Diagnosis and Management of Gallbladder Cancer

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Algorithmic Approach

While uncommon with less than 5000 diagnoses per year in the United States, gallbladder cancer (GC) is the most frequently diagnosed cancer of the biliary tract. It has a high mortality rate due to its frequently advanced stage at diagnosis [1]. Its incidence increases with age, and it is more common in women and blacks [2]. Risk factors include cholelithiasis, gallbladder polyps, obesity, and chronic infections of the gallbladder [3, 4].

Diagnosis of GC is made in one of three ways: preoperatively, intraoperatively, or postoperatively. Due to the asymptomatic nature of early GC, approximately 50% of diagnoses are incidentally discovered postoperatively on pathology [5]. The course of treatment and treatment goals are different for the varying presentations and therefore will be discussed separately.

A. Gallbladder cancer can be suspected preoperatively on various imaging modalities. Ultrasonography is the most common modality used for evaluation of the gallbladder and findings that suggest GC include an intraluminal or fixed mass, no discernable plane between the liver and gallbladder, and/or mural calcifications. While small lesions (<1 cm) can represent a variety of benign lesions, any lesion >1 cm is an indication for surgery as it carries a higher likelihood of malignancy [6]. Cross-sectional imaging with CT scan of the chest, abdomen, and pelvis or magnetic resonance imaging (MRI)/magnetic resonance cholangiopancreatography (MRCP) with chest computed tomography (CT) should be performed preoperatively to evaluate for metastatic spread and local invasion. Positron emission tomography (PET)/CT is done selectively. Endoscopic ultrasound can further differentiate between benign and malignant lesions and also has the ability to stage the tumor, although it is not commonly used. While there is no laboratory value that has sufficient specificity or sensitivity in the diagnosis of GC, an elevated CA 19-9 can be useful. After the workup is completed, the patient is deemed appropriate for surgery if the mass is locally resectable without metastatic spread. At surgery, diagnostic laparoscopy is performed to rule out distant metastases followed by resection at the same setting. If the gallbladder mass or polyp is between 1 and 2 cm without evidence of invasion, then a laparoscopic cholecystectomy with intraoperative frozen section is appropriate. Care must be taken to avoid entry into the gallbladder or bile spillage. Conversion to open surgery is warranted if findings suggest malignancy or there is no clear plane between the gallbladder and liver bed. If frozen section

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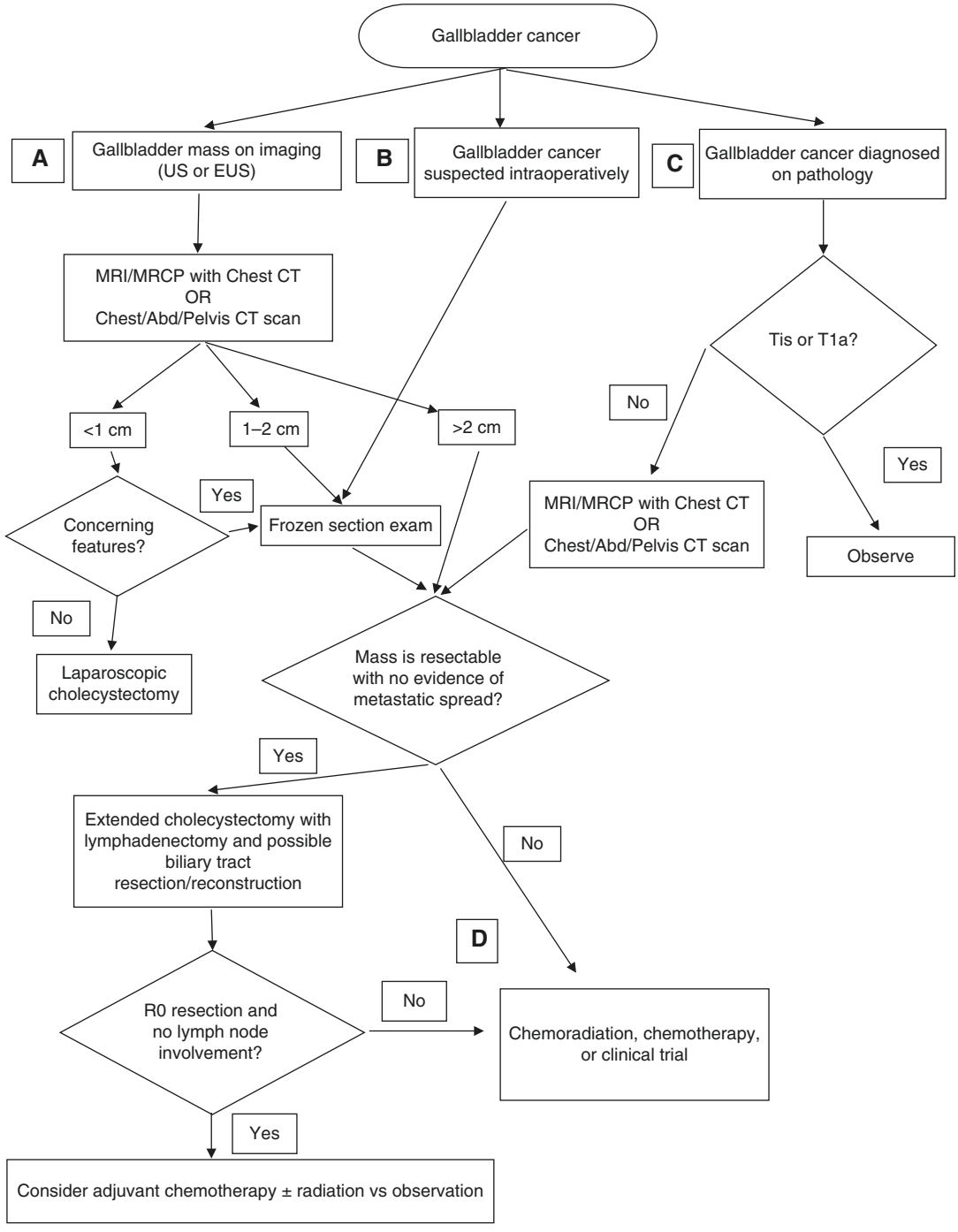
is positive, then oncologic surgery is undertaken at the same setting. If the gallbladder mass or polyp is greater than 2 cm, then an oncologic surgery should be undertaken from the outset. The operation of choice in GC is an extended cholecystectomy which involves resection of the gallbladder and hepatic bed to a negative margin (usually liver segments IVb and V but may require a more extensive hepatectomy), regional lymphadenectomy, and cystic/bile duct excision to a negative margin (if cystic margin is positive, a bile duct resection with subsequent reconstruction is necessary).

