

Treatment of T3 Gallbladder Cancer

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Abstract Until recently, advanced stage gallbladder cancer has been viewed with great pessimism and many patients abandoned as without potentially curative treatment option. Recent results have significantly improved due to a number of advances. Improvements in radiologic staging including positron emission tomography now allow selection of patients with disease treatable by local regional resection. With improvements in surgical and anesthetic techniques, aggressive surgery has proven T3 and T4 tumors to be resectable with safety and result in long-term survival.

Keywords T3 gallbladder cancer · Tumor · Surgery · Radiologic staging

Introduction

T3 gallbladder cancer comprises those tumors that perforate the serosa (visceral peritoneum) of the gallbladder and may

invade adjacent organs including the surrounding liver. Once the tumor penetrates the muscularis layer of the gallbladder, tumor cells have access to the lymphatics. Tumors growing through the serosa also have a high propensity for peritoneal dissemination. In a recent series, cases of T3 gallbladder cancer were found to have lymphatic metastases in 58% of patients, and peritoneal metastases in 42%.¹ This would explain the low (27%) likelihood of surgical resection for all T3 tumors encountered. Thus, one of the challenges is identification of disseminated disease both preoperatively and by minimally invasive methods to avoid the morbidity of laparotomy for those with unresectable disease.

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Improvements in Tumor Staging

Preoperative Imaging Cross-sectional imaging has improved tremendously over the last decade to allow definitive diagnosis of a majority of cases of unresectable disease. With a good computed tomography angiogram, invasion of the perihepatic vasculature can be well defined. Not only can the portal venous involvement by tumor be seen but involvement of the hepatic arteries can also be noted. Of particular importance is the status of the right hepatic artery, which passes behind the common bile duct in the region of the neck of the gallbladder. Patients who

are jaundiced from a biliary obstruction at this level are highly likely to have invasion of the hepatic artery. The reason this is important is that jaundiced patients tolerate hypoxia poorly. Thus, in patients with clear right hepatic arterial involvement, a right hepatic lobectomy may be necessary in order to achieve an R0 resection. Alternatively, a preoperative biliary drainage to relieve jaundice may be prudent to improve safety of the subsequent resection.

Magnetic Resonance Cholangiopancreatography This technique may also be useful in the patient who is jaundiced in helping define the level of biliary obstruction. We have found, however, that this test is most useful before any biliary drainage, when the bile ducts are very dilated. With improvements in multidetector computer tomography units in the last decade that now allow very precise assessment of liver, vascular, and even peritoneal involvement by tumor, the need for the more expensive magnetic resonance scanning has greatly diminished.

Fluorodeoxyglucose Positron Emission Tomography This type of scanning has evolved to become an important test in the management of gallbladder cancer. It is capable of confirming lymphatic metastases in this population of patients with high likelihood of such metastases. It is also capable of identification of peritoneal disease, including laparoscopic port involvement.² In a recent series of 126 patients with biliary or gallbladder cancers, 24% of PET scans performed as preoperative staging influenced therapy.²

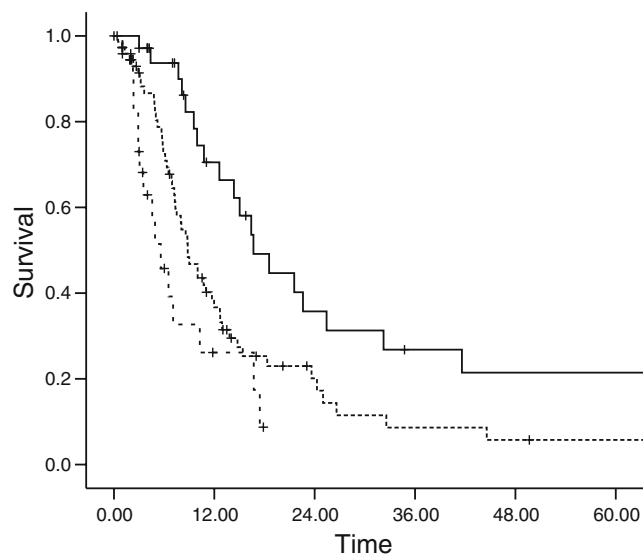


Figure 1 Survival of 137 patients with T3 gallbladder cancer. Survival for those treated with radical resection (n=35; solid line), with cholecystectomy (n=74; dashed line), and with only biopsy (n=24; long dashed lines) are shown. The 5-year survival rates were 0%, 5%, and 21%, respectively. $P < 0.0001$.

Table 1 Results of Surgical Management of Advanced Gallbladder Cancer

Author	Year	Parameter (N)	Survival (%)				
			Median	1 year	2 years	3 years	5 years
Kohya ⁵	2008	29	13	50	32	17	17
Coburn ³	2008	71	19	60	45	42	20
Reddy ⁶	2007	12	38	58	50	50	15
Fong ¹	2000	36	17	71	49	27	21

For T3 or T4 gallbladder cancer, we now consider fluorodeoxyglucose positron emission tomography an important staging tool in patient selection for radical surgery.

Extent of Surgery

Extent of Liver Resection By definition, T3 cancers transgress the gallbladder serosa. The cystic plate is the gallbladder serosa on the liver side. Thus, the minimal resection necessary is the gallbladder fossa, consisting of segments 4B and 5 of the liver. There are times that a bigger liver resection is necessary. The most clear-cut case is involvement of the vasculature of the right lobe, most commonly the right hepatic artery. In patients who have had a recent exploration and cholecystectomy for presumed cholelithiasis, a right hepatic lobectomy may also be necessary because the recent surgery may make it difficult to distinguish tumor from scars. This approach is supported by data. Figure 1 demonstrates the outcome for 123 patients with T3 gallbladder cancer treated either with no resection, simple cholecystectomy, or radical resection. All patients without surgical resection died by 18 months with a median survival of 6 months. The 5-year survival of patients subjected to simple cholecystectomy was 5%, while that for radical resection was 22%.

Extent of Lymph Node Dissection The likelihood of lymphatic dissemination is 58%¹ for a T3 gallbladder cancer. Therefore, from a theoretical standpoint, resection of the perihepatic lymph nodes is not only important for staging but also possibly important as therapy. This has been borne out by data. Recently, Coburn et al. examined surveillance, epidemiology, and end results data and analyzed the difference in outcome for the 1,114 patients not treated with a radical lymph node dissection compared with the 71 with documented lymphadenectomy. There was a survival advantage for those treated with lymphadenectomy.³

Recommendation In cases of T3 gallbladder cancer, the minimal operation with curative intent is cholecystectomy with segments 4B and 5 resections and a portal lymphadenectomy. For those with prior cholecystectomy, a right hepatic lobectomy

and additional resection of port sites may be necessary because of the high risk of port implantation of tumor.⁴

Outcomes

The perioperative mortality for such radical resections has greatly improved over the last two decades. Most recent series report an operative mortality less than 5%.

The long-term outcome of patients after radical resection clearly is superior to those treated with simple cholecystectomy or no surgery.⁵ Nevertheless, it is sobering that recent data still demonstrate that long-term survival and cure only occur in a minority of patients even after radical resection (Table 1). Only 20% seem to be long-term survivors. This is partly due to the resistance of these tumors to chemotherapy and radiotherapy. The search for effective adjuvant systemic and biologic therapies is, therefore, the most important issue in further improvements of outcome for patients afflicted with this dismal disease.

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