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The Journal of Association of Surgeons of Assam
Official Journal of Assam State Chapter of ASI

Contents & Contributors

Editorial

" Traction & Counter - traction" — A Basic Beauty in Surgery

Pulling a part of a human body in one direction is traction and the use of an opposing force to balance it, is counter-traction; - probably a simplified definition. Traction and counter-traction, along with maintaining excellent exposure is one of the fundamental principles of nearly all forms of surgical dissection. Its Newtonian: equal and opposite. Although in routine practice all of us think very little about this basic maneuver , still we all can appreciate that better exposure of operative field, stabilization and precise procedure is possible only with proper traction and counter-traction. However it is to be remembered that, when we give respect to tissue in return, it will give respect to us.

"There is never enough horsepower.....
just enough traction"

– Carrot Shelby

One of the great pleasures of operating is having an assistant who can read the Surgeon's mind on table, so that actions are co-ordinated and balanced. Constantly in motion , it is an ever changing dance as if we were tethered together by a silk cord and each move the surgeon initiates, perfectly mirrored by the assistant standing opposite side, keeping the cord absolutely taut. It happens in a constant flow with no exchange of words. It will be a mere injustice on my part, if I say that this beautiful maneuver (traction and counter-traction) is part and parcel of General Surgery only; rather in all corners of operation like Orthopedics, Obs-Gynae, Ophthalmology, ENT, Laparoscopy and even Robotics etc. etc., traction and counter-traction plays a pivotal role.

Philosophically too traction has an impact on our future plans and visions.

"Vision without traction
is merely hallucination....."

- Marrion Ato

Surgery has travelled a long way since the days of its father Sushrutaa and the journey still continues, exploring new horizon. Fractionization of General Surgery in to Bariatric, Onco, Robotic, AI has shown a great impact on our perception. But still this small basic trick of *traction* and *counter-traction* will not allow us a chance to delete its footprint in operations in the days to come.

Long live ASA
Long live JASA

Dr. Debabrata Dutta

Guest Article

A Case of Laparoscopic Right Anterior Sectionectomy after Partial S8 Resection using the Ccranio - Ventral Approach

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Abstract :

Laparoscopic hepatectomy has been rapidly widespread and currently highly difficult procedures such as sectionectomy have been also performed. We report a case of a laparoscopic right anterior sectionectomy using the cranio-ventral approach. The patient was an 80-year-old man who underwent laparoscopic resection of aliver metastasis from rectal cancer. 7 months later, the liver metastasis recurred in the dorsal region of S8, and the laparoscopic right anterior sectionectomy was scheduled. Although adhesions and scars due to the previous hepatectomy were observed, transection was performed from the root of the hepatic vein to peripheral side without significant blood loss.Pathologically surgical margin was negative. The patient was discharged on postoperative day 8 without any postoperative complications. The cranio-ventral approach may be useful in laparoscopic right anterior sectionectomyin cases of repeated hepatectomy.

Introduction:

Laparoscopic hepatectomy has been rapidly widespread and currently highly difficult procedures such as sectionectomy have been also performed. The hepatic veins run and serve as landmarks between the sections, and exposure of the hepatic veins is important for accurate sectionectomy. There are various approaches to the main hepatic vein, and we use a cranio-ventral approach in which transectionis performed from the root of the hepatic vein.

Case Report:

An 80-year-old man with a history of hypertension underwent a laparoscopic partial S8 resection after resection of the primary tumor for rectal cancer and a simultaneous liver metastasis. The main trunk of Glissonean pedicle of segment 8 (G8) and middle hepatic vein (MHV) were exposed to secure the surgical margin. A follow-up CT seven months after hepatectomy revealed the liver metastasis (Fig.1a)and the repeated hepatectomy was scheduled. His liver function was normal.Since the tumor was close to the previously resected lesion, the resection of the tumor including the scar was necessary, so theright anterior sectionectomy with combined resection of MHV was scheduled (Fig1b).

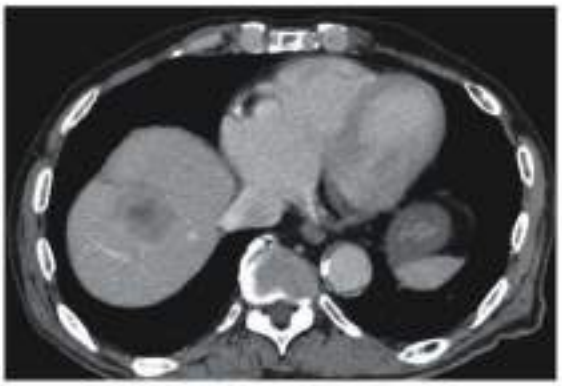

Fig1 a CT image

Enhanced CTshowed the 3 cm sized low-density area in dorsal area of S8 and it was close to the scar of the previous hepatectomy (arrowhead).

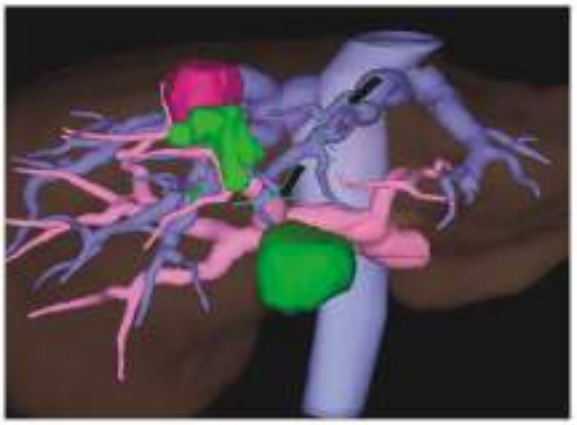

Fig.1b Pre operative Simulation 3D image

The feeder of the tumor was dorsal branch of G8, but the G5 bifurcation was close by, andright anterior sectionectomywas necessary to ensure surgical margin. The MHV was in the scar area, and a combined resection was necessary at the peripheral side of the V8 bifurcation. The line is transection line of veins and the Glissonean pedicle. Arrows shows the direction of dissection.

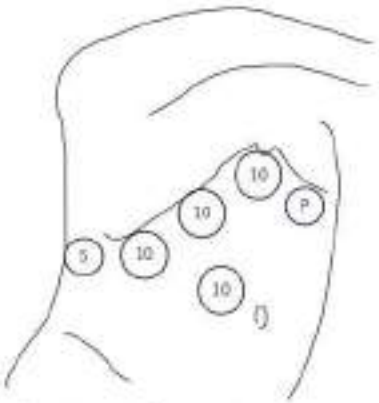

Fig.2 Port placement

P: port for Pringle maneuver

Intraoperative findings

Fig 3a

Dissection from the root of MHV. MHV was dissected from the root side. MHV: middle hepatic vein

Fig 3b

Dissection of RAGP. RAGP could be found behind V5. RAGP: right anterior Glissonean pedicle

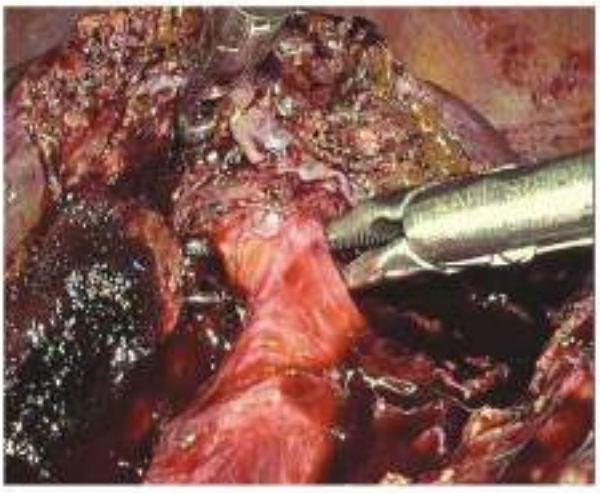

Fig 3c

Isolation of RAGP. RAGP was isolated after liver transection around it. Cistyc plate was continuous to RAGP. CP: cystic plate

Fig 3d

Dissection from the root of RHV. it was also dissected from the root and fully exposed. RHV: right hepatic vein

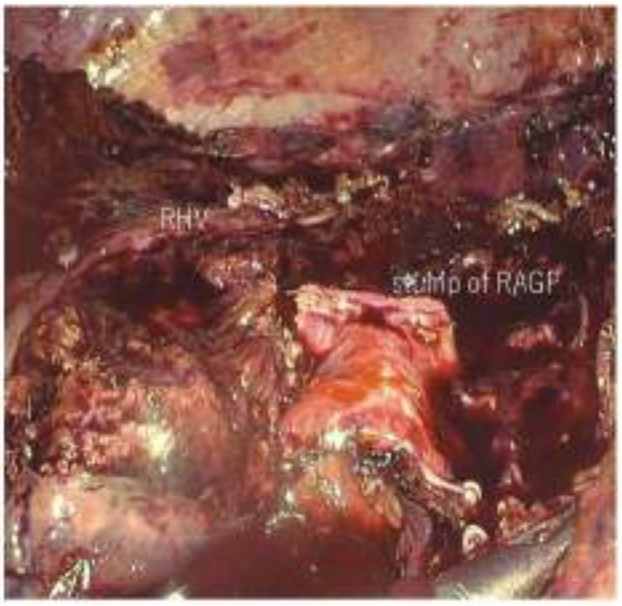

Fig 3e

Final view after removal of specimen.

Surgical procedure:

The patient was positioned in left semi-lateral position. We used a 3D flexible scope (ENDOEYE FLEX 3D®, OLYMPUS). The first port was inserted from the upper right side of the umbilicus using the open method. Three 10-mm and one 5-mm ports Kii Advanced Fixation Sleeve®, Applied Medical were inserted into the right subcostal area (Fig.2). After detaching adhesion at the previously resected lesion and around diaphragm, the root of the hepatic vein was dissected. Liver transection was performed under Pringle maneuver (20 min clamping, 5 min declamping) using CUSAEcel+®(Integra LifeSciences). Liver transection was started from the root of MHV to peripheral side, and then the MHV was isolatednear the scar at the peripheral side of the V8 bifurcation (Fig.3a).The liver transection was proceeded along V5 toward the hepatic hilum (Fig.3b) andthe right anteriorGlissonean pedicle (RAGP) was isolated following liver transection along the gallbladder bed from the caudal side(Fig.3c). The demarcation line was identified after clamping the RAGP and the tumor was confirmed within it. The RAGP was transected using linear stapler after cholecystectomy and liver dissection around the RAGP. The RHV was exposed from the root side and dissected toward peripheral side (Fig.3d), and the liver parenchyma was liftedand transected toward the demarcation line and then the resection was completed (Fig.3e). The operative time was 284 minutes, and blood loss was 400 ml. Since no bleeding or bile leakage from the cut surface was observed, and the drain was not placed.

Result:

The postoperative course was uneventful without any complication, and the patient was discharged on the postoperative day8.Pathological examination revealed liver metastasis from the rectal cancer and showed negative surgical margin.

Discussion:

The hepatic vein is important as a landmark in laparoscopic anatomical liver resection, and the main hepatic vein is exposed on the dissection plane. Safe exposure of the hepatic vein leads to maintenance of an adequate dissection plane (1)(2). An international consensus conference was held at the congress of the Japanese Society of

Hepatobiliary and Pancreatic Surgery in 2021 with the aim of identifying the anatomical landmarks and surgical approaches necessary to safely perform endoscopic surgery. Three types of approaches were classified and defined according to the site where the hepatic vein is first exposed: cranio-ventral approach, cranio-dorsal approach, and caudo-peripheral approach (1) (3). Care must be taken to avoid split injuries when exposing the hepatic vein, and lacerations are often stretched and difficult to stop when moving the device from the peripheral side to the rootof it(2). On the other hand, pulled-up injuries are caused by moving the device from the root of the hepatic vein to the peripheral side, but since they do not extend to the central side, hemostasis can be achieved by compression with gauze or soft coagulation (2). In addition, there is a capsule covering the entire liver including the Glissonean pedicles and hepatic veins called Laenec's capsule (5), and dissection from the root of hepatic vein maintains the strength of hepatic vein by dissecting at the layer that makes Laenec's capsule attach to the hepatic vein, which takes advantagein bleeding (6). On the other hand, it was reported that dissection from peripheral side of hepatic vein detaches the Laenec's capsule from the hepatic vein, resulting in venous wallfagile(7). For these reasons, we use the cranio-ventral approach when exposing the main hepatic vein.

The cranio-ventral approach is particularly useful when dissecting the Rex-Cantlie line, not only exposing MHV, but also allowing us to approach G8 and RAGP by dissecting along the hepatic vein. On the other hand, from the viewpoint of isolatingRAGP, there are extrahepatic, intrahepatic, and transfiss-ural approaches (8) and our approach to RAPG was the transfissural approach. Anatomically MHV and RAGP is close andRex-Cantlie line is easy to transect as it is an anatomical plane. Therefore, when the cranio-ventral approach is used for liver transection, the RAGP can be safely isolated without damaging the hepatic hilum such as bleeding and bile duct injury. We mainly use the cranio-ventral approach for the cases in which the transection line isRex-Cantlie line, and we can isolate the Glissonean pedicle in addition to creating dissection plane, so the extrahepatic Glissonean approach is not always necessary.

In this case, the cranio-ventral approach was useful because the simulation prior to hepatectomy showed that a combined resection of MHV was necessary, and the MHV needed to be isolated on the central side from the scar. Furthermore, the right anterior Glissonean pedicle could also be safely isolated with dissection along the hepatic vein toward hepatic hilum.

Conclusion:

The cranio-ventral approach may be useful in laparoscopic right anterior sectionectomy in cases of repeated hepatectomy.

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NOTE- This article is rapid dispatched due to a request from Dr Purujit Choudhury, Indian Surgeon visiting frequently the HPB center of this institute.This case is witnessed to

Dr. Choudhury.

Original Article

Surgical Site Infections in Acute Peritonitis Experience at a Tertiary Care Centre

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Abstract:
Introduction: The Surgical Site Infection (SSI) is a common post-operative complication and nosocomial infection causing substantial morbidity in the surgical patients. The incidence of SSI was found to be higher in emergency surgeries than that of elective ones. The burden of identifying the patients at risk of SSI and its prevention is necessary and is a challenging task to the treating surgeons. This observational study was undertaken to elucidate the incidence of post operative wound infection and its contributing factors among patients undergoing surgery for acute peritonitis and to identity the microbes associated with SSI with antibiotic sensitivity pattern.

Materials and Methods : : A total of 100 patients of either sex between the age group of 18 to 60 undergoing laparotomy for acute peritonitis were taken up for study. The data on its demographic incidence, associated of co-morbidities, nutritional status (HB%, serum proteins) ,duration of surgery, culture sensitivity of infected materials were collected. Chi-square test was performed for data analysis. Results and observations: This study showedwound infections(SSI) developing in 32 cases(32%). Male in the age group of 41-60 had maximum rate of SSI. The rate of infection was high when the operation proceeds for more than 2 hrs(P =0.0028) duration. The infection rate of SSI in patients with co-morbidity was higher (p=0.0022).E. coli being the most commonest organism found inthe wound showing highest sensitivity to gentamicin, Piperacillin + Tazobactum and imipenem/Meropenem. Conclusions: The incidence of surgical site infection increases with elderly male, Obesity, anaemia, hypoproteinemia,long duration of surgery.E.coli predominates as infective organism sensitive to penicillin, aminoglycosides and carbapenem group of drugs.and carbapenem group of drugs.

Keywords : Acute peritonitis-comorbidity-SSI-Ecoli-penicillin-carbapenem.

Introduction :The Surgical Site Infection (SSI) is the common post-operative complication and nosocomial infection causing substantial morbidity in the surgical patients. The incidence of SSI varies from 12-26%[1]when all abdominal surgeries are put together. The incidence of SSI was found to be higher in emergency surgeries. Surgery for Acute peritonitis is an emergency life saving procedure,

there is minimal scope for preoperative optimization of co morbid illness and chronic disease states. In trauma patients, there are additional risk factors including mechanism of injury, organs involved, severity, contamination of the wound, presence of foreign body, hemodynamic instability, blood transfusions[4] etc. SSIs lead to increased hospital stay, increased consumption of medical resources and financial burden on the patient. Inappropriate surgical prophylaxis adds to the cost of medical care and exposes the patient to toxic effects of drugs and promotes the development of antimicrobial resistance. The burden of identifying the patients at risk of SSI andits prevention is necessary and is a challenging task to the treating surgeon. This observational study was undertaken to elucidate the incidence of post operative wound infection and its contributing factors among patient undergoing surgery for acute peritonitis and to identity the microbes associated with SSI and the antibiotic sensitivity pattern.

Materials and Methods : In this study, a total of 100 patients of either sex between the age group of 18 to 60 undergoing laparotomy for acute peritonitis were taken up for study. All patients with immune-compromised state like, HIV, Autoimmune disorders, patients with previous laparotomies were excluded. The demographic incidence, association of co-morbidities, nutritional status (HB%, serum proteins),duration of surgery, culture sensitivity of infected materials were gathered. Post operatively the surgical site was assessed after 48 hrs up to 8 days . The status of surgical site at discharge also noted.

Data Management and Analysis: All data obtained from patients was entered into a proforma. At analysis, each item in the questionnaire was analysed separately using the tally method. Chi-square test was used for data analysis.

Results and observations : This study comprises 100 emergency cases undergoing various abdominal operation in surgical units of Guwahati Medical College and hospital, Guwahati. This present study comprising off 100 abdominal surgical wounds shows infection developing in 32 cases, the incidence of infection is 32%.All the patients 18 years to 60 years of age of either sex were included in this study. Infection rate was found be higher in the age group 51-60 years (45%) and least infection rate was found in the age group 18-30 years (10%). Incidence of infection increases with age which may be due to in decreased immunocompetence and accumulation of comorbid condition in old age group. Total number of male patients were 56 and female patients were 44 the incidence of wound infection was found to be more in males (35%) which may be attributed to a greater number of emergency cases (p value=0.6548). In this study, there were 80cases in class 3 contaminated one and 20 class 4 dirty cases. Out of 20 dirty types of wounds, 12 got infected and out of 80 contaminated types of wounds, 20 got infected(Table 1). Incidence of SSI in dirty wound (60%) is higher than the incidence of SSI in contaminated wound(25%).The difference was found to be statistically significant (P=0.006). Out of 32 patients, 17 (53%) develop SSI when the operation proceeds more than 2hrs and out of 68 patients, 15(22%) develop SSI when the operation proceeds more occur between 1-2 hours. The study shows there is gradual increasing trend in infection rate when the operation proceeds for more than 2 hrs and was considered statistically significant (P =0. 0028). The infection rate was higher in patients associated with predisposing factors. Obesity (100%) which was statistically significant (P=0.0307). Diabetes(66.67%) and hypoalbuminemia (66.67%) were the most common predisposing factors which were found to be statistically insignificant as sample size was limited(Table2).The infection rate of SSI in patients with predisposing factors was higher (50%) in comparison with patients without predisposing factors (20%).This association was found to be statistically significant (p=0.0022).

Table 1: Factors Associated with SSI for surgery in Acute Peritonitis:

1. Total numbers of study populations:100. 2.Total nosof SSI :32(32%).

Descriptions	Variables	Nos (%)	SSI (%)	*P* Value
Age	18-40	42	9	0.016673
	41-60	58	23	
Sex	Male	66	20	0.06548
	Female	34	12	
Type of wound	Dirty	80	20(25)	0.006
	Contaminated	20	12(60)	
Duration of Surgery	<2hrs	68	15	0.0028
	>2hrs	32	17	
Predisposing factors	positive	40	20	0.0022
	Negative	60	12	
Infective organisms	E-Coli		10(50%)	0.00001
	Klebsiella pneumoniae		4 (20%)	0.0092
	P. aeruginosa		4 (20%)	0.0092
	staph aureus		2(10%)	0.1002

The most frequent organisms cultured were E. coli, (50%, P value of 0.00001). Klebsiella pneumoniae (20%, P=0.0092) and P. aeruginosa (20%, P=0.0092) n which was statistically significant. Sensitivity of the infecting organisms was highest with Piperacillin+Tazobactum and Imipenem followed by Vancomycin.

Table 2: Morbidity Factors Associated with SSI for surgery in Acute Peritonitis:

1. Total numbers of study populations : 100. 2.Total nos of SSI :32(32%).

Descriptions	Variables (Total No/100)	Infected wounds/32(%)	PValue
ANAEMIA	4	2(50)	0.591
JAUNDICE	2	1(50)	0.5398
OBESITY	3	3(100)	0.0307
DIABETES	3	2(66.7)	0.2393
HYPOALBUMINEMIA	3	2(66.7)	0.2393
DYSELECTROLYTEMIA	3	1(33.3)	1
MALIGNANCY	5	2(40)	0.6539
SMOKING	5	2(40)	0.6539

Discussion : Despite the advances in the operative techniques and a better understanding on the pathogenesis of the wound infections, post operative wound infections continue to be a major source of morbidity and mortality for the patients undergoing operative procedures.In this study lowest incidence was found in 18-30 years (10%) of age group. The highest incidence was in the 51-60 years (45%) age group[1,2,3]. The incidence of SSI was higher in males (35%) than that of females (27%). In this study the number of cases with post operative wound infection in emergency surgery are 32 accounting for 32% of the incidence [4,5,6] .The reason of post operative wound infection being the most patientsoperated for emergency surgery had hollow viscus perforation with contamination of peritoneal cavity causing contamination of wound[7,8,9]. In the present study, the wound infection rate for contaminated and dirty cases is 25% and 60% respectively [10, 11,12]. In the present study it was seen that operation taking more than two hours of duration hadhigher rateof SSI (53%). Duration of procedure has been found to be an independent risk factor and any procedure that lasts longer than 120 minutes is indeed a high risk for surgical site infection [2,13,14]. In the present study infection rate in patients having predisposing factor/factors was found to be higher (50%) than to the patients without predisposing factors (20%). In this study all patients with Obesity (3/100%) resulted with SSI. Diabetes (66.67%) and Hypoalbuminemia (66.67%) were found to be other important predisposing factors for increased incidence of wound infection followed byhyperreninemia(50%), Anaemia (50%) andJaundice (50%) [4,15,16].The most common Organism encountered in post operative wound infection in this study was Escherichia coli (10/50%), followed by Klebsiella pneumoniae (4/20%) and pseudomonas (20%). In the present study, the E. coli being the most commonintestinal flora might have contaminated the wound[17,18,19]. This study reveals E. coli showing highest sensitivity to Gentamicin, Piperacillin + Tazobactam and imipenem/Meropenem. The Pseudomonas isolates showed good sensitivity to Piperacillin-Tazobactam, Ceftazidime and Imipenem. Staphylococcus aureus showed maximum sensitivity to Linezolid, Ofloxacin and Vancomycin.

