The POLYP-study: Guideline Adherence Leads to Overtreatment of Gallbladder Polyps

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ABBREVIATIONS

GB	Gallbladder
GBC	Gallbladder Carcinoma
TAUS	Transabdominal Ultrasonography
LC	Laparoscopic Cholecystectomy
FU	Follow-up
PA	Pathology

KEYWORDS

Gallbladder polyps

Management of gallbladder polyps

Guideline adherence

Gallbladder carcinoma

Follow-up

Special thanks to the participating study hospitals.

ABSTRACT

INTRODUCTION Gallbladder (GB) polyps are common but risk of malignancy remains low. Management guidelines rely primarily on polyp size as an indication for cholecystectomy. The surgical threshold with polyps >1 cm remains controversial and is proven to be insufficient. Currently, there is a growing concern for overtreatment and the need for improved diagnostic strategies. This study evaluates guideline adherence and current management of GB polyps in the Netherlands.

METHODS The POLYP-study is a nationwide prospective cohort study and aims to optimize patient selection for operative GB polyp management and to assess guideline adherence. Patient demographics, symptoms, imaging characteristics, follow-up data, and post-operative data were collected. If possible, histopathological analyses of excised GB polyps were collected as well. Given indications for surgical and conservative treatment were compared to the 2017 and 2021 guidelines.

RESULTS This study included 279 patients with GB polyps, of which 166 (59.5%) were females. Mean follow-up time was 30.2 months, with an average of 3.5 visits throughout follow-up. Polyp size at first visit was 7mm (± 2.8mm). GB polyps were incidental finding in 39.8% of patients. Guideline adherence remains sub-optimal according to the 2017 and 2021 guidelines; only 48.4% and 59.7% of patients reaching indication for cholecystectomy, underwent surgical treatment. Conservative adherence was even worse, with adequate follow-up duration after first visit in only 38.9% and 42.6% of patients following 2017 and 2021 guidelines. In total 77 patients underwent cholecystectomy, in 66 (85.7%) and in 65 (84.4%) this was a valid indication according to 2017 and 2021 guidelines, respectively. In 34 patients a polyp was present upon pathological analysis, cholesterol polyps were most common (26.3%), no malignant polyps were found. We identified a weak correlation (r=0.201) between pre-operative and post-operative polyp sizes, whereby possible measurement error pre-operative leads to incorrect indications for cholecystectomy.

CONCLUSION The study revealed a discordance between clinical practice and guidelines recommendations. While guideline adherence remains sub-optimal, strict adherence to the guideline may paradoxically result in overtreatment and futile cholecystectomies. The aggressive management of small GB polyps leads to excessive costs and unnecessary follow-up imaging, whereas the malignant potential of these polyps remains very small. This study underscores the importance of refining pre-operative patient selection and identification of potentially neoplastic polyps. Further research is required to develop advanced imaging techniques and enhance observer reproducibility in polyp assessment.

INTRODUCTION

Gallbladder (GB) polyps are defined as any elevated lesion of the mucosal surface of the gallbladder wall protruding into the lumen[1, 2]. Due to the widespread availability and improved image quality of ultrasonographic imaging such as transabdominal ultrasonography (TAUS) and computed tomography (CT), GB polyps are increasingly recognized[3]. It is estimated to affect approximately 5% of the global adult population[4]. Reported prevalence rates range from 0.3% to 12% in patients who underwent GB ultrasonography[3, 5-8]. These rates are similar to the prevalence rates of post-operative GB polyps found upon histopathological analysis following cholecystectomy (surgical GB removal), which are 0.004-13.8%[3]. Unfortunately, the reported incidence in adult populations rates vary greatly between studies and seems to be related to the population examined and the used study design. GB polyps have rarely been described in children, in whom they may occur as primary disorder or as a consequence of metabolic or genetic conditions, like metachromatic leukodystrophy or pancreatobiliary malunion[9].

