Surgical Management of Gallbladder Cancer

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Contents

Abstract

Gallbladder (GB) cancer carries a dismal prognosis with a 5-year survival rate of less than 5 % for advanced disease. Only 20 % of GB cancers are detected at an early stage when the disease is confined to the gallbladder. Improvements in surgical techniques have resulted in improved outcomes. We clearly understand that surgery is the only hope for survival and can have an impact on the natural history of the disease. In this article, we will summarize the most recent data with regards to the surgical options. Accurate diagnosis based on imaging and pathological staging will help us achieve better results. We will conclude by providing an algorithm to manage GB cancer based on T-staging.

1 Introduction

Gallbladder (GB) cancer is an aggressive disease. Because of its insidious onset, it is usually detected at an advanced stage. The five-year survival rate for advanced disease is less than 5 %. Surgery is the most effective and only curative form of treatment for GB cancer. Improvements in surgical techniques have resulted in improved outcomes. In this chapter, we will review data for surgical treatment and provide an algorithm of how to treat patients based on current evidence.

2 Epidemiology

Cancer of the GB is rare, but it is the commonest site of occurrence in the biliary tract. It is also the fifth most common tumor of the gastrointestinal tract. The estimated number of new cases from gallbladder (and other biliary) cancer in the United States (US) in 2012 was 9,810 new cases, including 4,480 males and 5,330 females. The number of deaths was 3,200 including 1,240 males and

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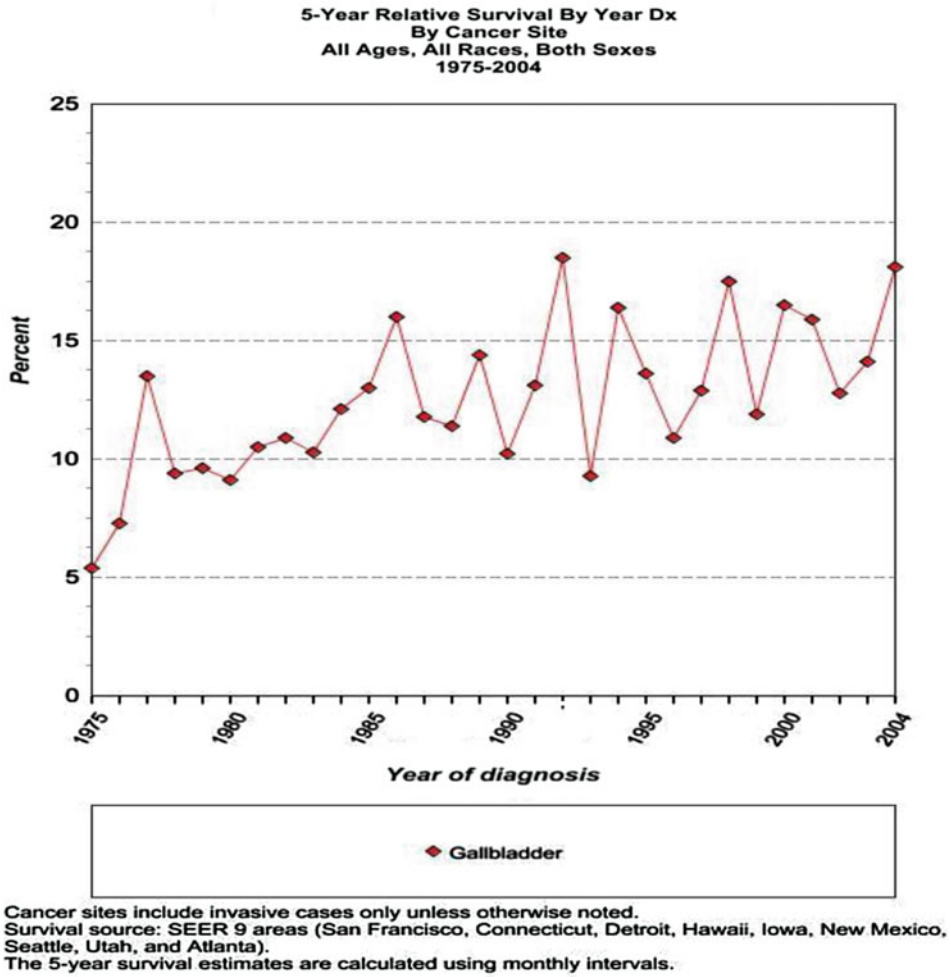