Conclusions: The incidence of surgical site infection increases with old Age,Male sex, Obesity,hypoproteinaemia, Anaemia, Jaundice, dirty wounds and prolonged duration of surgery. E.coli predominate in causing surgical site infection and the infecting organisms were sensitive to penicillin and carbapenem group of drugs.

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Chronic Pancreatitis – A Short Review.

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(Disclaimer- This is a compact review article. Part of it was presented in RAIPUR AIIMS, as a guest lecture and published in the Journal of the IMA sometime back under the authorship of the present author.)

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Introduction:

The incidence of chronic pancreatitis is 5 to 12 per 100 000 adults in industrialized countries, and the incidence is increasing. Treatment is multimodal, and involves nutrition optimization, pain management, and when indicated, endoscopic and surgical intervention.The prevalence of chronic pancreatitis is 50/100,000 people. Actual overall Incidence of Chronic Pancreatitis is around 7 -30 per 100,000.The incidence of CP varies between countries. European studies commonly show incidence rates around 7 per 100,000. Higher incidence rates of 14.4 per 100,000 is reported from Japan.

The leading cause of CP in Western industrialized countries is alcohol over-consumption (between 65% and 90%) followed by idiopathic (20–25%) and other rare etiologies (5%) .Chronic pancreatitis often develops in patients between the ages of 30 and 40, and is more common in men than women.

Chronic pancreatitis is sometimes due to an inherited gene mutation.
8 NEW patients are added per 100,000 populations per year in the US of A. But

- Autopsy suggest a higher prevalence rate for 0.04% -5% and
- In a quarter of patient (20-25%) no cause is identifiable

It is observed that the Life expectancy is reduced by 10-20 years. As well asMortality is increased 3.6 fold. The Expenditure burden is approximately 17000 USD per year per patient.Improvement of treatment gives additional 20 years of life to the patients.

Longstanding pre-existing CP is a risk factor for pancreatic cancer. (Smokers are more prone). Out of all 1.8% of these patients will develop pancreatic cancer within 10 years from the diagnosis and 4% after 20 years.In one study with 3290 person-years of observation, pancreatic cancers were diagnosed in 16 patients (2.20%, 0.49% per year) after a median follow-up of 2.4 years (range 1.4–6.6), with an age- and sex-standardized incidence ratio of 18.1 (95% CI 10.4–29.5). The underlying conditions in the 16 pancreatic cancers were classified as chronic obstructive pancreatitis (10/63%), chronic obstructive and calcifying pancreatitis (4/25%), chronic calcifying

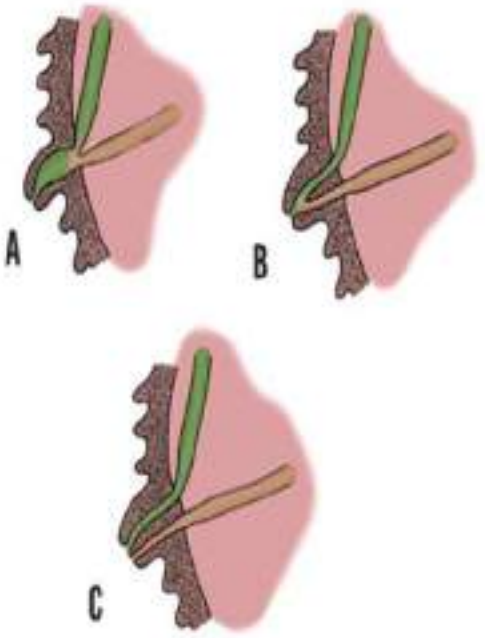
pancreatitis (1/6%), and autoimmune pancreatitis (1/6%). Factors associated with pancreatic cancer development included age, parenchymal calcification, pancreatic duct stricture, and serum CA 19–9 level. After adjustment, age over 60 years and serum CA 19–9 levels greater than 100 U/mL were independent risk factors for pancreatic cancer.

Some Historical Foot prints:

Bidloo (1685)-- Provided a description of the duodenal papillae, the junction of the pancreatic and common bile ducts, and the hepatopancreatic ampulla ,Vater (1720), redescribed the duodenal papilla originally described by Bidloo; it is now commonly called the papilla of Vater. MacBurney (1878), Used a duodenotomy and papillotomy to remove calculi in the papilla.Trendelenburg (1882), In the process of excising a sarcoma he removed the tail of the pancreas and the spleen. Oddi (1887), Observed and described the sphincter of the hepatopancreatic ampulla (sphincter of Oddi). Fitz (1889), Provided the first complete description of acute pancreatitis. Opie(1901), Established the common-channel theory of pancreatitis stating that Wirsung's duct entered the common bile duct proximal to their duodenal entrance. He also hypothesized that any stone wedged against the sphincter of this channel could cause bile to flow into the pancreas and pancreatic juice to flow into the biliary tract producing pancreatitis or cholecystitis. In the same report he noted that the islets of Langerhans were associated with diabetes because patients with hyalinized islet cells developed the disease. Ssoboleff (1902)-- Observed that acinar tissue atrophied after ligation of the pancreatic duct while islet tissue remained unchanged.Whipple (1940)-- Performed a one-stage excision of the entire head of the pancreas with total duodenectomy with 10-year survival. Kelly, Acosta (1974)-- Reported gallstone migration through the ampulla of Vater initiating pancreatitis.

Some Anatomy to understand the probable causes of continued pancreatitis.

Pic 1. Variations of pancreatic ducts. Degrees of suppression of accessory duct. A, Both ducts open into duodenum (60 percent). B, Accessory duct ends blindly in duodenal wall. C, Accessory duct ends blindly before reaching duodenum (30 percent). D, Accessory duct has no connection with main duct. E, Accessory duct absent.



Pic 2. . Variations in relation of common bile du and main pancreatic duct at duodenal papilla.
A, Minimal absorption of ducts into duodenal wall during embryonic development. Ampulla present.
B, Partial absorption of common channel. No true ampulla present.
C, Maximum absorption of ducts into duodenum. Separate orifices on papilla, no ampulla.

Let us see some Characteristics of the Chronic Pancreatitis now.

Chronic pancreatitis is a condition where protractedinflammation of pancreas characterized by the following features is associated. They are:

- Presence of lesions of chronic inflammation
- Loss of exocrine parenchyma
- Irreversible fibrosis
- Possible subsequent destruction of endocrine tissue
- Calcifications

Chronic (calcifying) pancreatitis is the most common form we see here. In this typean intraductal protein precipitate for various reasons, this calcifies with formation of calculi & obstructs the flow of pancreatic juice.

Types of calcifying chronic pancreatitis are differentiated as:

A. Alcoholic

B. Idiopathic chronic pancreatitis

C. Nutritional (tropical) pancreatitis

D. Hereditary Pancreatitis

E. Obstructive Chronic pancreatitis

Nutritional (tropical) pancreatitis is a special kind, which is seen in children and is of particular concern. The following peculiarities of the variant are worth mention.

- Onset in younger adults with intraductal stones
- Predominant in Kerala, regions of S America & Africa
- May be attributed to low protein diet
- Progressive disease with insulin dependent diabetes

Chronic Pancreatitis-Classification is based on microscopic finding in autopsies or specimen removed surgically. (As per histology)

- Chronic pancreatitis with diffuse or segmental fibrosis
- Chronic pancreatitis with or without focal necroses
- Chronic pancreatitis with or without calcification
- Chronic obstructive pancreatitis

Chronic Pancreatitis – Classification/ Grading according to the severity of Scarring in its parenchyma.

There are 4 grades of classification as per scarring. These are-

1. Grade I : Slight scarring (perilobular arrangement)
2. Grade II : moderate scarring
3. Grade III : High grade scarring (intralobular scars in greater areas)
4. Grade IV : complete scarring & destruction of exocrine parenchyma

The following chart will give some idea about the various classifications prevalent amongst the researchers in various corners of the world.

Previous classification of chronic pancreatitis

Classifications of Chronic pancreatitis	Major objectives, definitions, and criteria
Clinical description 1946	Description of the clinical presentation of chronic pancreatitis and its association with increased alcohol consumption
Marseille 1963	Description of morphologic characteristics and etiological factors of the disease; no discussion of the correlation between anatomic and functional changes; no categorization according to disease severity or clinical presentation; no inclusion of pancreatic imaging findings
Marseille 1984	Further description and subclassification of morphological changes; "obstructive chronic pancreatitis" listed as distinct form; no discussion of the correlation between anatomic and functional changes; no categorization according to disease severity or clinical presentation; no inclusion of pancreatic imaging findings
Marseille-Rome 1988	Further description of "chronic calcifying" and "chronic inflammatory" pancreatitis as distinct forms; description of etiological factors; no further elaboration of clinical, functional, or imaging criteria
Cambridge 1984	Classification of disease severity based on pancreatic imaging criteria (US, CT, ERCP); further discussion of etiological factors, pancreatic function, and testing for pancreatic insufficiency; morphologic characteristics not clearly defined
Clinical stages 1994	Detailed subclassification of chronic pancreatitis with correlation of etiological factors with different morphological forms of the disease; differentiation of clinical stages of the disease; linkage of pancreatic imaging findings and functional testing with stages of the disease
Japan Pancreas Society 1997	Description of clinical presentation and classification of disease in "definite" and "probable" chronic pancreatitis according to imaging findings, functional testing, and histological examination
Zürich Workshop 1997	Description of clinical presentation and classification of disease in "definite" and "probable" chronic pancreatitis according to imaging findings, functional testing, and histological examination
TIGAR-O 2001	Detailed categorization of etiological risk factors
ABC grading system 2002	Disease grading according to clinical criteria, but limited separation of different disease severities; not all clinical presentations can be categorized
Manchester system 2006	Disease grading according to clinical criteria, but limited separation of different disease severities; not all clinical presentations can be categorized

US, ultrasonography; CT, computed tomography; ERCP, endoscopic retrograde cholangiopancreatography

Pic. 3. Classification systems available to understand Chronic Pancreatitis.

The MANNHEIM factors of disease severity score is also another guideline for understanding the disease.

The M-ANNHEIM multiple risk factor classification of chronic pancreatitis

	M Pancreatitis with Multiple risk factors
A	Alcohol consumption Excessive consumption (>80 g/day) Increased consumption (20–80 g/day) Moderate consumption (<20 g/day)
N	Nicotine consumption (In cigarette smokers: description of nicotine consumption by pack-years)
N	Nutritional factors Nutrition (e.g., high calorie proportion of fat and protein) Hyperlipidemia
H	Hereditary factors Hereditary pancreatitis (defined according to Whitcomb) Familial pancreatitis (defined according to Whitcomb) Early-onset idiopathic pancreatitis Late-onset idiopathic pancreatitis Tropical pancreatitis (possible mutations in the *PRSS1*, *CFTR*, or *SPINK1* genes)
E	**Efferent Duct** Annular pancreas and other congenital abnormalities of the pancreas Pancreatic duct obstruction (e.g., tumors) Posttraumatic pancreatic duct scars Sphincter of Oddi dysfunction
I	Immunological Factors Autoimmune pancreatitis Sjögren syndrome-associated chronic pancreatitis Inflammatory bowel disease-associated chronic pancreatitis Chronic pancreatitis with autoimmune diseases (e.g., primary sclerosing cholangitis, primary biliary cirrhosis)
M	Miscellaneous and rare metabolic factors Hypercalcemia and hyperparathyroidism Chronic renal failure, Drugs & Toxins

The M-ANNHEIM classification is based on the assumption that, in the majority of patients, chronic pancreatitis results from the interaction of multiple risk factors (M). The different risk factors are grouped into the major subcategories of alcohol consumption (A), nicotine consump- tion (N), nutritional factors (N), hereditary factors (H), efferent pancreatic duct factors (E), immunological factors (I), and various rare miscellaneous and metabolic factors (M)
Hereditary and familial pancreatitis are defined according to Whitcomb. Hereditary pancreatitis refers to otherwise unexplained pancreatitis in an individual from a family in which the pancreatitis phenotype appears to be inherited through a disease-causing gene mutation expressed in an autosomal dominant pattern. Familial pancreatitis refers to pancreatitis due to any cause that occurs in a family with an incidence higher than would be expected by chance alone, given the size of the family and incidence of pancreatitis within a defined population. Thus, familal pancreatitis may or may not be caused by a genetic defect. Idiopathic pancreatitis is defined as pancreatitis in isolated cases within a family, in which all other causes of the disease have been excluded

Pic. 4. MANNHEIM Classification.

Clinical features of chronic pancreatitis.

Abdominal Pain

• This is indeed leading symptom in 80-90% of Chronic pancreatitis cases. Which is often described as low- situated, intermittent or chronic persistent, piercing or sharp pain. It is maximal in right or left upper quadrants in back or diffuse throughout the upper abdomen. It is also persistent, deep seated & unresponsive to antacids. This pain often increased by alcohol &ingestion of heavy meals (especially foods rich in fat). The pain lasts for several days.

• Symptoms usually subside after 3 to 7 days in uncomplicated cases.

Weight loss / fat and protein malabsorption

• Most will also have massive foul smelling greasy stools in about 25-33% with chronic calcifying pancreatitis (steatorrhoea). Fat & protein malabsorption when 90% loss of pancreatic secretory capacity is noticed with Sarcopenia.
• Both pain abdomen and Fat malabsorption will present in upto 70% of patients

Diabetes mellitus

• Present in 70% of patients in presence of radiographic calcifications.But it tends to ddevelop frequently in final stage of the condition before burnout.
• Prevalence in 30-70% of patients with steatorrhea& calcifications.

Pancreatic exocrine insufficiency (PEI)

• Defined as impaired exocrine function of pancreas, resulting in decreased pancreatic enzyme output & activity (50-70% of the CP Patients).

Management of Chronic Pancreatitis:

Strategies to improve pain control through behavioural modification, endoscopic measures, and surgery must also accompany management of the sequalae of complications that arise from endocrine and exocrine insufficiency.
Therefore, the treatment of Chronic Pancreatitis is divided into conservative, operative as well as Psychiatric involvement. An endoscopic subgroup is gaining ground too. Let us recapitulate about each a little.

Conservative management : Includes

• Proper balanced Diet and abstinence from alcohol
• Exocrine supplementation to deal with the Pancreatic Exocrine Insufficiency (EPI)
• Analgesics
• Pancreatic enzyme supplementation
• Endoscopic techniques like lithotripsy and Stenting
• Somatostatin and its analogue Octreotide (?)

Surgical treatment. It has few variants as given below.

These can either be **Drainage procedures like**

• LPJ (Lateral Pancreaticojejunostomy)
• Puestow's Procedure Etc.

Or **Resectional procedures like**
• Frey's (The famed Head coring technique)
• Berne's
• Beger Procedure
• Pylorus preserving Whipple's
• Duodenal preserving pancreatic head resection
• Classical Whipple's

In many cases Resectional and drainage combined procedures are adopted too.
The type of treatment of course depends on the severity of pancreatitis. The Resectional procedures like Beger's; Types of Pancreaticoduodenectomy are difficult procedures and best be tried in centers with vast experiences in managing such cases. The intrinsic scarring as well as extra pancreatic fibrosis make the procedures mentioned above not only difficult but extremely difficult at times.

In mild pancreatitis, general complications occur in less than 10% of patients and pancreatic inflammation subsides spontaneously. Studies show that surgery will eventually be required in about 40 to 75 % of patients with chronic pancreatitis during the course of their disease.
In England, over 1,000 people die from acute pancreatitis every year.

However only 3-10% of the Survivors of severe acute pancreatitis will progress into the Chronic Pancreatitis stage.

Pathogenesis or pathophysiology

Pathogenesis or pathophysiology of Chronic Pancreatitis is poorly understood but, the Etiology is well documented: These can be,
1. Excessive alcohol consumption
2. Cholelithiasis
3. Autoimmune
4. Genetic or hereditary
5. Anatomical variations (Divisum)
6. Nutritional
7. Smoking (Japan, 2016)

A series of mechanisms are postulated as to the pathophysiology of developing of Chronic Pancreatitis. These are-

i) The direct effect of toxic metabolites (e. g. tobacco, alcohol) on acinar cells,

(ii) A "two-hit" model in which an episode of acute pancreatitis causes activation of pancreatic stellate cells with subsequent fibrosis,

(iii) Ductal dysfunction causing obstruction secondary to formation of protein plugs,

(iv) Oxidative stress in acinar cells secondary to free radicals promoting fusion of lysosomes and

(v) A necrosis-fibrosis sequence as a result of repeated episodes of acute pancreatitis

To organize and classify patients with CP has led to development of multiple classification systems over the years, from Comfort et al in 1946 to the Marseille, 1983, Cambridge, 1999, Zurich and TIGAR-O systems amongst others . More recently, the M ANNHEIM , 2017, classification has sought to unify these systems and permit aetiology and clinical severity to be included in stratification. (Pic.3 & Pic. 4). Whilst these systems have contributed greatly to the study of Chronic Pancreatitis, none of them are specifically focused on a surgical approach. Although patients may be classified by these systems as "probable pancreatitis" (Zurich system), "moderate changes" (Cambridge system) or "M-ANNHEIM C", none of these though do not assist the surgeon in making the management decisions.

With the increasing evidence to support surgery in treatment of Chronic Pancreatitis, there is a need to stratify patients differently to aid the operative decision-making process.

The frequency of a pancreatic burnout increased with prolonged disease duration and was observed in a maximum of 38% of patients after 20 years of harboring the disease.

Development of a pancreatic burnout was significantly associated with alcohol consumption ($P < 0.05$, Mann-Whitney U test), but not with other etiological risk factors. After a disease duration of more than 10 years, the likelihood of a burnout was 8 times higher in alcoholic Chronic Pancreatitis than in nonalcoholic Chronic Pancreatitis (95% confidence interval, 1.5–42.0; P=0.015, logistic regression analysis).

Dite and colleagues studied the effects of Endoscopic therapy and surgery.

In a series, 72 patients were randomized to study the effect of surgery and therapeutic endoscopy.

Resection was the most common surgical procedure (80%) while surgical drainage was performed in 20% of patients.

Sphincterotomy and stenting (52%) and/or stone removal in 23% of patients were the most commonly performed intervention in the endoscopy arm.

Initial success rates for pain relief were similarly high (> 90% of patients with at least a partial pain relief after 1 year follow up) for both groups, these clinical outcomes changed noticeably after 3 and 5 years follow up

In the surgical treatment group 42% of patients showed a persistent complete pain relief after 1 year, which only slightly decreased to 41% after 3 and to 37% after 5 years. Endotherapy effect substantially decreased to 11% after 3, and to 14% after 5 years. Accordingly, the rate of non-responders was disappointingly high with 33-35% in the endoscopy arm versus only 12-14% in the surgical treatment arm after 3 and 5 years. Results were similar regarding the patient's body weight.

Dite and colleagues concluded that surgery seems to be superior to endoscopic treatment concerning long-term pain relief and body weight gain in Chronic Pancreatitis patients.

(It should be noted however, that endoscopic drainage techniques in this study did not meet current standards, as it did not include ESWL and for some patients only consisted of a sphincterotomy.)

At long-term follow up of up to 7 years, these numbers did not change considerably (38% vs. 80%). Additionally, endoscopically treated patients underwent significantly more re-interventions than surgically treated patients (8 vs. 3 at first follow up and 12 vs. 4 at the second follow up).

It could be concluded that surgical drainage is superior to endoscopic treatment and should be regarded as the preferred treatment option in patients with advanced disease.

In addition, At onset 8% has diabetes mellitus. After 10 years the number increases to 80%. At ten years 50-93% patients will have pain asking for reduction..

Finally of these patients, 50-68% will need surgery for pain or complications.

Some may need Total Pancreatectomy (TP). TP patients need active management of DM.

12 published articles indicated that Total Pancreatectomy with Islet Auto Transplant (TPIAT) is safe, with a 30-day mortality of 2.1% and a long-term mortality of 1.09 per 100 person-years,

Points to be noted here that :-

- Reduction of alcohol does not influence the pain.
- Continued indulgence lowers survival amongst the patients suffering from alcoholic Chronic Pancreatitis.
- Avoiding alcohol will improve exocrine function, But not endocrine function.

Two systematic reviews which carried out meta-analyses reported pooled insulin independence rates of 27% (95% CI: 21–33%) and 28.4% (95% CI: 15.7–46.0) at one year and 21% (95% CI: 16–27%) and 19.7% (95% CI: 5.1–52.6%) at two years, respectively.

Complications do occur in Chronic Pancreatitis.

