has been proven that the antibodies to denatured epitopes have no clinical effect in renal or heart transplantation. Fourthly, the difficulty in differentiation of complement versus non complement binding antibodies raises a question of clinical relevance. In 2010, Chin and colleagues modified the assay enabling detection of complement binding antibodies eliminating this obstacle. However, the clinical utility of using complement modified Luminex assays is still debated, with many studies indicating that the ability of HLA antibodies to give a positive signal in these assays is often just a function of the strength of the antibody.

Finally, another technical challenge of using SAB is the prozone effect. Here, a diluted serum gives a greater MFI than the undiluted serum, signifying an inhibitory effect which is removed by dilution. Inhibitory effect of IgM or complement component, C3 is postulated to be the cause. This can be overcome by heating serum or adding ethylenediaminetetraacetic acid (EDTA) to destroy complement or DTT to eliminate IgM.

#### **The Virtual Cross-match**

The utilization of highly specific and sensitive methods like Luminex SAB allows the characterization of a complete picture of the HLA immunization status of an individual patient. The "virtual crossmatch" (VXM) was hence established to predict the outcomes of a final crossmatch. Bielman et al. depicted that there was 86% concordance between the VXM and FCXM. VXM predicts the potential cross match negative donors, based on the HLA antibody profile of a patient and donor typing information. This methodology was successfully incorporated in to the kidney transplantation allowing transplants to proceed quickly with saving costs for testing and staffing.

The use of a VXM approach reduces laboratory workload, improves allocation efficiency and increases the rate of transplantation for sensitized patients and helps facilitate national paired exchange programs.

The potential challenge for VXM is the novel appearance of a DSA after a sensitization event, which was absent at the time of data gathering for VXM. Further, potential donors can be mistakenly excluded because of VXM false positives due to weak HLA DSA. In contrast, false negative VXMs can occur as solid-phase assays cannot necessarily accommodate all potential HLA antigens.

#### **PRA and c PRA**

PRA was used historically as a measure of the broadness of sensitization in transplant recipients. Traditionally, the recipient sera were tested against cells from a panel of HLA-typed donors using CDC. PRA was calculated as the percentage of positive reactions in the cell panel. A high PRA suggested that a candidate will immunologically react against a large section of the population. Bray et al. illustrated that PRA levels per se were not associated with allograft survival as long as HLA-DSA was not present which has subsequently been shown in other studies.

Furthermore, the introduction of SAB lead to a more precise definition of HLA antibody specificities in a recipient,



making the use of PRA obsolete and leading to development of a new formula known as calculated PRA (cPRA), or in the UK, calculated Reaction frequency (cRF)

The cRF is calculated as the proportion of donors which will be incompatible with the listed unacceptable HLA antigens of a prospective recipient. This is calculated against a pool of 10 000 actual deceased donors, and thereby gives an estimation of being allocated a suitable donor. The use of cPRA or cRF is a standardized method of estimating the possibility of the recipient having DSA via measuring the difference between antibody specificities and the prevalence of HLA alleles in a target population. cPRA reflects the broadness of sensitization more precisely and has a lower center-to-center variability matched with PRA.

As precise determination of DSA can be done, SAB technology has also revolutionized pre-transplantation risk assessment. This questions the utilization of broadness of sensitization hence, cPRA to predict the occurrence of rejection and allograft loss in an era with modern DSA assignment. Despite this ambiguity, cPRA is still widely used when deciding the choice of immunosuppression. But the new evidence suggests that cPRA values per se do not confer an immunological risk in absence of DSA. Whereas, HLA-DSA can be regarded as the most significant immunological pre-transplantation risk factor, the cPRA is mainly utilized to heighten access of sensitized patients to appropriate organs allocation systems.

### **Non HLA antibodies**

Even though the main targets of allograft immune response are the highly polymorphic HLA antigens, the contribution of non-HLA antigens is also implicated as evidenced by the development of ABMR in HLA matched organ transplantation between HLA matched siblings. Non-HLA antibodies can be autoantibodies or alloantibodies. Human Neutrophil antibodies (HNA), MHC Class I-related Chain A (MICA) Antibodies, Anti-endothelial cell antibodies (AECA), Antibodies Against Glomerular Basement Membrane, Peroxisomal Trans-2-enoyl-CoA Reductase (PECR), Phospholipase A2 Receptor (Pla2R) are known non-HLA antibodies.

Most of the well-studied non-HLA target antigens are not expressed on lymphocytes, hence are not detected on traditional lymphocyte (CDC/FCXM) crossmatch. Therefore, positive crossmatches in the absence of Luminex detected HLA-DSA may not be immunologically relevant and should not preclude a transplant.

Although there are numerous studies demonstrating role of non HLA antibodies in rejection and adverse graft outcomes, currently there is no consensus in the transplant community as to which patients to screen, the frequency of testing, when and how to desensitize or treat in situations of Non-HLA antibody identification. Further research is required to define these in future.

### **Conclusion**

The field of transplant immunology has advanced immensely over the past few decades. The presence of development of de novo DSA plays a central role in causation of graft loss hence characterization and quantification is of foremost importance. Multidisciplinary approach with the involvement of transplant physician, surgeon and clinical immunologist should be employed in careful Interpretation of different immunological tools and deciding on immunological risk of proceeding with transplantation.

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## The lateral stability of the knee, A review of the clinical Anatomy of the Popliteal hiatus and its clinical pathologies

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**Keywords:** Popliteal hiatus, Knee

### Abstract


As a modified hinge joint, the knee joint facilitates the erect posture and greater mobilization of the human body. Varus-valgus angulation, external-internal rotation, and anterior-posterior stability are primarily maintained by the tibial bony eminences, menisci, and the congruencies of the femoral and tibial articular surfaces. The primary restrainer for the valgus angulation is the medial collateral ligament (MCL). The primary restrainer for varus angulation is the lateral collateral ligament (LCL). Even though the LCL is the principal lateral stabilizer for the knee, it is supported by the surrounding ligaments, muscles, and tendons. Non-uniformity in the nomenclature of these structures and complexity in the anatomical arrangements lead to complexity of understanding and clinical interpretation. The popliteus is a very small muscle but a unique muscle to the knee with specialized functions. It is highly vulnerable to injuries during trauma with posterior lateral corner injuries of the knee. Proper history of the injury and clinical assessment will help in a proper diagnosis. However acute pain in the knee may interfere with a proper clinical diagnosis. During total knee arthroplasty, special care should be taken to minimize the iatrogenic popliteal ligament injuries during bone cuts and lateral release in soft tissue gap balancing.

### Introduction

The knee joint is a modified hinge joint that helps to achieve an erect posture and greater mobilization of the human. It is a complex structure with a femorotibial joint and a patella femoral joint. It is a synovial hinge joint and the largest joint in the human body. The femorotibial joint bears the body weight. It helps the mobilization with the greatest range of movements with internal, and external rotation (in the transverse plane), flexion, extension (in the sagittal planes), and varus, valgus stress (in the frontal plane). The patella-femoral joint gives the frictionless transfer of quadriceps contraction to leverage the tibia. Stress forces applied to the

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knee joint are very high during the function of the knee. The stability of the knee depends on the integrity of the knee's bony articulation, ligamentous, and muscular structures.

The ligamentous stability is maintained by the extra-articular medial collateral ligament (MCL), Lateral collateral ligament (LCL), and ilio tibial band with fibrous joint capsule. The intra-articular anterior cruciate ligament (ACL), and posterior cruciate ligament (PCL) had given the anterior-posterior motion stability. The two bony articulations in the joint with stabilizing ligaments facilitated the weight loading, and weight transmission of the knee joint in addition to flexion and extension. The knee joint acts as a static and dynamic stabilizer for running, walking, and jumping. Both medial and lateral stability of the knee is maintained by static and dynamic stabilizers. The knee joint stability in rotational planes, coronal and sagittal planes is primarily maintained by the tibial bony eminences, collateral ligaments, cruciate ligaments, menisci, and the congruencies of the femoral and tibial articular surfaces. The primary restrainer for the valgus angulation is the medial collateral ligament (MCL). MCL acts as the inner side stabilizer of the knee and attaches to the posterior superior aspect of the medial femoral epicondyle. And distally it gives two attachments to the medial surface of the proximal tibia. The LCL is the lateral side stabilizer of the knee, and it is a cord-like structure that proximally attaches to the lateral epicondyle of the femur, behind the popliteus groove. LCL distally attaches 1cm below the head of the fibula in the lateral aspect. Anterior and posterior cruciate ligaments and semilunar-shaped menisci further enhance medial and lateral stabilization of the knee.

The human knee is a complex joint with considerably different properties in the sagittal, frontal, and trans-verse planes.

The medial meniscus is larger with an open curve that encloses the horns of the lateral meniscus. The lateral meniscus is attached to the intercondylar area of the tibia immediately in front and behind the tibial eminence.

A complex arrangement of ligaments, tendons, and muscles maintains the lateral stability of the knee. The complexity of



structures and variances in nomenclature resulted in difficulty in understanding the functional anatomy of the lateral ligament stability. The purpose of this paper is to clarify the complexities of understanding the lateral stability of the knee.

In the anterolateral aspect, the principal joint stabilizers are the joint capsule and the iliotibial tract. The posterior lateral stabilization is a complex structural arrangement. In addition to the LCL, biceps femoris, popliteal tendon, arcuate ligament complex, popliteal menisci femoral ligament (PMFL) and popliteal fibular ligaments (PFL) act as postero lateral stabilizers. The anterior lateral part of the capsule is reinforced by the superior and inferior patella retinacular fibers and the vastus lateralis muscle and extends back to the lateral collateral ligaments and distally to the tibial condyles.

The posterior lateral corner stability has been explained as three-layer stability. Layer -I is the outer layer, which forms anteriorly by the iliotibial band and posteriorly by the bicep femoris tendon. Layer -II is the middle layer, formed by the patellofemoral ligament, lateral patellar retinaculum, and lateral collateral ligament. Layer -III is the inner layer formed by the popliteal muscle and tendon, arcuate ligament, fabella, fabella, fabella fibular complex, and lateral joint capsule.

The posterior capsular attachment to the lateral tibial condyle is interrupted by the emerging popliteal tendon (Figure 1). The oblique popliteal tendon which arises as an elongation of the semimembranosus tendon merges with the posterior capsule and strengthens the posterior capsule (Figure 1). A “Y-shape” condensed collagen band called an “arcuate” ligament starts from the fibular head and courses over the popliteus to merge into the posterior capsule. Its medial extension fibers join the fibers of the oblique popliteal ligament (Figure 1). During its course over the popliteus tendon, get firmly attach to the musculotendinous junction of the popliteus muscle. The arcuate ligament complex helps to stabilize the knee posteriorly. They primarily maintain the rotational stability and coronal and sagittal stability of the knee. Internally the

capsule is attached to the lateral meniscal outer ring and merging with the coronary ligaments and attaching to the lateral tibial condyles.

Popliteal fibular ligament is a well dominant anatomical structure in the lateral knee (Figure 1). It is the one of the main stabilizers of the lateral knee. It stabilizes the posterior translation of the knee, varus angulation and external rotation of the knee (Torzilli, Maynard and Warren, 1995). It originates just proximal to the myotendinous junction of the popliteus and inserts to the medial styloid of the fibular head and merges into the lateral collateral ligament attachment. Morphological appearance can vary as single, double or Y-shaped as describe by (K. Natsis et al., 2012). Posterior limb of the PFL inserted proximally in to the anterior PMF and stabilizes the lateral meniscus (Stäubli and Birrer, 1990).

Higgins 1894 first describes the popliteal muscle and its attachment to the lateral meniscus. In 1950 Last did an analytical description of the popliteal muscle and its tendinous fibers attachment to the head of the fibula and lateral meniscus. The popliteus muscle is a posterior lateral corner stabilizer of the knee. It is a unique feature of this muscle its origin is distal to its insertion. In the literature there are controversies about the origin and insertion of the popliteus muscle. The popliteus muscle originates from the posterior surface of the tibia, above the soleal line, and below the tibial condyles (Figure 1). It moves obliquely towards the lateral condyle of the femur with the formation of a cord-like tendon and attaches just below the lateral epicondyle of the femur known as popliteal sulcus. Popliteus tendon is located in the posterior lateral corner of the knee. It inserts onto the floor of the popliteal fossa and forms it (Figure 1). During its course it's give attachments to the posterior horn of lateral meniscus (the popliteal meniscal ligament) and popliteal fibular ligament to the fibula (Figure 2) Popliteus tendon traverses an extra synovial, extraarticular course. But popliteal tendon attachment at femoral condylar is intra capsular. It is partly intra synovial at the level of lateral meniscus.

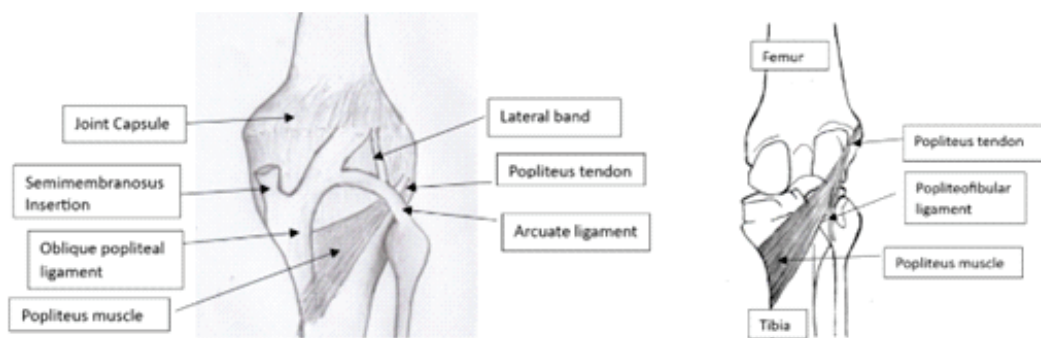


Figure 1

Bio mechanically popliteal complex act as a static and dynamic stabilizer of the knee. When the foot is on the ground and knee is fixed in full extension, the popliteus acts as an external rotator of the femur and as a lateral retractor of the lateral meniscus. But when the foot is off ground and knee is flexed it acts as an internal rotator of tibia. Popliteus action on lateral meniscus during knee flexion, prevents its impingement during knee movements.