The majority of GB polyps are found incidentally on imaging or during histopathological examination after cholecystectomy. This is because GB polyps are asymptomatic in the majority of the cases, and even if patients have symptoms, they are non-specific. Occasionally, symptoms seem similar to those of acute cholecystitis (e.g. nausea, vomiting, and episodic right upper quadrant pain). Interestingly, Kwon et al. found that the presence of symptoms was associated with malignant polyps, and increase of polyp size tended to increase chance of symptoms[10]. In another retrospective analysis (n=417), 64% of GB polyps were diagnosed during a work-up of unrelated illness. Abdominal pain and elevated liver function tests were present in 23% and 13% of cases, respectively[11]. The study reported no difference in symptoms between patients with benign or malignant polyps. Multiple mechanisms are proposed as an explanation for symptoms. However, an acute cholecystitis due to obstruction of the common bile duct and cholangitis due to fragments of the polyp breaking off and obstructing within the bile duct are the most accepted explanations[4].

Histopathology

The histopathological profile of GB polyps can be divided into two main categories: true and pseudo polyps (Figure 1.1). The latter consists of a wide variety of lesions including cholesterol polyps, inflammatory polyps, and focal adenomyomatosis[12]. They appear to compose around 70% to 95% of all GB polyps[2, 3, 13]. Cholesterol polyps represents the polypoid version of cholesterolosis, and are polyps composed of lipid-filled macrophages[14]. Cholesterolosis is also considered a pseudo polyp, resulting from abnormal deposits of lipids into the GB wall, which appears less pedunculated on TAUS

and is often an incidental finding due to absence of symptoms[14, 15]. Pseudo polyps pose no harm and have no malignant potential, whereas true polyps can be either benign of malignant. True benign polyps are most commonly adenomas, whereas malignant polyps are usually adenocarcinomas[12]. Evidence suggest that adenomas carry malignant potential, though other studies conflict with the validity of the adenoma-adenocarcinoma pathway[3, 16]. Even though approximately 5% of the global adult population is affected by GB polyps, only 3-8% of these GB polyps are malignant, a small but significant number[16]. Since GB polyps are common but gallbladder carcinoma (GBC) is rare, it is a diagnostic challenge to determine the malignant potential of a polyp and to determine which patients require (preventive) treatment[2]. The aim of current practice is to promote early detection and treatment of (possible) malignant polyps to improve survival rates of GBC. Currently, GBC is often discovered at stage 3 or 4, with a 5-year survival rate of 5% to 12%, while survival rates of stage 1 and 2 are >95% and 70%, respectively[3, 17].

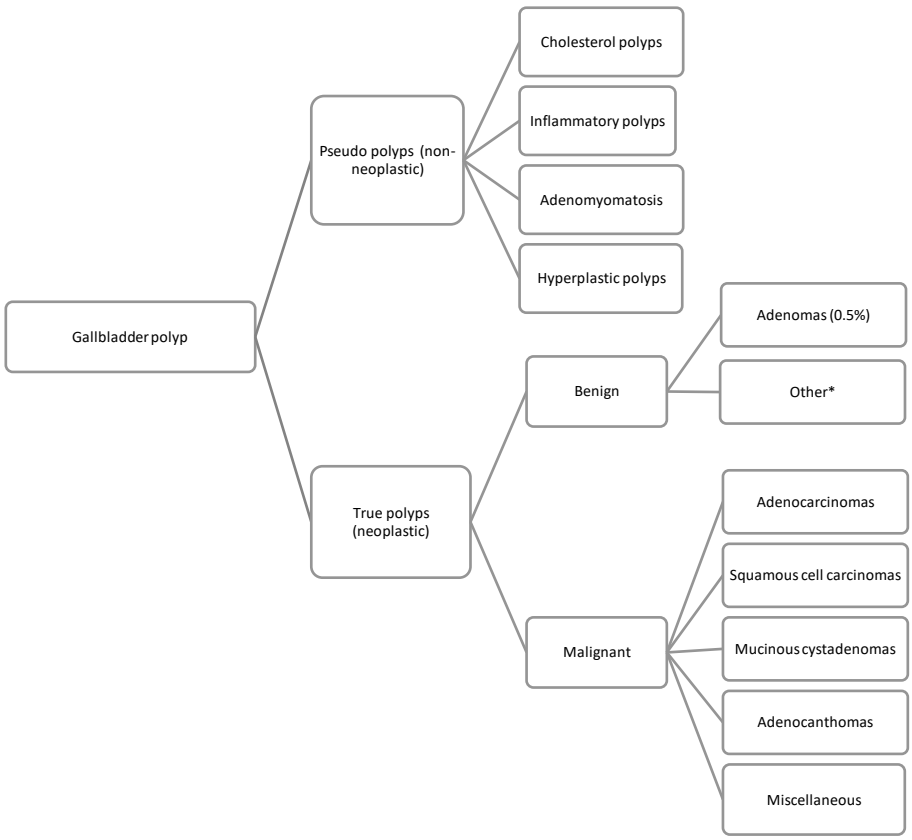

FIGURE 1.1. Classification of gallbladder polyps, based on Andren-Sandberg (2012). [18].