Fig. 1 Five-year survival for gallbladder cancer generated from surveillance epidemiology and end results (SEER) database [4]

1,960 females. Of these, more than half (about 60 %, which is almost 6,000 cases) were GB cancers [1]. Worldwide it is more common in Asia, East Europe and South America than the United States. The age-adjusted invasive cancer incidence rate in the US between the years 2005 and 2009 in males was 0.82 per 100,000 population and among females was 1.38 per 100,000 population [2]. Thus, it is more common in women than in men.

By the time GB cancer is detected, it is usually well advanced. Only 20 % of the cancers are detected in early stages—where the cancer has not spread beyond the gallbladder. The five-year survival rate for GB cancer in the United States based on more than 10,000 patients diagnosed between the years 1989 and 1996 are 80, 50, 28, 8 % and less than 4 % for Stages 0, 1, 2, 3 and 4, respectively [3].

Because of its silent onset, propensity for local invasion and rapid disease progression, treatment results have been dismal. The disease is usually diagnosed either incidentally after cholecystectomy or at an advanced stage, when it presents with jaundice, as a mass, peritoneal disease or ascites. With a clearer understanding of surgical anatomy, disease biology, advancement in imaging techniques and improvement in surgical procedures, the outcomes are better now. Appropriate workup of the extent of disease and radical resection can result in cure. There is no doubt that results for treatment for gallbladder cancer have improved over the 25 years [4] (Fig. 1). It is also clear from this figure that the majority of patients still die from this terrible cancer.

Gallstones and chronic gallbladder inflammation are two important risk factors for development of GB cancer. Cholelithiasis is an associated finding in the majority of cases, but less than 1 % of patients with cholelithiasis develop cancer. Stones larger than 3 cm are associated with a tenfold increased risk of cancer [5]. Porcelain GB was once suspected to be a risk factor for development of GB cancer, but recently this relationship has been questioned. Towfigh et al. [6] evaluated the pathology of 10,741 GB specimens between the years 1955 and 1998 and identified fifteen porcelain GB, and none had cancer. Similarly, Khan et al. analyzed 1,200 cholecystectomies and identified 13 patients with porcelain GB, and all were benign. They concluded that prophylactic cholecystectomy is not indicated for porcelain GB for risk of development of later cancer.

The most common symptoms caused by GB cancer are jaundice, pain, and fever. These symptoms are common for both benign and malignant diseases and that is a key reason for delay in diagnosis. Any GB mass or polyp found on imaging should lead to a high degree of suspicion for early cancer. Ninety percentage of primary GB cancers are adenocarcinomas, and they originate from the fundus (60 %), body (30 %) and neck (10 %). Among the morphological types, the papillary growth pattern seems to have better prognosis as this subtype tends to have little invasion. In contrast, the infiltrative pattern seems to invade early and grow along the subserosal plane (plane of dissection during simple cholecystectomy). The third morphological pattern is the nodular type, which shows early invasion, but the margins seem to be well defined; hence, they tend to have a better prognosis.

2.1 History of Biliary Surgery

Early part of the eighteenth century was the beginning of surgery for biliary diseases. In 1743, Jean Louis Petit, Paris, coined the term "biliary colic" ("colique hepatique"). He presented his seminal paper at the Paris Surgical Academy entitled "Considerations Concerning Tumors Produced by Retained Bile in the Gallbladder…." [7]. In the United States, John Bobbs [8] is credited with the first cholecystostomy in Indianapolis in 1867. A decade later in 1878, Theodore Kocher in Berne, Switzerland, who was trained under Billroth and Langenbuch did his cholecystostomy in two stages [9]. The Kocher maneuver named was first used for gastric surgery, and only later utilized for biliary surgery by Vautrin. Kocher also pioneered internal choledochoduodenostomy to remove common bile duct calculi. Along with Dr. Matti, he wrote the book *Hundert Operationen an den Gallenwegen* (A hundred operations on the bile ducts). Carl Langenbuch of Germany is credited with performing the first cholecystectomy at the Lazarus Hospital in Berlin in July, 1882 [10]. George Pack in 1955 was the first to report 3 cases, where radical liver resection (right hepatic lobectomy) along with portal lymph node dissection was performed for the treatment of gallbladder cancer [11].