These are

1. Stricture of CBD (5-9%)
2. Pancreatic Ascites (4%)
3. Pancreatico pleural Fistula- Rare
4. Extrahepatic Portal Hypertension
5. Splenic artery Aneurisms
6. Duodenal obstruction in the operated cases (12%)
7. Etc.

One must remember though that Chronic Pancreatitis cannot be cured and as per the present-day understanding can only be controlled. However, a good quality of life must be offered to these unfortunate patients.

The Gastrointestinal Quality of Life Index is a reliable score to consider here. The Gastrointestinal Quality of Life Index, a reliable and validated bilingual (German and English) instrument developed in 1989, was designed to assess QoL in patients with gastrointestinal diseases .The questionnaire constitutes 36 questions with five possible responses for each question. Each individual response is scored on a scale of 0–4 (0: least desirable; 4: most desirable) with all the responses summed to give an overall numerical score on a scale of 0–144. A higher overall score implies better QoL.

It is not a diagnostic tool and while it can moderately differentiate between healthy individuals and those with gastrointestinal diseases, it also does not distinguish between diseases.

There is another scale. The Abdominal Surgery Impact Scale (ASIS).

The ASIS questionnaire was initially designed to assess short-term QoL following abdominal surgery. The ASIS constitutes of 18 questions (scored on a scale ranging from 1 (strongly agree) to 7 (strongly disagree).

This is Categorized into six domains:

1. Physical limitations,
2. functional impairment,
3. pain,
4. visceral function,
5. sleep, and
6. psychological well-being.

The score can range from 18 to 126. The ASIS was found to be reliable for five out of six domains.

Conclusion-

To conclude it can be safely said that the treating surgeon must have the basic understanding on the disease. Without appreciating the following facts, management of Chronic Pancreatitis will be unsuccessful as the management not only targets physical but also the psychological well being.

Chronic Pancreatitis is a Major Disease

- The most common feature is pain
- It causes Morbidity in Young adults
- It is more in Men (working age group men)
- Only Conservatives give temporary relief
- Interventions are needed
- Endoscopic interventions are good for short term relief.
- More permanent relief and long lasting relief can be achieved only by surgery
- Resectional Surgery is better than Drainage only
- Frey's is a good procedure
- Abstinence from alcohol improves exocrine function
- Islet cell transplant is a feasible procedure after TP
- Some function, both the exocrine and endocrine improve after surgery.

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3D Printing and Bio Printing in Tissue Reconstruction - Current Concept

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Abstract : 3D technology is a new armamentarium in the field of reconstruction. Advances in this field involves synthesis of living tissues, known as 3D bioprinting with precise layering of cells on biological scaffolds with precisely controlledspatial distribution& growth factors resulting in reconstruction of bioidentical tissue for using in various type of complex reconstruction. Experimental studies followed by some clinical results shows promising outcome.[1]

Fig 1. Science of Bio printing: Experimentation 3D PRINTING MACHINES

It is important to mimic the Microenvironment typical of the tissue to be reconstructed. The other two main challenges are optimal cell viability and tissue vascularization.[2]

3D Bioprinting recapitulates the native architecture of tissues with precise deposition of cell containing bioinks. The spatiotemporal control over bioinks deposition permits for improved communication between cells and the extracellular matrix, which facilitates fabrication of Anatomically and physiologically relevant structures.

The physiochemical properties of bio inks, before and aftercrosslinking are crucial for bioprinting complex tissue structures. The cell viability during the printing process, post crosslinking of bioinks is critical for their mechanical integrity, physiological stability, cell survival and cell functions. Appropriate polymer selection is essential to maintain viability of encapsulated cells and achieve the necessary mechanical requirements for 3Dprinting.(3) The crucial bio ink characteristics at pre-extrusion stage include precursor cell viscosity, cell distribution, and biocompatibility. The critical bio ink at mid extrusion stage considers shear stress minimization through plug flow behavior, and post extrusion stage includes physiological stability post cross linking of 3D printed structures.

3D printed cell delivery scaffolds (Fig2) as beautifully illustrated[3]

Fig: 2 cell delivery, 3D printing, tissue regeneration. (Copied fromref:3)

There are three categories of 3D printing strategies.

1.Ink Jet – based printing (IBP)

2.Extrusion based Printing (EBP)

3.Light based printing (LBP)

Biomaterials & cells are generally referred to as 'bio inks '. Bio inks- including printable biomaterials, cells, and other biologics -are materials used in 3D bioprinting to develop tissue constructs and organoids. Bio materials provide appropriate micro-environments and structural supports for cell adhesion, migration, proliferation and - differentiation [4]

Types of 3D Bioprinting Technology:

a. Extrusion based bioprinting. Or microextrusion is the most common method of printing non biological 3D structures.

b. Pressure assisted bioprinting (PAB)

c. Laser assisted bioprinting (LAB) It is based on the deposition of biomaterials onto a substrate using a laser as the energy source.

d. Stereolithography (STL) (29th April 2022 internet)

The organ shortage is a global crisis and there is an increasing demand. With the development of 3 D printing technology, it is expected that not only tissue bio printing but organ construction will be a regular phenomenon in future.

Key words: 3D printing,3D bioprinting, Regenerative Medicine, scaffold,

INTRODUCTION:

3D printing is not only used for printing out surgical models & prosthetics but also 3Dprint can be used for reconstruction of complex tissues that can be implanted to replace various tissues &organs, the method known as 3D Bioprinting. In this method Bio inks are made from a mixture of chemicals, stem cells or living cells. The actual printing is carried out in scaffold consisting of a gel like base made up from Collagen, Gelatin, Hyaluronan, Silk, Alginate or Nano Cellulose. This development has revolutionized health care sector and in future it will definitely be a boon to the patients as well as the caregivers.[5]

3D bioprinting offers unprecedented versatility to co-deliver cells and biomaterials with precise control over deposition of layered cells.

The Process of Bioprinting goes through several stages.

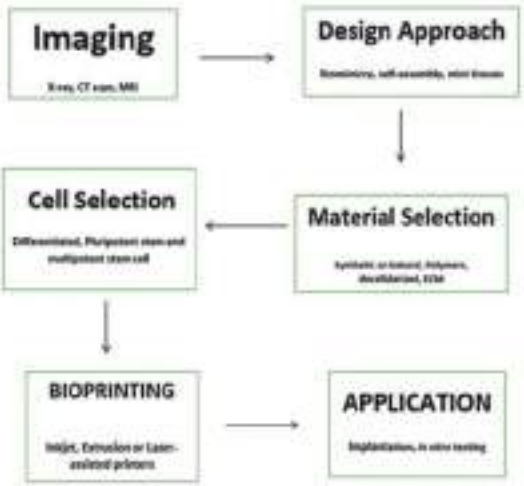

Fig 3: Stages of Bio printing.

1.Patient data imaging: A digital file is made from patients MRI & CT scans.

2. 3D modelling : A medically compatible CAD software to create a 3D CAD model of the implant.

3.Material/ Bio inks: One of the most crucial steps, which can directly impact the patient.The cartridges are loaded with Bio inks for bio printing.

2. Pre Bioprinting:The loaded cartridges and final setting of the image is rechecked to eliminate any occurrence of failure.

3. Bio Printing: The Bio Printer prints the model in a well-defined modelin a Gel like scaffold (Hydrogel). Layer by layer of printing continues at a moderate pace and deposited on the top of previously solidified layers and the completed object takes the desired shape.

4. Curing Stage: Once the printing is completed, the Bio printed structure is left in the Gel for maturation & growth.Various factors that influence the curing process are -Time, U V Light exposure, Temperature, Chemicals etc.
After sufficient maturation, the printed structure is separated from hydrogel to be used in implants or experiments.Most cases the support material is meltedaway to release the Bio-printed part easily. [5]

5. Post BioPrinting: After establishing cytocompatibility, the bio ink can be printed into complex shapes and geometrics. Various other additional biological and mechanical characteristics are need to be considered. Post printing considerations: a)Optical image analysis to examine quality, spreading and printability, b) Compressive mechanical Analysis to evaluate stability and compressive modulus of the 3D bio printed construct. C) Swelling & degradation Analysis of the bio ink, which is crucial in designing. Swelling can influence post printing mechanics. Effect of cellular compatibility is an essential partto understand bio ink – cell interactions and how the cell can be stimulated by Bio ink.
Software CAD was used to develop 3 D structures. However, the organ and tissue printing developed later. [5]

Achieving a synergistic balance of all properties is required to maintain printabilitywith active cellular viability and proliferation. For e.g., Viscosity influences the ability of bio ink to flow. Bio inks must overcome certain amount of stress, deemed yield stress. This yield stress is the minimum stress that must be placed on the material for flow to occur.

Collagen is the most abundant protein within the Human Body & is an important ECM component. Both ECM adhesion sites & mechanical properties are of paramount importance when selecting biomaterial constituents. The main goal of fabricated ECM is to provide adequate sites to the cell for binding, as well as a 3D architecture& mechanical stiffness similar to the native tissue

Most structures like the Ears,Nose, Facial bones,skin, Blood Vesselsetc. and other complex structures can be bio-printed avoiding complex &staged surgical reconstruction in major wounds, Burn etc.It has been tried to bio print a hair follicle and the research is on. So, in future, one can probably avoid long and expensive hair implant procedures.

Bioengineers and surgeons have also made advancement in reconstructing unique pattern of specific corneas. Bio printing Skin is possible with the naturally occurring pigmentation. Researchers used different type of skin cells – melanocytes.[5]). When it will be possible to be widely used, it is going to be a boon to the extensive Burn patients giving them a new life.

Reconstruction of various tissues is an integral part of Plastic Surgery. Clinically there may be circumstances where there is significant deformity, which may be quite difficult to reproduce with complex
3D geometry of the defect. Bioprintingdevice using biological ink, by reconstructing layer by layer over a scaffold has made it possible and revolutionized the health care sector.

The application of 3D bioprinting technology often involves multiple areas of tissue engineering, such as Skin, bone, cartilage etc. Moreover, the ECM of different tissue has different properties, and the cellular structure within different tissues varies. 03 Jan-2023. (Internet.)

For different actual clinical needs and applications in Plastic Surgery,e.g., Skin wound healing, Rhinoplasty, ear reconstruction, it is necessary to select the right bioprinting materials, pick or combine different bioprinting technologies., in order to finally develop a suitable bioprinting strategy. (internet).

For extensive and complex defects,quantity of tissue required to restore form and function may be a difficult task for various reasons which may not match patients healing capacity, and or tissues

regenerative capacity. Also, increased operating time, graft resorption, donor site morbidity, limited supply and most importantly the cost factor involved with long and difficult surgery are other determining factors.

Plastic and reconstructive surgery has come a long way in the area of reconstructions from simple to most complex using vascularized tissue to reduce resorption. Free flaps have become gold standard but still it has other disadvantages viz donor site morbidity and requires expertise in the field.

Tissue engineering provides a promising strategy and facilitates tissue repair by transplanting cells and biomolecules into biomaterial scaffolds. 3-D tissue engineering with printing on biological scaffolds has grown into a specialty in the past two decades. It employs a layer-by-layer manufacturing technique, andit is possible to reconstruct complex geometrical structures, which restores both aesthetic and functional goal.

HISTORY :

3D printing is gradually evolving into an emerging technology, that enables fabrication of biometric multiscale multicellular tissue in highly complex microenvironment, creates intricate cytoarchitecture with tissue specific structure with specific composition while maintaining mechanical integrity.

The first approach to creating 3D printing technology was made in May 1981 by Dr. Hideo Kodama, of the Nagoya Municipal Industrial Research Institutein Japan, who published details of a "rapid proto typing" technique. He came up with a layer-by-layer approach for manufacturing, using a photosensitive resin that was polymerized by UV light. 3D printing is an additive process whereby layers of material are built up to create a 3D part. This is opposite to subtractive manufacturing process, where a final design is cut from a larger block of material. As a result, 3D printing creates less material wastage.

Father of 3D printing is Chuck Hull& uses of 3D printing are manufacturing,architecture, custom art and design and can vary from fully functional to purely aesthetic applications. (Internet)

The concept of 3D printing was first described by David E.H. Jones back in 1974 [6] it was then established by video Kodama using photo hardening thermoset polymers for fabricating 3D plastic models as the early additive manufacturing (AM) process in 1981 [6]

Later in 1986a 3D printing methodology named" Stereolithography" was brought to light by Charles W. Hull, wherein layers of materialswere sequentially printed layer by layer and then cured to form solid structures by being placed under ultraviolet (UV) light [7]

Progress continued in 1999, when the first artificial organ made using bioprinting was printed by a team of scientist lead by Dr. Anthony Atala at the Wake Forest Institute for regenerative Medicine.

BASICS:(MATERIAL AND METHODS)

3D Bioprinting has been an emerging technique, used in multiple ways in most complex repairs. At first, it was used only for printing out presurgical models and prosthetics. Bioprinting prints three dimensional tissues and organs from specially formulated bio inks. The bio inks are made from a mixture of chemicals, stem cells or other living cells. Actual printing is carried out in a gel like base made from collagen, Gelatin, Hyaluronan, silk, Fibrin, alginate or Nanocellulose etc.– (sourceInternet)

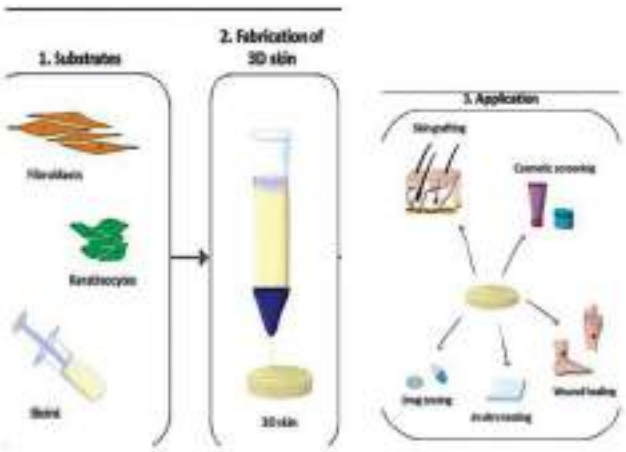

Fig 5: Processing& application of 3D Bio Ink as described by Li et al

Thermal inkjet Bioprinting Technology

A. A piezoelectric transducer generates a pulse that creates transient pressure resulting in droplet ejection

B. Pressure assisted Bio Printing uses solutions or pastes that is extruded through a microneedle.

C. Laser based Bio Printing consists of 3 parts: A pulsed laser source, a ribbon and receiving substrate.

The three basic steps in the 3D bioprinting process includes:

a) Pre-Printing/ Pre processing
b) Bioprinting technology to bio print a tissue construct and crosslinking to maintain a stable structure.
c) Post bioprinting.[8]

The components of bioprinting used in LASER ASSISTED BIOPRINTING include a hydrogel culture media, cells, proteins & ceramic materials. The speed of bioprinters is medium. It retains almost 95% of cell viability.
(https://thebiologynotes.com)

3D Bio Printing is based on 3 fundamental approaches. 1) Biomimicry or Biomimetics, 2) Autonomous cell assembly and 3) Mini Tissue building blocks [9]

The scaffold offers a surface upon which cells adhere, multiply, thriveand produce an extracellular matrix of structural and functional proteins & saccharides that create the living tissue [10]

So, broadly, three main technological systems of bioprinting include Inkjet based bioprinting, Extrusion based bioprinting & Laser based bioprinting. The three essential components of 3D bioprinting are CELLS, BIOMATERIALS AND GROWTH FACTORS.

Review of literature:
Bioprinting organs & tissue patches from a patient's own cells reduces the chance of rejection and can eliminate the need for organ donors (2nd dec 2022 https://www.brinter.com, benefits)

The purpose of 3D printing techniques is to fabricate tissue, organs, and biomedical parts that imitate natural tissue architecture. It also combines cells, growth factors and biomaterials to create a microenvironment in which cells can grow and differentiate in tissue structures. (http://www.sciencedirect . com...)

In the early 2000s researchers discovered that living cells could be sprayed through the nozzles of inkjet printers without damaging them. It was also stressed that to stay alive they need nurturing environments, food, water & oxygen. It is provided by a microgel, gelatin enriched with vitamins, proteins & other life sustainingcompounds. And for fastest growth and efficient cell growth, the cells were placed around 3D scaffolds made of biodegradable polymers or collagen so that they can grow into a fully functional tissue. Eradicating Transplantation waiting lists and Testing Drugs on Living Tissues. – Full overview of how 3Dbioprinting will break into healthcare revolutionizing organ donation& animal testing. (Dr Bertalan Mesko, PhD).Bone tissue, as the basic supporting and protective tissue of human body. There is enormous demands of bone transplantation and rapid progress has been made in this field. Bone tissue is filled with blood vessels that are involved in physiological activities such as nutrient transport, metabolism and bone hemostasis maintenance [11]

Skin is the first layer of protection of Human body from foreign substances. Early Skin replacement is a must to protect exposed body parts from infection and other hazards.Bio printing technology has been applied to produce skin substitute for the repair of damaged skin. The use of bioprinting will enable incorporation of other cell types in the dermis including hair follicles and sweat and sebaceous glands. This will enable regeneration of the skin tissue with structure and cellular composition resembling native tissue. [12]

Although bone has the intrinsic property of self-repair, in many cases, bone cannot fully regenerate and requires external stimulation. Current solutions may not be always effective. Hence there is need to explore alternative techniques. 3D bioprinting has been used to manufacture bone and blood vessels and extracellular matrices. [13]

Bone tissue is filled with blood vessels as nutrient transport, it is important to promote the repair of bone tissuewith blood vessels simultaneously for functionalized bone regeneration. It has been seen that sensory nerves and sympathetic nerves can participate in bone tissue regenerationthrough secreting neurotrophinsand neuropeptides [14-15]

Cartilage tissue is widely found in joints, auricles and trachea. It has poor ability of nutrients transportation, since there is no blood vessel within it. Therefore, once it gets injured, the damaged cartilage is hard to self-repair [16]. To better treat these defects, so called matrix associated autologous chondrocyte implantation has been proposed. 3D printed cell seeded scaffolds in cartilage repair, which will mimic natural cartilage tissue structures to prepare tissue engineered constructs with irregular shape., which expanded the application the field of cartilage tissue engineering. [16].

Complex Tissue Regeneration: The complex tissue is composed of two or more types of tissue with different properties and lineages.Some common examples are **osteochondral tissue, Tendon to Bone tissue, Bone Cartilage tissue** of joints is a typical complex tissue. Critchley et al [17] designed biphasic 3D printed scaffolds for treatment of osteochondral defects.

Muscle Tissue Regeneration:
Costantini et al [18] fabricated an artificial skeletal muscle by 3D bio-printed muscle precursor cells (C2C12)- laden hydrogel with fiber structures. This has been tested in vitro and in vivo in nude mice.

Spinal cord Regeneration:
Several researchers have developed 3D bio printed scaffolds for spinal cord regeneration. Koffer J et al [19] bio printed a neural progenitor cell (NPCs)-loaded scaffold by using microscale continuous projection printing method (M CPP) to repair the SCI.

Skin Colour: While surgery is the first challenge the hurdle is skin colour mismatch at the site of replacement. Researchers have developed a way that can make bio printing of skin is possible with the naturally occurring pigmentation. This process is truly revolutionary as published data suggests that different type of skin cells Melanocytes, Keratinocytes and fibroblasts and used 3D bioprinting to control the distribution of Melanocytes using a two-step drop on demand bioprinting strategy.[20]

Patients with Liver transplantation demands have two options. Either wait for healthy live donors or extremely long self-generation process of Liver tissue. Under the circumstances 3 D bioprinting of Liver tissue is particularly important for enabling more options for liver transplantation [21]

First developments in 3D printing, was first described as "Stereolithography"by Charles W.Hull [22] The definition of Bio fabricationhas been further refined to include "Bio printing "and "Bioassembly "as complementary parts of Biofabrication process [23]

Three-dimensional (3D) printing of scaffolds for tissue engineering applications has grown substantially in the past two decades. Unlike conventional autografts and allografts, 3D scaffold can satisfy the growing need for personalized bony reconstruction following massive craniofacial bone loss. Employing layer by layer manufacturing techniques it is possible to produce patient specific structures to rebuild complex geometries for aesthetic purposes and respiratory functions.[24] Applications of tissue engineering are many. With 3D Bio-Printing, different types of body tissue can be reconstructed. Thenthis generated tissue which has the potential for growth and maturation by placing in a suitable environment where it can replicate themselves further and form organs. Thus, it provides natural artificial organs with natural characters for transplants and surgeries.

Tissue engineering provides a promising strategy to facilitate tissue repair by transplanting cells and biomolecules into biomaterial scaffolds. (24)Bioprinting drug delivery system has been developed as delivery vehicles using printed cells, biocompatible tissue, specific hydrogels or implantable devices. This will provide localized and tissue specific drug delivery, allowing for targeted disease treatment with scalable and complex geometry. This will help to overcome limitations with higher organ donation and transplantation, which will otherwise result in organ rejection with individual immune responses. Bioprinting drug delivery (Wikipedia)

Organ Printing : Organ printing utilizes techniques similar to conventional 3D printing where a computer model is fed into a printer that lays down successive layers of plastics or wax until a 3D object is produced. In the case of organ printing, the material being used by the printer is biocompatible plastic. (Wikipedia)

In 2005, Kesari & colleagues made one of the first attempts to construct tubular hydrogel structures using drop on demand ink jet printing. [25]

A major challenge for 3D printing technologies is in the construction of medical devices and biological tissues & organs.

