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ORIGINAL ARTICLE

Outcome of Surgical Inspection of the Gallbladder in Relation to Final Pathology

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Abstract

Introduction Routine histopathologic gallbladder examination after cholecystectomy has been a point of discussion. The aim of this study was to evaluate the macroscopic examination by the surgeon in relation to the final histology.

Methods A prospective study was conducted to investigate the practice of macroscopic gallbladder examination by a surgeon compared to routine histopathology by a pathologist. All consecutive cholecystectomies were included between November 2009 and February 2011.

Results A total of 319 consecutive cholecystectomies were performed. Of all macroscopic examinations, the surgeon identified 62 gallbladders with macroscopic abnormalities, ranging from polyps to wall thickening or ulcers. In 55 (17.2%) cases, the surgeon judged that further examination of the specimen by the pathologist could possibly lead to additional and relevant findings. There was a strong agreement between the surgeon and the pathologist concerning the macroscopic examination (κappa = 0.822). The surgeon and the pathologist had disagreement on the macroscopic examination of 18 gallbladders, without clinical consequences for the patient.

Discussion The present prospective study shows that the surgeon should be able to select those gallbladders needing a microscopic gallbladder examination. Potentially, about 80% of this kind of routine histology can be reduced.

Keywords Laparoscopic cholecystectomy · Gallbladder carcinoma · Gallbladder cancer · Routine histopathologic examination

Introduction

Gallbladder carcinoma (GBC) remains a rare gastrointestinal malignancy with an extremely poor prognosis. This poor prognosis is due to the highly aggressive biological nature of the carcinoma, the lack of screening tools, absence of reliable biomarkers as well as the late onset of symptoms of advanced GBC.[1–7] The incidence of gallbladder cancers is very low (0.7 per 100,000 in the Western world, higher incidence is found in Asian countries) and shows a declining trend over the last decades.[8,9] The age-standardized incidence (ASR per 100,000 persons) was 2.6 for males and 2.1 for females in the Netherlands and 3.0 and 3.3 respectively in Europe.[9,10] Unexpected incidental carcinoma is discovered in 0.19–2.8% of patients after a cholecystectomy for symptomatic cholecystolithiasis.[5,11] Depending on the depth of invasion (T-status), additional surgery may take place to pursue a R0 resection.[8,9,12,13]

Whether a removed gallbladder requires standard histopathological examination in each patient has been debated. In the Netherlands, costs generated by routine practice amount to approximately 1.5 million euros annually. The only clinically relevant conclusion about histological evaluation of gallbladders is the exclusion of malignancy. We hypothesize that pathological examination of a macroscopic "normal" appearing gallbladder will not yield additional relevant information that leads to a change in the individual treatment plan.[14] At the very most, there is a confirmation of the perioperative findings varying from "normal gallbladder" to "prior or chronic inflammation." In other words, a macroscopic abnormal gallbladder would require microscopic verification

This paper is not based on previous communication to a society or meeting.

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of the diagnosis, and in the absence of macroscopic abnormalities, a cholecystectomy would suffice. Therefore, one might question the value of routine histopathological gallbladder examination by a pathologist.

The aim of the present study was to investigate the practice of macroscopic examination of the gallbladder by a surgeon compared to the routine histopathologic examination by a pathologist, defined as being the gold standard. This has not been evaluated prospectively before. Additionally, we wanted to investigate which percentage of gallbladders would require additional microscopic examination after being inspected by a surgeon.