In phylogenetic origin, among the lower vertebrate's popliteus attached to the fibular head. And fibula articulates with the distal femur with a fibular meniscus. In the phylogenetic development due to the upright posture in humans, fibula head migrates distally and fibula meniscus evolved as popliteal tendon .

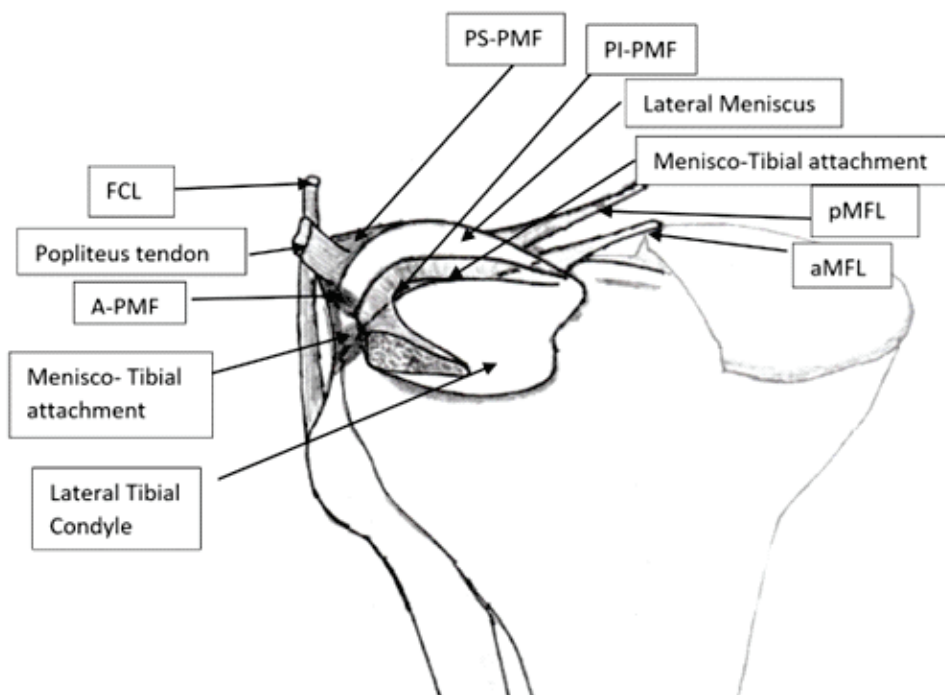
Musculotendinous kinesthetic studies of the popliteus muscle shows, popliteus has an inherent ability of stiffness regulation during the tonic and phasic activation of the muscle. It has shown human popliteus has 50% slow oxidative, 15% fast oxidative glycolytic and 35% fast glycolytic muscle fibers . This muscle fiber distribution supports the tonic regulatory posture control and sudden phasic position changes in function during locomotion.

***Significance of popliteal hiatus in the lateral posterior corner stability of the knee.***

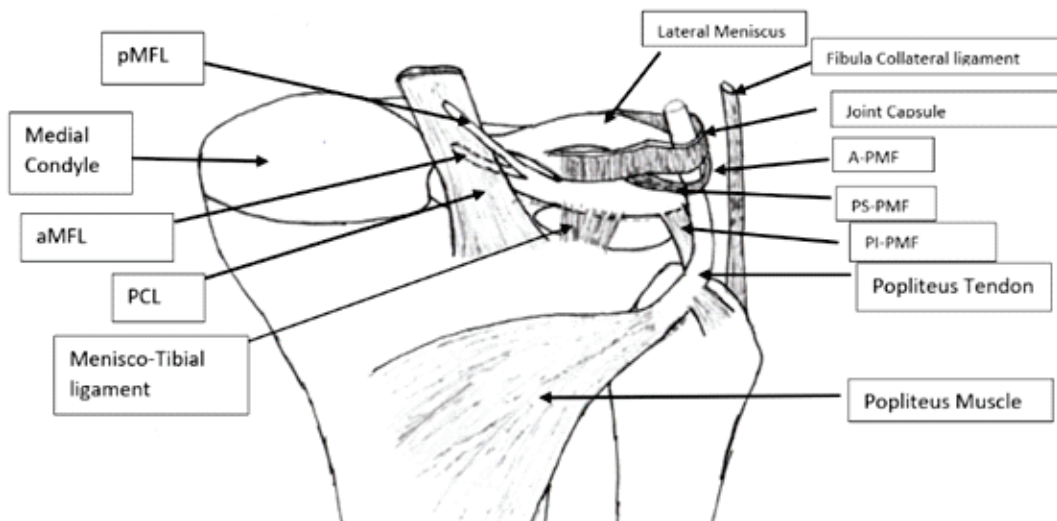
The complex structure of the popliteal hiatus is formed by the combination of the popliteal tendon, joint capsule, lateral meniscus, and the fascicles of the lateral meniscus (Figure 3). The popliteal tendon traverses through the popliteal hiatus before the popliteal tendon starts its intraarticular course .

Posterior corner stability of the lateral knee is integrated with the consistency of the integrity of structures of the popliteal hiatus, joint capsule and lateral meniscus. Cohn in his study described, popliteal hiatus as a constant structure of the lateral meniscus at the mid coronal plane. He schematically described popliteomeniscal fascicles (PMF) including the superior fascicle, inferior fascicles and the borders of the popliteal hiatus. He elaborated the significance of popliteal hiatal structures to the lateral stability of the knee . During the flexion and extension movements of the knee, popliteomeniscal fascicles (PMF-Figure 3 and 4) control the motion of lateral meniscus.

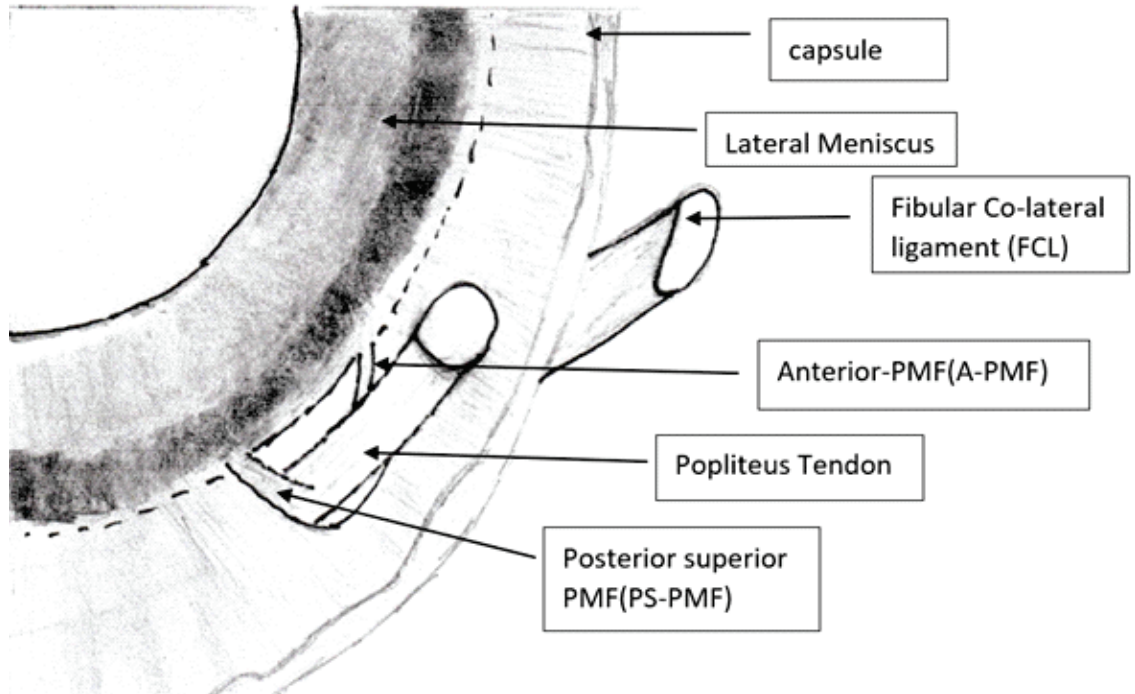
Popliteal hiatus has been described as an “aperture” in the continuation of the attachment of joint capsule to the lateral meniscus (Figure 4). There are three fibro fascicular connections which form peripheral string like attachment from popliteal tendon to the lateral meniscus outer border.



**Figure 2:** Illustrate the anterior superior view of the posterior lateral corner of the knee. Anterior popliteomeniscal fascicles (A-PMF), Posterior superior popliteomeniscal fascicles (PS-PMF), Posterior inferior popliteomeniscal fascicles (PI-PMF), Posterior cruciate ligament (PCL), Anterior Menisiofemoral ligament (aMFL), Posterior Menisiofemoral Ligament (pMFL) and Fibular Collateral ligament (FCL)



**Figure 3:** Illustrate the posterior superior view of the posterior lateral corner of the knee. Anterior popliteomeniscal fascicles (A-PMF), Posterior superior popliteomeniscal fascicles (PS-PMF), Posterior inferior popliteomeniscal fascicles (PI-PMF), Posterior cruciate ligament (PCL), Anterior Menisiofemoral ligament (aMFL), Posterior Menisiofemoral Ligament (pMFL).



**Figure 4.** Illustrate the superior view of the popliteal hiatus.

They are called popliteomeniscal fascicles (PMF) (Figure 2 and 4). It provides stability to the non-tethered part of the lateral meniscus and gives a static and dynamic stability to the lateral meniscus and popliteus tendon. The nomenclature of this fascicles are not very constant among the authors.

Popliteal hiatus is a more or less a transverse conical shape hiatus. This hiatus is formed with a superior aperture and an inferior aperture. The apex of the conical hiatus is placed anteriorly, and base is placed posteriorly. Anterior border of the superior aperture is formed by the anterior PMF (A-PMF). Posterior corner of the superior aperture formed by the by the posterior-superior PMF(PS-PMF), postero inferior corner is formed by the posterior- inferior PMF(PI-PMF), laterally by the joint capsule and medially by the superior lateral border of the lateral meniscus (Figure 4). Because of its oblique course, ill-defined anatomy, nomenclature of A-PMF is inconstant. Some authors named it as anterior inferior PMF due to the course of inferior medial portion of the popliteus tendon to the outer surface of the lateral meniscus. Because of its superior attachment to the lateral meniscus some authors named it as anterior superior PMF. However, the anterior PMF is the most appropriate name because it is anteriorly and superiorly placed structure. And it is the only anterior attachment of the popliteus hiatus. It is reasonable to name as anterior PMF(A-PMF) rather than as the antero superior PMF or antero inferior PMF. The nomenclature of the PMFs at postero superior corner of the hiatus as postero-superior PMF(PS-PMF) and the posterior inferior corner as posterior- inferior PMF(PI-PMF) are constant in the literature.

The lateral meniscal inferior outer margin attaches to the outer border of tibial plateau with lateral meniscotibial ligament (LMTL) (Figure 3). Posteriorly it continues as the posterior meniscotibial ligament (PMTL) and intersected with the posterior cruciate ligament (PCL) insertion posteriorly. LMTL start at the mid meniscal point of the inferior border and extend anteriorly. The LMTL is also refereed as the “coronary ligament”. Even though they are called ligaments, there are basically a mere thickening of connective tissues. There is no proper ligamentous attachment between the superior and inferior borders of the meniscus with joint capsule except at popliteal hiatus as described above. Inferior aperture of the popliteal hiatus is supported anteriorly by the lateral meniscotibial ligament (LMTL), posteriorly by the posterior meniscotibial ligament (PMTL), medially margin by the inferior border of lateral meniscus and laterally margin by the popliteus tendon (Figure 3).

Popliteal hiatus is connected distally with tip of fibula by popliteofibular (PFL) ligament and meniscofibular fascicle (MFF) (Figure 2). PFL is a constant and identifiable ligament, but MFF is an inconsistent in presence and merely a thickening of fibrous tissue.

Anterior popliteomeniscal fascicles (A-PMF)( Figure 3 and 4) originates from the inferior medial portion of popliteus tendon and inserts to the outer surface of the lateral meniscus anteriorly just anterior to mid coronal plane of the lateral meniscus. It follows the oblique course of the popliteus tendon from postero- inferior to antero superior. Inferiorly it merges with meniscofibular fascicle (MFF) and attaches to the fibular head.

Posterior superior popliteomeniscal fascicles (PS-PMF) (Figure 3 and 4), originates from the posterior surface of the popliteal tendon and attaches to the posterior superior border of the lateral meniscus near the posterior horn. With the margins of posterior superior PMF(PS-PMF) and postero inferior PMF(PI-PMF), it forms the popliteal recess.

Posterior inferior popliteomeniscal fascicles (PI-PMF) ( Figure 2 and 3) connects the deep medial part of popliteal tendon to the inferior outer margin of lateral meniscus. Some authors suggest it merely replaced the coronary ligament and given an indirect attachment to the meniscus for stability .