*Other benign neoplastic polyps include epithelial, papillary, nonpapillary, supporting tissue, hemangioma, lipoma, leiomyoma, granular cell tumor, hyperplasia, adenomatous, adenomyomatous, heterotropia, gastric mucosa, intestinal mucosa-, pancreas-, liver-, and inflammatory polyps.

Management of gallbladder polyps

The primary goal in GB polyp management is to prevent the development of GBC. A cholecystectomy is absolutely indicated for true neoplastic polyps, including adenomas due to their malignant potential[12]. Multiple factors associated with an increased risk of malignancy have been identified, including increasing age, gallstones, rapid polyp growth, gallbladder wall thickening, a sessile polyp on TAUS, Indian/Asian ethnicity, and symptomatic polyps[3]. However, these risk factors are still a subject of debate and change throughout the years. Studies tend to agree that with an increase in polyp size, the risk for malignancy increases as well, some studies reported that with a polyp size between 10 and 15mm, the chance of malignancy is 37% to 67%[3, 12, 19-21]. Pre-operative histopathological differentiation unfortunately remains a diagnostic challenge, and imaging techniques prove to be insufficient to discriminate between true- and pseudo polyps[2, 3, 22, 23].

The Joint Guidelines between the European Society of Gastrointestinal and Abdominal Radiology, European Association for Endoscopic Surgery and other Interventional Techniques, International Society of Digestive Surgery- European Federation, and European Society of Gastrointestinal Endoscopy were published in 2017 for the management and follow-up of gallbladder polyps[2]. In 2021, these guidelines were last updated (see appendix 1)[24]. The guideline of 2021 recommends cholecystectomy for all polyps with a diameter of ≥10 mm or polyps of 6-9 mm with additional risk factors for malignancy (age >60 years, presence or history of primary sclerosing cholangitis (PSC), Asian ethnicity, or a sessile polyp with wall thickening >4 mm) [2, 4, 12]. Interestingly, these risk factors differ from the risk factors mentioned in the guideline of 2017, where cholecystectomy is recommended in patients with polyp size 6-9 mm with risk factors of age >50 years, and Indian ethnicity. The difference in age is based on the study of Elsmary et al. which identified an age threshold of 60 years to be a significant risk factor for malignancy[3]. It is acknowledged that the threshold remains variable and arbitrary. Asian ethnicity was associated with the risk of malignancy in another study, including 43 articles and 11.685 patients, and therefore the risk factor was extended to Asian ethnicity[25]. Several studies suggested that the presence of a solitary polyp is also a risk factor for malignancy, however, additional details such as age and polyp size were inadequately reported[3, 8, 12]. Therefore, the risk factor of a solitary polyp was not added to the guideline, but it is recommended by the committee that in presence of one of the four risk factors and presence of solitary polyp regardless of polyp size, cholecystectomy should be considered[24].

With the updated guideline, the follow-up period was decreased to up to two years in the absence of growth, instead of the previously recommended five years. This update was based on a large

retrospective cohort study (n=622.227), which showed that growth over time is the natural course of a GB polyp and that subsequent growth was not associated with GBC, but also that the absence of growth does not guarantee subsequent stability[21]. Therefore, it was concluded that GB polyps <5mm could be discontinued from follow-up after 2 years in the absence of growth. However, the guideline does recommend considering cholecystectomy if the polypoid lesion grows by >2mm in 2 years or if the polyp grows to 10mm during follow-up[24].

The surgical threshold of 10mm remains controversial and shows to be little discriminatory to identify malignant GB polyps [2, 26, 27]. This causes significant overtreatment in surgical care, as nearly a third of patients would indicate incorrect treatment since their GB polyps exceed the threshold but are non-neoplastic in nature[12]. Another study implied that the 10mm threshold leads to unnecessary cholecystectomies, with reported specificity for predicting malignant polyps at the cut-off point of 10mm was around 19.6%, whereas the sensitivity is as high as 98.2%. Specificity increased as the cut-off point increased as well[27]. Polyp size >10mm is only rarely associated with GBC after the first year of follow-up, whereas polyps <10mm are almost never associated with future GBC. This was shown in a retrospective study (n=35.856) which showed that approximately 1 in 6 patients with GB polyps underwent cholecystectomy but only 0.2% of these showed histological evidence of GBC[21].