Method

This prospective consecutive case series study was performed in Máxima Medical Centre (MMC), a 614-bed teaching hospital in Veldhoven/Eindhoven, the Netherlands. Approval was granted by the local Medical Ethics Committee. All consecutive laparoscopic cholecystectomies performed between November 2009 and February 2011, were included. Anonymized patient characteristics, operative procedure, conversions to laparotomy, macroscopic examination of the gallbladder mucosa, necessity for microscopic analysis, and histopathology of the gallbladder were analyzed. All cholecystectomies were performed by one of 10 surgeons or by a resident (one of the 31 participating residents) under supervision of a surgeon. All cholecystectomies were performed laparoscopically, unless there were contraindications for performing laparoscopy resulting in an open procedure. The decision to convert from laparoscopic cholecystectomy to open cholecystectomy was made during surgery. Each extracted gallbladder specimen was macroscopically evaluated by the surgeon in the operating room before sending it to pathology. Findings were tabulated on a standard form (appendix 1). The gallbladder was incised longitudinally, from the cystic duct to the end of the gallbladder pouch. The number of gallstones were classified in groups (0; 1; 2–10; > 10), and the color of the mucosa was described. The mucosal wall was manually palpated in search of any abnormality of the gallbladder wall, including thickening, induration, ulcers, calcifications, or any masses. Hereafter, the surgeon had to fill in whether he/she would send the gallbladder for microscopic analysis or that no relevant additional findings from histopathological examination were to be expected (e.g., dysplasia or adenocarcinoma). Each gallbladder, however, was routinely sent in for further microscopic analysis by a pathologist to confirm or to disprove the macroscopic evaluation of the surgeon. The pathologist had no knowledge of the findings of the macroscopic inspection of the surgeon. Histological examinations were routinely performed according to pathologist guidelines.[15] One of 11 pathologist examined the gallbladder. Samples were taken from macroscopic anomalies and if not present only from the gallbladder fundus, body and neck, otherwise known as Hartmann's pouch, due to the predominant etiology of gallbladder carcinoma at these sites.[1] We compared the macroscopic examination of the surgeon to the macroscopic examination and the microscopic conclusions of the pathologist, as reported in the pathology reports.

Statistical Analysis

All data were analyzed using IBM SPSS Statistics version 24 (Armonk, NY: IBM Corp.). Agreement between macroscopic examination of the surgeon and pathologist was calculated by Cohen's kappa (κ) for interrater agreement. Magnitude for interobserver agreement was interpreted as follows: values < 0 indicating no agreement; 0–0.20, slight agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, substantial agreement; 0.81–1, strong to almost perfect agreement.[16]

Results

General Characteristics

During the study period, a total of 319 consecutive patients underwent a cholecystectomy. An emergency cholecystectomy was performed in 33 (10.3%) cases. Median age at presentation was 51 years (range 18–86 years). Female to male ratio was 2:1 (214 (67%) female, 104 (33%) male). Three-hundred and two patients were treated laparoscopically (94.4%). In 15 patients (4.7%), conversion to laparotomy was done, and 2 patients were treated by planned open cholecystectomy (0.6%). Table 1 shows the indication for cholecystectomy.

Table 1 Indication for gallbladder operation in 319 consecutive patients

	Patients, *n*	Percentage
Symptomatic uncomplicated cholecystolithiasis	227	70.9
Cholecystectomy a froid	31	9.7
Acute cholecystitis	29	9.1
Post biliary pancreatitis	18	5.6
Post ERC (P)	8	2.5
Gallbladder polyp	4	1.2
Cholangitis	1	0.3
Porcelain gallbladder	1	0.3

ERC (P) endoscopic retrograde cholangiopancreatography

Surgeon's Inspection and Palpation Versus Histopathology

A total of 257 (80.6%) were judged by the surgeon as normal and 62 (19.4%) were not, while the pathologist considered 255 (79.9%) normal and 64 (20.1%) not (Table 2). A strong agreement between the macroscopic agreement of the surgeon and pathologist was found (κappa = 0,822).

The surgeon and the pathologist disagreed on 18 (5.6%) gallbladders (Table 2). Of these, ten gallbladders were considered macroscopically abnormal by the pathologist, whereas the surgeon judged them to be normal. The pathologist found mucosal abnormalities in four out of ten gallbladders, wall thickening with focal wall rigidity in four out of ten, and a combination of both wall thickening and mucosal abnormalities in the remaining two. Additionally, two gallbladders contained enlarged nodes according to the pathologist. None of these ten gallbladders, however, had microscopic relevant abnormalities. Nine out of ten showed microscopically chronic inflammation and one revealed pseudopolyp.

Eight of the 18 gallbladders were considered macroscopically abnormal by the surgeon, whereas the pathologist judges them to be normal. The surgeon described two out of eight gallbladders fibrotic, one contained fibrosis of the cystic duct, three showed wall thickening, and two showed irregularities of the mucosa. All eight of these gallbladders showed chronic inflammation upon final histopathologic examination.

Not all macroscopic abnormalities were judged by the surgeon to be in need of microscopic examination, specifically 16 abnormal gallbladders were judged not to require further histopathologic examination. On the other hand, nine gallbladders without macroscopic abnormalities were judged to need microscopic examination for various reasons, such as the clinical indication for the cholecystectomy, a suspect patient history, or other (Fig. 1).