Meniscofibular fascicle (MFF) is basically a capsular thickening of the postero lateral corner of the knee. It is a tape like fibrous band extending from the inferior outer border of the lateral meniscus , directed distal and posteriorly towards the head of the fibula . On its path it crosses popliteal tendon obliquely blend anteriorly with anterior PMF and LMTL. It appears to be an interposition of soft tissue layer in between the outer border of tibial plateau and medial surface of popliteal tendon. Its functional component is not very clear but seems to be a protector of lateral meniscus on extreme extension of the knee and reinforce the posterior lateral part of the lateral coronary ligament.

#### ***Clinical significance of Popliteal hiatus and Its structures:***

Various injury mechanisms of force loading on lateral compartment of the knee can result in the destabilization of popliteal hiatal complex.

Iatrogenic injuries during surgical procedures can damage the popliteal hiatal complex structures.

High energy traumatic injuries can destabilize the posterior lateral corner of the knee. Knee injuries following sports and



motorcycle riding are highly suggestive for posterior lateral corner damage. Especially the varus angulation force, extensive external rotation of tibia, posterior translation of tibia. Especially the forced hyperextension or flexion when tibia is externally rotated can result for popliteal hiatal complex injuries. These injuries can be isolated or combination injuries of popliteal tendon, popliteomeniscal fascicles (PMF), popliteofibular ligament, meniscofemoral ligament. Or it could be a combination of multiple tissue injuries and resulting complex posterior corner injuries. Isolated injuries are rare and most of the time it is a complex injury in the posterior lateral corner of the knee.

Most of the posterior lateral corner injuries are associated with other complex injuries of the knee eg compete knee dislocations, anterolateral knee injuries and fractures in the distal femur or proximal tibia.

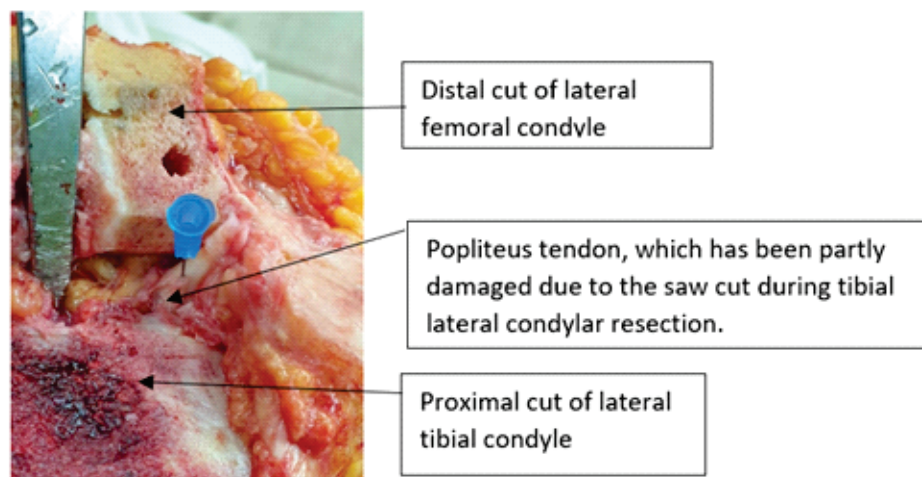
The correct clinical and radiological diagnosis of posterior lateral corner injuries are challenging. However, Magnetic resonance (MR) imaging has an important role in identification of posterior lateral corner injuries. Sometimes posterior lateral corner ligaments may not well be elaborated on MR images. Interpretation of MR images with normal anatomy and history of the mechanism is helpful to achieve a reasonable diagnosis. Inadequate treatment due to poor diagnosis can lead to lateral knee instability and chronic pain. Ignored or misdiagnosed posterior lateral corner injuries can lead for early degenerative changes in the knee.

Isolated popliteal tendon injuries are rare. Most of the time injuries happens at musculotendinous junction of the popliteus and extra-articular. Popliteal tendon tears can be intra-articular at the level of popliteal hiatus. Popliteus injuries are noted in 60%-68% of patients who had been

operated for posterior lateral corner injuries . Complete tear of the popliteus is usually associated with multiple ligament injuries of the knee. Anterior cruciate ligament (ACL) and posterior cruciate ligament (PCL) injuries can mask the diagnosis of posterior lateral corner instability. Popliteal tendon tears are graded to 3 grades, stretching injuries are graded as Grade -I, incomplete tears of the tendon are considered as Grade-II tears. Grade -III are complete tears of the tendon. Grade-II and Grade-III are due to high energy trauma. Most of the popliteus tendon tears are extraarticular which involves the musculotendon junction or the muscle. Intraarticular tears are also being reported . Micro- trauma and repetitive stress of the tendon can result in tendinopathy of the popliteal tendon and clinically experiencing chronic pain around the posterior lateral corner of the knee. High energy twisting injuries of the knee can result for the avulsion of the femoral attachment with or without a separated bony fragment. The presence of the sesamoid bone “cyamella” may be able to be visualized with X-ray. It should be taken into consideration on interpretation of radiological investigations for posterior lateral knee pain.

In 2012 H.K. Shin et al postulated the popliteomeniscal fascicles (PMF) isolated tears can result in pain in the lateral compartment of knee, locking symptoms of the knee, giving way symptoms and osteochondral lesions of the posterior lateral condyles of the femur (Shin et al., 2012).

Tendinosis and tendinopathies of the popliteus can be seen due to the repetitive stress on the popliteus. Long standing downhill walking and running can load a repetitive stress on the popliteus muscle and tendon . On the downhill weight bearing phase, popliteus continuously act to prevent lateral rotation of femur and forward displacement of femur. Patient will present with posterior lateral knee pain and local



**Figure 5:** Illustrate an iatrogenic injury to popliteus tendon.

tenderness. MR images will show oedema of the tendon and fluid surrounding the tendon.

### ***Role of Popliteal hiatus in total knee arthroplasty.***

In total knee joint arthroplasty, during the bone cuts of the distal femur condyle and proximal tibial condyle, popliteus can get damage. During the resection of lateral meniscus, if the surgeon is not careful on resection, popliteus tendon can get damage (Figure 5). If the lateral release of the knee to be done surgeons have to be extremely care full to prevent popliteal tendon injuries. Popliteus tendon damage will result in lateral instability of the knee.

### ***Surgical tips for prevention of popliteal injuries during Total Knee arthroplasty.***

Before performing the distal femoral bone cuts, by sliding the resection check guide (angel wing) in the cutting slot of the universal cutting block of the femur will give an idea about the bone cut level and the insertion of popliteus tendon at lateral femoral epicondyle. It will help to prevent iatrogenic popliteal injuries.

When using the oscillating saw blade to prepare the proximal tibia, over penetration of saw blade to the posterior lateral corner can damage the popliteal tendon. This can be prevented by keeping a metal protector (small Hohmann Retractor) in the posterior lateral corner of the knee.

During the resection of lateral meniscus, by keeping a (2-3) mm lateral meniscus outer margin will protect the popliteal tendon. And this procedure will protect the popliteal hiatus and Popliteomeniscal fascicles (PMF), which are help full in the lateral stability of the knee.

Removal of excess bone cement particles in the posterior lateral corner is very important to reduce post operative knee pain and irritation of popliteal tendon due to bone cement remnants.

In cases of extensive valgus deformities of the knee, there will be a requirement for lateral release of knee ligaments to balance the soft tissue gap. In such cases complete removal of lateral meniscus, release of Popliteomeniscal fascicles (PMF) and release of the posterior-lateral joint capsule will be adequate to achieve the desirable soft tissue balance. The ultimate option is the control release of the popliteal tendon by pie-crusting with 18G needle rather than sacrificing it.

Osteoarthritic loose bodies and degenerative substances can pass through the popliteal hiatus to the popliteal bursae and

result irritative symptoms or mechanical symptoms. Posterior lateral corner pain without a history of injury is suggestive for the diagnosis.

Other pathological conditions like synovial chondromatosis, synovial proliferations can continue to the popliteal peritendon area through the popliteal hiatus and to the popliteal bursae. It can trigger posterior lateral corner knee pain.

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## Radiological investigations in nephrolithiasis and: a narrative review.

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**Keywords:** X-ray kidney-ureter-bladder (X-ray KUB), intravenous urogram (IVU), ultrasonography (USG), non-contrast computed tomography of kidney-ureter-bladder (CT-KUB), magnetic resonance urogram (MRU)

### Abstract

Nephrolithiasis and ureterolithiasis are increasing in incidence and prevalence worldwide, which are significant clinical challenges in management. Radiological assessments are vital in early diagnosis and effective management to decrease morbidity and healthcare costs. This narrative review explores the role of various radiological investigations in nephrolithiasis and ureterolithiasis, focusing on their clinical implications and limitations. Plain X-ray of the kidney, ureter, and bladder (X-ray KUB) is a widely available, relatively inexpensive modality with limited sensitivity, mainly for smaller stones. However, it is most beneficial when assessing follow-up patients diagnosed with renal or ureteric calculi, but it is less effective in acute ureteric colic. Intravenous Urogram/Intravenous Pyelography (IVU/IVP) is an obsolete investigation and has largely been replaced by newer modalities due to numerous drawbacks. Ultrasonography (USG) is a widely available, relatively low-cost, non-invasive radiological modality without ionising radiation, considered first-line for children and pregnant patients. However, its sensitivity and specificity are traditionally lower than computed tomography and largely depend on the operator and patient factors. Computed tomography kidney, ureter, and bladder (CT-KUB) is the gold standard for diagnosing urolithiasis. It offers high sensitivity, specificity, and the ability to calculate the exact size and stone composition, but it comes with substantial radiation exposure. However, low-dose and ultralow-dose CT (LDCT-KUB) protocols reduce radiation to the patient significantly, compromising image clarity. Magnetic Resonance Urography (MRU) is a second-line investigation in obstructive uropathy, particularly in pregnancy and children. It provides vital anatomical and functional information without ionising radiation. Urology and radiology

professionals should collaborate to identify individualised and optimal radiological investigations, considering the risks and benefits associated with each modality.

### Introduction

Urinary calculi are a significant global health concern with a gradual incline in incidence and prevalence during the last few decades [1]. Clinical diagnosis of urinary calculi is achievable when symptomatic with classic clinical features. Large intrarenal calculi may be symptomatic and patients may seek medical advice due to haematuria or renal colic. Most ureteral stones are also symptomatic, leading to quick medical attention and diagnosis. However, the clinical suspicion is confirmed by imaging. Still, about 10% of urinary calculi are asymptomatic and found incidentally in imaging, probably due to the frequent use of high-resolution imaging modalities [1]. It must be noted that both symptomatic and asymptomatic calculi have a substantial potential to cause chronic kidney disease (CKD) and end-stage renal disease (ESRD). Hence, in addition to the clinical and biochemical clues, early radiological assessments are mandatory in managing urolithiasis to minimise morbidity, mortality, and healthcare budget.


In current clinical practice, many radiological investigations are available to diagnose urolithiasis. The test of choice depends on its cost, availability, relative advantages and disadvantages, and disease burden. [2]. However, the radiological investigation should describe adequate information to narrow down differential diagnoses with minimal hazard to the patient. Besides, the test should be able to monitor the response to treatment. Radiological investigations in urolithiasis include X-ray kidney-ureter-bladder (X-ray KUB), intravenous urogram/intravenous pyelogram (IVU/IVP), ultrasonography (USG), non-contrast computed tomography of kidney-ureter-bladder (CT-KUB), CT intravenous urogram (CT-IVU), and magnetic resonance urogram (MRU). This review will discuss such radiological modalities with their clinical implications.

### *Plain radiograph of the kidney, ureter, and bladder*

Like all other X-rays, plain X-ray KUB uses a single energy

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source to produce electromagnetic radiation to capture images of abdominal organs. The region imaged in the X-ray-KUB includes the area between the upper poles of kidneys to the inferior pubic rami.

Plain X-ray KUB is a readily available, relatively less expensive (~10% of the cost of CT-KUB) and simple radiological investigation. It utilises a significantly low radiation dose to the patient (about 0.5 mSv) compared to the radiation used in CT-KUB, in which the radiation dose is about 10-20 times higher than X-ray KUB [2]. X-ray KUB helps to detect radiopaque calculi in the urinary system. Approximately 80% of renal calculi are radiopaque, while 20% remain invisible in plain radiographs due to the inherent radiolucency of certain stones like uric acid and matrix stones [2]. Therefore, the location and growth of radiopaque calculi are monitored using a plain X-ray during follow-up. Further, X-ray KUB has a specificity of 99.1% in diagnosing urolithiasis [3].

However, X-ray KUB has several downsides. The overall sensitivity of X-ray KUB is about 49.1% in detecting renal calculi, and it has minimal value for diagnosing calculi < 5mm [3]. About 63% of ureteric calculi < 5 mm and 21% of calculi > 5 mm are not visible in plain radiography [3]. This is due to various factors, such as overlying bowel gas, colonic faecal shadows, soft tissues, and osseous structures, which obscure renal or ureteral calculi visualisation. In addition, pelvic venous wall calcification (phleboliths) and calcified lymph nodes are mistakenly detected as ureteric stones, particularly in approximation with the vesicoureteric junction [3]. The plain radiological appearance of phleboliths is traditionally described as rounded opacities with central lucency [3]. As per recent guidelines, the sensitivity and specificity of X-ray KUB are increased when plain radiography is combined with ultrasonography (USG), especially when the stone diameter is > 5mm [3].

