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**ABSTRACT:** A large number of patients with advanced gall bladder cancer present with surgical obstructive jaundice caused by infiltration of the common bile duct by a gall bladder neck tumor. The investigation of choice is magnetic resonance imaging with cholangiography and angiography, which delineates the extent of biliary ductal involvement and the involvement of hepatic artery and portal vein in the hepatoduodenal ligament. Positron emission tomography and staging laparoscopy are useful to detect distant metastases which contraindicate resection. Major hepatectomy in the form of extended right hepatectomy is required to achieve R0 resection; preoperative preparation includes biliary drainage and portal vein embolization. Duodenal involvement may necessitate hepatopancreatoduodenectomy, but it is not recommended for gall bladder cancer. Mortality, however, remains high and long-term survival is anecdotal. Very few patients are candidates for resection; most require palliation from biliary and gastroduodenal obstruction by nonsurgical (endoscopic and/or radiological) intervention. Jaundice in gall bladder cancer is akin to the yellow traffic signal – stop, look and, then only, proceed!

**KEYWORDS:** cholangiocarcinoma, cholangiography, gall bladder cancer, surgical obstructive jaundice, extended right hepatectomy

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## Introduction

Gall bladder cancer (GBC) is the commonest biliary tract cancer worldwide. The incidence rates, however, vary in different geographical areas – from low (<1 per 100,000 per year in the West) to medium (~5 per 100,000 per year in Korea and Japan) to high (>10 per 100,000 per year in Chile and northern Indian subcontinent).<sup>1</sup> A significant number of patients with clinically obvious GBC present with surgical obstructive jaundice (SOJ). Hawkins et al.<sup>2</sup> reported 240 patients with GBC operated at the MSKCC, NY, USA, between 1995 and 2002 – of those, 82 patients (34%) had SOJ. In another report from France, 110 of 424 patients (26%) with GBC had SOJ.<sup>3</sup>

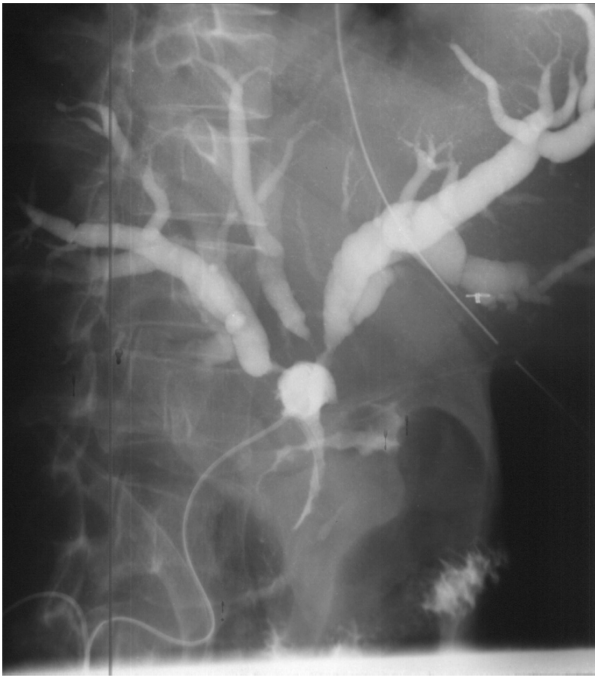
## Investigations

Jaundice in patients with GBC is most commonly caused by a gall bladder neck tumor infiltrating the extrahepatic bile ducts, common hepatic duct and common bile duct, in the hepatoduodenal ligament. Therefore, in patients with SOJ, not only the bile ducts but also the vessels in the hepatoduodenal ligament, ie, hepatic artery and portal vein, need to be evaluated. This necessitates cholangiography and angiography, which should preferably be in the form of magnetic resonance cholangiography (Fig. 1) and magnetic resonance angiography. Staging laparoscopy should be performed in all patients with GBC, including those with SOJ, to detect small peritoneal deposits that may not be picked up on computed tomography or magnetic resonance imaging.<sup>4</sup> It may be worthwhile to even get

a positron emission tomography scan to pick up abdominal or extra-abdominal distant disease.<sup>5</sup> The presence of distant metastases and distant (celiac, superior mesenteric, and aortocaval) lymph nodes and the involvement of the secondary biliary ductal confluence and hepatic artery and portal vein are contraindications for surgical resection.

