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ORIGINAL ARTICLE

The risk of incidental gallbladder cancer is negligible in macroscopically normal cholecystectomy specimens

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Abstract

Background: Cholecystectomy is usually carried out for benign indications. Most perform routine histopathologic examination to detect incidental gallbladder cancer (GBC).

Methods: Cholecystectomies performed at four hospitals in the Helsinki Metropolitan Area during 2010–2012 were analyzed retrospectively. Patients with preoperative suspicion of neoplasia, active malignancy, or in whom cholecystectomy was performed as a secondary procedure were excluded.

Results: A total of 2034 cholecystectomies were included. In ten patients (0.5%), GBC was identified, each with an associated macroscopic finding, including local hardness (n = 1), a thickened wall (n = 5), acute inflammation and necrosis (n = 1), or suspected neoplasia (n = 3). No GBC was found in macroscopically normal gallbladders (n = 1464). Of the ten patients with GBC, five underwent subsequent liver resection, four had metastatic disease, and one had locally advanced inoperable disease. Three of the five patients who underwent liver resection were alive and disease-free at final follow-up (median 48 months). The remaining seven patients with GBC died of the disease, with a median survival of 14 months (range 10–48 months).

Conclusions: Routine histopathologic examination of a macroscopically normal gallbladder does not improve diagnosis of GBC. A histopathological examination is, however, mandatory when a macroscopic abnormality is present.

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Introduction

Cholecystectomy (open or laparoscopic) is one of the most common surgical operations, with approximately 8000, 65 000, and 460 000 operations performed annually in Finland, UK, and USA, respectively.[1–3] Cholecystectomy is usually performed due to symptomatic or complicated cholelithiasis, and rarely due to a suspicion of neoplasm. Occasionally, surgeons encounter incidental gallbladder cancer (GBC) after routine cholecystectomy for a non-neoplastic indication. Therefore, in most centers, the excised gallbladder is routinely sent for a histopathological examination (HPE).[4–7] While GBC is relatively common in Asian countries, it is a rare malignancy in Western populations.[5,6,8–13]

The only possibility for curative treatment of GBC is early diagnosis and radical surgery.[9,14] According to current guidelines, cholecystectomy is sufficient for stage T1aN0 cancer.[15] However, for tumors beyond this stage, radical cholecystectomy with en bloc resection of adjacent liver parenchyma and regional lymphadenectomy is advised.[15] Overall survival remains exceptionally poor (5.1–9.5 months) in patients with unresectable GBC, but radical surgery extends the median survival to 35–53 months.[11,16,17] Several retrospective studies have shown a survival benefit for resection with lymphadenectomy after incidentally detected GBC,[17–20] and such an approach is recommended for T1b-T3 tumors.[15] Survival after

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incidental GBC does not appear to rely on whether liver resection is carried out in the same operation or during reoperation at a later stage.[16,17] Furthermore, incidental GBC has a better prognosis than symptomatic GBC.[14,17] For these reasons, routine HPE has been recommended to detect incidental GBC.[15] However, even if a reoperation and resection is recommended after identification of incidental GBC, it is not clear whether routine HPE of all excised gallbladders offers a diagnostic advantage over macroscopic examination and selective HPE for those with macroscopic abnormalities. The aim of this study, therefore, was to assess the rate of incidental GBC in macroscopically normal gallbladders.

Material and methods

This was a retrospective cohort study including patients treated in 4 hospitals in the Helsinki Metropolitan Area (Surgical Hospital, Meilahti Hospital, Jorvi Hospital, and Peijas Hospital), all of which are administratively part of the Helsinki University Hospital, with a total patient catchment area of approximately 1 000 000 individuals. Patients were identified from an electronic operative registry using the procedure codes for open and laparoscopic cholecystectomy (JKA20 and JKA21).

The aim was to collect at least 2000 patients undergoing cholecystectomy to detect at least 10 patients with incidental gallbladder cancer, assuming an incidence of 0.5%. Based on initial calculations, a 1.5 year time period was chosen, which was then extended by 2 months to obtain the target study population. Furthermore, the period was chosen such that a sufficient follow-up of at least 3 years from cholecystectomy would be available. The final index cholecystectomy period was from November 2010 to May 2012, and data were collected during 2016. Patients who had undergone open or laparoscopic cholecystectomy as their primary operation (i.e. not as a secondary operation performed concomitantly with an alternative primary operation) during the chosen time period were included. Exclusion criteria were: 1) clinical or radiological suspicion of gallbladder neoplasia prior to the operation, and 2) any active malignancy or malignancy that had been in remission less than 5 years.

Data were collected from electronic patient records in a preformatted SPSS sheet (SPSS Statistics ver. 22, IBM, Armonk, NY). Basic demographics, operative details, macro- and microscopic findings, and follow-up were extracted. The indication for surgery was defined as the main reason for cholecystectomy at the time of the operation, although other indications, such as previous episodes of cholecystitis or pancreatitis, might have been present. Cholecystectomies performed during an emergency admission were classified as emergent, whilst others were classified as elective procedures.

Any macroscopic description of thickening, tumor, polyp, or necrosis in the operation record was interpreted as a pathology of the gallbladder. The routine method to evaluate the resected gallbladders in these hospitals is to open the gallbladder after resection, inspect the mucosa, and mark the contents of the gallbladder (stones, sludge, etc). The end of follow-up was defined as the last verified contact or visit based on the electronic patient records. Patients whose gallbladder was not sent for HPE were crosschecked using the Finnish Cancer Registry (FCR) in 2015 to verify that no malignancies were missed in these patients. FCR covers the whole Finland with 96% completeness regarding solid tumors.[21] This study was approved by the institutional review board of Helsinki University Hospital and the National Institute for Health and Welfare.

Results

Patients

Of the 2317 patients identified, 2034 patients met the inclusion and exclusion criteria and were included in the study (Fig. 1). The basic patient and operative characteristics are shown in Table 1.

Micro- and macroscopic findings

The macroscopic description was normal in 70.0% and 60.8% of gallbladders, as assessed by the surgeon and pathologist, respectively (Table 2). Histopathological analysis was performed on 94% of gallbladders (n = 1916). Of the 118 gallbladders not sent for HPE, 112 were reported as macroscopically normal, while six exhibited a thickened or necrotic wall. Ten GBC were found by HPE. The macroscopic appearance of these gallbladders, as described by the surgeon, was as follows: local hardness (n = 1), thickened wall (n = 5), acute cholecystitis (n = 1), and neoplastic (n = 3). Thus, the rate of GBC in patients without signs of malignancy in preoperative imaging was 0.5% (n = 10). No GBC was found in patients with a macroscopically normal gallbladder. Of note, one other patient derived diagnostic benefit from HPE when a suspicion of primary sclerosing cholangitis was established on the basis of histopathological findings. In this patient, the gallbladder wall was also thickened. Patients whose gallbladders were not sent for HPE were crosschecked with the Finnish Cancer Registry for instances of missed GBC; however, none were identified.

Patients with incidental GBC

The male/female ratio among patients with GBC was similar to patients undergoing cholecystectomy (two-thirds female) (Table 3). The median age was 74 years (range 49–84 years), with only one patient younger than 50 years of age. Six of these patients (60%) underwent elective cholecystectomy, and none had a history of acute cholecystitis. Four patients underwent emergency cholecystectomy due to acute cholecystitis. Of note, nine patients had been evaluated with US, one with CT, and three with MRI prior to the operation without

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