Limitation of diagnostics

It is recommended that the primary investigation of polypoid lesions should be with the TAUS. It is the diagnostic modality of first choice since it is portable, low-invasive, safe and has relative low costs[28]. GB polyps have been described as hyperechoic structures, without posterior acoustic shadowing (as is the case with gallstones) and with a sessile (flat) or pedunculated (protruding) shape. Additionally, GB polyps are fixed to the gallbladder wall and should not be mobile secondary to the change of a patient's position [15, 28]. Based on ultrasonography characteristics it seems possible to differentiate between different types of polyps. Studies suggest that a solitary polyp, in absence of hyperechoic spots and with presence of intralesional blood flow favors a diagnosis of neoplastic polyps[29]. Another study reported multiple other characteristics that were significantly associated with neoplastic GB polyps, including larger size (>13.9mm), lower height/width ratio (>13.9mm), wider base >3.4mm and higher base/width ratio[30].

Even though multiple characteristics of neoplastic GB polyps have been described and recognized, there are numerous shortcomings in routine ultrasound assessment of GB polyps: including a low sensitivity in polyp identification, low specificity for polyp size estimation, and a disputable 10mm threshold[31].

TAUS has been shown to be inaccurate in measuring GB polyp size, as multiple studies mention a measurement error in the estimation of GB polyps[12, 32-34]. Guo et al. reported that polyp size is overestimated by 4.24mm, while cholesterolosis is even overestimated by 5.12mm, and may be inaccurately labeled as a true polyp[35]. A positive correlation between ultrasonographic size and size upon histopathological analysis has been found in high incidence populations, with a trend to overestimate the size about 3mm on TAUS[33]. However, this correlation was not found in other populations[36]. A systematic review by Bhatt et al. reported that 93% of polyps did not change size throughout follow-up, suggesting that the majority of reported size changes may be attributable to measurement errors[37]. Interestingly, Lee et al. (2020) reported that polyp size measurements on TAUS are highly repeatable and reproducible, however, they accepted a measurement error of 25% within their measurements[32]. Polyp growth to 10mm does not increase chance of malignancy throughout follow-up [24, 38], even though thorough follow-up is recommended in the guideline for polyps < 10mm. Another study reported that the accuracy of TAUS detecting GB polyps remains low, and that following GB polyps with TAUS should be reconsidered[36].

The aggressive management of (small) GB polyps may ultimately lead to patient harm. This includes frequent and long follow-up imaging with questionable benefit and unnecessary surgical intervention[39]. Improving pre-operative differentiation between true- and pseudo polyps is paramount in order to prevent both unnecessary morbidity due to the surgical treatment of benign GB polyps, as well as malignant degeneration of small, conservatively managed true polyps[40]. In addition, improved patient selection for cholecystectomy could significantly reduce healthcare costs related to GB polyps[41, 42].

METHODS

The POLYP-study is a nation-wide cohort study focusing on optimizing patient selection for surgical intervention for GB polyps by improving current methods for the pre-operative distinction and identification for benign and neoplastic polyps, based on clinical and histopathological characteristics. This prospective cohort study aims to assess the guideline adherence for the management of GB polyps. The study is coordinated by the department of Surgery of the Radboud University Medical Center (RUMC), Nijmegen, The Netherlands and has been approved by the Medical Ethics Review Committee of the region Arnhem-Nijmegen (CMO nr. 2018-4225). See appendix B for all participating study centers.

Patient selection and variable definitions

In total 389 patients from twenty-six different Dutch hospitals are included in the POLYP-study between April 2018 until September 2022. All patients with GB polyps requiring surveillance or surgical intervention were included. Patients were excluded if <18 years of age, unable to provide informed consent, or where no polyp size was available. In patients where GB polyps were diagnosed after cholecystectomy for gallstone disease upon histopathological analysis were excluded as well, as the initial adherence to the guideline is not applicable. Records between 2014-2022 were gathered. Inclusion of patients was done by participating study centers; informed consent was obtained by the coordinating study center for all included patients.