Discussion & Summary

In the past decades, tissue engineering strategy of integrating biological scaffolds and living cells has been a promising alternative for autograft and allografttransplantation.[26] Specifically, the tissue engineering scaffolds act as the artificial extracellular matrix (ECM) for supporting cell attachment, proliferation and delivery, finally creating functional constructs to replace/ repair injured tissues.[27] Therefore, tissue engineering scaffolds should possess several basic properties, such as excellent biocompatibility, sufficient mechanical support, good transportation capacity and suitable micro environment for cells [28]. 3D bioprinting methods has certain requirements for the printing environment and parameters since cells are sensitive to inappropriate conditions, which means that the bio inks and printing conditions, should be designed in detail in advance.

why we should use 3D printed scaffolds,for it gives almost near normal results,can avoid stressful and long surgeries, post-operative care, donor site morbidity, complex and challenging surgeries, Pediatric patient and when there is critical sized craniofacial boneloss and when enough tissue is not available in the body.

Advantages of 3D bioprinting:

1. Allows mimicking the real structure of desired tissue/ organ etc.Enables the scientists to more precisely engineer tissue
2. Possibility to revolutionize future medical treatment capabilities.
3. Possible creation of patient specific and organ specific and organ specific treatments.
4. Effects of drugs can be examined more accurately.
5. Decreases Animal testing.
6. Complicated and long surgeries may be avoided.
7. Possible to mimic real structure of complex anatomy, e.g., of Face, Ear, Nose, midface, eyesocket etc.

Disadvantages / Risk are Teratoma and cancer, dislodgement and migrations of implant

3D printed internal organs are still years off from being ready for implantation. Research is on across the world and days are not far off when bio printed custom made organs would be available.(Source-Internet).

Bio ceramics are popular material candidates for craniofacial bone regeneration, such as dental implants, alveolar ridge augmentation and maxillofacial surgery., due to their wear resistance and similarities in composition to the inorganic matrix of the bone. Hydroxyapatite(HA) is the predominant composition of bone matrix and possess biocompatible and osteoconductive properties.

Most of the bioprinters used for 3D organ printing can cost an average $100,000 while living tissue can be printed for about $1000. It requires highly skilled professionals and takes quite a long time to conduct research to ensure successful results. (Source: Internet)

CONCLUSION:

3Dbioprinting is basically a rapid phototyping and additive manufacturing technique used to fabricate artificial implants or complex tissue constructs through a layer -by-layer building process for patient specific therapy.

The first organ that has been artificially engineered 3D bioprinted is bladder, which was printed, covered in the recipients own cells, and then implanted in 1999.In Wake Forest university School of Medicine in Winston- Salem, North Carolina, cells from seven children with spina bifida were extracted and

used to grow thin sacs of tissue. (Source: Internet)

Despite promising advances in bioprinting, it is still immensely difficult to reproduce the delicate structure – function relationships of complex tissues and organs for example Kidney & Heart remains an aspirational goal. However, the formation of more simple tissues such as Adipose tissue for Breast Reconstruction, represents an important step in translational bioprinting research.There is a great need for breast reconstruction characterized by simplicity along with a low complication profile. 3D bioprinting adipose tissue for Breast Reconstruction M.P. Chae.... M W. Findlay,in 3D bioprinting for reconstructive surgery.[29]

The first 3D bioprinting center in India is in Bengaluru. Sweden headquartered CELLLINK, the global leader in developing 3D bioprinters, and the Indian Institute of Science (IISC), Bengaluru have opened the doors to the first Bioprinting center of Excellence in the Indian subcontinent.

Days are not far away when with more advancement in this field in future, we will get human tissue and organs like Heart, Lung, Blood vessels, Extracellular Matrix, Bone, Cartilage,Meniscus, Complex structures like Nose, Ear, Skin on order, all custom made. This will definitely reduce the requirement of complex reconstructions and make life easy for both patients and doctors. Most researchers put the idea of full-sized 3D printed organ transplantation in humans at somewhere between 20-30 years away. But will the doctor get the same satisfaction as in complex reconstruction planning & execution? only time will tell.

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Gastric Cancer Treated by R0-D2 Gastric Resection Followed by Adjuvant Therapy and Effect of Helicobacter Pylori.

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Abstract :

Helicobacter pylori(HP) a gm –ve bacteria invented in 1983 has been associated with diverse pathologies of varying severityin the gastric and extra gastric organs. We had studied the H. Pylori infection status and its association with the pathologic features and clinical outcomes in stage III gastric cancer(LAGC) patients treated with adjuvant therapy after curative resection(RO/D2). Between 2014 and January,2018, the records of 50 consecutive patients were retrospectively reviewed in the Deptt of Surgery, Gauhati Medical College. H. Pylori infection was confirmed by examination of pathological specimen (RUT+ HPE). The relationship between H. Pylori and the clinicopathological features was analyzed by Fisher exact test, Student's t test, and Kaplan-Meier method. Of the 50 patients, 11 patients (22%) were confirmed for H. Pylori infection. The median age was 65 years. Sixteen patients received chemotherapy and remainder received chemoradiotherapy. H. Pylori status did not correlate with the clinicopathologic features in significant. It was greater in non-neoplastic tissue than the tumor tissue (21% vs 8 %). Median follow-up was 20 months. During this period, 88.2% patients had experienced tumor recurrence, and 85.5% patients had died. Recurrence was observed in 87.5% patients and in 88.3% patients in H. Pylori-positive and H. Pylori-negative patients respectively (P=0. 92). Disease-free survival was 27 + 7 months and overall survival was 29 + 6 months in H. Pylori- negative patients. H. Pylori infection status did not have effect on the overall or disease-free survival . H. Pylori status might not be useful as a prognostic and predictive factor for clinical outcomes.

Keywords: Helicobacter pylori(HP). Gastric carcinoma , Prognosis. RUT (Rapid Urease Test),Locally advanced gastric cancer(LAGC).

Introduction:

Helicobacter pylori is considered the most common etiologic agent for infection-related cancers, which represent 5.5% of the global cancer burden [1].This bacteria was invented by by Australian microbiologist Rabin Warren and Berry Marshall in the year 1983. It is so common that more than 50% of the global population harbours the H. Pylori infection in the gastric mucosa and causes chronic inflammation that often persists for years. In addition, it also leads to genetic and epigenetic changes resulting in genetic instability [2]. Among infected individuals, approximately 10% develops peptic

ulcer disease, 1-3% progresses to gastric cancer, and 0.1% develops mucosa-associated lymphoid tissue lymphoma (MALT) [3]. Till date association of HP infected gastric cancer and role of it on prognosis is not able to ascertained. But researchers are striving on it to know is there any effect on outcome.After therelationship between H. Pylori infection and development of gastric cancer has been defined by both epidemiological and clinical prospective studies. H. Pylori was classified as a group 1 carcinogen for human by International Agency for Research on Cancer in 1994 [4]. Although many studies over the past two decades have revealed the strong correlation between H. Pylori and gastric cancer development, the effect of H. Pylori status on clinical outcome of gastric cancer patients has not been well documented, especially according to the stage. Currently, the available data have suggested that the influence of H. Pylori infection on the progression and clinical outcome of gastric cancer is still obscure [5-11]. In this study, we investigated the H. Pylori infection status and its association with the pathologic features and clinical outcomes in stage III gastric cancer patients treated with adjuvant therapy after curative resection.

Materials and Methods:

Between 2014 and 2018, the records of 50 consecutive patients who had a curative resection followed by postoperative chemotherapy or chemo-radiotherapy for the treatment of stage III gastric adenocarcinoma (according to the American Joint Committee on Cancer, 7 th/8th edition [2]) were retrospectively reviewed. Patients who had a previous gastric resection or had other coincident malignancies and those with Siewert (GE Junction) type I cardia adenocarcinoma were excluded from the study. Five patients were of proximal gastric cancer (not GE Junction type). All patients underwent subtotal/total gastrectomy with D2 lymphadenectomy with curative intent(R0) and all received chemotherapy or chemoradiotherapy postoperatively. Chemotherapy regimen was 5-fluorouracil. Chemoradiotherapy consist of 45 Gy of regional radiotherapy (1.8 Cy/day 5 days/week) for 5 weeks, in addition with 5-fluorouracil and leucovorin regimen. We analyzed clinicopathological features including age, sex, tumor location, type of gastrectomy, histological type of the tumor, Lauren classification, tumor size, T stage, N stage, lympho-vascular and perineural invasion, adjuvant treatments, type of patterns of metastasis, and survival outcomes. All patient's surgical specimens re-evaluated for H. Pylori infection.Pathologist rightly evaluated tumor and non tumor tissue. Patients were grouped according to the presence of HP infection and potential differences in clinical and pathologic characteristics between the two groups of patients were investigated.

Histopathologic Examination:

All resected gastric specimens were fixed in neutral-buffered 10% formalin. After tissue processing overnight, all tissues were embedded in paraffin and cut into 4- m sections. The sections were stained with hematoxylin-eosin for histology and Giemsa for detecting H. pylori. Histopathologicaly, analyses were established both in neoplastic and non-neoplastic areas of the gastric specimen by one pathologist who was unaware of the patient's clinical information. The histopathological findings of gastritis in non-neoplastic areas including glandular atrophy, intestinal metaplasia, inflammation, and H. pylori density were analyzed using the visual analog scale of the Updated Sydney System [13]. The density of H. pylori infection was graded as negative (normal) or positive (mild, moderate, marked) in neoplastic and non-neoplastic areas. Patients were regarded as morphologically negative for H. pylori if not detected in both areas. Otherwise, they were regarded positive for H. pylori.

Follow-up:

Follow-up evaluation included complete medical history and physical examination, chest radiography, and laboratory tests, including complete blood cell count, blood urea nitrogen, creatinine, liver function tests, and tests for tumor markers such as carcion-embryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9). The patients were reviewed every 3 months for 2 years, every 6 months for next periods (Good contact of patients were kept). Abdominal ultrasonography or computed tomography scan and chest radiography every 6 months .Endoscopy in 6-12 months was followed. Recurrences were

documented by clinical or radiologic assessment or both and were categorized as locoregional, systemic, or combined type of recurrences/metastases.

Statistical Analysis:

Descriptive statistics were used to calculate frequencies and percentages for all variables involved. The association between H. pylori infection status and clinicopathological features was compared using the Fisher exact test or the Pearson chi-square test. The Kaplan-Meier method was used to estimate the effect of H. pylori status on prognosis. The differences between the survival curves were tested by using the log-rank test. P values of <0.05 were considered statistically significant. All analyses were carried out using SPSS software (version 21.0; SPSS Inc, Chicago, IL).

Results:

Eleven out of 50 patients (22%) had H. pylori infection in stage III gastric carcinoma. The median age of the enrolled patients was 65 years, with a range of 35-79 years. Stage distribution was as follows : 31. 6% of patients in stage IIIA, 23.7% in stage IIIB, and 44.7% in stage IIIC.(IIIA=T2N3a/T3N2/T4aN1-2/T4bN0; IIIB=T1-2N3b/T3-4aN3a/T4bN1-2;IIIC=T3-4aN3b/T4bN3a-3b).14a H. pylori infection was not related to the level of serum CEA and CA 19-9 preoperatively. All patients had undergone surgery with curative intent either with total (5 patients, 10%) or subtotal gastrectomy (45 patients, 90%). Seventeen(34%) patients received 5-fluorouracil-based regimen, and the remainder received chemoradiotherapy.

H. pylori status did not correlate with the clinicopathologic features of gastric adenocarcinoma (Table 1). It was greater in non-neoplasic tissue than the tumor tissue (21% vs 8%), and only four patients (8%) had H. pylori infection in both non-neoplastic tissue and tumor tissue. In terms of relationship between. H. pylori status and histopathologic findings of gastritis, positive H. pylori infection, it had no correlation with inflammation, atrophy, and intestinal metaplasis (**Table 2).**

The median follow-up was 20 months. During the follow-up period, 78.4% had experienced locoregional recurrence or distant metastasis, 75.7% had died of gastric cancer-related complications. Recurrence were showed as follows : locoregional in three patients, both locoregional and systemic in four patients, and the remainder in systemic recurrence. Recurrence was observed in 87.5% and 88.3% in H. pylori-positive and H. pylori-negative patients, respectively .H. pylori infection status did not have a significant effect on the overall or disease-free survival and hence prognosis in this context.

Discussion:

In the present study, H. pylori status did not correlate with survival in gastric cancer patients. Additionally, H. pylori status could not predict recurrence in patients with gastric cancer. The clinicopathological features of H. pylori-positive patients were also compared with those of the group of patients with negative H. pylori status. "Statistical analysis" revealed that H. pylori status was not identified to be significantly associated with the clinicopathologic factors of gastric - adenocarcinoma.

In contrast to our study, a few recent studies have supported the role of H. pylori infection in gastric cancer prognosis. After Lee at al. [14] reported the significant association between sero-negative H. pylori status and poor outcome in 128 resected gastric cancer patients in univariate analysis, three large prospective studies investigated the prognostic role of H. pylori infection [10, 11, 15]. First, Meimarakis et al. [15] identified H. pylori status as an independent beneficial prognostic factor for overall and relapse-free survival in gastric cancer patients with curative resection, especially in early stages. The other prospective study by Marrelli et al. [10] indicated the negative H. pylori status was an independent prognostic factor of poor prognosis in patients with gastric cancer. A recent study by Wang et al. [11], in which they investigated the prognostic impact of H. pylori status on the prognosis of patients undergoing curative resection for gastric cancer in Chinese prospective cohort, showed that H. pylori positivity was a beneficial prognostic indicator, independent of other clinicopathologic variables.

The different findings between current and above mentioned recent studies might be attributed to several points. First, unlike previous studies, our study did not include patients with early gastric cancer; all patients are in stage III and received adjuvant chemotherapy or chemoradiotherapy as a routine treatment. In contrast, most of the patients have received no adjuvant treatment in the studies of Marrelli and Meimarakis et al. Second, different H. pylori detection mthods have been used. Although there are many methods used to detect the H. pylori, including culture, histopathological diagnosis, urease test, real-time polymerase chain reaction (PCR), serological analysis, and urea breath test, none of the methods of H. pylori detection is perfect. There is also no universally accepted standard diagnostic test for H. pylori. In concordance with many previous studies in the literature, we used only histopathological diagnosis for H. pylori detection [8, 11, 16]. And also RUT by gastroenterologist in our center. Since the combination of two or more methods might increase the sensitivity and specificity of a diagnosis of H. pylori infection to define the H. pylori status, Marrelli et al. Used the combination of methods PCR for vacA gene and serologic analysis, and Meimarakis et al. used bacterial culture, histological analysis, and serology. Nevertheless, we could not use the serologic test and PCR analysis due to the retrospective nature of our study. However, conventional serological analysis for H. pylori infection may not be an appropriate method for detecting a relationship between H. pylori and gastric cancer prognosis. It might be considered as the most accurate method for determining previous H. pylori infection, but not all of them are associated with gastric cancer [17]. In addition, it has been reported that 14% of PCR positive gastric cancer patients demonstrated negative serology for H. pylori [10]. On the other hand, H. pylori may be localized in or around the tumor and carcinogenesis related to H. pylori is considered to be localized rather than systemic in gastric cancer patients [16]. As a result, histopathological diagnosis and molecular methods may be likely to be most successful in detecting a relationship between H. pylori infection and gastric cancer prognosis.

The reasons why negative H. pylori status is associated with poor outcomes in gastric cancer patients remain to be defined. To date, several possible explanations are suggested to explain the correlation between a positive H. pylori status and a better prognosis. According to one of them, improved prognosis in gastric cancer patients with positive H. pylori status may be the result of local immune response to H. pylori infection [18, 18]. As a gram-negative bacterium, H. pylori stimulates the production of many inflammatory

Table 1: The association between clinicopathologic features and H. pylori infection status-

		H. pylori		
		Negative 39 pts	Positive 11 pts	P value
Age (year)		57.2±11.4	51.6±13.0	0.66
Gender	Male	27 (69.0%)	7 (64.3%)	0.59
	Female	12 (30.8%)	4 (43.7%)	
Tumor location	Upper third	4(10%)	1(2%)	
	Middle	2 (4%)	1(2%)	0.58
	Lower third	39 (78%)	9(18%)	
Resection	Total gastrectomy	4	1	0.59
	Subtotal gastrectomy	35	10	
Pathology	Adenocarcinoma	39	11	0.51
Lauren classification	Intestinal	37	10	0.65
	Diffuse	2	1	
Tumor size	Mean±SD	6.4±3.1	6.1±2.9	0.71
Tumor invasion				
	T3	39	11	0.38
N stage	N1	5	2	
	N2	9	3	0.94
	N3	25	6	
Stage	Stage IIIA	12	3	
	Stage IIIB	7	4	0.68
	Stage IIIC	17	7	
Lymphovascular invasion	Absent	10	3	0.51
	Present	29	8	
Perineural invasion	Absent	9	3	0.77
	Present	30	8	

Mediators such as cytokines which may promote the development of cellular and humoral immune response mainly of type -1 T helper cell which contributes to elevated antitumor

immunity [19, 20]. Improved immune response against the tumor improves survival rates of gastric cancer patients with H. pylori infection. In addition, it has been assumed that because H. pylori components mimic specific receptors or surface molecules on gastric epithelial cells, auto antibodies could induce a cross-reaction against gastric cancer cells [21].

However, several authors have raised doubts regarding the true prognostic value of H. pylori status, suggesting that H. pylori negativity may be simply related to more advanced tumor stage [22, 23]. When the disease is far advanced, parietal cells in the gastric mucosa are destructed and the lumen of the stomach becomes an alkaline environment, which is unfavourable for H. pylori. The organism is destroyed and the patient becomes H. pylori negative [22]. Actually, it was reported that the rates of histologically detected H. pylori positively in tumor tissue was higher for early-stage gastric cancer compared to advanced gastric cancer [24]. It is therefore not surprising that H. pylori positive patients whose disease is at a less advanced stage show higher survival rates than H. pylori negative patients with gastric cancer. Because the cohort consisted of patients with advanced (stage III) gastric cancer, the above mentioned scenario might be the reason of relatively lower rate of H. pylori positivity in our study. In the present study, the rate of H. pylori ++positivity was identified as 22% in gastric cancer patients. This value is lower than both the rates reported in most studies [7, 10] which vary from 17.5 to 86.2% and expected rates in Turkey where H. pylori infection is highly prevalent [25]. It might also explain the reason of the rate of H. pylori positivity was higher in non-neoplastic tissue than in tumor tissue in current and most studies in the literature [9, 11].

Table 2: H. pylori and chronic gastritis (according to Sidney classification) status in pathologic assessment of the surgical specimen-

		H. pylori		
		Negative 39 pts	Positive 11 pts	P values
Inflammation	Positive	29	7	0.57
	Negative	10	4	
Atrophy	Positive	9	3	0.41
	Negative	30	8	
Intestinal metaplasia	Positive	32	7	0.59
	Negative	7	4	

On the other hand, there are only a few studies suggested that H. pylori infection is also an independent prognostic factor in locally advanced and metastatic gastric cancer [8, 16]. One of them had a non-homogenous patient group which includes stages IB, II, IIIA, IIIB and IV and two groups of patients receiving different adjuvant chemotherapy regiments in contrast to our study. It reported H. pylori negative status was associated with poor outcome in all stages except stage IIIB. The others included only inoperable advanced gastric cancer patients and also did not use any chemotherapy regimen. The difference in survival rates of these studies may be due to a better response to different chemotherapy regimen in H. pylori positive patients.

The cohort included the patients with gastric cancer in same stage and received similar adjuvant treatment. This differs the current study from other studies in the literature. The current study was limited by a relatively small number of patients from single institution and retrospective nature, with consequent methodological limitations. Only histopathological method for H. pylori diagnosis was used. Because of the nature of the disease, survival in advanced gastric carcinomas is limited. This may be the reason that the effect of H. pylori status in gastric cancer prognosis might not be identified.

Conclusions:

H. pylori status does not seem to be associated with survival in stage III gastric cancer patients treated with gastrectomy (R0). Data from the current study suggest that H. pylori status might not be useful as a prognostic and predictive factor for clinical outcome of this group of patients. It should be noticed that this study consists of small number of patients. Considering previous reports and our study, the effect of H. pylori status on survival, especially in advanced stage gastric cancer, has to be validated with further studies. Associations and mechanism of H.pylori infection have not yet been defined sufficiently well to guide the clinician in treatment decisions.Overall role of HP in pathogenesis and outcome of gastric cancer yet to be ascertained and association is to be seriously considered and much research has been advocated .

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Review Article

Laser : A Short History and Simplified Physics

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It was Albert Einstein who in 1917 first proposed the theory of 'stimulated emission': the process by which photons (a 'packet of light energy') with the correct amount of energy could disturb an excited atom and cause it to drop to a lower energy level, in turn leading to the creation of another identical photon. The original photon interacting with the atom, as well as the photon subsequently released will be discharged simultaneously and will therefore have an identical wavelength and direction of propagation [Einstein, 1917].

The concept of stimulated emission was the foundation on which subsequent laser development would be undertaken.

Development of the MASER ('microwave amplification by stimulated emission of radiation') was the first giant leap. Microwaves are electromagnetic waves with fairly long wavelengths (1 mm to 1 m). In 1954, Gordon and colleagues tested the first MASER where stimulated emission at microwave wavelengths (in this case 12.5 mm) was demonstrated in an oscillator [Gordon et al. 1954].

The step from MASER to LASER (light amplification by stimulated emission of radiation) took 3 years. The idea was to extend the principle of stimulated emission from the microwave wavelengths to much shorter wavelengths, also including the optical range or visible spectrum of around 390750 nm. For this, one would need to build an optical oscillator that could generate coherent light by amplifying stimulated emission [Hecht, 2010]. Theodore Maiman was the first to succeed and in 1960 he built the first LASER using ruby crystals as an active medium [Maiman, 1960].