Eventually, 55 of the 319 cholecystectomies (17.2%) were judged to be in need for additional histopathology either because of acute cholecystitis or other clinical reasons, wall thickening, polyps, or suspicious mucosa by macroscopic examination (Table 3).

In this series no carcinoma, two gallbladders with focal metaplasia and one gallbladder with focal dysplasia were observed (Tables 4 and 5). All cases were selected for histopathological examination. No microscopic malignant or premalignant abnormalities would have been missed with surgical macroscopic evaluation alone.

Table 2 Macroscopic examination by a surgeon compared to the macroscopic examination by a pathologist

		Pathologist		
		Normal, *n*	Abnormal, *n*	Total, *n*
Surgeon	Normal, *n*	247	10	257
	Abnormal, *n*	8	54	62
	Total, *n*	255	64	319

Discussion

We conducted this prospective case series to collect evidence to support the use of *selective* histopathological examination after cholecystectomy and to refrain from current practice to routinely sent in all gallbladders for additional histology. To the best of our knowledge, this is the first study to address the macroscopic examination of the gallbladder by the surgeon in a prospective fashion. At preoperative imaging, no gallbladders were suspected for gallbladder carcinoma, while one patient was known with colorectal liver metastasis, one was categorized as having a porcelain gallbladder and four patients were suspected of having a gallbladder polyp. The latter is known to be prone for and associated with development of gallbladder malignancy.[17,18]

Routine histopathologic gallbladder examination after cholecystectomy has been a point of discussion for several decades. Recently, in 2016, the Dutch guideline "cholecystolithiasis" of the Dutch Surgical Society (NVvH) was changed concerning its policy in case of a macroscopic normal appearing gallbladder. For such gallbladders, one can refrain from routine histopathological inspection (level 2a—systemic review).[19–21] Several hospitals have implemented these changes in their current daily practice. Thus far, however, no one challenged the capability of the surgeon to adequately inspect the gallbladder macroscopically.

Based on the finding of the present study, the surgeon selected one out of six gallbladders for supplementary histopathological investigation. In most of these cases, there was a combination of wall, mucosal, and other abnormalities, deemed to be in need of further microscopic evaluation. However, all surgically described abnormalities corresponded well with the final microscopic analysis. No microscopic relevant abnormalities were missed after the macroscopic surgical examination, and histological examination revealed no additional relevant findings. Moreover, all other gallbladders that were sent in showed only chronic inflammation of the gallbladder wall without any other macroscopic or microscopic abnormalities. There was disagreement between the surgeon and the pathologist in a total of 18 gallbladders, being 5.6% in this series. Of these 18 cases, 10 are relevant to distinguish further, because these gallbladders might erroneously be judged as normal and discarded, whereas they in fact may contain relevant microscopic abnormalities. However, none of these disagreement cases showed any relevant microscopic relevant conclusions. This means that a surgeon can adequately discover whether a gallbladder needs further investigation or not.