## Surgical Management

Surgical resection with curative intent is the treatment of choice for GBC. This may involve a minor hepatectomy, ie, wedge of liver or segment IVB + V resection, or a major hepatectomy, ie, extended right hepatectomy (Fig. 2), both with or without common bile duct (CBD) excision. The standard surgical procedure for GBC is extended cholecystectomy, which includes the gall bladder, 2–3 cm wedge of liver in segments IVB and V, and lymphadenectomy (en bloc dissection of the regional lymph nodes along the hepatoduodenal ligament, the common hepatic artery, and the head of the pancreas). Extended cholecystectomy alone is not technically possible in GBC with SOJ because the cystic duct margin will be positive resulting in an R2 (gross residual disease) resection; common bile duct also, therefore, has to be excised. Extended cholecystectomy with common bile duct excision is, however, possible only if the primary biliary ductal confluence is not involved and there is no liver infiltration. The majority of patients with SOJ also have liver infiltration and will require right hepatectomy because the desired 2 cm margin cannot be achieved as the right main

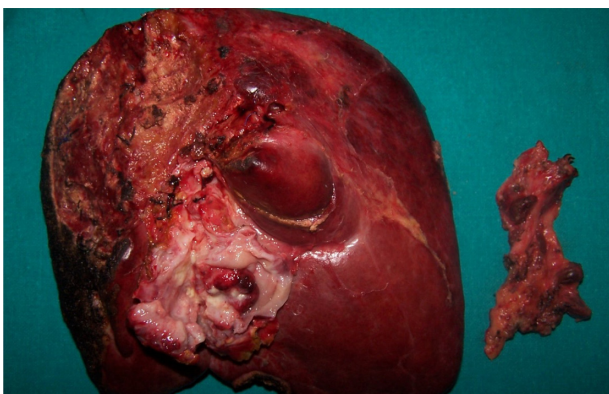


**Figure 1.** Cholangiogram in a patient with gall bladder cancer (GBC) and surgical obstructive jaundice (SOJ) showing hilar separation.

portal pedicle lies at a depth of only a few millimeters in the liver bed of the gall bladder neck. Hepatectomy in GBC has to include segment IV also resulting in extended right hepatectomy. Adjacent duodenum may also be involved requiring pancreatoduodenectomy to achieve an R0 (no residual disease) resection resulting in hepatopancreatoduodenectomy.

### Preparation

Patients with SOJ require preoperative biliary drainage in order to bring down the level of serum bilirubin and to improve the impaired mitochondrial function that is vital for liver regeneration after a major hepatectomy. One of the fatal complications after a major hepatectomy is postoperative liver failure. Functional liver remnant may not be adequate after extended right hepatectomy; preoperative portal vein embolization may



**Figure 2.** Extended right hepatectomy for gall bladder cancer.

be required to induce atrophy hypertrophy and increase the functional liver remnant. Preoperative biliary drainage and portal vein embolization are, however, invasive procedures with their own morbidity. Ebata et al.<sup>6</sup> reported 141 patients with GBC who underwent portal vein embolization – as many as 61 (43%) did not undergo subsequent hepatectomy; mortality in 80 patients who were operated was 13 (16%) and only 10 patients with GBC survived for 5 years.

### Results

Results, in terms of morbidity, mortality, and survival, in patients with GBC and SOJ in various series are summarized in Table 1. Mortality of major surgical procedures, eg, extended right hepatectomy and hepatopancreatoduodenectomy, remains high; in addition, outcome of these surgical procedures in patients with GBC is not very good. Risk stratification of 7,732 hepatectomy cases from the National Clinical Databases from Japan revealed GBC to be a factor associated with risk for 90-day in-hospital mortality.<sup>7</sup> Shimada et al.<sup>8</sup> reported 126 patients with GBC who underwent surgical resection between 1999 and 2009 – 35 of these underwent extended right hepatectomy – there was no mortality but morbidity was 46%; only three patients survived for 5 years. Composite resection of adjacent organs was a predictor of poor survival – even after R0 resection in 61 patients, those who required composite resection of adjacent organs had poorer survival (5-year survival, 16%; median, 0.8 years) than those who did not require composite resection of adjacent organs (5-year survival, 36%; median, 3.8 years); only 12 out of 100 patients lived beyond 5 years and five patients lived beyond 10 years.<sup>9</sup> In the report by Yang et al.<sup>10</sup>, patients with SOJ more often required composite resection of adjacent organs (23.4% vs. 2.8%) and had more postoperative complications (34% vs. 12%) and higher mortality (6.4% vs. 2.1%). Lim et al.<sup>11</sup> called hepatopancreatoduodenectomy a *highly morbid* operation with significant risk of death regardless of preoperative preparation – “though a sound conceptual approach, clinical experience does not support its use.” Ebata et al.<sup>12</sup>, with world’s largest experience of 33 hepatopancreatoduodenectomies for GBC over 23 years, concluded that hepatopancreatoduodenectomy for GBC remains controversial because of extremely poor survival.