#### ***Intravenous Urography/Intravenous Pyelography***

IVP is a minimally invasive investigation to image the urinary tract using serial plain X-rays after intravenous administration of non-ionic contrast media. It offers additional information compared to plain radiographs, including anatomy and pathology visualisation of the pelvicalyceal system, ureter, and bladder. Additionally, it demonstrates the relationship of calculi to each part of the urinary system and provides evidence of the functional status of the kidneys [4]. When performing percutaneous nephrolithotomy (PCNL) to remove complex renal and upper ureteric stones from the upper pole of the kidney, the success rates and possible complications are assessed using Guy's

Stone Score (GSS). Hence, GSS, based on IVP interpretation, is a reliable and simple tool for predicting the outcome, assisting in pre-operative planning, and counselling the patient [5].

However, many disadvantages of IVP have limited its use. One of the traditional concerns is that the use of an intravenous iodinated contrast medium has the potential to cause hypersensitivity (HST) reactions (incidence of mild HST <3%, moderate to severe <0.04%) against the contrast medium [6]. Another limitation of its use is the occurrence of contrast-induced nephropathy (CIN), particularly in pre-existing renal impairment and diabetes [6]. Small intrarenal non-obstructing calculi may not be visualised in IVP films, especially in inadequate bowel preparation and when the gas-filled bowel shadow obstructs the renal area. The IVU inadequately differentiates renal changes due to acute obstruction from residual changes in chronic ureteric obstruction [6]. Moreover, IVU has a moderate radiation dose (effective radiation dose is about 3mSv). Therefore, owing to many limitations, IVP has largely been replaced by newer radiological modalities such as real-time USG, CT, and MRU.

#### ***Ultrasonography***

USG is a commonly used non-invasive radiological modality that does not use ionising radiation. Ultrasound transducers generate and send high-frequency sound waves into the body tissue and then receive the echoes back to generate an image.

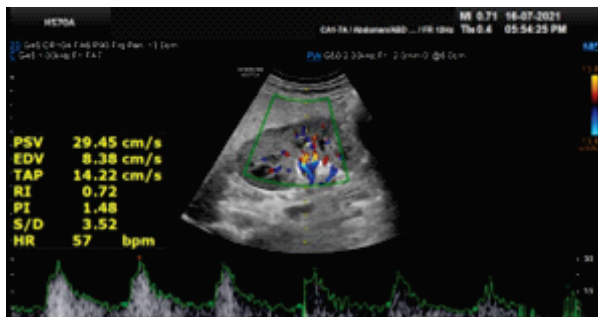
USG is a versatile investigation for diagnosing urolithiasis. Its wide availability, relatively low cost, safe bedside nature, and repeatability, especially in the follow-up of ureteric calculi, make it a valuable test for most urolithiasis cases. Besides, sonography has a significant advantage in detecting extrarenal pathologies that mimic acute urolithiasis. Major such pathologies as acute appendicitis, ectopic pregnancy, ovarian torsion, acute pyelonephritis, haemorrhage into an ovarian cyst, endometriomas, and aortic dissection

The non-ionisation property of USG makes it the first-line investigation in urolithiasis in children and pregnancy [6]. Doppler USG has a relative advantage in differentiating the obstructive ureteric system from the non-obstructive system due to ureteric calculi, especially with a short duration (6-24 hours) of symptoms [7]. Acute unilateral ureteric obstruction is suspected when the intrarenal resistive index (RI) is  $\geq 0.7$ , and the difference in mean RI (Delta RI) between obstructed kidney and non-obstructed contralateral kidney is  $\geq 0.06$ . (RI >7 and <7). Delta RI is more sensitive and specific than RI in acute ureteric obstruction [7]. However, these results can change based on the patient's age, body habitus, current NSAID usage, and comorbidities like diabetes, hypertension,

and heart disease [7]. The absence of ureterovesical jet dynamics in colour Doppler examination in an obstructed ureter is adjunct to greyscale sonography as a secondary finding to improve diagnostic accuracy [6]. (Figure 1) However, a ureteric jet does not entirely rule out the ureteric obstruction because a partial obstruction still shows a colour change with low frequency and velocity [6].

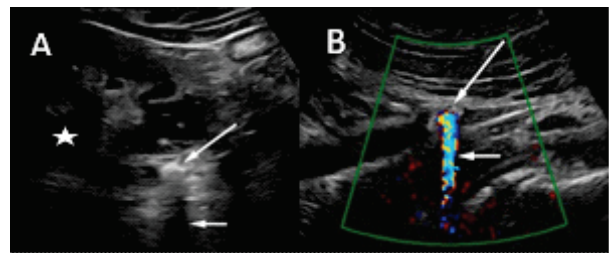
In USG, the posterior acoustic shadow is frequently seen behind the echogenic calculus, and it is an essential secondary sign in doubtful cases of urolithiasis (Figure 2A). When this sign is not visible due to the small size of the calculus and surrounding renal sinus fat, a colour Doppler twinkling artefact (A rapidly changing mixture of red and blue colours behind a strongly reflecting structure in colour Doppler) has shown an excellent secondary sign to locate the calculus (Figure 2B). It has been noted that the overall sensitivity and specificity of twinkling artefacts are 99.6% and 100%, respectively, in colour Doppler [8]. Furthermore, Point-of-care ultrasound (PoCUS) has received significant attention in managing acute urolithiasis in past decades. An emergency care physician performs the PoCUS to assess the degree of hydronephrosis as an indirect sign of suspected renal colic (Figure 3A). This moderately sensitive test significantly reduces the length of stay in an emergency room and medical costs [9]. Further, in PoCUS, ureterovesical calculi are easily detected when the urinary bladder is adequately filled (Figure 3B).

Despite its utility, USG has certain inherited limitations, particularly in detecting urolithiasis. The sensitivity and specificity of USG depend on factors such as ultrasound machine settings, techniques used, patients' body habits, and operator expertise. According to Toru Kanno et al., the sensitivity and specificity in identifying calyceal calculi are



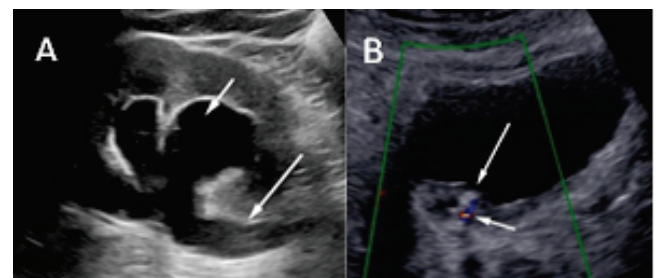
**Figure 1.** A patient with a suspected right-side ureteric calculus presents mild hydronephrosis and proximal hydroureter on ultrasound without a visible obstructing calculus. Duplex ultrasonography reveals the resistive index (RI) to be just above 0.7, indicating suspicion of a ureteric calculus.

78.9% and 83.7%, respectively, whereas for ureteric calculi, the sensitivity is 57.3%, and the specificity is 97.5% [10]. Moreover, mid-ureter calculi may not be readily visible, especially in obese patients, due to overlying bowel shadows and fat pads. The limited visibility of ureteric calculi < 5 mm further hinders accurate diagnoses, mainly due to the partial volume effect and lack of posterior acoustic shadowing [10]. Another drawback of USG is its tendency to overestimate the length of stones, particularly those < 5 mm, which can affect management decisions [10]. Additionally, USG may mistakenly detect vascular or parenchymal calcifications and renal fat as intrarenal calculi, leading to unnecessary interventions [10]. Furthermore, its sensitivity for detecting ureteric calculi in pregnant women is considerably low, ranging from 34% to 69% [11]. However, secondary signs like proximal hydronephrosis, hydroureter, ureteric jet sign, and RI values can improve diagnostic sensitivity. Still,



**Figure 2A:** A patient with right side upper ureteric calculus (long arrow) with posterior acoustic shadowing (short arrow). Note: Mild to moderate hydronephrosis and proximal hydroureter (asterisk)

**Figure 2B:** A patient with right side mid ureteric calculus (long arrow) with twinkling artefact posterior to the calculus (short arrow) in Doppler mode of ultrasound.



**Figure 3A:** A patient with acute left-side loin pain. Emergency ultrasound shows moderate hydronephrosis (short arrow) and proximal hydroureter (long arrow).

**Figure 3B:** A patient with suspected right-side ureteric calculus. Bedside ultrasound shows a calculus at the right ureterovesical junction (long arrow). Note: twinkling artefact posterior to the calculus (short arrow).

differentiating pathological hydroureter from physiological hydroureter may be challenging in the second trimester of pregnancy [11]. It is important to note that the physiological hydroureter may not extend beyond the internal iliac vessels, and the renal pelvic diameter typically does not dilate > 17mm [11]. However, when the initial ultrasound findings are inconclusive in pregnancy, a transvaginal ultrasound scan enhances the stone detection in the distal ureter with a sensitivity of 94% compared to 29 % in transabdominal USG [12].

#### ***Non-contrast computed tomography of the kidney, ureter and bladder.***

Computed tomography (CT) uses a rotating narrow beam X-ray generator to create cross-sectional images of the site of interest from different angles, and results are reformatted into multiple planes using computerised algorithms.

CT of the kidney ureter and bladder (CT-KUB) is performed without introducing intravenous contrast material. It has become the gold standard for assessing renal and ureteric calculi, surpassing other imaging techniques with high sensitivity and specificity of up to 98% and 96-100%, respectively [13]. The introduction of multidetector CT (MDCT) further enhances its capabilities, allowing the rapid detection of stones without requiring an intravenous contrast medium. In addition, The 3-dimensional reconstruction feature assists in precise localisation and size measurement of uroliths. Moreover, CT attenuation values of the stone provide the composition of the stone, which immensely helps the clinician to plan future management. These values, measured in Hounsfield units (HU), fall within specific ranges for different urinary calculi: Calcium oxalate monohydrate/dihydrate and brushite (1700-2800 HU), hydroxyapatite (calcium phosphate) (1200-1600 HU), cystine (600-1100 HU), struvite (600-900 HU), and uric acid (200-450 HU) [14]. (Figure 4A and Figure 4B). However, due to their radiolucent nature, CT-KUB may still face challenges in identifying certain rare calculi, such as protease inhibitor (indinavir)-induced stones and matrix stones [15]. Conventional single-energy CT-KUB has drawbacks in evaluating the density of stones since a substantial proportion of renal calculi contain mixed chemical materials [16]. Therefore, a single energy CT-KUB may not represent the actual density of the calculus. Additionally, density measurements of small stones can be inaccurate due to partial volume effects. DECT-KUB uses two different voltages (140kV and 80-100kV) and two separate detectors to quantify the chemical composition precisely, distinguishing uric acid and non-uric acid proportions in mixed stones [16]. DECT-KUB helps assess the stone site, size, and internal composition to manage urolithiasis. Kambadakone AR et al.



**Figure 4A:** Coronal view of non-contrast CT KUB shows a Staghorn calculus at the left renal pelvis. The density of the calculus is about 1296 HU.

**Figure 4B:** Coronal view of a non-contrast CT KUB shows bilateral ureteric calculi with proximal obstruction. The density of the right ureteric calculus is about 1163 HU, and that of the left ureteric calculus is about 1184 HU.

demonstrated that oral dissolution therapy can treat uric acid stones (< 400HU) while cystine stones (600-1100HU) are best managed with ureteroscopy or PCNL due to their hardness and resistance to shock wave lithotripsy (SWL) [14]. They further explained that non-uric acid, non-cystine stones <1 cm in diameter (500 HU-1000HU) can be treated with SWL or ureteroscopy, whereas large cystine stones (>1cm) with high density (>1000HU) in the lower poles of kidneys are treated with ureteroscopy or PCNL [14]. Therefore, knowing the chemical composition of the stone helps to plan the management option, avoiding unnecessary surgical interventions and treatment failures. Furthermore, CT-KUB is important in planning SWL to measure stone-to-skin distance (SSD). A distance > 10 cm from the centre of the stone to the skin surface indicates a high chance of failure [17]. Prior to PCNL for staghorn calculi removal, evaluating CT-KUB and multidetector computed tomographic urography (CTU) with intravenous contrast material is important to achieve success with minimal procedural complications.

These investigations accurately assess the orientation of the pelvicalyceal system (PCS), the exact location of the stone in the PCS, the position of the kidney, anatomical variations, and the relationship of the kidney to other surrounding organs like the spleen, liver, and colon specially retro-renal colon [18]. In addition, three-dimensional (3-D) coronal reformatted reconstruction and multiplanar assessments are beneficial to guide instruments in interventional procedures [18]. CT-KUB significantly evaluates residual stone fragments after PCNL and SWL [19].



Occasionally, ureteric calculi may not be visible in CT-KUB due to various reasons, such as small size, low density, volume averaging, paucity of retroperitoneal fat, confusion with phleboliths, respiratory movements during image acquisition, or recent passage of the stone [20]. Nevertheless, CT-KUB demonstrates helpful secondary signs to locate a stone, including hydroureter, perinephric fat stranding, tissue rim sign, and renal parenchymal density differences compared to the normal contralateral kidney [20, 21]. Hydroureter is more reliable than hydronephrosis because the latter may be misinterpreted with most of the normal renal pelvis or in an extrarenal baggy pelvis [20,21]. Perinephric fat stranding is thread-like soft tissue densities in surrounding perinephric fatty tissues. This results from inflammation or increased lymphatic pressure secondary to back pressure effects of the ureteric stones [21]. The tissue rim sign represents ureteral wall inflammation and oedema at the level of calculus obstruction. This sign distinguishes calculus from a phlebolith in the pelvis [21]. The renal parenchymal density difference is a critical parameter for ureteric obstruction as it is a measurement-based indicator. Parenchymal density is measured in the upper, middle, and lower segments of each obstructed kidney. A 5 HU or more density difference is an important secondary sign to predict the obstructed urinary system [22].

