

Routine versus selective histological examination after cholecystectomy to exclude incidental gallbladder carcinoma

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ABSTRACT

INTRODUCTION Gallstone disease is treated commonly with cholecystectomy. Malignant disease of the gallbladder may present similarly and has a poor prognosis. It is common for cholecystectomy specimens to be sent for histological examination to exclude malignancy. However, the incidence of incidental gallbladder carcinoma (IGBC) is low and it has therefore been suggested that macroscopic inspection of the gallbladder by the surgeon, followed by selective histological examination of abnormal specimens, may be safe and cost saving.

METHODS All cholecystectomies performed between 1 May 2003 and 1 September 2009 were identified from clinical coding. Pathology records were used to identify gallbladder malignancies; these were searched manually to identify IGBC. Pathology reports and case notes were cross-referenced to determine whether there were macroscopic abnormalities present. Annual cost savings were estimated by comparing the number of gallbladder specimens over one year (May 2013 – April 2014) with the total number of cholecystectomies performed in that time.

RESULTS Of 4,776 cholecystectomies identified, 12 (0.25%) were cases of IGBC. These cases had a higher median age (68 vs 54 years, $p < 0.001$) and a higher proportion were emergency operations (50% vs 12%, $p < 0.001$). All cases had some form of macroscopic abnormality, most commonly wall thickening ($n=6$, 50%). Only two cases (17%) had a visible tumour present.

CONCLUSIONS All cases of IGBC in this study had a macroscopically abnormal gallbladder. Our findings suggest it is safe to adopt a selective approach to histological examination. Savings of almost £20,500 per annum have been achieved.

KEYWORDS

Gallbladder – Cancer – Incidental – Histology

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Cholecystectomy is performed commonly for benign gallstone disease, either electively or as an emergency. Malignant disease of the gallbladder is rare in Western populations, with a recorded incidence of 0.9 per 100,000 men and 1.9 per 100,000 women in England.¹ On the other hand, incidence varies considerably around the world, with high incidence rates in northern India and Chile.² The disease carries a poor prognosis.³ In a high proportion of patients with gallbladder cancer (GBC), the diagnosis will be made as an incidental finding following cholecystectomy for presumed benign disease. It is estimated that 60–80% of GBC may present in this way.^{3,4} However, it is reported in the literature that incidental GBC (IGBC) is detected after only 0.19–3.5% of cholecystectomies for presumed benign disease.⁵

In many institutions, it is routine practice to subject all cholecystectomy specimens to histological examination. Nevertheless, as only a tiny proportion of these examinations reveal any unexpected malignant pathology, it has been suggested that this is unnecessary. Selective examination of macroscopically abnormal or high risk specimens

may be safe as well as more cost effective.^{6–9} Studies suggest high risk groups include older patients, patients converted from laparoscopic to open surgery, female patients, patients of Asian and African ethnicity, and patients with raised alkaline phosphatase levels prior to surgery.^{10,11} Other studies advocate routine histological examination of all specimens as the safest approach.^{5,12,13}

In view of this disagreement in the literature, our study sought to determine the frequency of IGBC in our institution and to establish whether selective histological examination of macroscopically abnormal specimens only would have detected these cancers. Secondary aims were to present the treatment given to patients with IGBC in our institution and to estimate the economic impact of a selective approach to gallbladder histology.

Methods

All elective and emergency cholecystectomies (laparoscopic and open) performed in our institution between

1 May 2005 and 1 September 2009 for presumed benign disease were reviewed retrospectively. Cases were identified from clinical coding data, which included demographic data (age, sex). Pathology records of gallbladder specimens were searched to identify all GBCs. These were then searched manually to exclude specimens where there was preoperative suspicion of cancer on imaging so as to identify only incidental cancers. The pathology reports and case notes of these patients were cross-referenced to see whether there was any intraoperative or macroscopic abnormality present that would have raised the suspicion of cancer. Furthermore, demographic and operative data from IGBC patients were compared with the non-cancer patients to identify potential risk factors for malignancy.