### Palliation

The majority of patients with GBC and SOJ are not candidates for resection. Uncontrollable cholangitis not responding to even parenteral antibiotics indicates biliary drainage and stenting – endoscopic or percutaneous<sup>13</sup>; self-expandable metal stents, though expensive, are preferred over plastic stents. Intractable distressing pruritus disturbing sleep is another indication for palliative stenting. Some patients with antroduodenal infiltration may have symptoms of gastric outlet obstruction and malignant gastroparesis, which can be palliated with antroduodenal stenting. Palliative surgical

**Table 1.** Results of resection in patients with gall bladder cancer (GBC) and surgical obstructive jaundice (SOJ).

SERIES DURATION	DESCRIPTION	NO. OF PATIENTS	R0 RESECTION	MORBIDITY	MORTALITY	SURVIVAL
Kaneoka 2003 <sup>14</sup>	GBC with BDI	32	<30%			3 year survival 6%; no 5 year survival
Hawkins 2004 (1995–2002)	GBC with SOJ	82	4 (5%)			No 2 year survival; median 6 mo 21% 2 year survival; median 16 mo
	GBC without SOJ	158	62 (39%)			
Agarwal 2007 <sup>15</sup> (3 years)	GBC with SOJ	51	14 (27%)	50%	7%	7 survived for 2 years
Nishio 2011	GBC T3/T4 N0/N1 including				9%	
	GBC with EBI	73				23% 5 year survival; median 1.5 years
	GBC without EBI	27				54% 5 year survival; median 15.4 years
Regimbeau 2011	GBC with SOJ	50	71%	62%	16%	19% 3 year survival; 4 survived 5 years
Feng 2012 <sup>16</sup> (2002–2010)	GBC with SOJ	117	32%			Median 6 mo (12 mo after R0 resection) Median 15 mo (18 mo after R0 resection)
	GBC without SOJ	134	63%			
Yang 2014 (2003–2012)	GBC resection with curative intent (R0/R1)					
	With SOJ	47	32%	34%	6.4%	6% 5 year survival; median 14 mo
	Without SOJ	145	63%	12%	2.1%	37% 5 year survival; median 43 mo

**Abbreviations:** BDI, Bile duct infiltration; EBI, Extrahepatic biliary infiltration; R0, Resection with no residual disease; R1, Resection with microscopic residual disease.

biliary or gastroduodenal bypass is rarely ever performed today. The role of noncurative palliative chemoradiotherapy remains unclear as anticipated survival in unresected GBC is very poor – median of 2–4 months and <5% at 1 year.

## Conclusion

A large number of patients with advanced GBC present with SOJ. Very few patients with GBC and SOJ are operable. Resection to achieve R0 status in these patients usually requires a major hepatectomy which, in turn, requires preparation with multiple invasive endoscopic and radiological procedures. Even fewer patients can finally be resected; resection in GBC with SOJ is *challenging*,<sup>9</sup> and mortality of resection still remains high and long-term survival is anecdotal. In unresectable patients, palliation for cholangitis and pruritus should be provided by nonsurgical intervention.

The presence of SOJ in GBC is akin to the yellow traffic signal – stop, look and, then only, proceed!

## Author Contributions

Conceived the concepts: VKK. Analyzed the data: VKK. Wrote the first draft of the manuscript: VKK. Made critical revisions: VKK. The author reviewed and approved of the final manuscript.

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