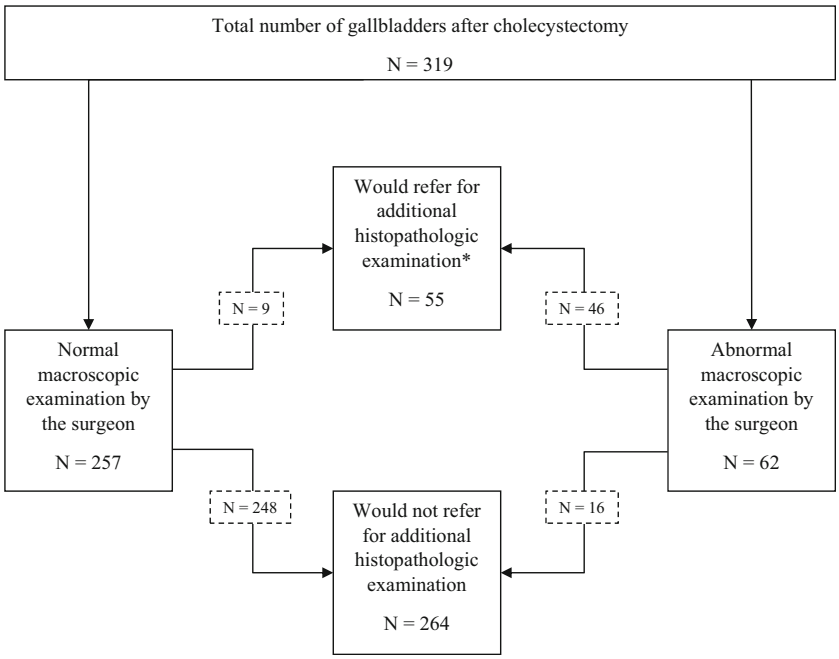

Fig. 1 Flow chart addressing the macroscopic examination of the surgeon and the number of gallbladders judged to be in need of additional histopathology. A single asterisk details in Table 3

With a "strong to almost perfect agreement," we conclude that macroscopic examination performed by the surgeon is comparable to final histology and is a safe policy to detect relevant abnormalities. The present findings are in line with the retrospective data of Vliet et al. who found that 13.5% would require further microscopic examination after a macroscopic surgical inspection.[19] Our study differs from their research by its prospective design, albeit that smaller numbers were evaluated. Moreover, Vliet et al. investigated the macroscopic examination of the gallbladder performed by a pathologist in contrast to the examination performed by a surgeon, as in the present study. Hence, that report could not criticize the capabilities of a macroscopic gallbladder examination performed by a surgeon. Besides, the conclusion of van Vliets' report suggests the necessity of a pathologist, and therefore would not result in a reduction of medical costs.

Of course, the present study has some limitations. The number of cases studied was limited; however, the percentage of potential referrals to histopathology is probably a good estimation for future calculations. Additionally, in over 300 consecutively removed gallbladders, no carcinoma was found, but this study was not set up to calculate the risk of missing a GBC if histopathology is only done selectively. Further research might be needed to make such a solid claim regarding gallbladder carcinoma and the practice of macroscopic examination by the surgeon. If a prospective study would be conducted, it should be conducted in a multicenter setting given the low incidence of (incidental) GBC. To make a valid claim in a prospective setting, one would need several thousands of gallbladders in a prospective cohort. Realization of this cohort is debatable and possibly futile.

Annual costs for routine examination of the gallbladder in the Netherlands encompasses 1.5 million euros. Histopathologic examination of a gallbladder costs circa €60–. A selective histopathologic examination of gallbladders, would result in a cost reduction of approximately 80%, which might translate into a reduction of roughly €1,245,000– nationwide. Alternative to an economic benefit, a selective pathologic examination gives pathologists the possibility to reallocate time and resources to other examinations, especially in countries with a shortage of pathologists.

In conclusion, surgeons are very well capable to perform a clinically relevant macroscopic examination of the removed gallbladder and draw conclusions based on that observations. Furthermore, *selective* histopathological examination might therefore result in a significant decrease in medical costs without compromising patient safety and outcome.

Table 3 reasons which warranted additional histopathologic examination of the gallbladder

Reasons for additional histopathologic examination	Number (*n*)
Macroscopic abnormalities of gallbladder wall or mucosa, including acute cholecystitis	46
Preoperative abnormalities on imaging	4
Suspected patient history	3
Clinical indication	2

Table 4 Histopathology results

	Patients, *n*	Percentage
Chronic inflammation	282	88.4
Acute inflammation	19	5.9
Miscellaneous	18	5.7

Table 5 Subdivision of miscellaneous histopathology results

	Total of 18 miscellaneous gallbladders	Percentage of total series (5.7%)
Eosinophil inflammation	3	0.9
Metaplasia	2	0.6
Dysplasia	1	0.3
Pseudopolyp	4	1.4
Adenoma	2	0.6
No abnormality	6	1.9

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Appendix 1 - standard form detailing macroscopic gallbladder examination

General characteristics

Name of patient
Patient identification number
Sex
Date of birth
Patients' age

Surgery characteristics

Date of surgery
Primary surgeon
Secondary surgeon
Indication for cholecystectomy
Setting: elective/emergency
Type of surgery: laparoscopy/conversion/open

Gallbladder characteristics

Doubt regarding anatomy, if so specify
Number of gallstones: 0; 1; 2–10; > 10
Gallbladder wall macroscopy
Gallbladder mucosa macroscopy
Color mucosa
Mucosal abnormalities
Other specified abnormalities
Macroscopic abnormalities: yes/no
Reason for histopathologic examination: yes/no. If no, specify

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