Toward the end of the twentieth century in 1985, Prof Dr Med Erich Muhe of Böblingen, Germany, did the first laparoscopic cholecystectomy [12]. Since then it has become the gold standard for removal of gallbladder for benign disease. At present, surgeons use other minimally invasive techniques to remove the gallbladder [13, 14]. Biliary surgery continues to evolve with the help of advancements in imaging with ultrasound in liver and biliary surgery [15], computerized tomography (CT) scan of the liver [16] and magnetic resonance (MR) imaging [17]. After popularization of laparoscopic cholecystectomy, there is a new presentation of gallbladder cancer, namely after minimally invasive cholecystectomy. The number of incidental cancers detected in the pathology specimen is approximately one for every hundred gallbladders that are removed for a presumed benign etiology [7].

2.2 Surgical Anatomy

Anatomically, the gallbladder lies in the subhepatic area close to Couinaud's liver segments 4b and 5. The GB wall is composed of an innermost layer of mucosa which is lined by simple columnar epithelium; beneath this is a layer of lamina propria. The GB wall lacks submucosa. A layer of muscular tissue (smooth muscle) is present beneath the lamina propria. The outermost layer is made up of thick connective tissue called adventitia which is present in the area where GB is attached to the liver tissue (GB bed). In the unattached area, facing the free peritoneal cavity, there is an outer layer of mesothelium and loose connective tissue called serosa. The subserosal plane is the least bloody plane of dissection during routine cholecystectomy. The cystic plate is the gallbladder serosa on the liver which is usually left behind after dissection in the subserosal plane. According to American Joint Committee on Cancer staging, the lymph nodal station N1 is defined as regional (hepatic hilus) which corresponds to nodes around cystic duct, common hepatic duct, portal vein and hepatic artery. N2 station refers to metastases nodes around celiac artery, superior mesenteric artery, periduodenal and peripancreatic nodes.

GB cancers spread by direct extension to contiguous structures or via veins draining segments IV and V to the liver. GB cancer can also spread to regional lymph nodes and to the peritoneal cavity by direct extension or after bile spillage. In addition, GB cancer has a propensity to seed and grow along needle track sites, including port sites. GB cancers very rarely metastasize via blood stream.

3 Presentation

There are three common presentations of GB cancer. The most common is a presentation as **incidental gallbladder cancer**. As such, it may be (a) detected during surgery (cholecystectomy) or (b) detected on postoperative pathology review of the resected gallbladder specimen. Gallbladder cancer can also be detected as a **large invasive mass in GB fossa detected on imaging.** Finally, it may be

detected as a **small mass or polyp in the GB found on preoperative imaging.** These presentations will be discussed separately.

1. **Management of incidental gallbladder cancer (IGBC)**

IGBC refers to GB cancer discovered incidentally at the time of surgery (cholecystectomy) or detected postoperatively in the GB specimen removed for a presumed benign pathology.

a. **Intraoperative detection**

Since the liberal use of laparoscopic technology for cholecystectomies in the early 1990s, there is increased detection of GB cancers. In a study by [18], almost 50 % of the cancers were discovered incidentally. If suspicion of gallbladder cancer arises during initial laparoscopic surgery for presumed gallstone disease or cholecystitis, intraoperative staging should be done. Metastatic disease should be ruled out by sending frozen section on any suspected lesion or lymph node. A thorough laparoscopic examination of the abdominal cavity should be done. The exploration should include inspection of the liver, including intraoperative ultrasound, gastrohepatic ligament, porta hepatis, pelvis and peritoneal cavity. Additionally, frozen section of the gallbladder should be sent when the diagnosis is in doubt, after resection, and to confirm negative margins. In one study, frozen section biopsy had an accuracy of 88 % [19] and sensitivity and specificity of over 90 and 100 %, respectively [20]. However, the accuracy of T stage which is critical for management though is less than 100 % [20].

