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Optimal surgical management for T2 gallbladder cancer-formal 4b-5 resection

This issue of *Surgery* features an interesting retrospective multicenter study by Chen et al on the surgical management of T2 gallbladder cancer (GBC), with one of the largest cohorts of patients to date.[1] They analyzed 512 patients accrued from 7 centers, 395 of whom had a wedge resection (WR) and 117 had segment IVb + V resection (SR). Of those, 112 patients undergoing SR were matched to 112 patients undergoing WR. No statistically significant difference in overall survival was found between matched patients undergoing SR compared to WR ($P = .886$); however, disease-free survival (DFS) was higher in the SR group compared to WR ($P = .04$). Patients in the WR group with incidentally identified GBC ($P = .016$), those with stage T2b ($P = .019$), and those with negative lymph nodes had a better DFS. SR patients had higher morbidity than WR patients. Jaundiced patients ($P = .013$), laparoscopic resection ($P = .028$), or surgeon inexperience with SR resections ($P = .041$) were independent risk factors for postoperative complications in the SR group.

In the treatment of incidental GBC, re-resection of T1b, T2a, T2b and T3 lesions is recommended unless they are contraindicated by comorbidities or advanced disease. The early reoperation is imperative once the histopathological findings have been confirmed and metastatic disease has been ruled out. If the histopathological analysis of incidental GBC T1a was not performed by a specialized unit or the specimen cannot be obtained for reevaluation in a specialized unit, reoperation could be considered. Recurrence reports in T1a cases are usually related to an incomplete histological examination; therefore, when in doubt about the histological analysis and depending on the patient's conditions, re-resection could be proposed. The location of the tumor, either on the peritoneal or hepatic side of the gallbladder (T2a and T2b, respectively), plays a role in subsequent management as well as prognosis, and each is associated with a pattern and rate of specific recurrence survival. T2b tumors could spread to the liver without penetrating the serosa, so a margin of safety during excision requires liver resection. However, it is not clear whether liver resection is equally indicated in T2a tumors.[2]

Some circumstances could not be taken into account in this paper, such as the incidental finding of a tumor during an urgent cholecystectomy for acute cholecystitis, with or without inadvertent intraoperative bile spillage, which may influence the plan for any subsequent surgical intervention. In any case, there are insufficient data about the clinical significance of these specific cases.

As Chen rightly describes, China has a high prevalence of GBC, as does Chile, where more thorough pathological examinations are routinely done, which may improve the management of the patients, including an earlier rescue procedure done within the standard 8 weeks.[2] In countries with a low prevalence of GBC, ultrasound and computed tomography or magnetic resonance imaging studies do not have the same level of methodical scrutiny than in higher prevalence countries, which may affect the oncological results of the resections, worsening those of WR compared with SR. Insufficient staging preoperatively and lack of intraoperative frozen section are also likely to lead to under-recognition of GBC and thus under-treatment, as a simple cholecystectomy rather than an oncological resection is likely to be performed.

Timing of reoperation is often appropriately delayed by the inflammatory process found during the initial cholecystectomy to decrease complications from the second surgery. In the consensus conference at Brazil, Coimbra et al recommended the second surgery within 2 to 4 weeks, depending on patient fitness, the staging of the tumor, and the time of admission to the specialist referral center hospital.[2] Some studies have shown that increasing this time interval has prognostic implications.[3]

Studying the venous drainage of the gallbladder, Sugita et al observed that micrometastasis of the GBC can be found in segments IVb and V.[4] Kohya et al defined the subserosal score (ss) to analyze cancer invasion in the subserosal layer (ss minimum, ss medium, and ss massive) by vertical and horizontal tumor spread. The authors showed that segment IV to V hepatectomy contributed to better survival for ss medium and ss massive GBC. They concluded that SR with extrahepatic bile duct resection and lymphadenectomy should be the standard operation for the treatment of patients presenting with this degree of invasion.[5]

From an anatomical point of view, the definition of WR has a wide variability since the depth of the resection is not standardized. This factor, along with the variability of the techniques performed in 7 different hospitals in the present study, may greatly influence the results, which could have rendered better data in favor of SR. Given the wide differences in recurrence rates from distinct countries and even within the same country, with 5-year survival rates ranging from 30% to more than 70% in T2 GBC,[6] we must advocate that SR plus hilar lymphadenectomy is likely to be a more standardized technique and thus the more appropriate resection to improve DFS.

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In tertiary specialist centers, SR does not carry a higher morbidity than WR but contributes to a better DFS, except in those cases with positive hilar lymph nodes or poorly differentiated carcinoma. Hilar lymphadenectomy can also be performed more extensively in the upper part of the hilum in SR than in WR.

In conclusion, patients with an incidentally detected GBC on initial cholecystectomy should be sent to a high-volume center for further operative intervention, ideally SR and hilar lymphadenectomy. Accurate pathological diagnoses and staging of GBC are essential in guiding further management and are best performed in specialized units. Patients with a preoperative diagnosis of GBC should be sent to a high-volume center for SR and hilar lymphadenectomy, performed by open surgery if jaundice or pathological hilar lymph nodes are present. SR and hilar lymphadenectomy is safe and oncologically appropriate when performed by experienced surgeons in a specialist center, and with the risk of micrometastases and the best DFS, SIVb + SV in T2 GBC should be proposed.

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Conflict of interest/Disclosure

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