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Review Article

Changing role of laparoscopy in the management of patients with cirrhosis

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Abstract

Cirrhosis was previously a contraindication to laparoscopic surgery. The associated coagulation defects, portal hypertension and nutritional disorders were seen as risk factors for high morbidity and mortality. Open surgery in cirrhotic patients over the years have witnessed poor outcome. However, as experience with laparoscopic surgery continues to grow, several studies have described the use of laparoscopy for the diagnosis of cirrhosis as well as the treatment of various surgical conditions among cirrhotic patients. This article reviews the effect of laparoscopy on the cirrhotic patient and describes the increasing role of laparoscopy in management of cirrhosis as well as its proven benefits.

Key words: Cirrhosis, laparoscopy

INTRODUCTION

Cirrhosis is a chronic, diffuse and progressive condition characterised by fibrosis and conversion of normal liver architecture into structurally abnormal nodules.[1] It induces various physiological and metabolic changes in the body which may worsen with disease progression. These changes, including fluid retention, coagulation defects and poor resistance to infections, can increase the peri-operative morbidity and mortality in cirrhotic patients. This observation led to various recommendations advocating the use of non-invasive procedures for the diagnosis and treatment of patients with cirrhosis. Earlier studies however show that different imaging techniques have varying specificity in the diagnosis and staging of liver cirrhosis.[2-5]

Open surgical procedures in cirrhotic patients are associated with high morbidity and mortality.[6-9] At the onset of laparoscopic surgery, liver cirrhosis was either an absolute or a relative contraindication; however current literature has increasingly shown that the use of laparoscopy in the diagnosis of cirrhosis and treatment of various disease specific and non-specific surgical conditions in cirrhotic patients is safe and offers many advantages.[10-13]

AIM

This study aims to evaluate the role of laparoscopy in the management of patients with liver cirrhosis over the years with emphasis on the increasing use of laparoscopy in the diagnosis and treatment of specific and non-specific surgical conditions in cirrhotic patients. This will include a review of:

- The risk of laparoscopy and laparoscopic surgery in cirrhotic patients,
- Previous role and current trends in the use of laparoscopy in the diagnosis of liver cirrhosis, and
- Safety and efficacy of laparoscopy in the treatment of various surgical conditions in cirrhotic patients.

MATERIALS AND METHODS

A literature search was performed using the following search engines: HINARI, Google, High Wire Press, Pubmed and the online Springerlink MetaPress Library available at the Laparoscopy hospital, New Delhi

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India, where this study was carried out. The following terms were used for the search: "Laparoscopy in Liver cirrhosis"; "Liver cirrhosis, diagnosis"; "Laparoscopic surgery in cirrhosis"; "Surgery and Cirrhosis" and "Surgical procedures in cirrhosis".

A review of the articles that matched the search criteria was then carried out.

GENERAL CONSIDERATIONS

Pathophysiology of liver cirrhosis[14,15]

Liver cirrhosis may be caused by Hepatitis C or B infection, alcoholic liver disease, non-alcoholic fatty liver among others. The central histological finding in cirrhosis is the development of hepatic fibrosis with an alteration in the normally balanced processes of extracellular matrix production and degradation. The extracellular matrix which is composed of collagens, glycoproteins, and proteoglycans depends on the activities of stellate cells, which in cirrhosis may become activated into collagen-forming cells by a variety of paracrine factors. Such factors may be released by hepatocytes, Kupffer cells, and sinusoidal endothelium following liver injury. With disease progression, there is increased collagen deposition in the space between hepatocytes and sinusoids (the space of Disse) and diminution of the size of endothelial fenestrae leading to the capillarisation of sinusoids. The capillarisation along with constriction of sinusoids by stellate cells, contribute to the development of portal hypertension in cirrhosis.

Several indices have been proposed for the estimation of the surgical risk in a patient with cirrhosis.[16-20] Of these, the Child's classification and the modification proposed by Pugh *et al*, (1973) remain the most widely acceptable.[18,21,22] As will be shown later, the outcome of both open and laparoscopic procedures in cirrhotic patients is influenced by the preoperative Child's class.