If frozen section confirms GB malignancy and the lesion is resectable, then an extended cholecystectomy should be performed after conversion to an open procedure [21]. If expertise is not available, then surgery should be deferred. The patient should then be transferred to an experienced center. Such approach is reasonable and does not affect the prognosis [22, 23].

b. **Cancer discovered incidentally in postoperative pathology specimen**

The most common presentation of early GB cancer is incidental discovery after unsuspected cholecystectomy in the pathology specimen. In a study by Duffy et al., 47 % of the GB cancers were detected after laparoscopic cholecystectomy [24, 25]. In those patients, a careful review of the GB specimen for the level of invasion (T staging), assessment of resected margins and search for malignancy in the nodes if any retrieved is important. Also, these patients need to be worked up carefully to rule out any metastatic disease. Documentation of spillage of bile or gall stones during the initial surgery must be done, as GB cancer is notorious to spread and recur at port sites and peritoneal surfaces. Further management after cholecystectomy is based on staging and surgical margins.

3.1 Management Based on T Staging

For **carcinoma in situ (Cis)** and **T1a lesions** (i.e., lesion confined to the mucosa), the treatment recommendation is simple cholecystectomy. Most often, these lesions are identified after cholecystectomy as incidental cancers found in the specimens. A high degree of suspicion is required to identify GB cancer by preoperative imaging. In a study of 27 patients with T1a lesions, eight of whom underwent lymph nodal dissection; none had lymph nodal metastasis [26]. A careful review of the pathology for the level of invasion and negative margins is important. There is no need for additional surgical procedures or re-exploration in these patients if the staging workup is negative. The five-year survival rate for Cis and T1a lesions ranges from 85 to 100 % [27–29].

3.2 Tumors Confined to Muscularis Propria (T1b)

According to the AJCC staging system, 7th edition, T1b lesion is one which invades the muscularis propria but does not involve the perimuscular connective tissue. Many studies show T1b lesion treated by laparoscopic cholecystectomy alone had a 5-year survival rate of around 90 % and in some others as high as 100 % [19, 27–29]. However, whether an operation beyond a simple cholecystectomy is needed remains controversial.

Otero et al. [30] concluded that for T1b lesions, additional procedures are needed after cholecystectomy, which was a recommendation shared by Principe et al. [31] and in the review by Miller et al. [23]. Most data, however, argue against radical resection. The occurrence of lymph nodal metastasis was only 3.8 % in the study by You et al. [26]. Similarly, in a study in 1996 by Tsukada et al. [32], all 15 patients with T1 lesions had no lymph nodal metastasis. De Aretxabala et al. concluded after their study in 46 patients that lesions with invasion of muscle layer do not need additional procedures following cholecystectomy.

It must be stated that the 2009 NCCN guidelines mention additional hepatic resection and lymphadenectomy for T1b lesion [33]. We do not routinely perform such radical resection except in cases with clinically positive lymph node metastases. Our reasoning is since lymphatics are only present in the subserosal layer; those tumors that have not yet fully penetrated the muscularis layer have a minimal risk of lymph nodal involvement. Hence, nodal dissection is not required for T1b lesions. However, an open discussion with the patient is worthwhile. There is convincing enough data to demonstrate that early-stage cancers that have not