CT-KUB has been identified as a gold-stranded test to differentiate renal calculi from various differential diagnoses. Up to one-third of patients with acute flank pain, initially suspected of having ureteric calculi, may have alternative diagnoses that significantly impact patient management [22, 23]. These alternative diagnoses include gynaecological conditions (ectopic pregnancy, haemorrhagic ovarian cysts), gastrointestinal and hepatobiliary conditions (acute appendicitis, diverticulitis, cholecystitis, pancreatitis), and vascular conditions (ruptured aneurysms) [23]. Furthermore, CT-KUB can diagnose unrelated incidental findings in the urinary system, such as neoplastic conditions and congenital abnormalities/anatomical variants.

### **Disadvantages of CT**

Despite its immense merits, CT-KUB has a few drawbacks. Radiation exposure is a significant limitation. One significant limitation is the high radiation exposure, ranging from 5 to 10 mSv, which is over three times the radiation dose of IVP [14]. Young patients with urinary stones who undergo repeat CT scans are at risk of accumulating high cumulative radiation doses, which may lead to radiation-induced neoplasms [24]. When the lifetime cumulative radiation dose is more than 100 mSv, it is associated with a 1 in 200 risk of radiation-induced neoplasms [25].

Therefore, to overcome these drawbacks, researchers have proposed various low-dose CT (LDCT) protocols to address these issues, reducing radiation dose by 75% to 90% without compromising diagnostic accuracy [26]. These protocols use techniques like reduced tube voltage (kV) and tube current(mA), while advancements in CT hardware and software enable high diagnostic performance with lower effective radiation doses (1-4 mSv) [27]. (Figure 5A and Figure 5B) LDCT and even ultra-LDCT demonstrate a sensitivity and specificity of 94.1% and 100.0%, respectively, in detecting urinary calculi [27]. It can also detect alternative diagnoses with sensitivity and specificity of around 92% and 96%, respectively [27]. Furthermore, CT-KUB does not provide much information about the functional state of the kidneys. The cost and availability of the test have limited its free usage in certain hospitals.

To minimise unnecessary radiation doses to patients, paramedical teams, physicists, and radiologists should discuss introducing low-dose and ultra-low-dose CT protocols during CT imaging. Additionally, medical teams should consider alternative diagnostic methods and justification before requesting a CT to minimise unnecessary radiation exposure.

### **Magnetic resonance urography**

Magnetic resonance imaging (MRI) is a non-ionic imaging modality to acquire comprehensive soft tissue images using a powerful magnetic field, radio waves and a complex computer system. Magnetic resonance urography (MRU) is a modified MRI technique that provides a detailed assessment of the urinary system, including the collecting system, renal parenchyma, and surrounding structures, with or without IV contrast. Two different methods of MRU studies are available. Heavily T2-weighted turbo spin-echo sequences visualise static water in the urinary system for image contrast without intravenous contrast material. (Figure 6A) On the other hand, gadolinium contrast material is injected



**Figure 5A:** Standard dose axial view of CT-KUB (120 kVp and effective dose of 12mSv)

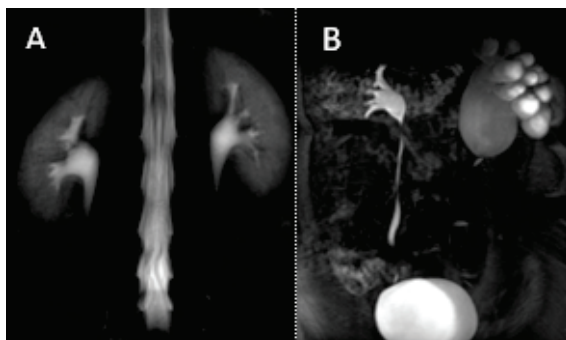
**Figure 5B:** Low dose axial CT-KUB (100 kVp and effective dose of 2 mSv). Despite high image noise, small calculus (<3mm) is still visible. (arrow)



intravenously, and renal excretion of Gadolinium-containing urine is imaged using fast T1-weighted gradient-echo sequences, mimicking IVU [28]. (Figure 6B)

MRU is considered a second-line investigation in obstructive uropathy, particularly in pregnancy and children [28]. It has many advantages over other imaging modalities, such as demonstrating the 3D anatomy of renal parenchyma, pelvicalyceal system, ureters, and bladder without ionising radiation. Semins et al. described that the MRU has a sensitivity of 84 % and a specificity of 100 % to detect calculus using a half-Fourier acquisition single-shot turbo spin-echo (HASTE) MRU with a 3-T MR scanner [29]. Additionally, MRU can differentiate physiological urinary tract dilatation in pregnancy from hydronephrosis caused by urolithiasis [30]. The HASTE technique is used in pregnancy during the second and third trimesters without intravenous Gadolinium as a complementary test to sonography. Additionally, MRI can provide functional information on the kidney in obstructive uropathy for non-pregnant subjects, mainly when chemical exchange saturation transfer (CEST) MRI is utilised with an intravenous contrast medium [30].

A few drawbacks of MRU are poor sensitivity in detecting non-obstructing and small obstructing calculi, relatively high cost, not being freely available in most centres, and time-consuming. Furthermore, it is not recommended during the first trimester of pregnancy.



**Figure 6A:** Magnetic resonance urogram (MRU) to demonstrate the renal pelvi-calyceal system. Static water in the urinary system used as image contrast without intravenous contrast material.

**Figure 6B:** A male patient with incidental left hydronephrosis. Excretory phase of contrast MRU demonstrates dilated left renal pelvis with markedly narrowed pelviureteric junction. Case courtesy of Roberto Schubert, Radiopaedia.org,

## Conclusion

Early diagnosis of urinary calculi and understanding the nature of urinary tract obstruction are crucial in managing urolithiasis. Different radiological modalities play a vital and sometimes complementary role in this regard, with their selection depending on clinical features, availability, and patient factors. X-ray KUB is commonly utilised in follow-up patient care in many centres despite its low sensitivity. However, the value of IVP is currently limited, and many contemporary modalities have replaced it. Ultrasonography is the first-line imaging tool in paediatrics, non-obese patients, and pregnancy. However, non-contrast CT-KUB is considered the gold standard technique for diagnosing urolithiasis despite radiation being a significant drawback. To address this concern, many centres have modified conventional CT protocols, especially for follow-up examinations, using LDCT and ultra-LDCT protocols, which have shown promising results. Being a recent non-ionic investigation, MRU plays a vital role in pregnancy and children. Urology and radiology professionals should collaborate to identify individualised and optimal radiological investigations for each patient, carefully considering the risks and benefits associated with each modality.

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## We report you decide.

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Before the era of medical imaging, surgical decisions were primarily based on subjective assessments. When the diagnosis was unclear, the 'open and see' approach was commonly adopted in the past. With the advent of medical imaging, decisions began to be supported by objective evidence, enabling focused and planned surgical interventions. Imaging has now become an integral part of modern-day surgical practice, with crucial decisions often relying heavily on imaging results. However, it is important to note that although imaging provides fixed visual data, its interpretation and reporting are subject to human involvement. Therefore, human errors in interpreting imaging results are a reality. Incorrect decisions based on misinterpretations can lead to disastrous outcomes for the patient.

### Errors in reporting

Errors in radiology reporting can be categorized into two types: cognitive errors and observational errors. Cognitive errors occur when the reporter fails to comprehend the observation, whereas observational errors arise when the radiologist overlooks an abnormality. Real-time reporting errors have been noted to occur in only 5%, whereas retrospective assessments have documented rates as high as 30% (2). In a study comparing specialist neuro-radiologists and general radiologists revealed a 13% incidence of major errors and 21% incidence of minor errors in generalists (1). Additionally, communication failures may occur during the production of the printed report. Several factors may contribute to these errors, including equipment malfunction or misuse, workload implications, and cognitive biases.

It is interesting to note that the performance of trained human activities does not follow a Gaussian distribution. Rather, performance is expected to adhere to an initial standard, with some individuals exhibiting exceptional performance, referred to as "Pareto distribution" (2) (Figure 1). However, whether training can completely overcome the natural

distribution seen in Gaussian distribution to perfect Pareto distribution is questionable. There will always be individuals on the left of the standard.

### Is it an error?

When a clinician makes an error in a court of law, they are liable to be charged with negligence or malpractice. Visual comprehension of an object and its interpretation is a highly subjective human quality. Hence, whether an incorrect interpretation can be considered an error remains a matter of debate (3). However clinicians are held legally and morally accountable and responsible for the decisions, whereas the accountability of the imaging report is less direct, often adopting the perspective of "we report, you decide." Relying solely on a report in clinical decision-making can potentially lead to detrimental consequences.

### We are accountable

Clinicians bear the ultimate accountability for patient outcomes. We must exercise caution before blindly relying on a report, recognizing that it should not be considered the definitive conclusion. At times imaging modality may have its limitations in sensitivity. Hence employing clinical judgment, questioning, and engaging in discussions with radiologists while providing necessary information, further tests and seeking a second opinion when necessary, are essential practices. It is imperative that clinicians develop the skill to understand imaging themselves and make own judgments,

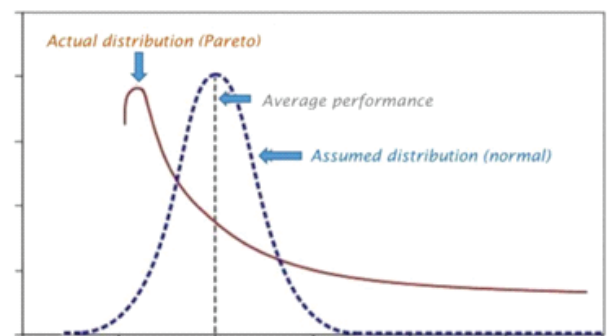



Figure 1.

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applying the knowledge of what to look in an image study. Providing feedback on outcomes allows the reporter to engage in reflection and improvement. Further clinical services have progressed significantly in the domain of sub-specialization. It is equally important to recognize areas of sub-specialization and foster parallel development in radiology. In conclusion, radiology has improved the outcomes and how we practice medicine. However, its application should be judicious.

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## Leiomyosarcoma of the Inferior Vena Cava and its tributaries, a case series and review of the literature.

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### Introduction

Leiomyosarcoma of the Inferior Vena Cava (IVC) (1) and its tributaries are rare accounting for only 0.5% of all adult sarcomas. However, it is the commonest primary tumour of the IVC. Due to its rarity, large series describing such cases are lacking. The diagnosis is often delayed and incorrect diagnoses are made due to its nonspecific nature of the presentation. This report describes a series of three patients who presented with nonspecific abdominal symptoms and diagnosed to have primary leiomyosarcoma of the IVC.



**Figure 1.** Leiomyosarcoma of the Inferior Vena Cava in the retro hepatic segment

### Case 1

A 51-year-old female presented with nonspecific epigastric pain. An ultrasound scan of the abdomen revealed a hypo echoic, well defined, lobular mass postero lateral to the suprarenal IVC (Level II) (fig1). The lesion was invading the IVC. Further evaluation with contrast enhanced Computed Tomographic scan (CT scan) was done. The CT scan revealed a well-defined 3x3.5 cm mass arising in relation to the right adrenal gland. The mass was invading the postero- lateral surface of the IVC. There was no invasion into the adjacent structures.

A surgical exploration and excision of the lump was planned. During surgery the tumour was found to be in the suprarenal area posterior to the IVC, and was well defined. It was attached to the posterior wall of the IVC and was invading into it. Tumour was mobilized from the surrounding tissues. It was excised with the cuff of the IVC. The IVC was directly repaired with 4/0 polypropylene sutures.


Histology revealed a leiomyosarcoma (with malignant spindle cells, Mitotic count of 8 per10 High Power Field (HPF).The tumour was positive for smooth muscle actin (SMA) and desmin, indicating smooth muscle cell origin but it was negative for S 100 thus excluding a malignant nerve sheath tumour). The tumour was reaching the resection margin at one area. However a positron emission tomography (PET) CT scan done after 2 months did not show any residual tumour. After 308 days of follow up, the patient is well with no clinical and imaging evidence of recurrence.

### Case 2

A 52-year-old female presented with nonspecific abdominal pain. Imaging revealed a well-defined 6x4 cm dumb-bell shaped tumour invading the posterior surface of the infra renal IVC (level I). Patient underwent tumour resection with a cuff of the IVC. Histology revealed a leiomyosarcoma (tumour with atypical spindle cells with a mitotic activity of 3 to 4 per 10 HPF. The tumour was positive for SMA and desmin; it was negative for S 100). The patient was referred to the oncologist for further management. After 1230 days of follow up, the patient is well with no clinical and imaging evidence of recurrence.

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### Case 3

A 66-year-old female presented with nonspecific abdominal pain. Imaging revealed left sided retroperitoneal mass near the left kidney. A radical nephrectomy was performed. At surgery it was found that the tumour was arising from the left renal vein. Histology revealed a differentiated (pleomorphic) leiomyosarcoma extending into the renal vein. 3 months later the patient returned with nonspecific abdominal pain. A CT scan of the chest and abdomen was done. It revealed multiple metastases in the lungs and the liver. The patient was referred for palliative care.

### Summary of results

In the above described cases, all were females (100%). The mean age at presentation was 56.3 years (51 - 66). All presented with nonspecific abdominal pain. The locations of the tumours were in the suprarenal IVC (n-1), infrarenal IVC (n-1) and the left renal vein (n-1). The mean tumour size at presentation was 4.75 cm (3.5 - 6.0). All patients underwent surgical resection in our series. Both IVC tumours were removed with a cuff of IVC. A direct repair of the IVC was done. One patient who had a primary leiomyosarcoma of the left renal vein (Case 3) underwent radical nephrectomy. At a mean follow up of 542.7 days (90 - 1230), one patient was diagnosed to have metastases in the lungs and liver two months after the surgery and died in 90 days. The other two patients are well with no clinical or imaging evidence of recurrence.