B. If a suspicious mass is encountered intraoperatively, it is recommended that the operation be converted to open in order to have better tactile feedback and minimize the risk of entering the gallbladder. It is also accepted to stop the operation at this point and refer the patient to a high-volume center. An open cholecystectomy should then be performed without bile spillage and the mass sent for frozen section exam. If the mass is adherent to the liver bed, it is important to resect a portion of the liver in order to avoid violating the tumor and seeding the peritoneum. If the frozen section exam is positive for malignancy and the surgeon is comfortable with proceeding, an extended cholecystectomy and lymphadenectomy should be done. If the surgeon is not comfortable proceeding, closing the patient with referral to a high-volume center is the preferred course.

C. Gallbladder cancer is diagnosed most commonly on pathologic exam of a cholecystectomy specimen done for benign biliary disease. Management is dependent on the tumor staging. If the tumor is Tis or T1a with negative margins, no further resection is necessary, as this does not convey a survival benefit [7]. If the tumor is T1b or greater, cross-sectional imaging of the chest, abdomen, and pelvis should be performed preoperatively to evaluate for metastatic spread and local invasion. If no metastatic spread is found, then diagnostic laparoscopy followed by potentially curative hepatic resection, lymphadenectomy, and cystic/bile duct excision should be performed. This second procedure is required due to the high incidence of residual disease and therefore does convey a survival benefit [8].

D. Surgery is the only potentially curative therapy for GC. Five-year survival for stage IA carcinoma is 50% compared to 2% in stage IV carcinoma [9]. If an R0 resection is achieved on final pathology with no lymph node involvement, observation or adjuvant chemoradiation versus chemotherapy is reasonable. There are no historical randomized controlled trials (RCT) to guide adjuvant therapy for biliary tract malignancies. However, a recent RCT of 447 patients with biliary tract malignancies (18% were GC) showed a survival benefit with single agent capecitabine in the adjuvant setting [10]. While further studies are needed to compare capecitabine with current adjuvant therapy regimes (gemcitabine and cisplatin [11]), it emphasizes the need for multidisciplinary care. In addition, there have been retrospective studies that have shown a survival advantage with radiation alone and chemoradiation [12, 13]. There are no data with regard to surveillance, but a reasonable schedule could include repeat imaging every 6 months for 2 years and then annually for 5 years. If the resection has a positive margin or there is gross residual disease or regional lymph node involvement, the patient should be referred for adjuvant chemoradiation versus chemotherapy. There is no role for palliative, debulking, or repeat resections as these procedures do not convey a survival or palliative benefit. If the patient has obstructive jaundice, endoscopic or percutaneous stenting is preferred over biliary bypass. Multidisciplinary cancer care teams are important to guide the management of this disease.

Gallbladder cancer is an uncommon yet often fatal malignancy. However, in selected patients, surgical intervention can be curative. It is therefore prudent for surgeons to develop a systematic management plan in the event that GC is diagnosed on pathologic review or during routine cholecystectomy.



Algorithm 91.1

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