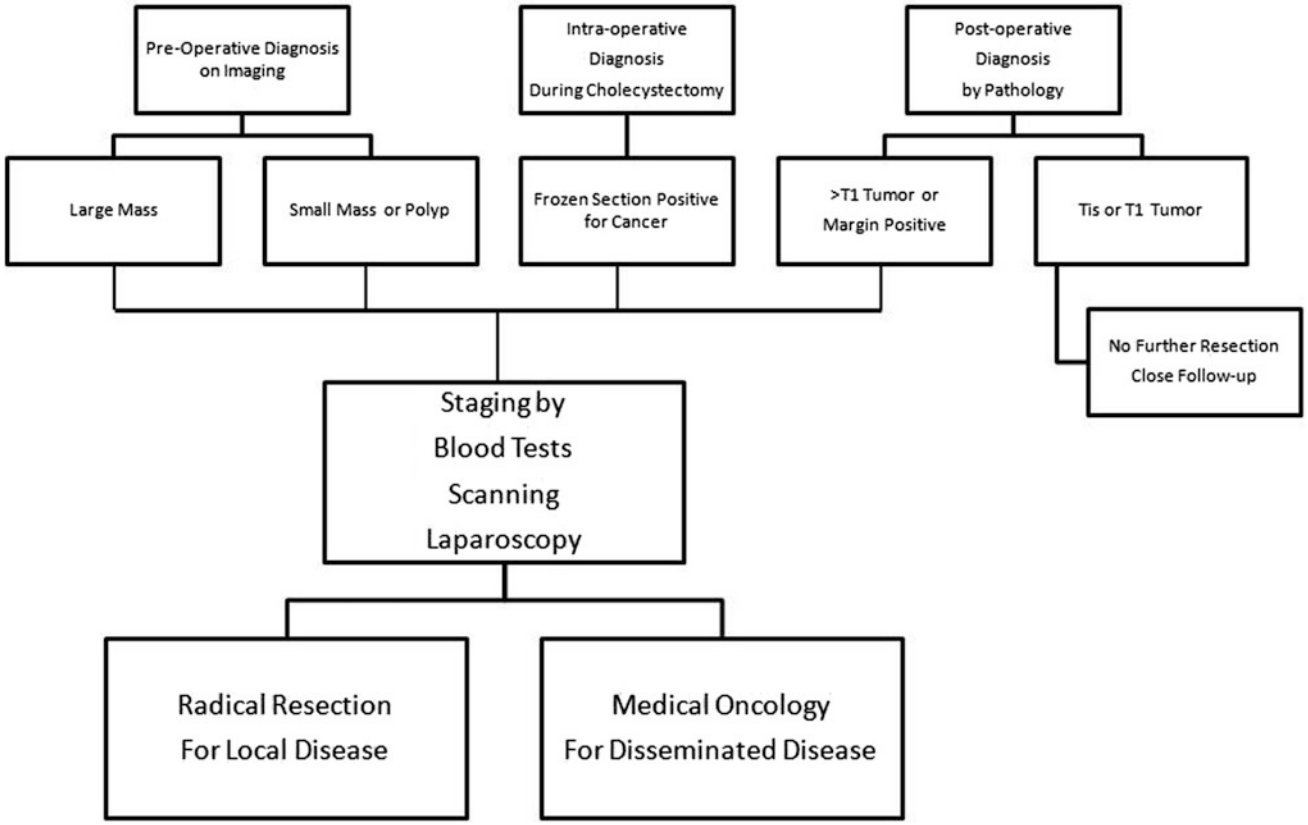

Fig. 2 Algorithm of management of gallbladder cancer

penetrated through the entire muscularis layer can be adequately treated by cholecystectomy alone [34, 35].

In those patients where diagnosis of T1 GB cancer is made after initial cholecystectomy, a careful review of the specimen for level of invasion and margins must be done. Patients will need an additional procedure only if the margins or lymph nodes are positive or the depth of invasion is higher than T1. Postoperatively if CT and CEA levels are normal, they will need routine follow-up as shown in algorithm (Fig. 2).

3.3 Tumors Penetrating Full Thickness of the Muscularis Propria into Subserosa: T2 (stage 2)

Tumors that penetrate through the entire thickness of the muscularis layer but do not involve the serosa are defined as T2 lesions and have been grouped as stage 2 per the AJCC staging (Table 1). The subserosa (avascular) is the space between the muscle layer and the outer serosal layer. Lymphatics are present immediately outside of the muscle layer in the subserosa. Hence, T2 lesions have a high incidence of lymph nodal metastasis ranging from 20 to 40 % (Table 2). While performing a simple cholecystectomy, this is the plane where the gallbladder is dissected off the GB fossa from the liver. The serosa on the GB fossa that is present on the liver surface and which is left behind after dissecting the GB along the avascular subserosal plane in a simple cholecystectomy is called the cystic plate. Therefore, a conventional cholecystectomy in a T2 lesion will result in high likelihood of positive margins as the tumor plane may be violated. Hence, these patients have to be subjected to additional exploration if R0 resection needs to be achieved.