### Discussion and conclusions

Leiomyosarcomas accounts for only 7% of all soft tissue sarcomas. Primary leiomyosarcoma of the IVC are rarer accounting for only 0.5% of all adult sarcomas. However, it is the commonest primary malignant tumour of the IVC.

It originates from the smooth muscle cells of the media of the vein. As it grows, it extends both into the vessel (intravascular part – i.e. tumour thrombus) and to the outside of the vein wall (extravascular). This extravascular part of the tumour could be misdiagnosed as tumours arising from the surrounding tissues e.g. Adrenal tumour. On microscopy the tumour consist of bundles of spindle cells. The mitotic activity differs depending on the tumour grade. On immunohistochemical staining, the leiomyosarcoma is positive for desmin, vimentin and SMA.

Since the time it was first reported in 1871, only about 400 cases are reported until now. It commonly affects females (female to male ratio of 4:1). It affects 50 to 60 year age group as the cases reported in this series.

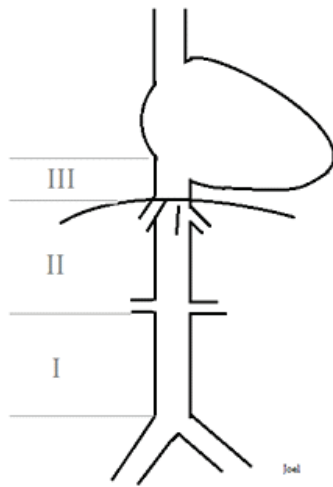
Patients commonly present with nonspecific symptoms, while specific symptoms occur according to the location of the tumour and the completeness of the IVC occlusion i.e. Lower limb oedema, hepatic venous outflow obstruction (HVOO), etc. Due to the nonspecific nature of its presentation, the diagnosis is often missed or delayed.

Contrast enhanced CT scan of the abdomen is the imaging of choice. If supra hepatic extension (level III) is detected or suspected, a trans-esophageal echocardiography (TEE) should be performed to confirm the atrial extension, to detect the invasion into cardiac muscle and to plan the intervention. Intra operative TEE helps to monitor the tumour during surgery i.e. for migration, embolisation, etc.

For the purpose of description, the proximal extent of the leiomyosarcoma of the IVC is classified into 3 levels. The level I extends from the beginning of the IVC (the confluence of the common iliac veins) to the lower border of the renal

**Table 01-** Summary of the cases

Case	Age	Gender	Presentation	Vein	Imaging finding	Surgery	Histology	Follow up
1	51	F	Nonspecific abdominal pain	Supra-renal IVC	Hypo dense, well defined, 3.0 x 3.5cm, lobulated mass	Excision with IVC cuff, direct IVC repair	Leiomyosarcoma - Malignant spindle cells, mitotic count of 8 /10 HPF. Positive for SMA and desmin, negative for S 100	Well at 1230 days
2	52	F	Nonspecific abdominal pain	Infra-renal IVC	6.0 x4.0cm dumb-bell shaped tumour	Excision with IVC cuff, direct IVC repair	Leiomyosarcoma - A typical spindle cells, mitotic activity 3 to 4/10 HPF. Positive for SMA and desmin, negative for S 100	Well at 308 days
3	66	F	Nonspecific abdominal pain	Left renal vein		Radical nephrectomy	Differentiated (pleomorphic) leiomyosarcoma	Developed metastases in lungs and liver, died in 90 days



**Figure 2.** Level of the IVC involvement (according to Kieffer E, et.al.)

veins. The level II extends from the renal veins level to the lower border of the hepatic veins. The level III is above the level of the hepatic veins(1).

Surgical excision is done with curative intent. Options depend on the extent of the tumour, the presence of IVC occlusion and the IVC wall infiltration by the tumour. For the level I tumours the proximal and distal control of the infrarenal IVC is adequate. During excision of the tumours in the suprarenal and retro hepatic area (level II), the main sources of bleeding are the renal veins and the hepatics veins. Therefore control of the infra renal IVC, renal veins, supra hepatic IVC and the hepatic hilar vessels are needed (to achieve total hepatic vascular exclusion). For the tumours extending above the hepatic venous level (Level III), sternotomy and cardiopulmonary bypass is needed.

For the intra luminal tumours which are not adherent to the wall of the IVC, the tumours can be excised with a cuff of the IVC. And for tumours which are attached to the wall of the IVC the tumour and the segment of the IVC need to be excised.

The options for IVC reconstruction include; direct repair, repair with a patch, excision of IVC and reconstruction with synthetic graft. Excision of the IVC and ligation of the ends is done if the IVC is already occluded with adequate collateral flow. However before the IVC is ligated, the distal stump pressure is measured and if the stump pressure is more than 30mmHg (1), reconstruction of the IVC is recommended to avoid venous hypertension i.e. In the lower limbs.

The consensus on adjuvant chemo and radiotherapy is lacking due to the rarity of the IVC leiomyosarcoma (8). Although in the past adjuvant chemotherapy and the radiotherapy was considered as ineffective (9), there are recent reports to suggest that there is a survival benefit with these modalities (10).

Overall the leiomyosarcoma of IVC is associated with poor prognosis with a 5 and 10 year survival of 31.4% and 7.4% (11).

Therefore leiomyosarcoma of the IVC and its tributaries should be considered as a differential diagnosis, especially if the tumour lies near the IVC or it extends into the IVC. Well planned surgical excision with vascular control provides the best chance of survival.

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## Recurrent Ureteric Obstruction due to an intraluminal hematoma following live donor renal transplant

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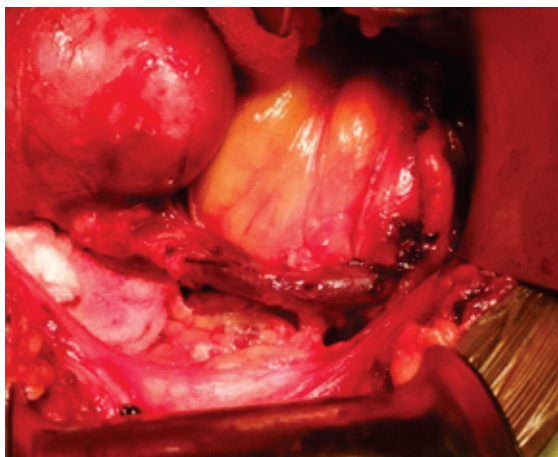
**Keywords:** Renal Transplant, End Stage Renal Disease, Ureteric Hematoma, Post Kidney Transplant Complications

### Introduction

Kidney transplant is a well-established, definitive treatment modality for end stage renal disease (ESRD). Ureteric obstruction is a cause of anuria following kidney transplant and it accounts for 1-5% of cases with graft dysfunction [1]. Commonest cause of ureteric obstruction following kidney transplant is the development of ischemic stricture and other rare causes include lymphocele, extrinsic compression or intraluminal blood clot [1], [2]. We report a rare case of recurrent ureteric obstruction due to an intraluminal hematoma despite surgical evacuation and ureteric stenting, and its treatment course.

### Description

This is a 56-year-old male with ESRD diagnosed for three years and had been on regular hemodialysis for two and half years. His was also known to have hypertension, ischemic heart disease (single vessel disease) managed with dual antiplatelet therapy, peripheral vascular disease (Fontaine I)



**Figure 1.** This picture shows completely occluded ureteric outflow due to an organized hematoma

and poorly controlled diabetes mellitus. After thorough assessment and multidisciplinary meeting, he was prepared for live donor kidney transplant with a compatible donor, who was a 53-year-old lady without any medical co morbidities.

The left kidney of the donor was harvested uneventfully. The recipient's iliac arteries were exposed through retroperitoneal approach with a Rutherford Morrison incision, and it was decided to anastomose the renal graft to right internal iliac artery due to severe atherosclerosis disease of external iliac artery. The kidney was reperfused after 2 hours of cold ischemic time and the allograft had a good thrill at the hilum. Uretero – vesical anastomosis was done using 5/0 PDS and a 6Fr ureteric stent was placed with a use of guide-wire. Total surgical time was four hours and the blood loss was approximately 300ml.


Post reperfusion urine output was low despite adequate fluid resuscitation, Frusemide infusions, and catheter readjustment. Post-transplant renal graft duplex revealed normal blood flow in renal artery and vein. However there was moderate hydronephrosis with high resistive index of 0.8 throughout the kidney.

The decision was made to re- explore the renal graft after urgent multidisciplinary meeting in post-operative day 1. Exploration revealed well perfused renal graft with good thrill at renal hilum. However, the ureter was found to be obstructed by an organized hematoma despite the ureteric stent being in situ.

Ureteric hematoma was evacuated and ureter and bladder were flushed with heparinized saline. Urine flow was noted immediately following hematoma evacuation. Patients' urine output improved dramatically despite mild to moderate hematuria until 7 hours following the reopening, where he became acutely anuric for 3 consecutive hours. Renal duplex revealed moderate hydronephrosis and high resistive index of 0.9 throughout the kidney. Urgent team meeting comprising nephrology, urology, interventional radiology, and transplant surgical team was done, and it was decided to proceed with percutaneous nephrostomy insertion for decompression of the renal graft. Percutaneous nephrostomy was inserted 10 hours

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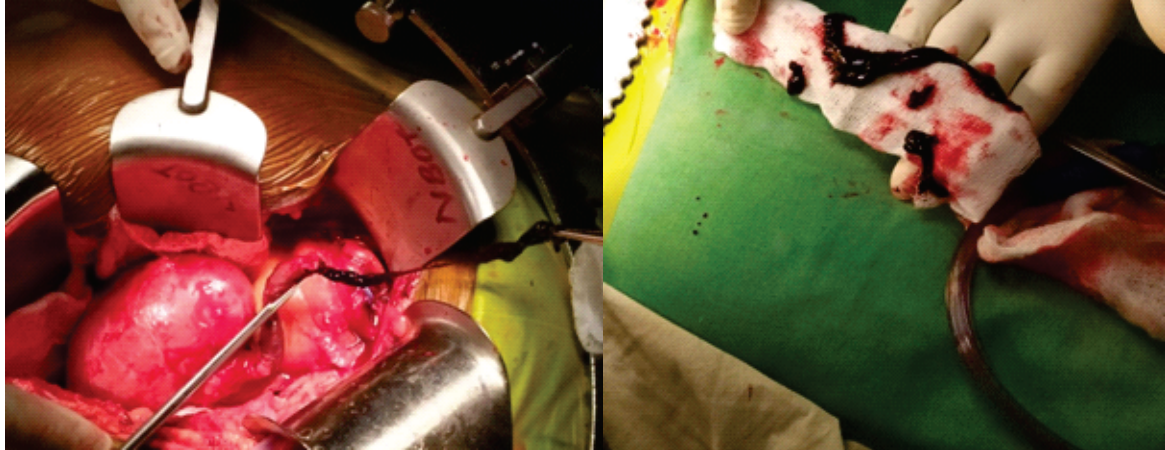
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**Figure 2 and 3 :** Open retrieval of the hematoma

post re-exploration and urine output was detected through nephrostomy.

Post nephrostomy urine output was normal and the rest of recovery of the patient has been uneventful. He became polyuric from 4th day of post nephrostomy and increased in subsequent days. Patient received intensive care for 8 days and transferred to surgical ward for further care.

Patient's serum creatinine level dropped from 347 micromole/l to 124 micromole/l. The nephrostomy tube was removed as there was good urine output through the urinary catheter by day 8th day following the procedure. Patient was discharged on day 10 following the transplant.

### **Discussion**

Ureteric obstruction in a transplanted kidney could be early or late. Early obstruction is often related to ureteric ischemia, a narrow anti-reflux tunnel at the uretero-vesical anastomosis or external compression by a lymphocele or hematoma, whereas late obstruction is usually due to ischemic fibrosis or vasculitis.

Obstruction of ureter in a transplanted kidney due to recurrent blood clots is an extremely rare event (2-10%), and it should be identified and treated promptly in order to preserve the renal graft function. This complication can pose a risk to graft, and, occasionally, to patients' survival [1].

According to literature search using PubMed data base, urethral obstruction, urine leak and vesico-ureteric reflux were the most common complications following renal transplant, and traditionally these patients were managed with open surgical techniques which carried higher patient morbidity.

However, with the recent advances in medicine, percutaneous / endoscopic approaches like percutaneous nephrostomy has been used to successful to treat ureteric obstruction following renal transplant [3].

Another study conducted on 582 post renal transplant patients between 1986 to 1993 in New York, states that modern endourological procedures have replaced the open reconstructive surgeries in the majority of the patients with urethral obstruction [4].

In our patient, the possible risk factor for recurrent ureteric obstruction due to a hematoma includes placement of ureteric stent with the use of blind uphill guidewire which could have injured the renal pelvis.

Once ureteric obstruction is suspected or confirmed immediate steps should be taken to minimize the kidney damage. Our patient once diagnosed initially was reopened to relieve the ureteric obstruction. However, ureteric obstruction was progressive despite the stent in situ. Following a multi-disciplinary team meeting, we had opted

for percutaneous nephrostomy as a temporary measure. Following this the patient's urine output significantly improved and the creatinine level dropped.

Percutaneous nephrostomy poses a risk of bleeding, sepsis and injury to the surrounding viscera; however, these can be mitigated by ensuring adequate platelets, hemoglobin and the coagulation time. While the sepsis can be managed with intravenous antibiotics. However, it being a minimally invasive procedure the benefits of percutaneous nephrostomy outweigh the risks.