A single patient diagnosed initially with cancer had her specimen re-examined by a regional hepatobiliary unit and the diagnosis was revised to severe cholecystitis. This patient was excluded from the study.

The economic impact of selective histology was estimated by obtaining the total number of cholecystectomies performed at our institution for a calendar year (1 May 2013 – 30 April 2014) from clinical coding. During this time period, a selective approach to gallbladder histology was being used. This figure was compared with the number of gallbladder specimens processed by the pathology department during the same time period. The difference between these, along with the total cost per specimen, was used to estimate the savings made.

Statistical analysis

Parametric data were analysed using Student's t-test (Excel®; Microsoft, Redmond, WA, US) and categorical data with Fisher's exact test (QuickCalcs; GraphPad Software, La Jolla, CA, US). A *p*-value of <0.05 was considered statistically significant.

Results

During the study period, 4,776 patients underwent cholecystectomy in our institution. The median age of these patients was 54 years (range: 14–90 years) and the male-to-female ratio was 1:5. Overall, 544 procedures (12%) were undertaken as an emergency.

A search of the pathology records yielded 12 cases of IGBC (0.25% of all cholecystectomies performed). The male-to-female ratio was 1:2 and the median age of these patients was 68 years (range: 48–84 years). This was a statistically significant difference in age (Student's t-test, *p*<0.001). Six (50%) of these were emergencies. This was a significantly higher proportion than for benign cases (527 patients, 12%; Fisher's exact test, *p*=0.001). The majority of the IGBC cases were adenocarcinomas (*n*=10, 83%). There was one mixed adenocarcinoma and one poorly differentiated carcinoma, possibly metastatic in nature.

Nine (75%) of the patients with IGBC had died by the time of writing. The mean postoperative survival in these cases was 12.8 months (range: 4.2–29.1 months). Of these, 8 (89%) died from their GBC. The remaining patient died following surgery for an advanced right-sided colon cancer 29 months

after cholecystectomy, having declined radical biliary resectional surgery. Five patients received chemotherapy following diagnosis, one of whom is still alive at the time of writing. Two patients received palliative care only and one received palliative radiotherapy. Two underwent radical resectional surgery at a tertiary hepatobiliary unit. One of these patients is still alive at the time of writing, five years after diagnosis. The other developed peritoneal disease and received palliative chemotherapy, passing away 21 months after cholecystectomy. Postoperative treatment information was not available for one patient (Table 1).

Regarding macroscopic appearance, all of the 12 cases of IGBC had some degree of macroscopic abnormality (Table 1). The most common was inflammation or thickening of the gallbladder wall (*n*=6, 50%). Other abnormalities included perforation, fistulation and necrosis. In two cases (17%) a tumour was visible at the time of surgery.

In most cases, surgery was difficult. There were six subtotal cholecystectomies (50%) including one open subtotal cholecystectomy and three cases (25%) were converted from laparoscopic to open surgery (Table 1). Only three procedures (25%) were laparoscopic total cholecystectomies.

Between 1 May 2013 and 30 April 2014, 809 cholecystectomies were performed. This compares with 535 gallbladder

Table 1 Management of malignant specimens following cholecystectomy, macroscopic abnormalities and surgical approach in these patients

	<i>n</i>
<i>Treatment</i>	
Surgery (+/- adjuvant therapy)	2
Chemotherapy only	5
Radiotherapy only	1
Palliative care only	2
No treatment	1*
Not known	1
<i>Macroscopic abnormalities</i>	
Thickened / inflamed wall**	6
Mass / tumour	2
Necrotic tissue	2
Fistula	1
Perforation	1
<i>Surgical approach</i>	
Complete laparoscopic	3
Subtotal laparoscopic	5
Subtotal open	1
Laparoscopic converted to open	3
*Patient offered radical surgery but declined. Died following surgery for advanced colon cancer.	
**Based on the judgement of the surgeon and/or pathologist	

Table 2 Summary of economic analysis and estimated annual savings. Data for 1 May 2013 to 31 April 2014.