Hence, for a T2 lesion, the recommendation is a cholecystectomy, along with resection of sufficient liver to achieve a negative margin, and a regional lymph node dissection. Such an operation is known as an extended or radical cholecystectomy. The incidence of nodal disease in T2 lesion has been reported from 23 % in a series by Konstantinidis [36] to as high as 61 % by Duffy et al. [24]. This group of patients benefit from re-exploration and additional radical or extended resection to achieve negative margins. Similarly, Ogura et al. [35], Japan, reported after a nationwide survey that 5-year survival rate for 499 patients with T2 carcinoma was 37 %. Among them, 44 % of patients had lymph node metastases. In a study by Fong et al., those with T2 lesions after prior cholecystectomy who never underwent a subsequent re-exploration and additional procedure had a 5-year survival rate of 19 %. By comparison, those who

Table 1 Seventh edition of AJCC staging

AJCC staging 7th edition			
Primary Tumor (T)			
TX—primary tumor cannot be assessed T0—no evidence of primary tumor Tis—carcinoma in situ T1—tumor invades lamina propria or muscular layer T1a—tumor invades lamina propria T1b—tumor invades muscular layer T2—tumor invades perimuscular connective tissue; no extension beyond serosa or into liver T3—tumor perforates the serosa (visceral peritoneum) and/or directly invades the liver and/or one other adjacent organ or structure such as the stomach, duodenum, colon, pancreas, omentum or extrahepatic bile ducts T4—tumor invades main portal vein or hepatic artery or invades two or more extrahepatic organs or structures *Regional Lymph Nodes (N)* N0—no regional lymph node metastases N1—metastases to nodes along the cystic duct, common bile duct, hepatic artery and/or portal vein			
N2—metastases to periaortic, pericaval, superior mesenteric artery and/or celiac artery lymph nodes *Distant Metastasis (M)* M0—no distant metastasis M1—distant metastasis			
Anatomic stage/prognostic groups			
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage IIIA	T3	N0	M0
Stage IIIB	T1-3	N1	MO
Stage IVA	T4	N0-1	MO
Stage IVB	Any T Any T	N2 Any N	M0 M1

Table 2 Results of cholecystectomy alone versus additional re-exploration and resection for T2 lesions

Author, year, country	N	Only cholecystectomy 5-year survival (%)	Re-exploration and additional radical resection			
			N	Nodal disease (%)	Positive margins (%)	5-year survival (%)
Shirai, 1992 [28], Japan	35	40	10	30	20	90
Fong, 2000 [22], USA	16	19	37	33	NR	61
Chijiwa, 2001 [55], Japan	NR	17	28	39	21	59
Wakai, 2002 [56], Japan	6	50	7	28	0	100
Toyonaga, 2003 [57], Japan	25	65	18	20	63	38
Foster, 2007 [58], USA	10	38	19	33	NR	78

N number of patients; *NR* not reported

underwent further radical procedure for T2 lesion had a survival rate of 61 % (Table 2) [22]. Similarly, De Aretxabala reported a 5-year survival of 70 % for patients treated by radical re-resection versus 20 % 5-year survival for simple cholecystectomy alone [37]. Most data over the past 15 years have consistently shown that T2-stage patients benefit the most from radical cholecystectomy that included a segment 4, 5 liver resection and regional lymphadenectomy. Radical re-resection is not only safe but also rational therapy for T2 cancers.

Two factors need to be addressed in treatment of T2 tumors are the extent of lymph node removal and extent of liver resection along with the GB removal. We know that GB cancer has a high propensity to involve lymph nodes. The presence of lymph nodal disease in T2 lesions ranges from 20 to 39 % in different studies (Table 2). In a study by Shirai et al. [38], lymphatic drainage mapping using a dye was done to follow the drainage pattern from gallbladder. They found that the first echelon group of lymph nodes were cystic or pericholedochal nodes and the second echelon

Table 3 Results of surgical treatment for advanced (T3/T4) lesions

Author, year, Country	N	Stage	3-year OS (%)	5-year OS (%)	Comment
Gall, 1991 [59], Germany	9 11	III IV	11 9	NR NR	
Onoyama, 1995 [42], Japan	12 14	III IV	44* 8*	44* 8*	
Nakamura, 1999 [60], Japan	23	IV	17	11	Morbidity—60 % Mortality—nil
Fong, 2000 [22], USA	58	III/IV	28	28	
Kondo, 2002 [40], Japan	9 29	III IVa(M0) IVb(M1)	44 24 7	33 17 3	
D'Angelica, 2009 [61], USA	63	III/IV	NA	25	

* Incidentally discovered GB cancers after laparoscopic cholecystectomy; *OS*—overall survival

group of nodes were located around the portal vein, hepatic arteries, and postero-superior to the head of pancreas, which correspond to the N1 nodes as per the AJCC TNM staging, 7th edition [39]. Although it is not uniform throughout the world, the extent of lymphadenectomy for T2 disease ranges from cystic node removal alone to *en bloc* portal lymphadenectomy and in some series combined with pancreatoduodenectomy. It must be noted that combined liver resection and pancreatic resections, done usually to improve nodal clearance, have a mortality rate of nearly 18 % [40].

