



Routine or selective histopathology of the gallbladder

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Introduction

The issue of selective versus routine histopathology of removed gallbladders has been discussed for many years within the surgical communities. The pro arguments for routine histopathology of the gallbladder after laparoscopic cholecystectomy include the fear of overlooking an incidental cancer. There are, however, numerous studies in the literature where local departments have retrospectively reviewed thousands of histopathology reports and found a negligible or no risk of overlooking an incidental gallbladder cancer (1-4). Two reviews summarized the available evidence and came to the same conclusion that routine histopathology may not be justified (5,6).

Macroscopic abnormalities found preoperatively or in the operating room

An interesting study from Turkey was recently published in the *Annals of Surgical Treatment and Research* (7). They reported a large sample of 11,680 operations and found 40 incidental gallbladder cancers (0.3%). All the specimens were sent for routine histopathology, and they showed that most of the gallbladder cancers had wall thickening on preoperative ultrasound examination (>3 mm). This parameter could therefore be a factor to be considered if a selective approach for histopathology would be chosen in the future.

A review interestingly found that studies that opened the specimens intra-operatively identified all cancers by

their macroscopic appearance (5). Thus, reports have found that all cases of incidental gallbladder cancer evaluated by routine histopathology had macroscopic abnormalities when the specimen was opened in the operating room (2-4). These abnormal appearances could be anything from a visible tumor to simple wall thickening, and the latter could argue for sending all specimens with cholecystitis for histopathology if a selective approach is chosen.

Other factors

A review compared prevalence of incidental gallbladder cancers based on geographic region and found higher prevalence in Asian studies (median 1.2% of operations) compared with the Western studies (median 0.4% of operations) (6). A report from India found that 3.9% of the examined gallbladders showed neoplastic pathology (8)—a prevalence much higher than is normally seen in Western countries.

There is also an issue concerning age of the patient. In all the published reports age of patients with incidental gallbladder carcinoma has been above 50 (9), 60 (5,7), or 70 years (2).

Harms

An interesting study was recently published in *British Journal of Surgery* on the subject (10). They found in a Dutch population only 22 of 10,041 (0.2%) of specimens

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with malignancy with clinical consequences. They also reported that if the surgeons would have employed a selective policy and only sending the gallbladders with macroscopic pathology to histopathologic examination, then they would have saved 78.1% of the gallbladder examinations corresponding to a cost of approximately 700,000 Euros. Malignancy with clinical consequences would have been missed in seven of 7,846 patients, and no patient benefitted from the clinical consequences drawn upon histopathological examination, and in fact two were harmed with futile additional surgery. Of 15 patients in whom malignancy with clinical consequences would have been diagnosed, one benefitted (residual disease radically removed), two potentially benefitted (palliative systemic therapy), and four experienced harm (futile additional surgery). This is an interesting study since they also reported harms by routine histopathology, which has not previously been reported or discussed. From their results it does not seem justified to employ routine histopathology since harms may outweigh the very small chance of making an early diagnosis of a gallbladder carcinoma; a diagnosis that will most likely not change the disease trajectory to the better for the patient.

Thus, one aspect that supports selective histopathology is the low percentage of patients undergoing salvage surgery. In many cases, this is due to patient comorbidity with reduced life expectancy, or the fact that the gallbladder carcinoma was radically treated by simple cholecystectomy. Consequently, the population not amenable to surgical salvage could also be excluded from routine histopathology.

Discussion

The need for routine or selective histopathological evaluation of gallbladder specimens following cholecystectomy may depend on factors such as macroscopic appearance of the gallbladder, ethnicity, or age. This would mean that a macroscopically normal gallbladder in patients of Western ethnicity under the age of 60 may not require formal histopathology. When operating in parts of the world where prevalence of incidental gallbladder cancer is higher than in Western countries this situation may be different. It is, however, interesting that sending all gallbladders for routine histopathology may even be harmful for some of the patients based on the newly published Dutch study (10). The situation is therefore not as simple as diagnosis of malignancy.

It would be correct to discuss it locally at hospitals,

regions, and countries as well as scientific societies, and only if a local guideline recommends abstaining from routine histopathology then it should be implemented to avoid putting responsibility on the individual surgeon.

Many of the published studies have reported that all or most of the gallbladders with cancer would have been found by simply opening the specimen in the operating room in conjunction with the surgical procedure. Thus, if a selective approach is chosen, then the decision of sending the gallbladder for histopathology should include macroscopic evaluation of the opened specimen in the operating room. This could be combined with factors such as thickened gallbladder wall and patient's age as well as geographical area.

It is, however, important to consider the downsides of sending all gallbladders for histopathology. There is no evidence to support that we gain survival in patients with incidental gallbladder carcinoma by sending all gallbladders for histopathology, and we may indeed harm patients because of futile re-resections and chemotherapy with limited or no effect on overall survival. Another important issue is that most patients with an incidental small carcinoma will most likely be cured by the simple cholecystectomy, and with routine histopathology we put these patients in states of anxiety with further workup and control regimens for long periods. "First do no harm" seems to be more relevant than ever.

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appropriately investigated and resolved.

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