Technical Aspects of Gallbladder Cancer Surgery

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KEYWORDS

• Gallbladder cancer • Incidental • Nonincidental • Laparoscopic • Robotic
• Segment IVB/V • Biliary tract cancer

KEY POINTS

- Gallbladder cancer is a rare disease that may be diagnosed incidentally following cholecystectomy or nonincidentally, often with more advanced disease.
- The principal aim of surgical resection is attainment of negative margins.
- Jaundice is considered an ominous sign in the presentation of gallbladder cancer.
- Minimally invasive resection techniques are well described in the surgical treatment of gallbladder cancer.
- The roles of adjuvant and neoadjuvant therapies in the treatment of gallbladder cancer remain poorly elucidated.

INTRODUCTION

Gallbladder cancer is a rare disease, although it is the most common disease of the biliary tract. Its incidence has increased over the last 20 years. This increase may be a result of the increasing prevalence of laparoscopic cholecystectomy, which is responsible for incidentally discovered gallbladder cancer.[1] Despite the increasing incidence of gallbladder cancer, laparoscopic cholecystectomy has permitted earlier detection and improved survival of what was once considered a disease associated with a dismal prognosis.[2]

In this review, an updated description of gallbladder cancer is divided into 2 sections based on presentation: disease that presents incidentally following laparoscopic cholecystectomy and malignancy that is suspected preoperatively. Elements pertaining to technical aspects of surgical resection provide the critical focus of this review

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and are discussed in the context of evidence-based literature on gallbladder cancer today.

EPIDEMIOLOGY

The estimated incidence of gallbladder cancer is approximately 2 per 100,000 of the population in the United States.[3] As of 2015, there are an estimated 10,910 cases in the United States annually, including other biliary tumors, compared with only approximately 9250 cases in 2008.[3,4] The incidence seems to be significantly higher in women (3:1) and more commonly occurs in patients older than 40 years.[5] Incidence of gallbladder cancer is based on the central etiologic factor of cholelithiasis, with variations in geography and race mirroring the incidence of gallstone disease. For example, the incidence of gallbladder cancer in Norway, where cholelithiasis rates are low, ranges from 0.2 to 0.4 per 100,000 people. Conversely, the incidence of gallbladder cancer ranges from 9.3 to 25.3 per 100,000 among Chilean Mapuche Indian women, in whom gallstone disease is more prevalent.[6] Furthermore, mortality rates seem to also be higher in Andean populations within South America.[7] Finally, even within the United States, the incidence among Native Americans in the state of New Mexico is approximately 14.5 per 100,000, a rate that is dramatically higher than the national average.[8]

CAUSE AND PATHOGENESIS

Cholelithiasis is considered a primary etiologic factor in gallbladder cancer, which results in chronic mucosal inflammation, dysplasia, and subsequent malignant transformation, with the development of porcelain features clinically.[7] Only approximately 0.3% to 3.0% of patients with long-standing cholelithiasis will develop gallbladder cancer, highlighting the rarity of gallbladder cancer.[9] Interestingly, in a case-control study that compared gallstones in patients with and without gallbladder cancer, there were significantly more stones and heavier stones in patients who developed gallbladder cancer.[10] Despite this, the mechanistic association between gallstones and frank malignancy is not fully established. In a study by Jain and colleagues,[11] the investigators examined 350 gallbladder specimens from patients with gallstones and found mucosal hyperplasia in 32.0%, metaplasia in 47.8%, dysplasia in 15.7%, and carcinoma in situ in 0.6% of specimens. The investigators were able to show loss of genetic heterozygosity in 2.1% to 47.8% of preneoplastic lesions at 8 different loci for several tumor suppressor genes associated with gallbladder cancer but showed no loss of heterozygosity in normal gallbladders, thereby suggesting a possible mechanistic association between gallstones and gallbladder cancer beyond inflammation and neoplasia.

In keeping with other gastrointestinal malignancies, progression from adenoma to carcinoma has also been stipulated in gallbladder cancer, particularly in sessile adenomata greater than 1 cm in size.[12] Although adenomatous polyps exist in only about 1% of gallbladder specimens, up to 7% of lesions harbor malignancy.[13,14] Cancer was more likely to exist in isolated, broad-based polyps, with increasing size. A size cutoff of 1 cm is often considered relevant.

Although porcelain gallbladder does not automatically imply malignancy, gallbladder cancer may occur in approximately 1 in 13 patients with a porcelain appearance.[15] These data are still debated, as demonstrated by a recent case series evaluating the risk of gallbladder cancer in patients with a porcelain gallbladder. This series found 13 patients with porcelain gallbladder identified among 1200 cholecystectomy patients. None of the 13 patients had evidence of carcinoma.[16]