For curative surgery, an adequate portal lymphadenectomy is required with resection of CBD as the periportal lymph nodes are closely related to CBD, and its removal facilitates nodal clearance. A full Kocher maneuver should be performed; the CBD should be transected close to the pancreas posterior to the duodenum to clear lymph nodal tissue behind the duodenum and pancreas; the portal vein and hepatic artery should be skeletonized, and all tissue should be swept superiorly along with the divided CBD. At the confluence of the right and left hepatic ducts, the CBD should be divided and a Roux—en—Y hepaticojejunostomy should be performed. This regional lymphadenectomy should include periportal, peripancreatic and celiac nodes, and any aorto-caval or superior mesenteric nodes should be included if possible. This entire procedure is justified for any cancer which is $T \geq 2$ as they have high incidence of lymph nodal disease (Table 2). Combined radical resection with pancreaticoduodenectomy should be reserved for very fit patients.

2. **Large invasive mass detected on imaging (locally advanced)**

Although resection is the treatment of choice for large GB cancer, only 25 % of the patients are candidates for a curative procedure due to the advanced presentation of the disease [41].

Treatment for advanced tumors (T3 and T4): For T3 and T4 lesions, there is an increased risk of nodal disease as well as peritoneal and systemic metastasis. A careful workup that includes imaging studies and staging laparoscopy should be performed to rule out M1 or N2 disease. If these patients are referred after initial cholecystectomy, there will often be a residual mass in the imaging done postoperatively, as well as positive margins in the specimen.

Although radical surgeries, including hepatic lobectomies and extended lobectomies, for advanced disease have been performed since 1990s, there was controversy whether such procedures are justifiable when associated mortality and morbidity was high. There is no doubt that such extensive liver resections are necessary to get a clear margin that is the first step toward long-term survival. However, morbidity and mortality for such operations in the 1990s were quite high. As safety of liver resection has improved, more studies are reporting substantial survival benefit of such procedures. Onoyama et al. [42] reported from Japan, a 5-year survival of 44 and 8 % for stage III and IV GB cancers that underwent radical resection. These patients should be evaluated for major liver resection, which includes assessment of liver residual volumes to maintain adequate hepatic function after surgery.

If the lesion is deemed resectable and patient is medically fit, the patient should be explored for radical resection. This usually includes a liver resection and lymphadenectomy, with or without bile duct resection. In some cases, resection may also include contiguous organs like colon or part of the stomach for tumor clearance. Doty et al. [43] reported in a small series of five patients, the safety of combined pancreatoduodenectomy for nodal clearance along with liver resection for GB cancer. But, combined pancreas and liver resections have resulted in a high mortality of up to 21 % in a study by Nimura et al. [44].

As in Table 3, more studies show better outcomes after radical operations for T3 and T4 lesions. These data indicate that radical surgery for advanced disease may be potentially curative. In selected group of patients, extended radical resection is the only hope for long-term survival.

3. **Small mass or polyp found on imaging**

Any polyp more than 1 cm, solitary, sessile, growing or vascular in nature should raise suspicion for cancer [45]. Similarly, any irregular wall thickening and evidence of ultrasonographic invasion at the liver interface in an older patient should arouse suspicion [46]. US is a good modality to evaluate the direct extension of GB cancer [47], but it is not very useful to evaluate lymph nodes. If a suspicious mass is found in the gallbladder on preoperative imaging, patients need further workup to evaluate the extent of disease. Metastasis needs to be ruled out with CT, MRI, PET (positron emission tomography) and staging laparoscopy. When metastasis is ruled out, these patients need exploration and radical resection.

3.4 Complications

GB cancer is a disease of elderly population. Most of the patients are in their seventh or eighth decade of life with age related co-morbidities. The curative procedures described for treatment of advanced disease are extensive procedures posing significant risks. The mortality associated with such radical procedures ranges from 1 to 7 % in many series. The mortality increases up to 18 % in one series when liver resection was combined with pancreas resection for adequate nodal clearance [44]. Hence, risks of resection should be weighed against the benefits before undertaking such radical procedures for GB cancers [35].