Physiological effects of pneumoperitoneum on patients with liver cirrhosis

A major difference of open and laparoscopic procedures is the creation of pneumoperitoneum for visualisation of the abdominal cavity. Studies have shown that along with other effects, there is decreased cardiac output, splanchnic blood flow and portal venous flow following pneumoperitoneum.[23-25] Theoretically, pneumoperitoneum was initially considered unsafe in cirrhotic patients since they already have varying degrees of alterations in hepatic blood flow and general haemodynamics. Tsubio *et al*, (2002) studied the effect of carbon dioxide pneumoperitoneum on the haemodynamics of cirrhotic rats and observed a marked decrease in splanchnic organ blood flow (particularly hepatic blood flow), which persisted up to one hour after desufflation.[26] This suggests that impaired hepatic arterial buffer response may play a role in the decreased hepatic blood flow in cirrhosis. Other studies have shown that the resulting relative ischemia leads to some immediate hepatocyte damage with consequent elevation of various hepatic enzymes such as SGOT and SGPT as well as an impairment of the functions of the Kupffer cells within the liver.[27,28] The implication of this in the clinical setting is a possibility of hepatic failure intraoperatively or in the early postoperative period. Few clinical studies have also showed transient increased levels of alanine aminotransferase, aspartate aminotransferase, alcohol dehydrogenase and glutathione S-transferase in patients undergoing laparoscopy.[29-31] The levels usually return to normal within 72h after surgery. These changes, though not very rare, are usually subclinical in human. Within the limits of our literature search, no report of hepatic failure attributable to laparoscopy alone in a cirrhotic patient was found. This may indicate that more factors may be involved in the response of cirrhotic patients to the effect of pneumoperitoneum and should be a subject for further research.

Safety considerations in cirrhotic patients undergoing laparoscopic procedures

The Surgeon: Schiff *et al,* (2005), while concluding that laparoscopic cholecystectomy is safe in cirrhotic patients, stated that "… tremendous amount of patience is necessary (in the procedure) because conversion (to open surgery) does not help to control coagulopathy.[32] In their study, three of the 24 cirrhotic patients who had laparoscopic cholecystectomy were converted to open and two of these were due to surgeons' inexperience. This and other findings in the literature suggest a role of the experience of the surgeon in the success of the procedure in this group of patients.

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Anaesthetic techniques in cirrhotic patients: As previously noted, hepato-splanchnic perfusion may be impaired in cirrhotic patients. This implies that adequate circulation must be maintained in the patients throughout the period of anaesthesia. In addition, some anaesthetic drugs may have specific effects on liver circulation. While isoflurane increases hepatic regional blood flow, halothane is noted to increase hepatic arterial resistance. Fentanyl, Vencuronium and Pancuronium do not significantly affect hepatic blood flow and may be preferable in cirrhotic patients.[33]

Preoperative preparation: Preoperative preparation of the patients in elective cases is important. This will include correction of coagulopathy with parenteral Vitamin K administration and or transfusion with fresh frozen plasma, lowering of portal hypertension with medications, attainment of fluid and electrolyte balance as well as control of infection where present. Garrison *et al,* (1984) had identified absolute serum albumin concentration, presence of infection or contamination and number of seconds partial thromboplastin time is deviated from its control value as the three main preoperative variables that predict surgical outcome in cirrhotic patients.[34]

Operative techniques: Some authors have advocated a number of operative techniques to help minimise the morbidity associated with surgery in cirrhotic patients undergoing laparoscopic procedures.

Klopfenstein *et al*, (1998) demonstrated in anaesthetised pigs that CO_2 insufflation after a head-down tilt will lead to an increase in portal venous blood flow while a head-up tilt before CO_2 insufflation decreases both the portal venous and the hepatic arterial blood flow.[35] This has not been sufficiently studied in humans and the beneficial effects of positioning on the hepatic circulation in cirrhotic patients need to be further studied.