Clinical data was gathered on baseline characteristics (age, gender, date of birth, general medical and hepatobiliary history, and ASA-classification), indication for diagnostics (GB polyps in previous imaging, abdominal pain without previous imaging, gallstones, cholecystitis, or other), and symptoms (colic pain, nonspecific abdominal pain, nausea and/or vomiting, dyspepsia, icterus, weight loss, or no specific symptoms reported i.e. incidental finding). Diagnostic imaging was reported as type of imaging (TAUS, CT, MRI, EUS, or other) and indication for imaging. Each visitation was recorded including date of imaging, present symptoms, imaging (yes/no), and if indication for cholecystectomy was present (polyp >10mm, growth >2mm, polyp >6mm with risk-factors, or other present gallstone disease). If multiple indications were present, cases were allocated according to polyp size, not growth.

Upon imaging of the GB polyp(s), the following details were, if reported, extracted: number of polyp(s), polyp size, change in polyp size between visitations, and presence of gallstones. Polyp size was classified as the largest measurement in millimeter from the (first) imaging report, in case of multiple polyps the size of the largest polyp present was recorded. Number of polyps was classified as counts or as 'multiple, number not specified'. If during follow-up imaging size was marked as 'unchanged' but no specific size was given, then the size of the previous visit was recorded for the follow-up visit. If the polyp was not visible on imaging at any time during follow-up or size was not mentioned, then size was recorded as zero. Polyp sizes were compared pre- and postoperatively based on initial imaging and histopathology reports. Type of histopathology was reported as non-neoplastic or neoplastic, and with a subtype of pathology.

Guideline adherence was compared to the guidelines from 2017 and 2021. Based on polyp size a guideline classification was assigned after each visit. Initiated treatment after each visit was recorded as conservative (with specific follow-up time) or operative. Reasons for change in policy or not following guidelines were, if present, recorded. Type of surgery was defined as laparoscopic

cholecystectomy (LC) or open cholecystectomy (OC). Pre-operative characteristics (inspection of GB) and per-operative complications were reported. Post-operative complications were defined according to the Clavien-Dindo classification and recorded until 90 days post-operatively. Post-operative mortality was defined as death within 90 days due to any cause. Duration of study follow-up was defined as time (in months) from date of diagnosis until date of last visit or mortality. Patients were considered to have visited once throughout follow-up and were left out of analysis for follow-up (FU) time.

Research question

What is the adherence to the 2017 and 2021 European guidelines in the management of GB polyps?

Outcome measures

- Adherence to the European guidelines for management of GB polyps, published in 2017 and updated in 2021[2], after first visit and during follow-up. This is defined as the number of patients having an indication for cholecystectomy versus those who actually received cholecystectomy, or those who received conservative treatment with adequate follow-up time.
- Polyp size as indication for cholecystectomy and a comparison of pre- and post-operative polyp sizes and GB polyp characteristics.
- Treatment outcomes in terms of surgical complications, pathohistological characteristics of GB polyps, and the number of patients with a histopathological diagnosis of neoplastic gallbladder polyps.

Statistical analysis

Baseline patient- and polyp characteristics were described using means and standard deviation for normally distributed variables; median and interquartile range (IQR) for non-normally distributed continuous variables; counts and percentage for discrete variables. For descriptive statistics for polyp size, sizes of zero were considered missing to have an adequate representation of mean polyp size. Missing data was not imputed. A p-value <0.05 was considered significant. Spearmans' coefficient was used to determine the relationship between the pre- and post-operative polyp sizes. Statistical analysis was conducted using SPSS version 28 (IBM SPSS Inc. Chicago, IL).

RESULTS

Between April 2018 and September 2022, 389 patients were approached for participation in the study. In total 110 patients were excluded (no informed consent (n=61), no recorded polyp size (n=48), missing data (n=1). A total of 279 patients met the inclusion criteria and were included for analysis. The population consists of 166 females (59.5%) and 113 males (40.5%); with mean age of 60 years (± 13.3 years). In 111 patients (39.8%) the GB polyps were incidentally found during diagnostic imaging unrelated to the gallbladder and no symptoms were present. Nonspecific abdominal pain was present in 50.2% of cases, and was in 34.8% of cases the reason for diagnostic imaging. Other reported symptoms were nausea/vomiting, dyspepsia, colic pain, and weight loss present in, respectively, 15.1%, 8.2%, 10.8%, and 9% of cases. In the majority of cases (24.4%) the suspicion of gallstones was reason for diagnostic imaging. TAUS was the first imaging modality used in 275 cases (98.5%), in 14 cases additional CT was performed and in one case additional MRI imaging. All additional imaging was unrelated to the GB polyp.