It is the active medium (also referred to as the lasing medium) in a laser that determines the wavelength (and therefore color) and frequency of the light that it emits. The wavelength and frequency are inversely proportional to one another.

In simple terms the design of a laser is basically that of a laser medium placed within an optical resonator, which is defined by two mirrors. Light at the characteristic laser wavelength receives amplification whenever it passes through the excited laser medium.

The reflective surfaces of the optical resonator ensure many passes of the light beam through the medium, leading to repetitive amplification. Excitation energy is required for this amplification process and can be derived from an electrical current. A fraction of the amplified light inside the optical resonator escapes as a beam of light out of one or both mirrors.

Early lasers used gas as active medium: nitrogen (N), carbon dioxide (CO2), helium (He) and neon (Ne). Liquids as medium soon followed: the so-called 'dye lasers', because the lasing agent is an organic dye [Gross and Herrmann, 2007]. Dye lasers have the advantage of being able to generate amplified light with a wider range of wavelengths. Some are even tunable. One of the earliest (1964) solid-state lasers utilized Nd:YAG (neodymium-doped yttrium aluminium garnet) as a medium; this is still popular today [Geusic et al. 1964].

A classification of laser output of particular practical importance in urology is that of pulsed wave (PW) versus continuous wave (CW). During CW operation the output of the laser is continuous and of constant amplitude. The clinical effect is a more controlled interaction with the tissue. PW operation on the other hand, delivers forceful bursts of laser energy, which is useful for stone fragmentation [Teichmann and Herrmann, 1994].

A basic understanding of the light-tissue interaction of lasers is required in order to fully appreciate important aspects such as penetration depth, thermal effects and reflection. These technical terms have major clinical significance. When laser light meets tissue, a percentage of the laser beam will be reflected. The reflected radiation is lost for the surgical purpose and may also cause unintended thermal damage to surrounding areas. Absorption is the most important interaction of laser light with tissue. A chromophore is required in order to achieve absorption: body chromophores accessible for laser light include blood, water and melanin. Absorbed laser light is converted to heat and depending on the amount of heat, the clinical effect will be tissue coagulation or vaporization. Absorption depth is dependent on the wavelength of the laser.

Over the course of the last four decades, many possible applications of lasers in urology have been investigated. This 'trial and error' era of the 1980s was a crucial step in the process of evolution of this technology. Every imaginable use was explored, with varying degrees of success and applicability. In the end, the safe and effective have remained, and are constantly being refined.

Today, the types of lasers most commonly used in urology include: .
Nd:YAG;
Ho:YAG (holmium:YAG);
Thu:YAG (thulium:YAG);
CO2 (carbon dioxide);
LBO (lithium triborate);
diode laser;
Thulium fiber laser.

Laser applications in urology

Stones

Initial reports on the use of the pulsed dye laser for stone fragmentation appeared in 1987 [Dretler et al. 1987]. This was a very promising new technology enabling endoscopic fragmentation of more than 8095% of stones and urothelial injury being rare. Drawbacks were very high initial costs and expensive disposables (coumarin dye), as well as trouble with fragmentation of notoriously 'hard' stones composed of calcium oxalate monohydrate (COM) and cysteine [Floratos and de la Rosette, 1999].

The FREDDY (frequency doubled double-pulse Nd: YAG) laser was the next step in laser lithotripsy, and consists of a KTP crystal incorporated into a Nd:YAG laser [Marks and Teichman, 2007]. This enables the laser to produce two pulses: a 20% green light component at 532 nm and an 80% infrared component at a wavelength of 1,064 nm. This combination works in synergy to enable highly effective stone fragmentation, mainly via a mechanical shockwave with very little thermal effects. Another major advantage is the extremely low risk of damage to the ureteral wall when using this laser [Yates et al. 2007]. Unfortunately the 'hard' types of calculi also present a challenge to this laser, as is the case with the pulsed dye lasers [Dubosq et al. 2006]. Another problem is that the FREDDY laser is only able to

effectively fragment dark or colored stones that absorb the green wavelength. Some urologists later referred to it as the 50% laser because only about 50% of stones could be treated with it.

The alexandrite laser was introduced in 1991 and even though initial results were promising, there was never widespread acceptance of this laser for use as a lithotriptor [Pearle et al. 1998].

Owing to the high costs when investing in a urological laser, the ideal would be to have a system with applications in various pathological conditions. The drawback of the FREDDY lasers negligible effect on soft tissue is that it can be exclusively used for stone procedures. The use of the Ho:YAG laser in BPH surgery was discussed earlier and this laser has also become the one most commonly used for lithotripsy [Lee and Gianduzzo, 2009]. Fragmentation occurs through a photothermal effect and requires direct contact of the laser tip with the stone [Pierre and Preminger, 2007]. A major advantage is minimal retropulsion effects during stone fragmentation [Cinman et al. 2010]. What puts this laser 'at the top of the food chain' is its ability to fragment all types of stones, including cysteine, brushite and COM [Leveillee and Lobik, 2003]. The holmium laser can either reduce stones to tiny fragments that are easily cleared from the collecting system with outflow or irrigant, or larger stones can be broken up and fragments removed using baskets or grasping forceps [Bagley, 2002].

Benign prostatic hyperplasia

The ability of the laser to ablate prostatic tissue with minimal hemorrhage has concentrated most of the interest in urologically applied lasers to benign prostatic hyperplasia (BPH) [Anson et al. 1994]. Despite tremendous advances in the surgical and minimally invasive treatment of BPH, transurethral resection of the prostate (TURP) is still considered the 'gold standard'. The risks of TURP are always mentioned when discussing the reasons for seeking alternative treatment modalities for BPH. Bleeding certainly remains a concern, especially in patients on some form of anticoagulation (heparin, coumarin related compounds, antiplatelet agents) or those with prostates in excess of 6080 g. On the other hand, with the availability of transurethral resection in saline (TURiS), the TURP syndrome is nowadays considered by many to be a relatively rare complication [Sarf et al. 2010].

Although removal of benign prostatic tissue using a laser was first described in 1986, it was only in 1990 that introduction of the 'side-firing' (deflecting device at the tip: 6090) laser prompted more widespread use of this modality. The Nd:YAG laser was initially the laser most commonly used and is also the one most extensively studied. One of the earliest techniques used for Nd:YAG laser treatment of BPH was called 'visual laser ablation of the prostate' (VLAP) [Norris et al. 1993]. This involves lasing prostatic tissue in a noncontact fashion to create an area of heat-induced coagulative necrosis that extends about 10 mm into the tissue. The method is reasonably simple to learn and perform, is safe in anticoagulated patients and carries no risk of the TURP syndrome. However, edema and prolonged sloughing of the coagulated tissue leads to irritative lower urinary tract syndrome (LUTS) and urinary retention requiring catheterization, often for long periods (3 months), in up to 30% of cases [Cowles et al. 1995].

Another approach in which the Nd:YAG laser can be used is the contact mode, which leads to real-time destruction of prostatic adenoma. A 'contact tip' converts laser light to heat, which induces vaporization and immediate creation of a cavity. As with VLAP, no tissue is available for histology, but this approach has the advantages of immediate relief of obstruction, early catheter removal and decreased

postoperative LUTS and urinary retention. Tissue ablation advances slowly (so-called repetitive 'painting'
of the surface that needs to be ablated) and it is therefore not suitable for prostates larger than 40 g. In addition the hemostatic effect is not as good as with VLAP [Floratos and de la Rosette, 1999].

Apart from VLAP and contact ablation, the Nd:YAG laser can also be used for performing interstitial laser coagulation (ILC) of the prostate.

First described in 1993 by Hofstetter, the main feature of this method was preservation of the prostatic urethra and its urothelium [Hofstetter and Alvarez, 1993]. The procedure is performed by placing laser-diffusing fibers directly into the prostatic adenoma, either via the transurethral cystoscopic approach, or the perineal approach. Laser energy then produces coagulation necrosis within the adenoma, which subsequently undergoes atrophy [Perlmutter and Muschter, 1998]. As is the case with VLAP, this method is safe in anticoagulated patients, but substantial tissue edema also usually necessitates prolonged (721 days) postoperative catheterization. Retreatment rates are problematic: as high as 20% at 2 years, 41% at 3 years and 50% at 54 months. Several authors have concluded that this modality should probably be restricted to selected, high-risk patients. It can be safely performed with a combination of local anesthesia and intravenous sedation [Daehlin and Fruga˙rd, 2007].

KTP laser, green light laser, frequency-doubled Nd: YAG laser and photoselective vaporization of the prostate (PVP) all refer to the same modality. Passing the Nd:YAG laser beam (wavelength 1064 nm, invisible) through a KTP crystal doubles the frequency and halves the wavelength (532 nm, visible green light). This wavelength is A Zarrabi and AJ Gross http://tau.sagepub.com 83 strongly absorbed by hemoglobin and therefore has a very short absorption depth in well-vascularized tissue such as the prostate [McAllister and Gilling, 2004]. It is used in a noncontact fashion, causes immediate vaporization of prostatic tissue and is a virtually bloodless procedure. Due to the limited absorption depth, necrosis of the tissue underlying the vaporized area, with subsequent edema, is not a problem. Some authors have reported discharging patients on the day of surgery without a catheter, even those with prostates sizes in excess of 100 g [Barber and Muir, 2004].

Application of the KTP laser has changed tremendously over the years. It started out as part of the 'hybrid technique' that involved VLAP with the Nd: YAG laser followed by bladder neck incision using the KTP laser at a lowpower setting (34 W]. The theory of these 'hybrid techniques' was that the additional KTP laser incisions would reduce the Nd:YAG laser's troublesome postoperative irritative symptoms and need for prolonged catheterization [Barber and Muir, 2004]. Further research was aimed at increasing the power output of the KTP laser, initially to 60W. Although originally a pulsed wave laser, modifications to the system furthermore facilitated the delivery of pulses so rapidly that the effect of continuous wave delivery was created. All of these improvements heralded the 'high-power' era of KTP lasers: they were now being used for prostate vaporization independently from the Nd:YAG laser. Today, 'high-power' KTP laser prostatectomy refers to a power output of 80W.

The 120 W lithium triborate (LBO) laser was the next step in the evolution of the 532 nm lasers. The aim with this system was to overcome the still relatively slow tissue ablation ability of the 'high-power' 80W KTP, which leads to timeconsuming procedures in patients with large prostate glands [Wosnitzer and Rutman, 2009]. Not only is energy transfer and tissue ablation faster and more efficient, but the working distance is also increased (working distance for KTP is 0.5 mm, for LBO it is up to 3 mm), making the LBO laser technically simpler to use. Unfortunately, a drawback of the higher power setting is a reduction in the hemostatic ability, as demonstrated in a recent study in an ex vivo model [Heinrich et al. 2010].

The Ho:YAG laser is a pulsed laser with a wavelength of 2140 nm. Some consider it to be the pinnacle of evolution of urological lasers: not only is it ideally suited for procedures on the prostate, but it is also extremely effective as an intracorporeal lithotriptor for most stones. In addition it can be used in the setting of ablation of urothelial tumors and incision of strictures of the upper and lower urinary tract [Kuntz, 2006]. The following features of the holmium laser make it such a useful instrument in prostate surgery:

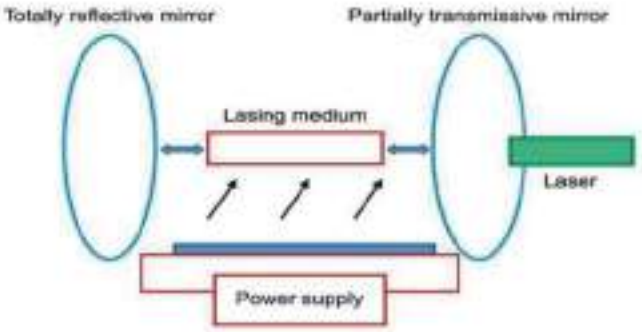
- Absorption depth in the prostate is only 0.4 mm, creating a high energy density sufficient for vaporization.
- Dissipating heat causes simultaneous coagulation of small blood vessels to a depth of about 2 mm.
- This enables precise, char-free and virtually bloodless incision in prostatic tissue.

The holmium laser proceeded through many of the same 'evolutionary processes' as the some of its predecessors. Initially, it was also used in 'hybrid techniques' (VLAP with the Nd:YAG laser followed by creation of a tunnel and bladder neck incision with the Ho:YAG laser, to attempt shortening of the post-operative catheterization time) just like the early KTP lasers [Gilling and Frauendorfer, 1998]. The next step was prostate vaporization in the same 'painting' fashion as the Nd:YAG and KTP lasers. Although the procedure (called HoLAP, holmium laser ablation of the prostate) was easy to learn and effective, it was once again too time consuming when dealing with larger prostates. This led to the development of HoLRP (holmium laser resection of the prostate) which basically simulates traditional TURP [Gilling et al. 1996]. Chips of prostatic tissue are resected with an end-firing laser fiber and the chips are then removed via the urethra. This method is not only technically quite difficult to master, but operative times are still too long in patients with large adenomas. Refinement of the holmium laser technique and development of an efficient tissue morcellator led to HoLEP (holmium laser enucleation of the prostate)-finally size was no longer an issues. This procedure simulates open prostatectomy where the entire adenoma is removed at the level of the surgical capsule. The Ho:YAG laser ensures bloodless incision followed by blunt dissection using the cystoscope and laser fiber as an 'index finger' [Elzayat and Elhilali, 2006].

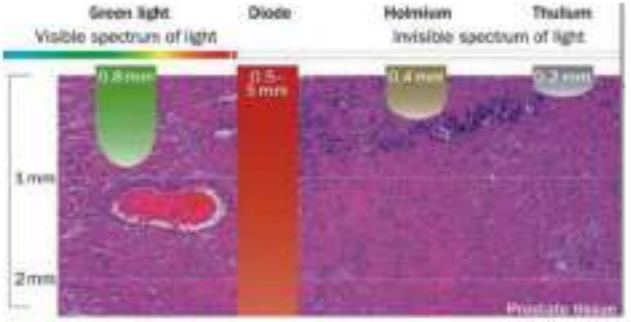
The Thu:YAG laser is the newest addition to the urologists laser armamentarium and use of this Therapeutic Advances in Urology 3 (2) 84 http://tau.sagepub.com laser for BPH surgery was first published in 2005 [Xia et al. 2005]. This report described the socalled 'thulium laser resection of the prostate tangerine technique'. The next step was vaporesection (simultaneous resection of TURP-like chips and vaporization of tissue), which was proven to be safe and effective [Bach et al. 2009]. The final leaps came with 'Thu:YAG vapo-enucleation', followed by ThuLEP (thulium laser enucleation of the prostate) [Bach et al. 2010]. When compared with the holmium laser, thulium seems to deliver improved vaporization ability, ensuring smooth tissue incisions. This allows the surgeon to accurately remove the adenoma at the level of the surgical capsule, as this plane is easier distinguishable. Virtually any sized prostate can be removed transurethrally using this technique.

Diode lasers have been around for a long time, but their clinical application has thus far been limited when compared to the other lasers. There now seems to be some renewed interest in these lasers as an alternative to KTP or LBO for vaporization techniques. As mentioned previously, for KTP and LBO lasers power versus hemostasis is somewhat of a 'catch 22' situation: the increased power of the 120W LBO certainly cuts down on operative times, but this is at the cost of hemostatic ability, which is much better when using the lower powered 80 W KTP system. However, lower power means longer duration of procedures. A recent report on a 980 nm diode laser device demonstrated better hemostasis during prostate vaporization when compared with a 120W LBO laser. Unfortunately the diode laser was also associated with a higher incidence of complications such as postoperative irritative symptoms and epididymitis [Chiang et al. 2010].

Components of Laser



Optical Penetration Depth



Era of Thulium fiber laser

Still in the early phases, but has revolutionized the field of urology with applications in both stones as well as BPH.

Our Journey so far

2011 – First use of Holmium laser for stones in the North Eastern region.

2015 – First use of Thu YAG laser for BPH in the North Eastern region.

2019- First use of Thulium fiber laser for stones as well as BPH in the North Eastern region.

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Robotic Collrectal Surgery : Our Experience From a Tertiary Care Centre

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INTRODUCTION :

Robotic surgery, which is regarded as the new revolution, is one of the areas of surgery that now garners the most interest. One of the most notable developments in surgery during the last decade of the 20th century was the emergence of laparoscopic procedures. However, there are several technical challenges with laparoscopic surgery, like limited range of motion and poor hand-eye coordination[1]. These limitations have been replaced by advancements in robotic surgery with their useover the past twenty years.Compared to laparoscopic surgery, robotic surgery have some advantages including the change in ergonomics, articulating wrists that eliminate the surgeon's tremor enabling more complex and precise movements, seven degrees of freedom, and "immersive" 3D visualisation that improves depth perception[2]. By doing so, it increases skill-set of the operator, makes it easier to carry out complicated procedures in narrow spaces (like the deep pelvis), enhances identification and preservation of the nerves, vasculature, adjacent organs and shortens the learning curve[3].

Similar to conventional surgery or laparoscopic procedures, robotic surgery necessitates skills and a learning curve. Since simulators are simple to use and the computerised interface permits using two consoles, helping the trainees to harness the art of surgery quickly and by augmenting the skills robotic surgery hasshortened the learning curve, noted in laparoscopic surgery[4].Many different forms of gastrointestinal malignancies, including esophageal, gastric, hepato-pancreatico-biliary and rectal cancers are currently treated with robotic surgery.Robotic surgery has a significant role in such challenging surgeries and in decreasing the post-operative complications[5].

Laparoscopic Total Mesorectal Excision for rectal tumours is oncologically equal to and provides short-term benefits over the open technique. The robotic system clearly outperforms traditional laparoscopy due to its better precision and dexterity. The articulation of the robotic instruments allows the surgeon to follow the proper plane of dissection for circumferential mobilization of the rectum[6].

The earliest mention of robotic colorectal surgery appeared in 2000, and the first report of a robotic TME appeared in 2006. Robotics is slowly getting adopted for the colon and rectal surgeries, with only 2.8% of such cases being performed as of now. The cost of robotic surgery systems as well as continuous maintenance and repair, recurring instrument cost, and additional team training, is a significant factor in explaining this low rate [7].

A meta-analysis of 7 studies, including the randomised trial by Park and colleagues, discovered that using robotics during right colectomy was linked to lesser blood loss, a lesser amount of postoperative challenges, and rapid recovery of bowel function than laparoscopy. Although surgical duration was longer, there were no difference in the duration of hospitalisation, likelihood of converting to open procedure, anastomotic leakage, or haemorrhage[8]. Other trials have indicated marginal benefits for robotic right colectomy . Luca and colleagues observed that robotic surgery was related to a shorter hospital stay and the removal of at least fifteen lymph nodes when comparing right-sided colon tumours to open surgery[9].Although these benefits come at a higher financial expense, robotic TME offers an effective therapeutic option in the hands of a skilled rectal surgeon with adequate patient selection and extensive practise [10].

MATERIALS AND METHODS:

This study was designed as a prospective study and involved consecutive patients who had undergone elective roboticcolorectal surgeries between June 2021 and June 2022.

The data regarding the patient demographics, clinicopathological characteristics, operative details and postoperative outcomes,were prospectively obtained from our computerised database. The 30-day postoperative complications were graded according to Clavien–Dindo classification system [11]. The TNM Classification of the American Joint Committee on Cancer staging system (8th edition) was used for staging purposes[12] Patients older than 18years and with colorectal pathology(including cancers, diverticulitis, rectal prolapse) admitted to Department of Colorectal Surgery, GEM Hospital and Research Centre, Chennai, South India were included in the study. Patients who had undergone emergency procedureswere excluded. The study was approved by the Ethics Committee of GEM Hospital (approval number: 22243).

Surgical technique:

All the surgical procedures were performed by one senior colorectal surgeon (CA) using standard robotic ports and CME-CVL technique for cancers. Pneumoperitoneum was created using Veress technique. The ureter identification was facilitated by routine usage of immediate preoperative cystoscopy guided intra-ureteral instillation of Indocyanine green (5mg ICG) dye into bilateral ureters which is used in all colorectal cases in our centre. The number of ports required to complete the surgery was standardised for the type of surgery. We used a 10 mm camera port 2 cm above and 2 cm lateral to the umbilicus. One 8 mm (R1) working port in the RIF and one 8 mm (R2) port in the left lumbar region , 8-10 cm away from the camera port were placed for robotic manipulation. We used the third robotic arm (R3) for retraction in only 2 cases of subtotal colectomy and 2 cases of Ultralow anterior resection, mostly placing it in the suprapubic position. One 10 mm port in the Right upper quadrant and one 5 mm epigastric port were used as assistant ports. The R1 8mm port was converted to 13 mm port at the end of the surgery for distal rectal transection using staplers. Extra ports were required in 3 patients who underwent subtotal colectomy and total proctocolectomy with Ileal pouch anastomosis.

All patients underwent Medial to lateral dissection with strict adherence to the principles of malignancy using the Complete mesocolic excision (CME) with central vascular ligation technique (CVL), as routinely used in our unit in all cases of malignancy. Extracorporeal (from an approximately 5-cm suprapubic incision) / Intracorporeal resection and side-to-sidestapled or end to end circular stapled anastomosis were performed variably.

Statistical Analysis:

The descriptive statistics are presented as means ± standarddeviations and frequencies (%). The normality of the data for continuous variables was visually assessed using quantileplots and histograms and was confirmed using the Shapiro–Wilk test. Associations between variables were evaluated

using Student t test or the Mann–Whitney U test (for continuous variables) and Pearson x2 test or Fisher exact test (for categorical variables), where appropriate. All tests were 2-sided, and P values <.05 were considered statistically significant. The relevant data were extracted from the database and imported into Statistical Package for the Social Sciences (SPSS), version 16.0 (IBM, Chicago, IL), for analysis.