Following percutaneous nephrostomy tube insertion, our patient made a faster recovery in transplanted kidney function. Nephrostomy tube was draining urine while the intrinsic Urokinase (in the urine) would dissolve intraureteric thrombi [5].

### Conclusion

Great caution must be administered during insertion of a stent along with a guidewire in renal transplant. Ureteric stent will not prevent complete occlusion of the renal outflow by an organized hematoma. In such situations, the best modality in treating ureteric obstruction is percutaneous nephrostomy.

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### Learning Points:

- Ureteric obstruction accounts for 1-5% of cases of anuria following kidney transplant, of which the most common cause is the formation of an ischemic stricture.
- Obstruction of ureter in a transplanted kidney due to recurrent blood clots is an extremely rare event (2-10%)
- Ureteric obstruction following kidney transplant can be effectively managed with minimally invasive procedures such as percutaneous nephrostomy.
- Minimally invasive techniques are preferred over open nephrostomy as it carries lesser patient morbidity.

## Acute abdominal distension in an one year old due to ingestion of unknown foreign body

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**Keywords:** intestinal obstruction; foreign body; enterotomy; super absorbant polymer beads; duplication cyst

### Introduction

Foreign body ingestion is a significant issue in children and causes morbidity depending on the type and size of the foreign body. Smooth and small foreign bodies are likely to be passed without any problem(1). However, smooth foreign bodies may get stuck in the gastrointestinal tract and result in obstruction, localised pressure necrosis, and ultimately, perforation. In such situations, children require surgical or endoscopic intervention to remove the foreign body<sup>1</sup>. Super absorbent polymer beads have emerged as popular product for use as a children's toy or home decoration. These beads absorb water due to the hydrophilic effect and can enlarged by 200 times their original size<sup>3</sup>. When these small beads (6mm) are swallowed they increases in size within the gastro intestinal tract and may lead to intestinal obstruction(2). The radiolucent nature of these beads makes it difficult to identify on plain radiographs and can result in delayed diagnosis. In this case, the child initially presented with aspiration symptoms and the cause was unknown. Over the following weeks she developed progressive abdominal distension and intestinal obstruction. This case highlights the challenges of diagnosis and provides an overview of literature on such cases.

### Case presentation

A one-year-old girl, otherwise fit and well, presented to emergency department (ED) with episodes of choking and vomiting at home. She was assessed, observed and discharged after normal chest X-ray. The following week she developed persistent non-bilious vomiting, anorexia, decrease stool frequency, and abdominal distension. On the 12th day after initial presentation, she presented to ED with tense abdominal distension and low grade pyrexia. She was clinically dehydrated, had a non-tender abdomen without palpable masses and reduced bowel sounds. Her supine abdominal X-ray (Fig 1) showed no free gas, but dilated small bowel loops

consistent with a small bowel obstruction. An abdominal ultrasound scan(Fig 1) was performed that revealed multiple fluid filled bowel loops with a spherical lesion (3cm in diameter) in the left flank of the abdomen that was atypical for a duplication cyst and was likely to be a foreign body. A CT abdomen and pelvis(Fig 2) was performed and it revealed dilated small bowel down to distal ileum with collapsed large bowel distal to the intraluminal circumferential foreign body in the distal ileum.

A laparotomy was performed through right upper transverse incision which demonstrated (Fig 3) grossly dilated small bowel loops down to the distal ileum and a palpable spherical foreign body at the level of a calibre change at the distal ileum. Distally there was collapsed distal ileum and collapsed colon, and at the level of the calibre change the bowel was circumferentially pale, but intact and viable. An enterotomy was made 10cm proximal to the discrepancy and the spherical foreign body was delivered after decompression. Distal bowel patency was confirmed with palpation and the enterotomy site was closed with 5/0 PDS

### Discussion

Online retailers highlight the features of absorbent polymer water beads as non-fading, non-toxic, 100% biodegradable, non-flammable, mushy, multi-coloured materials. The beads can help in developing colour recognition, concentration, counting, social and fine motor skills(3). They state that they are safety tested, and they do highlight that they are for children aged 5yrs and older. Parents and teachers who buy water beads should recognise the associated risks and ensure that young children do not use these products unsupervised.

This one year old child has presented initially with choking and vomiting episodes but a foreign body ingestion was not witnessed. The identification of the "Orbeez" bead ingestion only became apparent after the abdominal CT images were shown to the parents and they recalled that the child was playing with "Orbeez" beads in the house two weeks earlier. This case provided diagnostic challenges and highlighted the importance of a thorough history, appropriate imaging, to suspect and define the cause of obstruction. Although the

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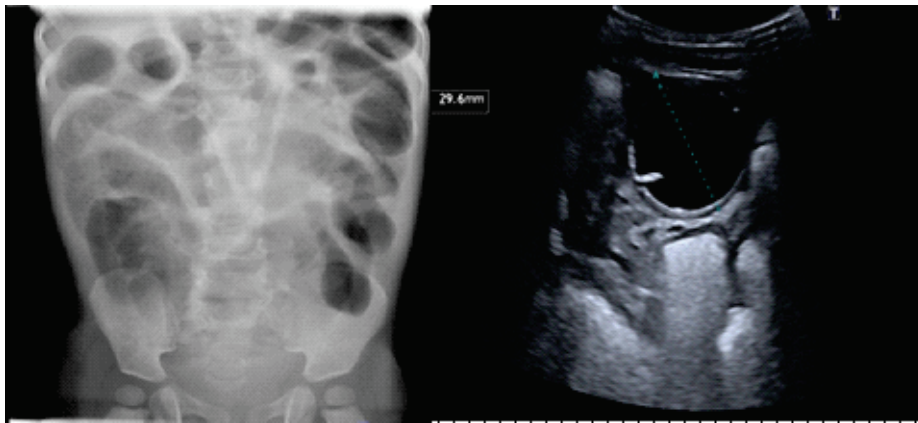
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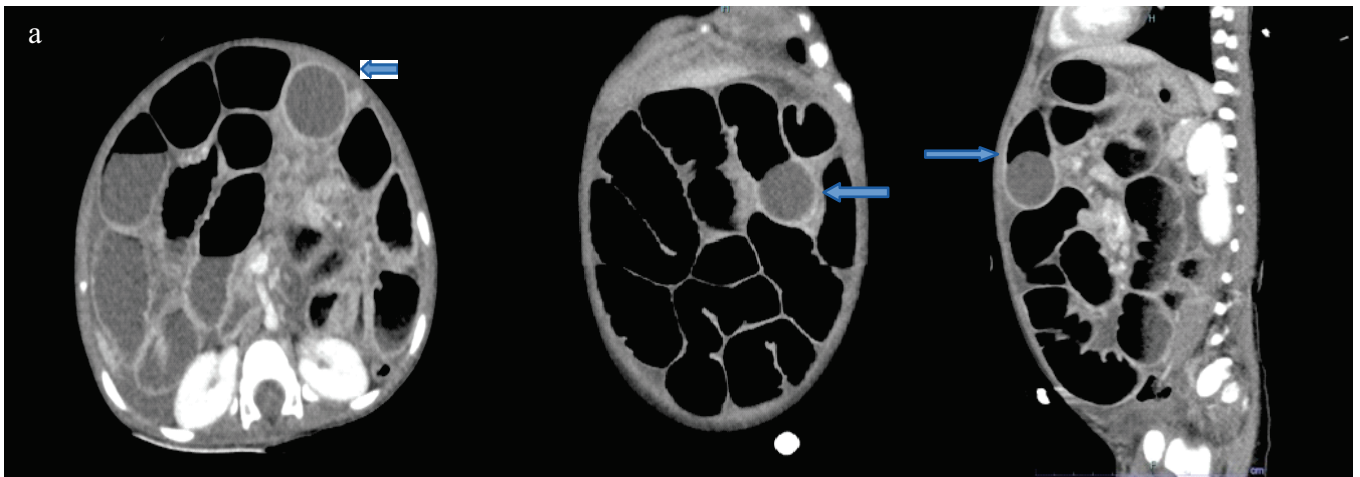
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**Figure 1.** (a)Supine X-ray abdomen and (b)ultrasound scan appearance which raised suspicion of duplication cyst.



**Figure 2.**CT abdomen and pelvis showed the small bowel obstruction with spherical foreign body.



**Figure 3.** Laparotomy shows (a)grossly dilated small bowel and collapsed distal bowel and (b)delivering of the foreign body through enterotomy

radiological imaging clearly demonstrates the foreign body, the exact nature of the sphere was better understood by a preoperative search on polymer beads and intraoperative findings.

According to the literature, there are several cases reported related to these water beads. In a similar case to ours it was initially suspected that the spherical lesion was a duplication cyst but at laparotomy “Orbeez” balls were identified and a small bowel resection with anastomosis was performed(2). Another case describes a child who aspirated a water bead and suffered recurrent chest infections before the bead was removed by bronchoscopy after a year(4) . A further case report describes a water bead that blocked the external auditory canal and was removed urgently but required followed up with myringoplasty for tympanic membrane damage(5).The majority of incidents occur in young children in outdoor settings with boys being affected more often(6). Therefore, parents and teachers should supervise children regardless of their age when they are playing with these beads and they should be kept away from young children to help prevent associated morbidity.

### Conclusions

Water beads or super absorbent polymer ingestion and aspiration can cause serious morbidity in children. Parents and teachers should have adequate knowledge about the associated risks and these cases should be reported in order to raise awareness.

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### Learning Points:

- There are few cases reported in the literature about the outcomes of super absorbent beads but in this case the child presented with choking but developed intestinal obstruction. Therefore, this should be recorded to raise awareness.
- When otherwise well children present with unusual or acute symptoms, consider appropriate imaging as an adjunct to ensure prompt diagnosis.
- Appropriate imaging and a pre operative literature search enabled a simple enterotomy, rather than small bowel resection.
- There should be raised awareness of the harms of such beads, for both parents and schools. Dangers should be displayed clearly on such manufactured goods/toys.

## A case of Castleman's disease presenting as left axillary tumor

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**Keywords:** Castleman's disease, POEMS syndrome, Interleukin-6

### Introduction

Castleman's disease is an uncommon disease affecting the lymph nodes [1]. It can manifest with a wide range of symptoms that affect people of all age groups. One of the major risk factors for this disease is immunosuppressive states like retrovirus, immunosuppression therapy, etc. We present a case of localised Castleman's disease presenting as left axillary swelling.

### Case Report

A 53 year old male presented with a swelling in the left axilla of 1-year duration, which was gradually increasing in size. It was not associated with pain and discharge. On examination, there was a single, non-tender, firm, large mass in the left axilla approximately 8 x 6 cm size, extending behind the pectoralis major muscle (Figure 1). Ultrasound of the left

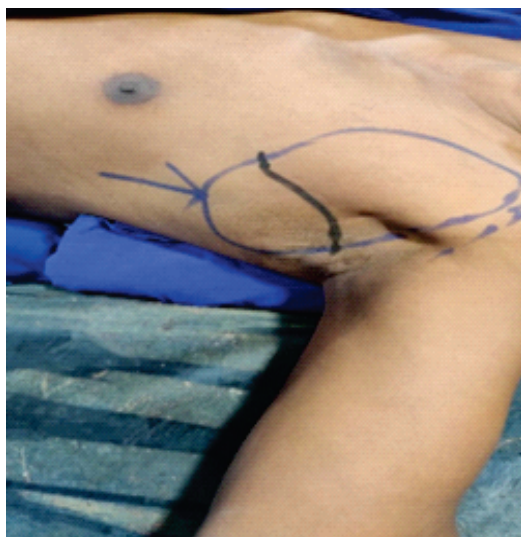


Figure 1. Left axillary swelling

axilla was performed which showed a well-defined hyperechoic lesion measuring 6.2 x 4.0 cm which was suspected to be a fibro-lipoma. To confirm the diagnosis, image guided biopsy was taken from the left axillary swelling which showed occasional reactive follicles with angiofollicular change, parafollicular vascular proliferation, hyalinization with sheets of plasma cells and negative for a focal lesion. We proceeded with MRI scan of the left axilla to find out the extension of the swelling which revealed an enhancing lesion measuring approximately 6.5 x 5.2 cm in the left axillary region, which was found to be abutting the intercostal muscles and ribs, lifting the pectoralis minor anteriorly. The lesion was also displacing the brachial plexus roots, subclavian vessels, with no evidence of chest wall invasion (Figure 2, 3). A differential diagnosis of Neurogenic tumor, was suspected from the findings.

Under general anesthesia, left axillary tumor, was removed successfully (Figure 4). Intraoperatively, it was evident that the tumor was abutting but not involving the brachial plexus or the subclavian vessels and also not invading the muscles. With meticulous dissection, complete removal of the tumor achieved.

Histopathological examination showed lymph nodal tissue with several follicles at the centre of which venules, with



Figure 2. MRI scan showing a large mass lesion in the left axilla

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small amount of hyaline were seen with lollipop appearance. There was vascular proliferation and area of fibrosis intersecting the follicles, showing reactive sinus histiocytosis. It was diagnosed as hyaline vascular type of Castleman's disease. Later on, he was evaluated and tested for retrovirus which was found to be negative and interleukin-6 levels which were unremarkable. Immunotyping was performed which did not detect monoclonal gammopathy. And the lymphoma panel tests were positive for CD 3, CD 20, CD 10, BCL 6, CD 138, CD 21, CD 23, Kappa, Lambda. Ki-67 was in a lower level of range. BCL 2 was negative. These results were consistent with Castleman's disease. As this could be a systemic disease, PET CT whole body was taken which showed hypodense nodules in both lobes of the thyroid (SUV max 5.6) in right lobe, largest measuring 0.8 x 0.7 cm. Other than thyroid nodule, no other metabolically active disease noted in the body. FNAC of right lobe of thyroid nodule was done and it was reported as atypical cytology (BETHESDA CATEGORY V). He was recommended surgery in view of the atypical cytology for which the patient chose to defer.