Friel *et al*, (1999) advocated the use of open technique using Hassan's trocar for access to prevent inadvertent puncture of an umbilical varix or placement of the trocar in the right paramedian position when umbilical varix is already present.[32] Other techniques advocated include subtotal cholecystectomy in cases of severe inflammation leaving the back wall of the gallbladder on the liver bed. The use of mechanical compression from introduced surgical sponges to achieve haemostasis with additional haemostatic modalities such as oxidized cellulose, topical haemostatic agents, application of ultrasonic energy via a harmonic scalpel and the use of argon beam coagulator which can be inserted through an operative port have also been described.[36]

A major safety consideration in the operative technique of patient with cirrhosis is the risk of transmission of Hepatitis B or Hepatitis C virus from the patient to the members of the operating team as these viruses are well known aetiological factors in cirrhosis. Precautions for safe passage and disposal of all sharp objects used intraoperatively are to be strictly adhered to.

ROLE OF LAPAROSCOPY IN DIAGNOSIS OF LIVER CIRRHOSIS

The diagnosis of liver cirrhosis is important in the evaluation and management of the patients. Histopathology of a liver biopsy specimen is the gold standard for diagnosis but the invasive procedure required as well as the associated complications encountered by initial researchers led to the preference for imaging and biochemical studies.[37,38] However, the accuracy of liver ultrasonography which is the most commonly used imaging modality in the diagnosis of cirrhosis has been the subject of much debate. While features of portal hypertension and marked architectural distortions in late stage disease can be easily identified on ultrasound, many studies have reported low specificity and sensitivity of ultrasound findings when correlated with histopathological reports especially in early cirrhosis. Other studies have however shown that high resolution ultrasound analysis of the liver is of high accuracy in diagnosing cirrhosis.[3,4,39-43] In some cases, macronodular cirrhosis is erroneously diagnosed as metastatic disease on ultrasound leading to confusion, repeated biopsies and inappropriate treatment.[44]

With improved expertise and increased use, diagnostic laparoscopy and biopsy are now commonly employed in cirrhosis. Laparoscopy enables direct visualisation of the liver surfaces, usually both liver lobes, which can vary in their degree of nodularity with disease progression.[45] This advantage has been highlighted in many studies comparing laparoscopic biopsy to blind

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and ultrasound guided percutaneous biopsy in cirrhosis.[46-48] No study has however compared laparoscopic liver biopsies to transjugular biopsy method while different studies have affirmed that the sensitivity and specificity of pathological features identified at laparoscopy are close to 100% since laparoscopic biopsies are directed at macroscopically identified targets. [Table 1][49-52] This is in contrast to percutaneous biopsy where the specimen may be too small or fragmented and therefore inadequate for definitive confirmation of cirrhosis. False negative findings with blind biopsies in cirrhosis have been estimated to be up to 10-15%.[53-55]

In large patient population studies, Orlando *et al* (1990) and Henning *et al* (1994) have reported complication rates from diagnostic laparotomies for liver biopsies that are similar to those reported for percutaneous biopsies in previous studies by Linder (1967) and Piccinino *et al* (1986).[38,48,55,56]

Laparoscopy also allows application of direct pressure or a heater probe to attain haemostasis in the event of bleeding from a biopsy site and may hence be carried out safely despite haematological abnormalities (e.g. PTR>1.3; Platelet <80,000/mm$^{3)}$ which routinely contraindicate blind percutaneous biopsy.[57]

The use of diagnostic laparoscopy has therefore expanded in liver cirrhosis so much that Vargas *et al* (1995) recommended that diagnostic laparoscopy should be incorporated into the training programmes for gastroenterologists in America.[58] Haydon and Hayes, (1997) also advocated that physicians in the United Kingdom should be the ones performing diagnostic laparoscopy.[59]

Table 1: Sensitivity and specificity of pathological features identified at laparoscopy (Adapted from Jalan *et al.* (1995)[52])