RESULTS:

In our study, 58 patients underwent Robotic surgery for colorectal pathology and all patients (mean age 57 years (range 34-88); males =37, females =21) were included for analysis.

Table 1: Patient characteristics- Sex

SEX	NO(%)
MALE	37(63.8)
FEMALE	21(36.2)
TOTAL	58(100)

Table 2: Patient characteristics- Age

AGE	MALE	FEMALE	TOTAL
31-40	6	2	8
41-50	6	2	8
51-60	7	5	12
61-70	7	9	16
71-80	8	2	10
81-90	3	1	4

Out of these, 12 patients underwent anterior resection, twenty patients underwent low anterior resection, fifteen patients underwent ultra-low anterior resection, three patients underwent right hemicolectomy, two patients underwent Subtotal colectomy, three patients underwent ventral rectopexy for rectal prolapse, one patient underwent Abdominoperineal resection, one patient extralevator abdominoperineal resection and one patient underwent Total proctocolectomy with ileal pouch anal anastomosis. There were no conversionstoopen surgery required.Mean body mass index was 20.8 ± 2 kg/m2.

Table 3: Types of surgeries performed

SURGERY	TOTAL (%)
ROBOTIC AR	12(20.68)
ROBOTIC LAR	20(34.48)
ROBOTIC ULAR	15(25.86)
ROBOTIC RIGHT HEMICOLECTOMY	3(5.17)
ROBOTIC RECTOPEXY	3(5.17)
ROBOTIC SUBTOTAL COLECTOMY	2(3.44)
ROBOTIC TPC+IPAA	1(1.72)
ROBOTIC ELAPE WITH PROSTATIC SLEEVE RESECTION WITH END DESCENDING COLOSTOMY	1(1.72)
ROBOTIC APR	1(1.72)

Indications for surgery were mainly malignancy in Sigmoid and rectumwhich was noted in 86.2% (50) cases. Three cases were for rectal prolapse and two of them was for sigmoid diverticulitis. Majority of the tumours were locally advanced and potentially resectable: cT3–75.47% (40/53) and node positive 66.03% (35/53) cases.

43.39 % (23/53) cases were post neoadjuvant therapy, majority being post Chemoradiotherapy and 2 cases post Total neoadjuvant therapy.

Only 7 cases required covering loop ileostomy. Our criteria for creating a diversion intraoperatively was based on requirement of more than 3 staplers for rectal transection and difficult dissection in a few cases post neoadjuvant therapy.

Two patients presented with acute large bowel obstruction and were preoperatively treated with colonoscopic stenting and underwent curative surgery in the same admission. Concomitant procedures in the form of Liver wedge metastasectomy (1), Total laparoscopic hysterectomy and bilateral salphingo oophorectomy (1), Only bilateral oophorectomy (1), Partial cystectomy (1) and Prostatic sleeve resection (1) were done based on spread to contiguous or distant sites.

In patients who underwent ventral mesh rectopexy, one patient had a cholecystectomy and the other patient had a concomitant repair of her left inguinal hernia with a mesh. Post operative period was uneventful in both patients.

Operative outcomes

Mean duration of surgery was 200±53.07 minutes overall for all left sided resections. It was 98±13.07 minutes for ventral rectopexy and 316±26.24 minutes for cases requiring subtotal or total colectomy.

Patients with CME-CVL technique had mean intraoperative blood loss of 86.3±26.5ml.

Postoperative Course

Postoperative course was uneventful in most cases. Nasogastric tube was removed and oral liquids were allowed in all patients on POD 1. On an average, bowel movements were first recorded on POD 2. Most of the patients did not require injectable analgesics after 2 days and were off oral analgesics after 3 days.

One patient developed colonic pseudo obstruction post LAR on POD 2 requiring colonoscopic decompression and neostigmine injection and was discharged on POD 10.

One patient with mid and lower rectal carcinoma post NACRT who underwent LAR developed anastomotic leak on POD 4 requiring Laparoscopic lavage and diversion loop ileostomy.

One patient with lower rectal cancer post NACRT who underwent ULAR, developed Per rectal bleeding which was diagnosed as anastomotic dehiscence with bleeding after discharge in the third week and was readmitted for diversion ileostomy.

One patient with locally advanced carcinoma recto-sigmoid who underwent anterior resection with covering ileostomy required local exploration and refashioning of stoma for stomal retraction on POD 4.

Three patients in the rectal cancer group had clinic- radiographically demonstrated paralytic ileus all of whom were managed conservatively. One patient who underwent LAR developed minor chylorrhea and was managed conservatively. The average hospital stay post operatively varied with different groups of patients. There was no postoperative mortality.

Lymph node harvest in the final histopathology was significantly high (mean 17) across all the groups (right/ subtotal/ total/ left colectomy).There has been no recurrence in the malignancy cases on follow up of 2 years for most patients.

Table 4: Operative and Post operative outcomes

DISCUSSION:

The laparoscopic approach for colorectal cancer has long been shown to have superior perioperative results and is non-inferior in terms of the oncological outcomes compared to open resections [13]. The da Vinci surgical system is equipped with a three- dimensional camera, articulated instruments with seven degrees of movement and an added advantage of physiological tremor filtration.This can minimize the risk of injury to vessels and other vital organs as well as givingan edge over laparoscopy in oncological resection.

Robotic surgery represents a major leap in the quality of surgical instruments, offering the possibility of a minimally invasive approach to technically complex procedures, in anatomical locations which are generally difficult, like the thorax or the pelvis. The technological advantage provided by the robotic approach may help overcome some of the technical difficulties underlying laparoscopic CME-CVL or TME, like the use of straight instruments or surgeon's fatigue during a prolonged procedure especially with a narrow pelvis, obese patients and low rectal tumors, leaning the balance towards minimally invasive procedure.

The computerized interface offered by surgical robots eases surgical training through shortening learning curves to make them more complete, and reducing the morbidity and mortality. Our present study critically reviews the feasibility and safety of the use of the robotic technique for colorectal surgeries in terms of perioperative and short-term oncologic outcomes.

Robotic surgery at our centre, which already is a high volume tertiary care referral centre in South India for advanced laparoscopic surgeries, was instituted using a Da Vinci Si platform. After the initial phase of exploring options for correct port positions and docking difficulties experienced during different phases of surgery in multi-quadrant surgeries (like subtotal colectomy or total proctocolectomy), our team started using the robotic technique selectively, only for technically difficult cases and those requiring dissection in the pelvis, for the judicious use of robot.

In a study by Rohila et al [14], the average blood loss was 235 ml with multi-visceral resections associated with higher blood loss of 925 ml andaverage operating time for standard rectal surgery was 280 min. In a study by Ramachandra et al [23], Mean blood loss was 110 ± 90 ml. Mean total operating time, docking and surgeon console time were 182 ± 66 min, 11 ± 6 min and 140 ± 22 min, respectively. In our study, mean intra-operative blood loss of 86.3±26.5ml. We had no multi visceral resections except one case with simultaneous liver wedge resection who had an estimated blood loss of 178 ml. In our series, mean duration of surgery was 200±53.07 minutes overall for all left sided resections. However it was comparatively less (98±13.07 minutes) for ventral rectopexy and higher (316±26.24 minutes) for cases requiring subtotal or total colectomy.

We had no cases of conversion to open surgery. Large series have however reported conversion rates of 5–10% [15-17].

In their study, Ramachandra et al [23] had three cases had clinic- radiologically documented paralytic ileus which resolved with conservative management, One case had chyle leakage requiring conservative management and one case had an anastomotic leakage which was managed with an exploratory laparotomy and a diversion loop ileostomy. Rohila et al [14] reported eight patients (4%) with anastomotic leak, out of which seven patients needed re-exploration. The leak rates reportedly were significantly higher in patients receiving LCRT vs. SCRT (7/122 vs. 0/24, p = 0.000). This is comparable with the complications described in our study.

From an oncological point of view, the nodal status is crucial. Number of nodes harvested is considered a marker of surgical expertise and is a surrogate outcome of survival[18]. The American Joint Committee on Cancer recommends the removal of at least 12 lymph nodes to ensure an accurate pathological staging of colon cancer after colectomy [19]. In the present series, we found a mean lymph nodal yield of 18 ± 4. The improved lymph node yield with robotic approach is in accordance with other studies [20-22].

The hospital stay in patients undergoing left sided resections(AR, LAR, and APR) in our series was 6.4 days. This is slightly longer than that published in previous large studies [16-17]. A Korean study had reported a longer hospital stay for robotic ULAR (hospital stays 09 days in robotic group) [24].

The ROLARR trial [15] reported that laparoscopy is non-inferior to robotic. Hence,patient selection and judicious use of robotic platform to justify the cost is important. Rohila et al [14]have data showing that the robotic colorectal surgery costs approximately 1. 5 lakh rupees more than laparoscopic surgery. Considering the large number of resource constrained countries worldwide, and patients living in such countries with no insurance coverage, it is logical to use the robotic services judiciously.

The data from our series demonstrate the technical feasibility and short- term safety of robotic CME in line with Ramachandra et al [23] and Bae et al [25].

Our study has few limitations as it is a small series with a single centre experience. Nonetheless,our results are consistent with multiple other larger studies with a similar objective.A longer follow-up is required to assess the long-term outcomes of local recurrence and cancer-free survival. When seeking for an approach that offers the best combination of oncological, functional, and patient-recovery outcomes, robotic approach seems to be the best option for the treatment of rectal cancers when compared with open, laparoscopic, or trans anal approach. This, however needs more objective evidence from ongoing randomised trials.

CONCLUSION:

The application of Robotic technique is a very significant development in thelast few decades in the management of colorectal cancer. A major overhaul in the technique including usage of 3D camera, novel instrumentation, firefly technology have led to its widespread adoption. Clinical and pathological outcomes of the robotic technique are now well described. Significant advantages of minimally invasive surgery have been shown,such as early recovery, lower complication rates and a shorter length of hospital stay as well ergonomic relevance for the surgeon. Hence, Robotic colorectal surgery is a safe, feasible, and standard method for both benign and malignant colorectal pathologies.

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Biliary Anatomical Variation in a Patient with a Large Choledochal Cyst Malformation Requiring Complex Biliary Reconstruction Surgery : A Case Report

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Abstract:
The choledochal cyst is a congenital anomaly of the bile duct more commonly found in the pediatric age group. The anatomical anomalies and size of choledochal cyst varies, but main mode of treatment of choledochal cyst is the total excision followed by bilio-enteric reconstruction. 13 years old patient presents with right upper quadrant abdominal pain and was diagnosed with a large choledochal cyst. A contrast MRI with MRCP of abdomen revealed choledochal cyst, however due to the large size of the cyst communicating with bile duct cannot be ascertained. Complete excision of choledochal cyst and hepaticojejunostomy was planned. Surprisingly on intra operative finding, all the three hepatic ducts were separately opening into the choledochal (i.e. left hepatic duct, right anterior sectorial duct and right posterior sectorial duct). The choledochal cyst was completely excised and complex biliary reconstruction with triple hepaticojejunostomy was carried out. The type of choledochal cyst and their anatomical abnormalities may not always be possible to diagnosed pre operatively. In this case, the complex biliary anatomy diagnosed intraoperatively and reconstruction was challenging and very rarely performed.

Keywords :Triple Hepato jejunostomy, Choledochal cyst, Biliary Reconstruction

Introduction :
Choledochal cyst is a congenital anomaly of the bile duct, more commonly found in the pediatrics age group [1].Approximately 85% of children present with two of the three symptoms of right upper quadrant mass, jaundice or intermittent colicky abdominal pain. In comparison, 85% of adults present with only one out of the three symptoms [2]. The exact etiology of Choledochal cyst is unknown; however, delay in diagnosis and treatment of choledochal cyst have been associated with a number of complications, including stone formation due to biliary stasis, inflammation, infections, pancreatitis, cholangitis and obstruction [3, 4]. One of the most critical steps in the management of a patient presenting with a choledochal cyst is correct surgical planning based on an accurate classification of the choledochal cyst [5]. However, the type of biliary reconstruction employed is based on the surgeon's personal preference in many cases. In this case report, we discuss a case of a large type 1

choledochal cyst in 13 years old girl with biliary anatomical variant which has three separates bile duct draining into choledochal cyst.

An extensively search of PUBMED, GOOGLE SCHOLAR, MEDLINE, SCOPUS, EMBASE with following key words triple hepatojenunostomy ,choledochal cyst, biliary reconstruction did not shows any satisfactory result. Although biliary anatomical variant are not uncommon, but presence of three separate bile duct associates with a choledochal cyst is very rare. The complex biliary reconstruction performed in this case, has not been reported in literature earlier as per the search mention above.

Case Presentation :

13 years old girl child without co-morbidities or surgical history came to our hospital. On primarily evaluation, patient presents with right upper quadrant abdominal pain, since 7 days. No history of fever and jaundice. On examination of patient, general examination was unremarkable, on palpation of abdomen a lump was felt on the right hypochondrium approximate size 12 x 10 cm that is moving with respiration.

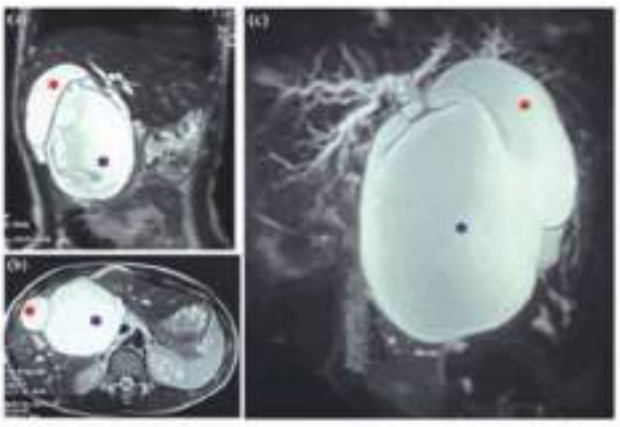

Figure 1: Preoperative Axial imaging in the form of contrast MRI with magnetic resonance cholangiopancreatography (MRCP) of the abdomen

(a) Large Cystic duct dilation of the common bile duct (blue star). (b) Grossly distended gall bladder (red star) (c)multiple intrahepatic biliary radical dilation (IHBRD) due to compression.

Significant laboratory value are AST of 248 U/L (Ref. range 5-26 mg/dl), ALT of 367 U/L (Ref. range 24-40 U/L), total bilirubin of 4.7 mg/dl (Ref. range <1.0 mg/dl), alkaline phosphate of 517 U/L (Ref. range 40-150 U/L), Glutamyl-transferase (GGTP) level of 371U/L (Ref. range 10-20 U/L), albumin- 4.4g/dl (Ref. range-3.5- 5.0g/dl).

Ultrasound of whole abdomen revealed a large common bile duct cyst measuring 100 mm x 67 mm suggestive of choledochal cyst. Axial imaging in the form of contrast MRI with magnetic resonance cholangiopancreatography (MRCP) of the abdomen revealed gall bladder is grossly distended and measuring11.0 cm in length with no calculus within. Fig. 1a and 1b (T2 weighted fat suppression image). A large cystic structure is seen adjacent to the gall bladder measuring 9.0 x 8.1 x 11.3 cm volumes (428cc) and appears to communicate with gall bladder at one end and the other end appears to connect with the common hepatic duct Fig. 1c (T2 weighted fat suppression image). Others finding are liver -14.7cm no focal lesions, spleen -7.6 x 2.7 cm, right kidney -10.3 x 4.3 cm, left kidney -9.2x 3.8 cm and no gross lymphadenopathy or ascites noted. Based on the clinical symptoms, biochemical and radiological findings, patient was diagnosed as a case of large choledochal cyst. The patient was planned for excision of choledochal cyst with roux-en-y hepaticojejunostomy after informed consent and pre-anesthetic checkup. Intraoperatively a Large choledochal cyst was seen on opening of the abdomen Fig 2 (a)

The cystic duct was communicating with choledochal cyst and common hepatic duct, in which distal end of CBD was not able to trace Fig 2 (b). Gall bladder is distended without adhesion; further carefully choledochal cyst was dissected from duodenum, head of Pancreas and from the portal vein. The choledochal cyst was completely dissected all around except the hepatic duct and the upper part of cyst wall which was adherent to the under surface of liver. To confirm the biliary anatomy, we did an intra-operative cholangiogram through the hepatic duct and the adherent cyst to which it was attached to under surface of liver Figure 2 (b), (c), and (e).

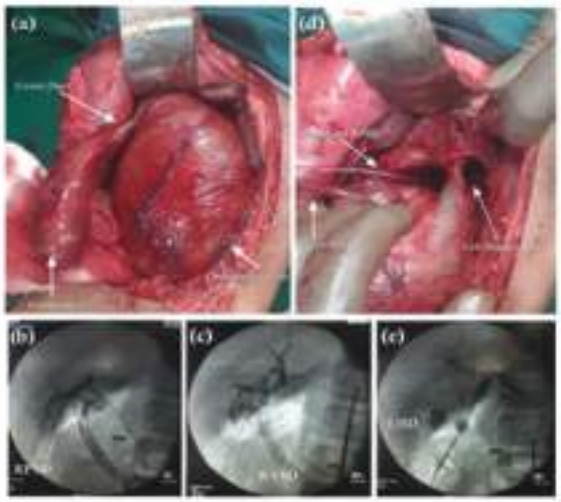

Figure 2: Intraoperative photograph

(a). white arrow shows distended gall bladder, cystic duct and choledochal cyst. (d). White arrows pointed shows cystic duct and the choledochal cyst was communicating with RPSD, RASD and LHD. (b). Right posterior sectorial duct (c). Right anterior sectorial duct (e) . Left hepatic duct.

Further, the choledochal cyst was completely excised and a complex biliary reconstruction performed at three separate bile duct opening with Hepaticojejunostomy (end –to- side) in which left hepatic duct (LHD), right anterior sectorial duct (RASD), and right posterior sectorial duct (RPSD) anastomosed with PDS 5-0 interrupted sutures Fig 3A, B. After finishing jejunojenunal anastomosis, a 28G drain is placed in right subphrenic space.

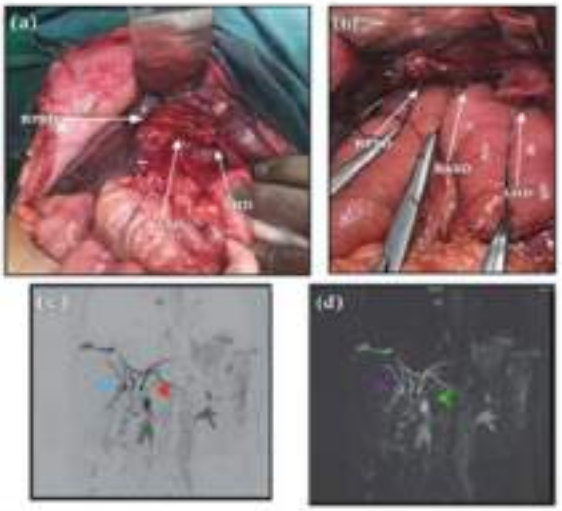

Figure 3: Intra-operative photographs (a). White arrows pointed left hepatic duct (LHD), right anterior sectorial duct (RASD) and right posterior sectorial duct (RPSD) draining into choledochal cyst (b) White arrows pointed Triple hepaticojejunostomy anastomosis had been completed by suture between jejunum and three separate bile duct. (c) and (d) MRCP image at 1 months post-operatively arrows show hepaticojejunostomy sites with three separate duct draining into jejunum

Post-operative, period was uneventful ,patient was allow to take orally on POD day 2 which was gradually increase to normal diet POD day 4 . We did ultrasound whole abdomen on pod 6 which didn't show any intra-abdominal collection and subsequently drain was removed on POD day 7.The patient was discharged on post-operative day 7. After 1 month, MRCP reveals normal hepaticojejunostomy sites. There is no suggestion of any anastomotic stenosis or upstream biliary dilation as shown in figure 3 (c) and 3(d). Complete summary of the pre- and postoperative liver function finding discussed in table 1

Liver function test	Preoperative values	Day 4 Postoperative values	1 months Postoperative values	Reference ranges
Total bilirubin (µmol/L)	4.7	1.6	1.0	0.2-1.2 mg/dl
Direct bilirubun (µmol/L)	2.5	1.0	0.3	0.0–0.6 mg/d
Alkaline phosphatase (U/L)	517	283	241	40-150 U/L
Gamma-glutamyl transferase (U/L)	371	218	36	10-20 U/L
Aspartate transaminase (U/L)	248	66	37	5-26 U/L
Alanine transaminase (U/L)	367	121	29	24-44 U/L
Serum albumin (gm/L)	4.4	3.1	3.6	3.1 g/dl

Discussion:

In 1959, Alonso Lej et al. reported the first clinical series of patients with choledochal cysts [6]. Todani et al. classified choledochal cysts into five types. Of these, 90 to 95 % of choledochal cysts are type I cysts [7]. In this case report patient has type 1 choledochal cyst which was intra-operatively diagnosed.

Ultrasonography and MRCP is used to diagnose choledochal cyst. Normal anatomical variants of the biliary tree or other anomalies in choledochal cyst are detected occasionally by Cholangiography or direct vision at the time of surgery and frequently necessitate some procedure for their Correction. An aberrant posterior hepatic duct draining into the distal common hepatic duct, however, seems to be rare [8].