3.5 Role of Palliation

The median survival for unresectable GB carcinoma is 2–4 months. Palliation is required to relieve pain, jaundice and bowel obstruction. For unresectable cancer, radiologic and endoscopic approaches for biliary drainage have replaced surgery. If a surgical bypass is indeed necessary, then segment III bypass should be done to relieve jaundice because of the advanced disease at porta hepatis. Systemic chemotherapy and radiation therapy have very little effect on these tumors. If patients are willing, they should be enrolled in investigational trials as a last option. For pain relief, celiac ganglion block can be offered. For bowel obstruction, patients need gastrointestinal bypass procedures.

4 Special Considerations

4.1 Port-site Resection

GB cancer is notorious for seeding and growing along needle biopsy tracts and port sites. Review of operative records after detection of IGBC in the pathology specimen is essential to identify GB perforation or bile spillage. In one study, the risk of port-site recurrence following laparoscopic cholecystectomy was 9 % when the initial operation on GB was without perforation. On the other hand, the incidence goes up to 40 % if GB perforation occurs during initial cholecystectomy [48]. Paolucci 2001 reported 174 cases of recurrence at port sites after laparoscopic cholecystectomy and 12 cases in the surgical scar in open cholecystectomy, with an incidence rate of 14 %. Recently, a study by Maker et al. [49] reported that port-site metastases was as high as 19 % and resection of the port sites did not improve survival or disease recurrence. They also state that resection should not be considered mandatory during definite surgical treatment [48–52]. At this time, we are not sure whether these port-site recurrences are just isolated areas of metastases or a marker of diffuse peritoneal disease.

4.2 Role of Staging Laparoscopy

Laparoscopy is helpful in prelaparotomy staging of GB cancer to identify occult metastases, especially peritoneal metastases. Any suspicious area needs to be biopsied because previous inflammation can make it difficult to differentiate scar tissue from tumor. Diagnostic laparoscopy complements high-quality imaging in detection of peritoneal disease which is common in advanced disease. In cases of previous cholecystectomy, biliary spillage and gallbladder perforation increase the chance of intra-abdominal spread [53].

Disseminated disease is relatively uncommon in patients with incidental GB cancer, and staging laparoscopy provides a very low yield. In one study by Vollmer et al. up to 50 % of patients were found to have unresectable disease at the time of laparoscopy [54]. However, patients with poorly differentiated T3/T4 or positive-margin gallbladder tumors are at high risk for disseminated disease, and targeting these patients may increase the yield of staging laparoscopy [53, 54].

5 Summary

Gallbladder cancer is an aggressive disease. Radical surgery offers the only form of cure. Improvements in surgery have resulted in improved outcomes. The rarity of gallbladder cancer prevents us from conducting randomized control studies regarding surgical options, and majority of the cases are unresectable at presentation. In an elderly patient, any mass or polyp >1 cm in the GB on imaging should raise suspicion for cancer. Because of its indolent nature, any long-term obstruction of mid common bile duct (CBD) should be considered GB cancer until proven otherwise.

Appropriate staging workup with the help of US, CT, MRI, chest imaging, PET and staging laparoscopy will help us to correctly stage these tumors. N2 and M1 disease have to be ruled out, because these findings preclude any surgical intervention. In advanced cases, MRCP, PTC or ERCP may be required to evaluate the extent of the disease. For early-stage GB cancer, (T1)-cholecystectomy alone seems to be an adequate procedure, if the margins are negative. For any lesion, ≥T2 will require standard extended cholecystectomy which includes removal of lymph nodes around porta hepatis, peripancreatic, celiac axis and superior mesenteric artery. The common bile duct may have to be resected for adequate lymphadenectomy. Also, liver segments 4b and 5 needs to be removed to achieve R0 resection. In selected patients with T3 and T4 lesions, adequacy of liver functional reserve needs to be assessed before any major hepatic resection. Most of these patients are elderly; hence, their general medical condition should be evaluated before any major procedure. We now understand that surgery remains the only form of therapy that has had an impact on the natural history of the disease.

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