Pathological feature	Sensitivity (%)	Specificity (%)
Fatty change	96.4	100
Fibrosis	100	95
Inflammatory activity	94	95
Cirrhosis	100	97.5

THERAPEUTIC ROLE OF LAPAROSCOPY IN CIRRHOSIS

Laparoscopic cholecystectomy in cirrhotic patients

Post-mortem examinations have revealed an incidence of gallstones twice as high in cirrhotic patients as in the general population.[60-62] This is commonly attributed to accelerated pigment stone formation. Small size, friable bilirubin stones are the most common type seen in cirrhosis.[63,64] With the increased incidence, symptoms of gallstones and its complications are also frequently seen in cirrhotic patients thus indicating cholecystectomy and hence cholecystectomy may be the commonest laparoscopic procedure performed in cirrhotic patients.

Open cholecystectomy (OC) in cirrhotic patients is associated with poor outcome. Many studies have reported high rates of morbidity (5-30%) and mortality (7-25%) compared to 0.5-1% mortality in non-cirrhotics.[49,50,56,57] These poor outcomes have led to the development of many multifactorial indices to more accurately estimate the surgical risk in cirrhosis.[18-20,65] However across the various stages of the disease, open procedure still has a high rate of complications.

At the inception of laparoscopic surgery, cirrhosis was listed either as an absolute or a relative contraindication.[66,67] However with increased experience with laparoscopy, several studies across the world have demonstrated that laparoscopic cholecystectomy (LC) is safe and effective with fewer complications compared to OC. [Table 2][12,13,68-71] Specifically, LC is associated with less intraoperative

Table 2: Recent reports on laparoscopic cholecystectomy in patients with liver cirrhosis

Reference	No.	Child-Pugh classification			Morbidity	Mortality
		A	B	C		
Morino, 2000[69]	33	27	4	2	0	0
Fernandes, 2000[71]	48	38	10	0	4	0
Clark, 2001[73]	25	14	9	2	0	0
Yeh, 2002[74]	226	193	33	0	15	2
Cucinotta, 2003[70]	22	12	10	0	14	0
Curro, 2007[68]	50	35	15	0	15	0

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bleeding and shorter duration of hospital stay and fewer postoperative complications. Visualisation is much better than with open cholecystectomy and the small vessels that may not be seen at open surgery appear larger during laparoscopy allowing for better haemostasis. It is also particularly useful in liver transplant candidates since it is associated with fewer postoperative adhesions.[71]

Certain problems may be encountered during laparoscopic cholecystectomy with a cirrhotic liver. There may be difficulty with traction of the liver, inadequate exposure of the hilum, adhesions around the gallbladder and the hilum with difficulty in identifying anatomical landmarks as well as increased vascularity of the gallbladder bed. The use of additional ports as well as performance of retrograde cholecystectomy or modified subtotal cholecystectomy in selected cases can be helpful.[72]

The safety of LC is however more documented for patients with Child-Pugh's class A and B. The experience of Yeh *et al* (2002) with LC in 226 cirrhotic patients represents the largest series published so far. However no patient with Child-Pugh's class C was operated upon. This is similar to the patient population in most of the studies as shown in Table 2 Curro *et al* (2005) compared 4 Child-Pugh's class C patients who had LC with 38 Child-Pugh's A and B patients in the same centre and found a morbidity rate of 75% in the Child-Pugh's C patients compared with 26% in the A and B group. The authors further advised that surgery in Child-Pugh's C patients should be avoided except in acute emergencies where conservative procedures such as gallbladder aspiration and partial cholecystectomies may be considered. A meta-analysis of LC in cirrhotic patients, (Puggioni and Wong, 2003) was inconclusive in either recommending LC for patients with Child-Pugh's class C cirrhosis or not due to inconclusive data in most of the studies reviewed. It is not clear whether many surgeons consider the risks of morbidity and mortality to be so high as to withhold even emergency surgeries in these patients or that the data on this group of patients are not included in the different publications. It would seem that indications for surgery in these patients should be limited to emergencies such as cholecystectomy for acute cholecystitis. Even in such instances, percutaneous drainage of the gallbladder and other conservative procedures may suffice.[68]