The incident of malignancy ranges between 5% and 30% over a lifetime, most commonly occurring in the seventh decade and almost exclusively occurring in types I and IV. Interestingly, malignancy has been seen in the nondilated intrahepatic biliary tree in type I choledochal cysts [9].

The most frequent late complication after bilioenteric anastomosis is cholangitis, which is sometimes associated with intrahepatic lithiasis [10]. Furthermore, a stricture of the biliary-enteric anastomotic site is the most important complication which actually determines the long-term outcome and can occur in all types of bilioenteric anastomosis [11]. However, once anastomotic stenosis occurs in hepaticojejunostomy, it is difficult to treat. In cases with intrinsic anastomotic stricture, percutaneous transhepatic cholangio-drainage (PTCD) and balloon dilation of the anastomosis can improve the stenosis but induce prolonged tube placement, leading to cholangitis, bile stasis, and inflammatory stenosis of the bile duct at the drain placement site [12,13]. Any anastomosis should be done at the hilum or very near to the hilum for wider stoma to prevent anastomotic stricture, as described by Todani et al [14].

Therefore, before going for surgical intervention, definitive radiological evaluation of the character/classification of the disease should be done as the procedure of choice varies in different types of choledochal cyst [15] .But decision of surgical intervention also changes by intraoperatively findings.

Conclusions:

Comparing with existing case reports, no such case has been reported yet, in which complex biliary reconstruction was performed with three separate hepaticojejunostomy anastomosis. The attempt to completely excise the choledochal cyst should be done in all cases. In spite of preoperative axial imaging, we have to be prepared for biliary anatomical variation during surgeries as shown in this case report.

Declarations

List of abbreviations:

LHD- left hepatic duct
RASD- Right anterior sectorial duct
RPSD- Right posterior sectorial duct
IHBRD-intrahepatic biliary radical dilation
POD- Post operative day
MRCP-Cholangiopancreatography
PTCD- Percutaneous transhepatic cholangio-drainage

Ethics approval and consent to participate:

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institution Ethics Committee, Apollo Hospital, Guwahati, Assam, India.

Consent for publication:

Written informed consent was obtained from patient for publication of this case report and accompanying images without any personal detail.

Availability of data and materials:

All data is available based on a reasonable request.

Competing interests:

The authors have no conflict of interest to report.

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Authors' contributions.

DJB contributed in initial manuscript preparation and approval of the final version of the study. He also contributed in preoperative diagnosis of the patient, performing the operation, post-operative surgical care and treatment. RP contributed in data acquisition, complete manuscript preparation and approval of the final version of the study. All authors have read and approved the manuscript.

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Resectability of Gall Bladder Cancer with Jaundice – the Role of PTBD and Neoadjuvant Chemotherapy - Our Experience

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Introduction:

Gall bladder cancer (GBC) is a dreadful condition with grave prognosis as most of the patients present at an advanced disease owing to their vague signs and symptoms.Most of the end stage GBC patients have involvement of hepatic hilum leading to jaundice. Earlier there was no curative treatment for these patients. The incidence of curative resection in GBC with jaundice is only around 7-30% (1). Palliative treatment is still the main form of treatmen-tavailable in these patients. But now it has been observed that with involvement of multidisciplinary team we can achieve curative treatment in few patients. In jaundiced patients, biliary stasis can be relieved by PTBD and these patients can be taken up for surgery after downstagingthe tumor by neoadjuvant chemotherapy.The aim of the study is to see the outcome of patients with GBC with jaundice undergoing PTBD followed by neoadjuvant chemotherapy to downstage the disease for curative surgery.

Materials and methods

The definitions used in this study are:
Jaundice is defined as serum bilirubin level of more than 3 mg/dL and serum ALP more than three times the normal reference level (50-136mg/dL).

TNM Staging was done by American joint committee on cancer (AJCC) classification, 8th edition.
Complete response (CR) to neoadjuvant chemotherapy is described as the no disease left for at least 4 weeks.

Partial response (PR) is described as >50% disappearance of disease for 4 weeks (≥30% in RECIST criteria(2)) and no new disease.

Stable disease (SD) is when both partial response and progressive disease criteria are not met.

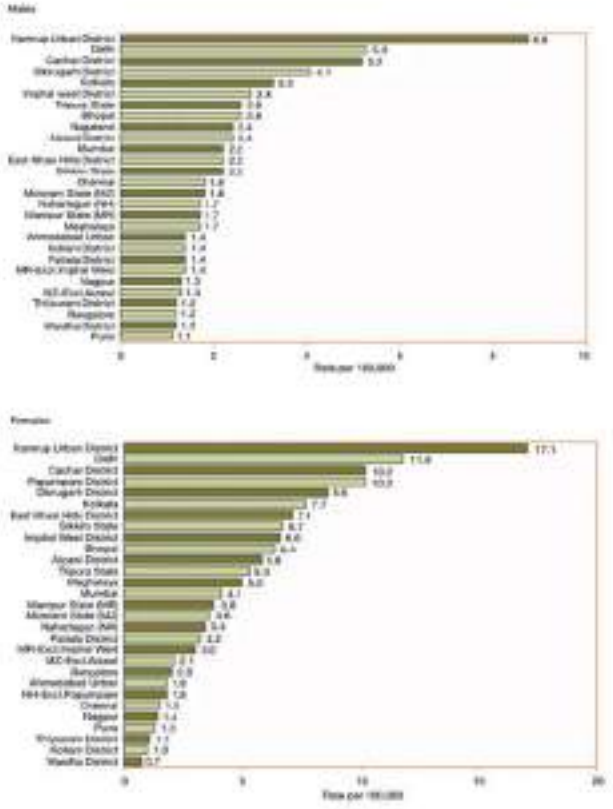
Progressive disease (PD) is described as >25% (≥20% for RECIST) increase in the already existing lesions or if the new lesion appears.

Clinical benefit rate (CBR) is defined as the total percentage of cases that had complete response, partial response, and stable disease after neoadjuvant chemotherapy. (3)
Radical (R0) resection is when the distance of margin to tumor is 1mm. Overall survivality (OS) is the number of days between date of surgical exploration and death due to any cause.

Post-operative mortality is death due to any cause <90 days post-operatively.
Long term survival is defined as survival >2 years.

Disease burden

Carcinoma GB has a dismal prognosis having a 5-year survival rate of <5%. (4). The incidence of GBC in north India is 10-22/100000 population (5). India accounts for 10% of the global cancer burden.Out of 28 most affected districts in the world, 14 districts are in northeastern region. Moreover, Kamrup district is the most affected district worldwide for both males and females comprising of about 8.8 per lakh and 17.1 per lakh population respectively (6).



Spread of gall bladder cancer

Since the gall bladder lacks outer serosal layer on its hepatic side, cancer can easily spread to liver by local encroachment. Also, liver can be involved via portal tracts in advanced GBC. While involvement of segment IVb and segment V is considered local spread, involvement of any other lobe is considered distant metastasis. Distant liver involvement is associated with poor prognosis (7-11).

Cause of jaundice in carcinoma gall bladder

Jaundice occurs in about 30-60% of all gall bladder cancers (12-14). Biliary obstruction occurs due to direct hilar infiltration or due to compression by enlarged hilar lymph nodes. It can also occur if there is lymphatic infiltration or intraluminal tumor extension. Jaundice can also be present in GBC patients with underlying chronic liver disease which is unrelated to carcinoma. Biliary stasis leads to biliary sepsis, inflammation, hepatic toxicity and also increases the morbidity and mortality postoperatively.

Percutaneous Transhepatic Biliary Drainage

Percutaneous transhepatic biliary drainage (PTBD) helps in decreasing the complications by resolving cholestasis, reducing bacterial proliferation and improving the nutritional status.In fact, PTBD can be done in those patients who have poor nutritional status.Though PTBD is technically very successful in biliary drainage and has almost no immediate procedure-related complications but is associated with some complications like peri-catheter bile-leak, dislodgement of catheter and bleeding. ERCP is not done in our patients as most of the jaundiced patients have hilar involvement and ERCP has less role in relieving jaundice in these patients. Also, it has more complication rates than PTBD (15,16).

Evaluation of patients is done by CECT triple phase and contrast MRI

A good quality CT scan can solve diagnostic problems and helps in assessment in most of the patients as FNAC and trucut biopsy are contraindicated in potentially resectableGBC patients. In triple phase CECT scan, patient is given oral contrast and arterial phase is taken 20-25 seconds after injection of intravenous contrast. The portal venous phase is taken in 50-70 seconds and delayed venous phase in 120 seconds after intravenous contrast. This type of CT scan gives the information about involvement of vascular structures (artery, portal vein), liver involvement, lymph node involvement, involvement of surrounding structures as well as distant metastasis. It also gives the view of segmental anatomy of liver which is very helpful for surgeons during liver resection. The yield of contrast MRI is same as that of CECT but the information about bile duct infiltration is better in MRI.

Lymph node dissection

Lymph node metastasis is the most important and independent prognostic factor in GBC patients (17, 18). Lymph node involvement in GBC patients is often not accurate preoperatively by CT scan and MRI. But 18-FDG PET-CT can detect occult lymph node metastasis (LNM) with a sensitivity rate of 56%(19). The LNs along the CBD and in the gall bladder triangle are to be removed completely in all cases as they are the first LNs to drain. Any otherLN is removed if it is more than 1 cm in size or it is hard on palpation. The LN stations are different according to different groups. According to the Japanese Society of Hepato-Biliary-Pancreatic Surgery (JSHBPS), there are 3 metastatic LN stations (20). N1 includes CBD LNs and GB neck LNs. N2 includes posterior portal LNs, common hepatic artery LNs, posterior suprapancreaticoduodenal LNs. N3 includes celiac artery LNs, superior mesenteric artery LNs and para-aortic LNs. The UICC group identifies 2 metastatic end points for GBC. N1 group includes LNs near CBD and GB neck. N2 comprises of the remaining LNs.According to UICC and AJCC guidelines the involvement of 13a lymph nodes (nodes at the posterior aspect of the pancreas head) is considered distant metastasis whereas the Japanese society considers it to be same as regional lymph node involvement as the prognosis of both are same.

Approach to treatment

Patients performance status is assessed by American Society of Anesthesiologists (ASA) physical status classification system(21).After thorough assessment of CT scan, MRI and PET CT scan, the extent of disease and lymph node involvement is evaluated. There are no definite management guidelines for patients with locally advanced GBC. If there is a chance of resectability even if the disease is involving more than 2 organs we planned the patients for curative resection after PTBD and NACT.

Neoadjuvant chemotherapy

Neoadjuvant chemotherapy with gemcitabine and cisplatin is indicated in patients with advanced GB cancer for down staging the disease. Patients having stage III or greater were given neoadjuvant chemotherapy. It was given for 3 cycles and post neoadjuvant chemotherapy CECT scan was done to see the disease regression.

Surgery types

Curative surgeries done in our institute are En-bloc cholecystectomy with liver wedge resection of 2-3 cm and varied lymph node dissection (N1, N2). CBD involvement is assessed macroscopically and CBD excision is done if found to be involved by the tumor or is compressed by extensive nodal disease.

Multi-visceral resections such as duodenal sleeve/duodenectomy, colonic sleeve/segmental colonic resections, distal gastrectomy and hepatico-pancreatico-duodenectomy is done in patients with obvious infiltration of adjacent organs.

Adjuvant chemotherapy

Adjuvant chemotherapy is proven to be beneficial postoperatively. Gemcitabine and cisplatin is given for 6-8 weeks on day1 and day 8 in a 21 days cycle.

Discussion

Earlier jaundice was associated withirresectability as well as post-operative mortality in GBC patients. In our study, the outcome of gall bladder cancer patients presenting with jaundice had much better outcomes in relation to 5-year survival rate and morbidity when they have undergone PTBD followed by neoadjuvant chemotherapy when compared with patients without PTBD and chemotherapy. Preoperatively, percutaneous transhepatic biliary drainage (PTBD) is helpful for decreasing the complications postoperatively by resolving cholestasis.

Jaundice in GBC patients was associated with increase rate of major complications in a study conducted by Elise A.J. et al when compared with non-jaundiced patients (22). In their study,jaundice was not an independent adverse prognostic factor in those patients undergoing curative resection. But surgery was only done in those patients where the cancer was limited (where R0 was feasible) and has not invaded the CBD. The resection of CBD was found to be an independent predictor for major complications.In this study, the major post-operative complications occurred in lesser numberof jaundiced patients without receiving NACTwhich when compared with other studies was very less. It implies that presence of jaundice does not imply unresectability (22). And if these patients were to be treated by NACT, the chances of OS may have been

increased. The tumor location on CECT was also different between jaundiced patients and non-jaundiced patients undergoing surgery (22). In the jaundiced group of patients, the location of tumor was more commonly found in the neck area or a diffuse tumor, whereas in non-jaundiced patients it was more common in the fundus or body.

Neoadjuvant chemotherapy causes downstaging of the patients which further required less aggressive surgical resection procedure.In a study done by Shah Naveed et al (23)which reviewed 6 studies on NACT in GBC,it was found that 30.47% patients showed progressive disease (PD) even after receiving neoadjuvant chemotherapy (NACT) and the clinical benefit rate, CBR (CBR = CR + PR + SD) was 67.38%. Out of 67.38% patients which showed clinical benefit after NACT, and only 51.66% were operated out of which only 40.71% were resectable (CR). R0 resection rate was 91.81% among patients who underwent surgical resection but there were variations in the six studies, i.e., in one study it was 25.0% (24) and in two of the papers it was 100% (25,26). Also, the median OS was 18.5-50.1 months in patients who underwent curative resection after neoadjuvant chemotherapy, which was better than the patients who did not have surgery after NACT (range 5.0-10.8 months). The patients who had CSR had a higher rate of event-free survival than those who did not (median 25.8 vs 5.0 months) (27). In their study, they also found that NACT in advanced GBC showed CBR of 67.38% after surgical resection and most of the patients had R0 resection (91.81%). The median OS was also significantly better in patients undergoing curative surgical resection after NACT than those who did not undergo curative surgery. It was found that only 40. 71% patients of advanced GBC had a CSR after NACT in their study. Also, 2.8% cases with clinical benefit from NACT were found to be inoperable upon exploration. (23)

Goel et al. had a very low mortality rate (4.2%) after surgical resection in patients receiving NACT (28). This was very low compared to other studies probably because they had no major liver resection surgeries and also the disease burden was decreased after NACT. The resection rate was also high (62%) after NACT because of disease downstaging.

Sirohi et al. in their study concluded that NACT (Gemcitabine and platinum based regimen) increases the resectability and survival of patients with locally advanced GBC.(29). Overall response rate (RR) was 67.5% and 46% of patients underwent R0 resection. The overall survival and progression-free survival was significantly better in patients undergoing surgery after NACT.

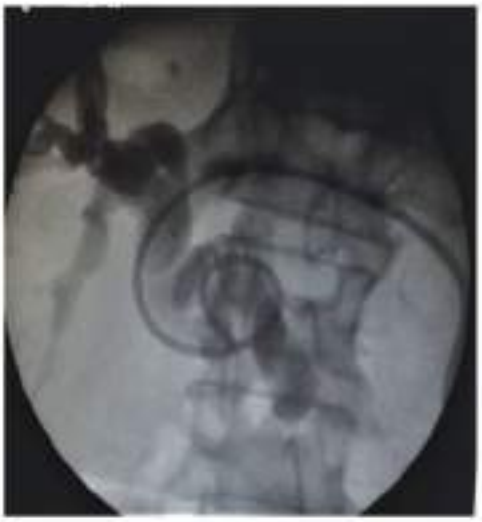
The assessment of NACT response is done by CECT in most of the institutes after 3-4 cycles of chemotherapy. Creasy et al. measured the response using CECT after 8 weeks of chemotherapy(25). On the other hand, Chaudhari et al. used CECT and PET to see the response of chemotherapy (27).

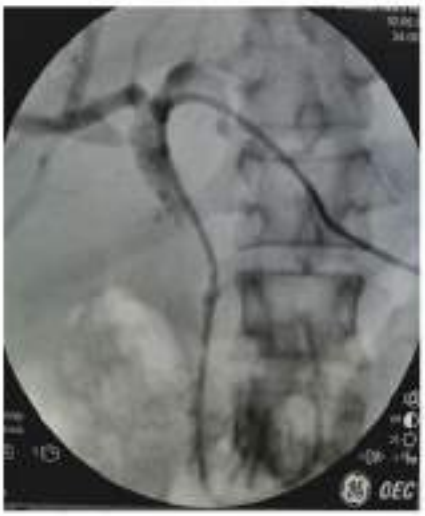
In most of the studies related to GBC, there is not a clear mention of the interval of NACT and curative surgery. In our study, CSR was performed after 3 weeks from the end of NACT cycle so as to get the maximum benefit of chemotherapy induced shrinkage of the tumour and not long enough for the tumour to metastasize or grow locally.

Chan et al. and Kang et al. studied the effectiveness of surgery in advanced stage IV GBC patients (30,31).

Jin Hong Lim et. al found that lymph node count of less than 6 was an independent prognostic factor for the OS and disease-free survival in T2 and T3 GBC patients. It is recommended to dissect a minimum of 6 lymph nodes in advanced GBC surgeries. But sometimes due to difficult anatomy, the yield is less.

Previously, jaundice was an obvious sign of inoperability but, now this notion is changed. Many studies have proven that jaundice is just a sign of advanced disease which can be controlled by PTBD. In a study by Sugumaran et. al, the overall survival of GBC patients with jaundice was better in patients undergoing curative resection than the patients receiving palliative treatment (32). Also, the OS was better in CR patients receiving adjuvant chemotherapy than the patients who did not. The resectability rate was 41.5% even without NACT and the R0 resection was achieved in 85% cases. Therefore, it can be expected that the result of CSR will be way better if NACT is given in those patients.

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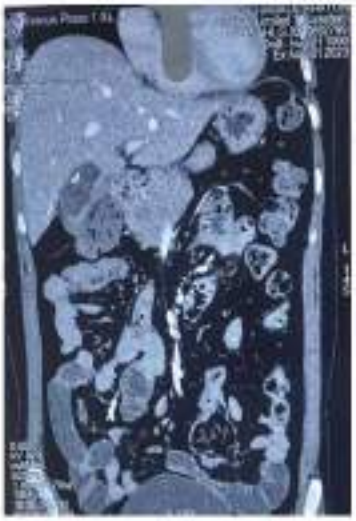

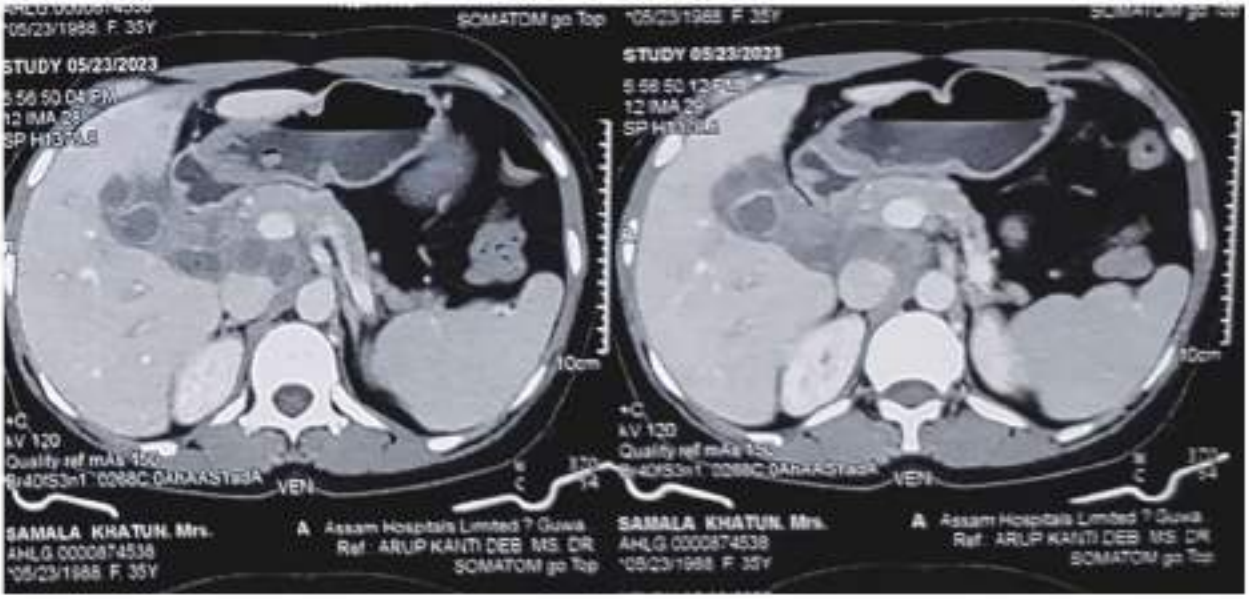
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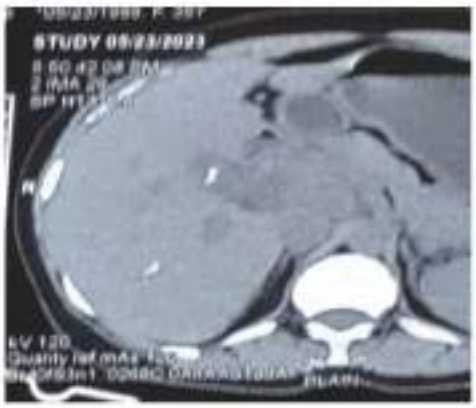
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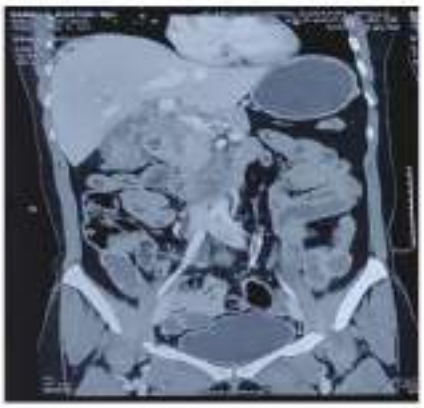

The most important deciding factor for long term survival is the R0 resection. Even if the disease is locally advanced and involving other organs, if there is a possibility of R0 resection then it is the most important prognostic factor for long term survival. Jaundice also is not a contraindication for surgery because the serum bilirubin levels can be lowered by doing PTBD. In a study done by Engineer et al., it was found that even if you do radical resection like pancreaticoduodenectomy, the 5-year survival rate was 30-42% (33). Higuchi et al found that in advanced GBC cases without NACT, the R0 resection rate was 61.3% and 5 – year survival rate was 52.4% (34).