Number of cholecystectomies performed	809
Number of gallbladders not sent for histology	274
Cost per specimen	£62.12
Pathology department savings	£17,021
Total estimated annual savings (incl 20% trust overheads)	£20,425

specimens processed by the pathology department during the same time period. The total cost per specimen is estimated at £62.12, with a further 20% cost per specimen to cover trust overheads. This gives an estimated cost per specimen of £74.54. As 274 gallbladders (34%) were not sent for histology, the total annual saving is estimated at £20,425 (Table 2).

Discussion

The findings in this study reflect what is already known about IGBC, namely that it is very rare and carries a very poor prognosis. The low rate of IGBC reported in this study (0.25% of cholecystectomies) is consistent with previously published data.⁵ The symptoms of malignant gallbladder disease closely mimic those of benign gallstone disease,⁵ making preoperative diagnosis difficult. There is little doubt that thorough histological examination of malignant specimens is very important to determine prognosis and plan further treatment.⁵ However, the vast majority of cholecystectomies in this series were for benign disease. It is reasonable to ask whether selective histological examination of high risk or suspicious specimens only is a safe and cost effective approach.

In this study, all 12 cases of IGBC had some degree of macroscopic abnormality (Table 1). On the other hand, many of these features (such as thickening of the gallbladder wall, inflammation and fistulation) are seen commonly in benign disease and are non-specific for cancer. Cases of IGBC were more likely to undergo cholecystectomy as an emergency and the median age of these patients was higher. In addition, a high proportion of these cases were difficult cholecystectomies and the conversion rate from laparoscopic to open surgery in this group was high at 25%.

It can therefore be concluded that any macroscopically abnormal gallbladder specimen, any emergency surgery specimen or any specimen from an open or subtotal procedure should be subjected to histological analysis. Owing to the non-specific nature of many of the macroscopic changes seen in IGBC, caution should be exercised and if there is any doubt, the gallbladder should be sent for histological examination. This is especially true for patients over 50 years of age. However, in younger patients where there is no difficulty in performing surgery and where no macroscopic abnormality is seen on postoperative inspection of the gallbladder by the surgeon, it is reasonable not

to send these specimens. If this approach is employed, the surgeon must inspect the specimen thoroughly, including opening the specimen to examine the mucosa. Agreement between surgeons and pathologists should also be sought before such an approach is introduced.^{14,15}

Savings of almost £20,500 per annum are estimated to have been made through adopting this approach. This is only an approximation as it is not known how consistently this approach is being applied across the hospitals in our trust. (The decision whether to send a specimen for histology is made by the operating surgeon and there is no fixed protocol or guideline in place.) Nevertheless, this represents a significant annual saving, especially in the current context of financial pressures on the National Health Service.

Study limitations

We acknowledge the limitations of retrospective studies. However, the small number of cases of IGBC over a long period of time makes prospective data collection impractical. These findings are from a single region of the UK and may not be generalisable to other countries, particularly those with a higher incidence of GBC. Over the period studied, there have also been changes in procedures for preparing specimens in the pathology department. Formerly, the specimens were prepared by medical staff (usually a consultant). Conversely, they are now dissected by a trained biomedical scientist. This is unlikely to have any bearing on the results of this study but it does represent a potential source of inconsistency in how specimens were handled.

Conclusions

The findings of this study are consistent with previously published data in terms of overall incidence of IGBC⁵ and the demographics of high risk patients.^{10,11} We describe an alternative approach to subjecting every cholecystectomy specimen to histological examination. However, surgeons wishing to adopt this approach should be cautious and exercise careful judgement in deciding whether to send a specimen.

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