### Discussion

In 1954, Dr. Benjamin Castleman first described 2 cases of localised mediastinal lymph node enlargement, which showed vascular proliferation with endothelial hyperplasia, lymphoid follicles with germinal center involution. The disease was named after him. It is a rare lymphoproliferative disorder, which can affect any organs in the body. This disease was expected to involve mediastinal lymph nodes. It also involves the axilla, abdomen, pelvis, breast etc. It initiates an inflammatory process, by releasing cytokines leading to organ dysfunction. It is classified as hyaline vascular (75-

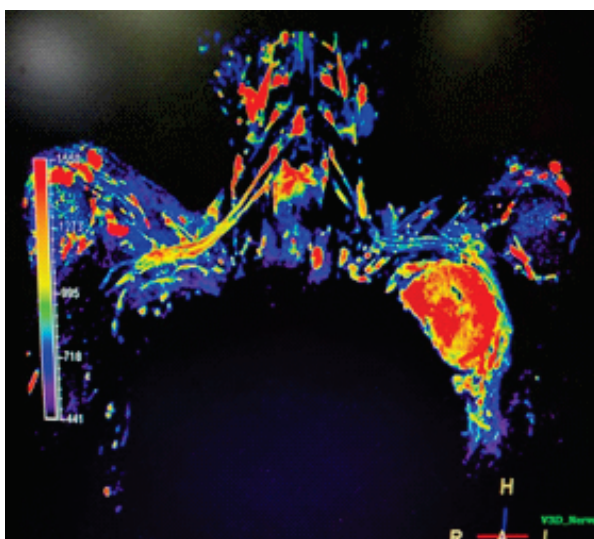


Figure 3

78%) and plasma cell (22-25%) based on microscopic examination. It can be unicentric or multicentric. Unicentric type will manifest as localised symptoms with regional lymph nodal involvement. It has an excellent prognosis with excision of involved lymph node. Multicentric is an aggressive type often progressing to lymphoma. It presents with generalised systemic symptoms, abnormal blood investigations. It can be idiopathic or associated with Human Herpesvirus (HHV-8) requiring systemic therapy. Recently, multicentric type is further subdivided into HHV-8-associated which is also known as Kaposi sarcoma-associated herpes virus (KSHV) [2], POEMS associated and idiopathic. TAFRO (thrombocytopenia, anasarca, fever, renal dysfunction / reticulin fibrosis, and organomegaly) is a variant of idiopathic multicentric type which exhibits hypogammaglobulinemia [3]. Multicentric forms an inter relationship with HIV, POEMS Syndrome (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammopathy and Skin changes - hyperpigmentation) and interleukin-6 levels. POEMS syndrome is also known as Osteosclerotic myeloma or Takatsuki or Crow-Fukase syndrome. HHV-8 influences the level of production of interleukin-6. The lymph nodes of Castleman's disease exclusively secretes an excess of interleukin-6 from the germinal centre by B cells. There will be abrupt decrease in the interleukin-6 level with the tumor being removed. If the level does not lower, anti-IL-6 antibody like Tocilizumab, Rituximab are used for multicentric type [4].

In our patient, with the evidence of histological examination, we finally confirmed that axillary mass was due to the Castleman's disease. After the procedure, he was evaluated thoroughly without evidence of systemic involvement. Since it was a localized disease, he did not require any further treatment.



Figure 4. Intra-operative image of the left axilla showing tumor



Bo-Kyoung Seo et al. reported a similar case of axillary swelling, incidentally detected in a 45-year-old female without any symptoms [5]. Upon further evaluation with CT scan and USG guided biopsy, they had come to a diagnosis of Castleman's tumor. The tumor was excised. According to this study, only 2% of Castleman's disease manifesting with axillary presentation. USG Doppler is essential in differentiating malignant from benign lymph nodes.

### Conclusion

Castleman's disease is an atypical disease which can only be confirmed with histological examination. It should be further evaluated with PET CT scan, as it can produce lesions in the lymph nodes anywhere in the whole body and to get the knowledge of its aggressiveness which really helps in deciding the management protocol.

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### Learning Points:

- .Castleman's disease is a rare benign lymphoproliferative disorder that can affect any system of the body.
- It is classified as unicentric and multicentric variety. Diagnosis is mainly confirmed by histopathological examination.
- Treatment varies according to the type of the disease. Hence PET CT scan of whole body is needed to differentiate these types.
- Unicentric type requires local treatment whereas multicentric type requires systemic therapy.

## Spontaneous cholecystocutaneous fistula: a rare complication of gallbladder disease

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**Keywords:** Cholecystitis · Cholecystocutaneous fistula · Hepaticojejunostomy · Fistulogram · Gallstones · Laparotomy · Bile ducts

### Introduction

Fistula is an abnormal condition, which results from abnormal connection between two epithelialized surfaces. Biliary fistulas are rare complications of gallstones, linkage between the biliary tract and various organs. There are two main groups of biliary fistulas: internal and external [1]. An internal biliary fistula forms a connection between the gallbladder and the gastrointestinal tract, typically resulting from chronic cholecystitis [2]. On the other hand, an external biliary fistula establishes a link between the gallbladder and the abdominal wall, with potential causes including spontaneous occurrence, postoperative complications, post-traumatic events, or iatrogenic injuries to the biliary tract [1,3].

Cholecystocutaneous fistula (CCF) belongs to the category of external biliary fistulas, creating a connection between the gallbladder and the skin. There are less than 100 cases of cholecystocutaneous fistula reported. The first reported case of CCF was in 1670 by Thilesus, who described this phenomenon for the first time. Nevertheless, during that

period, fistulas were a frequent complication arising from untreated cholecystitis [5]. As per a study conducted in 2005, a total of 226 cases have been documented, with fewer than 25 reported in the past five decades [4]. We don't see much of gallbladder fistula case in current practice due to rapid advancement in imaging, increased understanding of disease process and timely intervention either interventional radiologically or surgically. Mostly gallbladder calculus disease associated with fistula but at times we do see gallbladder carcinoma present with cholecystocutaneous fistula.

Commonest place of fistula opening is right hypochondrium which is self-explanatory due to underlying gallbladder but other known places are buttock, umbilicus and right inguinal region [4]. This entity is commonly seen in debilitated elderly over 60 years of age. However, cases have been reported in patients aged as young as 24 years. We report a case of a cholecystocutaneous fistula in a patient with previously undiagnosed gallstone disease.

### Case Summary

A 59-year-old woman with the history of hypertension and dyslipidemia was referred to our institution from a private sector with abdominal pain and discharging sinus in the epigastrium for 2 years. She has had excision biopsy of epigastric sinus 1 year back at a different hospital and histology revealed active chronic inflammation.




**Figure 1.** Fistulous opening in the epigastrium



**Figure 2.** Arrow showing the fistula

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Ultrasound of the abdomen showed 2cm tract in anterior abdominal wall in the epigastrium appears to communicate with peritoneal cavity, in favour of fistula formation with background chronic cholecystitis and gallbladder calculi. Subsequently CT fistulogram was performed and findings were diagnostic of cholecystocutaneous fistula.

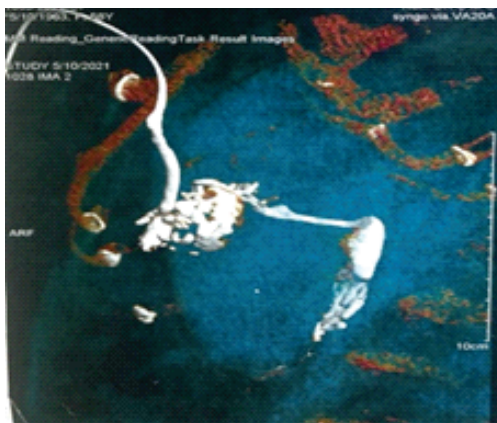
Liver function tests were normal, and there were no contraindications for surgery under general anesthesia. We performed laparoscopy and decided to convert to open surgery due to the density of the adhesions specially at the Calot's triangle. At laparotomy, the fistulous tract was demonstrated and found to enter the fundus of the gallbladder. Gallbladder was thick, fibrotic, and hard in consistency and was seen to adhere to the liver, with surrounding hard induration of the liver, and also the cystic duct - common hepatic duct junctional area, raising the suspicion of carcinoma of the gallbladder. There were several large and hard stones within the gallbladder. We proceeded with en bloc excision of aponeurotic muscle, skin and fistulous tract together with the gallbladder, and a 5cm cuff of the liver, and cystic duct - common hepatic duct junction, and the common bile duct down to the level of the superior border of the duodenum. A jejunal Roux-en-Y loop was raised, and end to side hepaticojejunostomy performed with 5/0 Polydioxanone interrupted sutures. A subhepatic drain was left in situ and patient received broad-spectrum antibiotics during and after surgery. The patient made a slow but uncomplicated recovery and was discharged home well on post-op D6. Superficial wound infection was noted on D9, which was managed with oral antibiotics and by D20 wound was completely healed. Histology of the specimen confirmed acute on chronic cholecystitis with a fistula between the skin and the gall bladder lumen, without evidence of malignancy or tuberculosis.

## Discussion

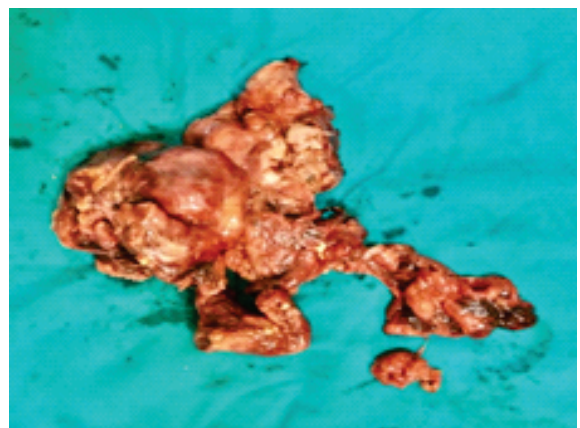
The better understanding of pathology and evolution of sophisticated investigations lead to a rare occurrence of spontaneous cholecystocutaneous fistula. Over the past 50 years, less than 20 cases of spontaneous CCFs have been reported [4]. A neglected biliary tract disease is being the culprit of CCF. They are painless and right upper hypochondrium being the commonest location. However, they have been reported at the umbilicus, left costal margin, right iliac fossa, right groin and the back [5]. A pyogenic granuloma, infected epidermal inclusion cyst, chronic osteomyelitis of ribs, enterocutaneous fistula, discharging tuberculosis and metastatic carcinoma should be considered as mimics of CCF by external appearance [5]. The patency of the cystic duct determines the nature of the discharge which can be purulent, mucoid or bile.

In a recent analysis by Kaminsky concerning the prevalence of biliary fistulas to the gastrointestinal tract, the majority were observed to be connected to the duodenum (60%), followed by the colon (24%), stomach (6%), and choledochal duct (5%). Out of all, only 2% cholecystocutaneous abscesses or fistulas are accounted. Key factors increasing the risk of spontaneous cholecystocutaneous fistulas (CCFs) encompass older women (> 50 years of age), steroid therapy, a history of typhoid, bacterial spread, trauma, immunocompromised conditions, etc.

The pathophysiology of CCF can be studied step by step in following manners: cholecystocutaneous fistula is a sequelae of cystic duct blockage leading to increased gallbladder pressure, either caused by stone or malignancy. As a result of increased intraluminal pressure, blood and lymphatic flow is compromised to gallbladder, result in mural necrosis and perforation.



**Figure 3.** 3D Constructed fistulogram



**Figure 4.** Resected gallbladder with fistulous tract

In literature, perforation classically described as acute, subacute and chronic. These fistulas, as presented in our case, frequently arise from the fundus of the gallbladder. Famous surgeon Nayman coined the term “empyema necessitatis” – A state prior to spontaneous rupture, also known as “burrowing abscess”.

Based on the underlying etiology, the external biliary fistula management differs. The septic presentation requires adequate antibiotics, analgesics and fluid resuscitation. Not all external biliary fistula warrants surgical intervention because a proportion of patients exhibits spontaneous healing. So, in elderly or debilitated patients major interventions can be avoided. Cholecystostomy and cholecystectomy are the possible surgical options. As cholecystostomy carries the possibility of further stone formation in the gallbladder, cholecystectomy is usually the treatment of choice.

In conclusion, gallstones-disease related complications can be prevented by early laparoscopic cholecystectomy. In patients with anterior abdominal wall discharging sinus should warrant early referrals. Rare possibility of malignancy should be kept in mind while dealing with spontaneous CCF. In these cases, proper preoperative planning with imaging like CT scan is pivotal. At last, patient's clinical status, local expertise and best post-operative outcome decide whether

laparoscopic versus open and one-stage versus two-stage approach.

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### Learning Points:

- Early laparoscopic cholecystectomy for gallstones may prevent chronic cholelithiasis complications.
- High level of suspicion needs to be maintained in patients with discharging sinus located in the anterior abdominal wall.
- Rare possibility of malignancy should be kept in mind while dealing with spontaneous CCF.
- Judicious use of CT as imaging modality should be considered to rule out the diagnosis and for proper preoperative planning.