Laparoscopic hernia repair in cirrhosis

In a report of 14 cirrhotic patients who underwent laparoscopic incisional and umbilical hernia repair, Giulio *et al* (2006) observed that though open repair in cirrhotic patients has significant recurrence rates and frequent wound infections, laparoscopic repair yields less morbidity and fewer recurrences.[10] The study further highlighted that the preservation of the anterior abdominal wall in laparoscopic repair avoids the interruption of collateral veins which are not infrequently distended in cirrhotic patients.

McAlister (2003), in an editorial titled "Management of umbilical hernia in patients with advanced liver disease" observed that the tendency for umbilical hernia to develop in patients with chronic liver disease is high and opined that in addition to the abdominal distension and abdominal muscle weakness which may predispose to hernias generally in them, umbilical hernia may be commoner due to transmission of additional pressure to the umbilicus via the porto-systemic venous communication.[75] He noted that previous attempts at umbilical hernia repair in cirrhotic patients were followed by different complications. The suture era witnessed a high rate of recurrences while the era of prosthetic mesh had fewer recurrences but a greater rate of wound complications. Laparoscopic umbilical hernia repair in cirrhotic patients appears to offer advantages over the open methods. He further proposed an algorithm for the management of umbilical hernia in these patients. Emergency repair is necessitated when there are associated complications such as incarceration, bowel obstruction or impending rupture. Elective repair is to be considered in other patients after controlling coagulopathy and ascites. In liver transplant candidates, elective repair should be delayed for a formal repair with transplantation.

Successful laparoscopic repair of recurrent incarcerated umbilical hernia in a cirrhotic patient with refractory ascites has also been reported.[76] In the report, the authors used dual mesh prosthesis and advocated meticulous sterile fashion of mesh insertion and fixation. This is important since ascitic fluid infection, which may occur after surgery may affect the hernia mesh repair. The possibility of mesh migration due to

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the ascitic fluid can be reduced by placing the mesh in a preperitoneal space.[75]

Laparoscopic management of ascites

The pathogenesis of ascites in cirrhosis is multifactorial.[77] Mild to moderate ascites is commonly treated medically, however in refractory ascites, surgical procedures may be required. Laparoscopic assisted peritoneo-venous shunt insertion has been advocated especially when peritoneal biopsy and or abdominal exploration are required for a definitive diagnosis.[78] Similarly, laparoscopic placement of peritoneal dialysis catheters may be done in refractory ascites with renal impairment.[79]

Other laparoscopic procedures in cirrhotic patients

Cobb *et al* (2004) reported 52 laparoscopic procedures performed on 50 cirrhotic patients.[11] These procedures, including cholecystectomies, splenectomies, colectomies, diagnostic laparoscopies, ventral hernia repairs , Nissen fundoplication, Heller's myotomy, gastric bypass and radical nephrectomy had a morbidity rate of 16% but no mortality. Tsugawa *et al*, (2001) had earlier compared open and laparoscopic appendicectomies among patients with liver cirrhosis.[80] They reported fewer rates of wound infection and wound bleeding in the laparoscopic group. Many other laparoscopic procedures including laparoscopic liver resections for hepatocellular carcinomas[81,82] and laparoscopic ultrasound with radiofrequency ablation[83,84] are now routinely done in cirrhotic patients in some centres.

CONCLUSION

The risk of laparoscopy, though real, is not significant enough to contraindicate the procedure in cirrhotic patients. Laparoscopy is being used increasingly in the diagnosis and treatment of these patients. Many studies have also shown that basic and advanced laparoscopic procedures are associated with fewer postoperative complications when compared with open procedures. However, its safety in Child-Pugh's class C patients is not yet proven hence surgery in such patients may be limited to conservative procedures in emergency cases. We advocate further research into the effects of prolonged pneumoperitoneum on the hepatic function in cirrhotic patients.

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