Chaudhari et al., (27) in their study observed major morbidity of only 7% in patients undergoing curative resection after NACT. It's very less compared to other studies. It could be because they have not considered surgical resection in those GBC where major hepatic resection or venous reconstruction were required. They managed those patients with palliative intent only. Their curative surgical resection rate was 41.2% after NACT and response rate(RR) was 52% the clinical benefit rate (CBR) was 70% which shows a good response of NACT to downstage the disease as well as morbidity associated with it.
Other studies found a high morbidity in GBC patients who were operated after NACT. Dixon E et al (35) had morbidity of 30-40%, but their patients had much more aggressive surgeries for locally advanced GBC.

Keto et al. (24) found that neoadjuvant chemotherapy was effective in downsizing the tumour in unresectable locally advanced BTC(biliary tract cancer) patients. Curative surgical resection was possible in 36.4% cases after administration of Gemcitabine for 3 weeks. Half of the patients had R0 resection and half had R1 resection. Their sample size was small and the effectiveness of NACT was not significant because they used only gemcitabine which is not so effective until it is combined with platinum-based chemotherapeutic agents.

Ozer et al in their study found that the GBC patients with LNM undergoing surgery after NACT and then receiving adjuvant chemotherapy had a longer median OS than patients undergoing radical surgery alone (36).

Adjuvant chemotherapy after CSR is the treatment of choice in locally advanced cancers (37,38). In a study, patients with advanced GBC patients with R1 resection had improved long term outcomes after receiving post-operative adjuvant chemotherapy (39).

Our experience

Patients admitted for gall bladder cancer with jaundice were evaluated retrospectively from 2014 to 2022. Before 2019, we excluded jaundiced patients with bilirubin >10 mg/dl and cholangitis from major resection. But 2019 onward, we are treating all jaundiced patients with PTBD. We are presenting an interim data from January 2019 to December 2022. We have resected 157 patients. We have done 52 PTBD in this period. Out of these, 45 received NACT, 7 patients were lost/could not complete CT due to ill health. Only 18 patients entered into CSR (R0 resection). Patients with metastatic disease which could not be operated were excluded from the study.

Neoadjuvant chemotherapy

After bilirubin <4mg/dl, Gemcitabine 1000mg/m2 and cisplatin 25mg/m2 was given intravenously in each cycle every week for 3 cycles and after completion, the patients were reviewed with CECT and blood investigations for signs of improvement. The response was assessed by Response Evaluation Criteria in Solid Tumors (RECIST) criteria.

Selection of patients for curative resection: GBC patients with jaundice without metastatic disease, or involvement of major vessels, portal involvement or patients with poor performance status. But the extent of radical surgery was dependent on the preoperative, intraoperative assessment of the tumour. Bile duct resection is done whenever possible in all cases presenting with jaundicewith the aim of getting a negative margin.

Surgical strategy

Radical cholecystectomy was done in all patients. Regional lymph node dissection (N1 dissection) was also performed in all cases, which included lymph nodes around the hepatoduodenal ligament (i.e., around cystic duct, hepatic artery, portal vein and bile duct) and around gastrohepatic ligament. In some cases(when palpable), N2 dissection was

performed which included N1 dissection with celiac LNs, pancreaticoduodenal LNs and para-aortic LNs. It was totally dependent on the specific case where the surgeon suspects involvement of the N2 LNs.The minimum number of lymph nodes to be resected for complete dissection was 6. CBD excision was done in all cases where the surgeon has suspected involvement either by palpation or if there is macroscopic evidence of infiltration or if the CBD was compressed by enlarged lymph nodes. Resection of bile duct was performed on reasonable grounds which was solely the decision of the surgeon after thorough inspection. If there was infiltration of adjacent organs e.g., duodenum, stomach, colon, pancreas, then they were managed accordingly by duodenectomy, distal gastrectomy, colonic resection and hepaticopancreaticoduodenectomy.Complications were assessed by Clavien-Dindo classification (40). The most common complication was bile leak, bleeding.

After surgery, adjuvant chemotherapy was given with Gemcitabine and cisplatin for 6-8 weeks on day1 and day8 in a 21 days cycle. After 3 weeks, the patients were evaluated. The patients were followed up after every 3 months for 24 Months.Follow-up was done with blood CEA, CA19.9 levels and routine blood investigations. CECT was done once every year for 5 years. Recurrence was identified if there was radiological diagnosis of involvement or high blood CEA or CA19.9 levels.

Histopathological examination

Although FNAC and histopathological examination is still the gold standard for diagnosis of GBC, it is not a pre-requisite but it is desirable for NACT or CSR. Radiological diagnosis is enough for undergoing curative resection if there are radiological features suggesting local advancement of malignancy. In fact, it has been found that there are cases of seeding of cancer cells while doing fine needle aspiration cytology (41) which will upstage the disease. The histopathological examination also seems to differ in GBC patients having jaundice and those without jaundice. The GBC that are involving the neck of gall bladder or are infiltrating in a diffuse manner are more likely to present with jaundice clearly because they are in vicinity of CBD and are more likely to involve CBD. The T2a disease were less likely to cause jaundice because they are in the peritoneal side whereas, T2b diseases had more chances of invading the liver and cause jaundice. Also, gall bladder lacks the serosal layer on the liver side which increases the chances of invasion into liver by T2b GBCs.

Conclusion

Many studies have evaluated the result of NACT before CSR in locally advanced GBC and found it to be effective to increase the overall survivality as well as decreasing the morbidity. But there are very few studies to see the result in GBC patients with obstructive jaundice. In our study, we found that the mere presence of obstructive jaundice is not a contraindication for abandoning curative surgical resection. There are other factors which contribute to the result of curative resection. With Neoadjuvant chemotherapy, a lot of the advanced GBC which were unresectable at the time of diagnosis can be downstaged which helps to get R0 resection. Also, overall survivality of the patients with advanced GBC can be prolonged with lesser morbidity by doing PTBD and NACT before curative resection. The mere infiltration of other organs like colonic or duodenal infiltration did not matter much until there was a chance of getting R0 resection. Further RCTs are needed to prove the definite effectiveness of PTBD followed by NACT and CSR as our study is composed of a small population. As our study does not have a control group, further studies and RCTs are required in the future to come up with a standard protocol for these patients. our study is providing interim data of retrospective study. Further prospective study data will be provided.

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Lateral Geniculate Artery Perforator Based Propeller Flap for Defect Repair in Pre-Patellar Squamous Cell Carcinoma.

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Abstract:

Wide local excision with negative margins is the recommended treatment for cutaneous malignancies. However, they often leave large, unsightly defects which cannot be closed primarily (because of size) or by split skin grafting (because of depth of clearance exposing periosteum or joint capsule). In such cases, local pedicled flaps are a life (and defect) saver. Propeller flaps based on musculo-cutaneous perforators allow freedom to be harvested in a wide range of areas and allow rotation of upto 180˚ to cover loco-regional defects

Keywords:

squamous cell carcinoma, cutaneous malignancy, wide local excision, propeller flap, local flap, perforator flap, distal thigh flap, lateral geniculate artery

Introduction:

Squamous cell carcinoma (SCC) is a common cutaneous malignancy strongly associated with older age and UV ray exposure,occurring most commonly in the sun exposed areas of the skin. Risk stratification of SCC is based, among a number of factors, on the size, differentiation and depth of invasion of the lesion[1]. The standard of care is wide local resection (WLE) with negative margins and closure of the defect either primarily, by skin graft or by loco-regional flaps. Cutaneous defects around knee joint are a difficult proposition for closure as underlying joint capsule or periosteum is often exposed which is thus unsuitable for skin grafting; also the bulk of the underlying muscle hinders primary closure. Hence the concepts of local flaps come into play, more specifically fascio-cutaneous flaps based on the extensive vasculaturearound the knee joint.

Case report:

A 74 years old gentleman presented to the OPD of Surgical Oncology, ******** with the complaints of a progressively increasing ulcerative growth on his left knee for the last 4 months. He was a farmer by occupation, used to working in the fields wearing dhoti or shorts. There was no history of trauma or burns. On clinical examination a 7 x 8 cm ulcero-proliferative mass was noted on the lateral aspect of the left knee joint with enlarged palpable left inguinal lymph nodes. Wedge biopsy of the lesion revealed squamous cell carcinoma and

FNAC of the inguinal node revealed metastatic squamous cell carcinoma. An MRI scan of the left knee to gauge the depth of invasion showed the lesion to be free from the underlying joint capsule and patellar periosteum. Because of the need to go to the periosteum to get an adequate oncological clearance, a decision was made to reconstruct the WLE defect with a local propeller flap.

Prior to surgery, help was sought from institutional radiologists to mark the underlying perforators based on the superior lateral geniculate artery (SLGA) upon which the local flap could be based. A musculo-cutaneous perforator through the vastus-lateralis muscle arising from the SLGA was identified and marked approximately 5 cm proximal to the lateral femoral condyle. The malignant lesion was excised with 1cm circumferential margins and depth upto, but not including the patellar periosteum and the joint capsule. Left inguinal lymphadenectomy was also done.

The resultant defect was 8 x 6 cm over the antero-lateral part of the left knee joint. Marking of flap based on the previously noted pedicle was done allowing 0.5 cm more than the size of the defect to allow for flap contraction. The length of the flap from the pedicle at the proximal part was kept longer than the distal part to allow for adequate cover of the defect after rotation of the flap. The incision was taken down beyond the deep fascia and the flap was carefully harvested between deep fascia and underlying muscle and mobilised all around the pedicle which was seen to pass through the vastus lateralis and supply the overlying skin. Vascularity of the flap was checked by the presence of punctate haemorrhage at the edge of the flap farthest away from the pedicle i.e. the proximal end.

The flap was rotated 150° inferiorly to cover the WLE defect and sutured at the edges. The cutaneous defect at the donor site of the flap was closed partly with split skin grafting (SSG) and partly primarily.

Post-operatively, the viability was monitored by comparing the temperature over the flap with the surrounding area and also looking out for color change of the flap. On day 4, mild epithelial discoloration was noted at the edges of the distal end of the flap. It was observed till day 7, and upon no further progression, the patient was discharged uneventfully. On follow-up at day 12, flap was intact and healthy, except for mild superficial epidermal discoloration at the distant edges, which is expected to heal primarily without hampering the viability of the graft.

Post-operative histopathology report showed squamous cell carcinoma with clear margins.

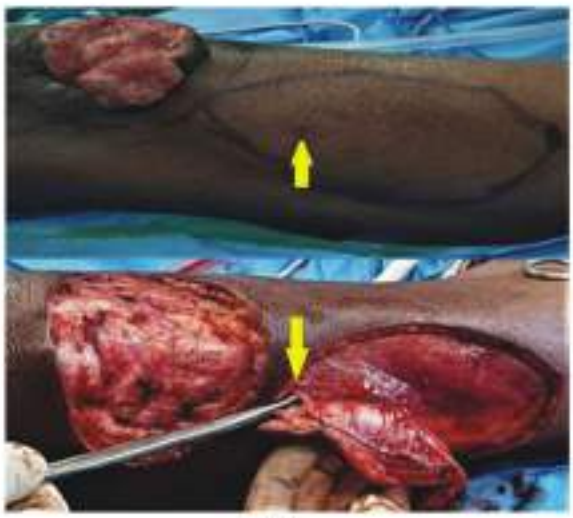

Fig. 1

Ulcer, defect and flap after being harvested (arrow marks the pedicle)

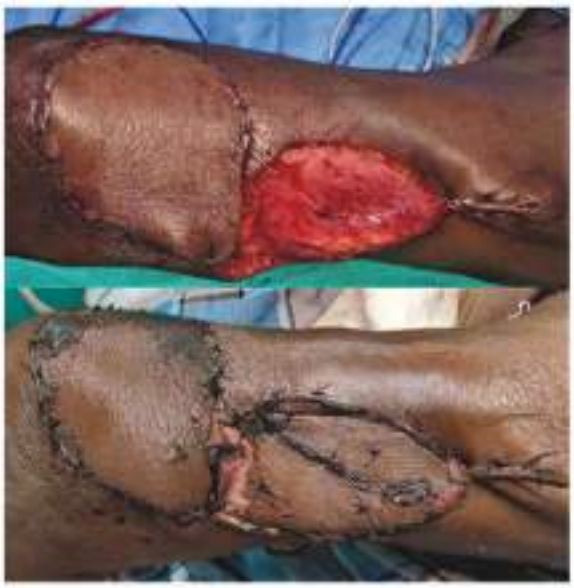

Fig. 2
Flap after inset and on Day 12

Discussion:

Cutaneous squamous cell carcinoma is a relatively common malignancy related to old age and prolonged cumulative exposure to sunlight. The treatment of choice is primarily surgical; WLE with clear margins and addressing the regional lymph nodes when necessary. The primary concern in oncology is to obtain negative margins in all dimensions; however, the resultant defectis often too large for a primary closure. Moreover, defects overlying the periosteum or joint capsule are not amenable for SSG. In this situation, local flaps come to the rescue.

A propeller flap is an adipo-cutaneous or fascio-cutaneous flap based on a vascular pedicle. The name propeller is based on the fact that the length of the flap exceeds its width and the pedicle is based on the center with the two parts of the skin island on two sides of the pedicle like the blades of a propeller. It can be subcutaneous pedicled, perforator pedicled (in this case) or supercharged pedicled[2]. It was first described by H. Hyakusoku et. al. in 1991, who rotated it 90° to cover defects following release of burn contractures[3]. This was further modified in 2006 by G. Hallock[4] who was successful in increasing the rotation range upto 180°.

A large number of vessels arising from the popliteal artery and the anterior tibial artery form a rich vascular anastomosis around the knee joint. Of these, one of the most consistent vessels is the superior lateral geniculate artery arising from the popliteal artery [5]. It gives a perforator approximately 3-8 cm (average 5cm) from the proximal end of the lateral femoral condyle, which supplies the overlying skin and subcutaneous tissue in a radial manner. Fascio-cutaneous islands can be based on these perforators and used as a rotation or propeller flap to reconstruct defects around the knee joint. The advantage of propeller flaps is the freedom it allows to be harvested based on a single perforator and avoids the need for a named vascular pedicle, which may not be available around the defect.

Conclusion:

Defects following WLE of SCC may not amenable for primary closure or SSG owing to the dimensions or base. In such cases, local perforator based flaps are useful to fill the defect. The SLGA perforator based propeller flap can be successfully used for defects on the antero-lateral part on and around the knee joint.

Patient consent : written and verbal patient consent has been taken.

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A Rare Case Report of Brunner's Gland Adenoma.

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Introduction:

Brunner's glands, is located in the wall of the first few centimetres of the duodenum, mainly between the pylorus of the stomach and the papilla of Vater of duodenum. These glands secrete large amounts of alkaline mucus containing bicarbonate ion in response to

a. tactile or irritating stimuli on the duodenal mucosa
b. vagal stimulation, which causes increased Brunner's glands secretion concurrently with increase in stomach secretion
c. gastrointestinal hormones, especially secretin.

The function of the mucus secreted by Brunner's glands is to protect the duodenal wall from digestion by the highly acidic gastric juice emptying from the stomach [1]. Brunner's glands, were described by the anatomist Brunner in 1688.

Brunner's gland adenomas (BGA) are rare, benign tumors arising from Brunner's glands in the duodenum. BGA are usually found incidentally on endoscopy. Usually BGA are asymptomatic, however they can present with hemorrhage or small bowel obstruction. There have been less than 200 cases reported in the literature since itsitsfirst description by Curveilheir in 1835[2]. In a study of a case series of 215 000 autopsies17 (0.008%) patient were found to have brunner's gland adenoma[3]

CASE REPORT :

A 56 years male visited primary hospital OPD with generalized weakness for 6 months and malena for 1 week. On evaluation, Pancytopenia was found and patient was referred to our hospital. Haematological workup & Bone Marrow study led to the diagnosis of Hypocellular marrow, and patient started on Tablet Cyclosporine (immunosuppressant) 100mg twice daily and inj. Romiplostim (fusion protein analog of thrombopoietin) 250mcg once weekly.

An upper GI endoscopy was done which showed (Figure 1) a large pedunculated duodenal polyp at D1-D2 junction with Antral Gastritis. Endoscopic punch biopsy of the polyp showed benign epithelial cells; which is negative for malignancy. CECT whole abdomen that showed (Figure 2) a large pedunculated duodenal polyp(6.9 x 2.2 x 2.0 cm).

After optimization, Endoscopic resection of the polyp was tried but was unsuccessful due to high vascularity around the polyp. Thereafter, patient underwent laparotomy: Duodenotomy & resection of the polyp was performed. Post operative period was uneventful. Histopathological examination of the polyp showed circumscribed tumour in submucosa with proliferation of normal appearing brunner's gland, arranged in lobules separated by fibroconnective tissue, suggestive of Brunner gland Adenoma. Patient is now undergoing monthly follow-up in department of haematology for hypocellular marrow.

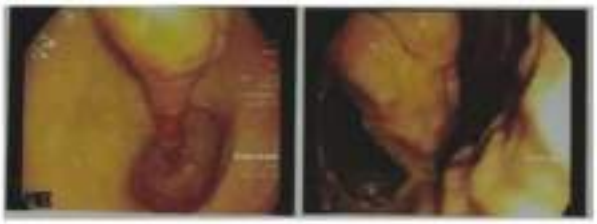

Fig 1: Endoscopic image of the polyp at D1-D2 junction of Duodenum

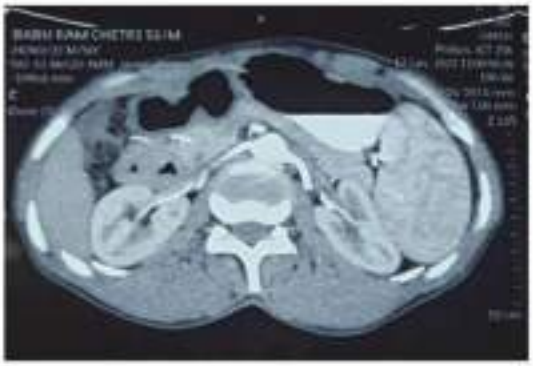

Fig 2: CECT whole Abdomen showing Polyp at at D1-D2 junction of Duodenum

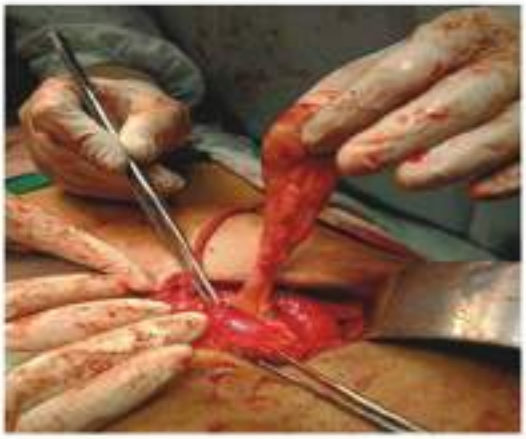

Fig 3: Intra operative image of the Polyp after Duodenotomy

Discussion: Brunner's gland adenomas are rare benign tumours arising from the Brunner's glands of the duodenum. BGA has a tendency to be predominant in the fifth or sixth decade of life with equal gender distribution [4]. Clinical presentation is variable. However, the majority of cases are asymptomatic or can present with symptoms like hematemesis, melena, nausea, vomiting or chronic abdominal pain.

In symptomatic patients, the most common clinical presentations is gastrointestinal bleeding which manifests in the majority of cases as chronic loss of blood with iron deficiency and anaemia or less frequently, when erosion or ulceration of the tumour occurs, patients can present with melena or hematemesis.

The exact pathogenesis of BGA still remains unclear. Some have suggested that the Brunner's glands are stimulated to undergo hyperplasia by increased acid secretion [5]. Franzin et al [6] have reported an association between BGA and hyperchlorhydria in patients with chronic gastric erosions and duodenal ulcers, but Spellberg et al[7] have not found regression of the lesion with acid secretion inhibitors.

The diagnosis is usually made by radiological studies followed by upper gastrointestinal endoscopy, which can also provide definitive treatment. Endoscopy demonstrates the tumor in the duodenal lumen and facilitates biopsy from the lesion. Endoscopic ultrasound helps to establish a preliminary diagnosis depending on the layer from which the lesion arises and also from the characteristic appearance of the lesion. Computed tomography can be used to delineate the extraluminal extent of large adenomas. Differential diagnosis includes leiomyoma, lipoma, carcinoid tumor, lymphoma, aberrant pancreatic tissue, prolapsed pyloric mucosa, and foreign body.

Endoscopic or surgical removal of the adenoma has been suggested in symptomatic patients to prevent development of complications. Local excisionof the lesion is the main treatment and may be done by either endoscopic snare-cautery technique or excision of the mass via duodenotomy [8]. Local recurrence after surgery is rare[9].

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