Table 1.

Follow-up

Of 92 patients (32.9%), only one imaging record was available, these were considered to have visited once throughout follow-up. Two or more visits were made by 187 (67.0%) patients, with mean FU time of 30.2 months (± 31.7 months) from first diagnostic date until date of last visit. With an average of 3.5 visits (± 1.9) with imaging throughout FU and a total 2.7 visits (±2.0) with imaging for the entire study group. No patients deceased during follow-up.

Polyp sizes

Polyp size at first visit was 7mm (± 2.8mm, min-max 2-16) of which 56 (20.1%) were ≥10mm, 85 (30.5%) between 6-9mm, and 138 (49.5%) <6mm. The number of polyps ranged from 1-20, and in 79 cases the number of polyps was described as 'multiple, number not specified'. Almost half of patients (46.6%) had one polyp on first imaging, which was >10mm in 29 patients. Polyp growth between visits was <1 mm on average. Between the first and second visit 15.9% of cases reported a polyp size growth >2mm. In 25 cases (8.9%) the GB polyps disappeared on imaging, seven of these patients were discontinued from surveillance according to records. Throughout FU, solitary polyps occurred most in all visits, 'multiple, number not specified' was second most common.

Table 2.

Guideline adherence after first visit

Retrospective classification according to the guidelines of 2017 and 2021, showed that 159 and 129 patients had indication for cholecystectomy after first visit, respectively. In total 43 patients received cholecystectomy after the first visit according to records. Polyp size with possible additional risk factors was a valid indication in 37 of these cases. Six patients received operative treatment for other reasons, being wish of patient (n=1), due to abdominal pain (n=1), suspicion of cholelithiasis (n=2), and unknown (n=2).

Conservative treatment was initiated for 190 patients after first visit, in 46 cases the FU period was not recorded, and therefore, recorded as missing. Three patients were discontinued from FU, even though there was an indication for FU (one with polyp size <6 plus risk factor, and two with polyp <6mm without risk factors). For seven patients with polyp size >10mm conservative treatment was initiated with different FU times (FU 1 year (n=3), FU 6 months (n=2), other FU time (n=2)). For 29 patients with indication for FU of 6 months this was adequate according to guidelines 2017 (polyp size <6 with risk factors (n=18), polyp size 6-9mm without risk factors (n=11). If classified according to the guideline of 2021, the same number of patients (n=29) had an adequate FU time of 6 months, but the indication differs (polyp size <6 with risk factors (n=10), polyp size 6-9mm without risk factors (n=19). Thirty-nine (guideline 2017) and 31 patients (guideline 2021) with polyp size 6-9mm with risk factors had an indication for cholecystectomy but were treated conservatively, and therefore had an FU after 6 months. A total of 80 patients had a FU after 1 year, but in only nine cases (2017) and 21 cases (2021) this was the adequate FU-period. Of these, three patients had an absolute indication for cholecystectomy (polyp >10mm) or FU should have been 6 months (n=68, guideline 2017; n=56, guideline 2021). Thirty-three patients received other conservative treatment, of which in 19 cases no specific agreements were made regarding FU, consequently leading to no FU in most patients. Overall, records of indications were poorly maintained and are an inadequate representation of actual operative indications. Therefore, the clinically set indications could not be compared to the guideline indications.

Table 3.

Guideline adherence during follow-up

After first FU visit, 19 patients received cholecystectomy of which 17 had a valid indication based on polyp size according to the 2017 guideline (polyp >10 (n=11), polyp 6-9mm with risk factors (n=5), polyp size <6 with risk factors (n=1)). Two patients had no indication for cholecystectomy according to the guideline, but were operated due to presence of abdominal pain.

After the second, third, fourth, and fifth follow-up visit, a total of seven, two, five, and one patient(s) received cholecystectomy, respectively. Three of these patients had no indication according the guidelines, but it was patients wish in one, suspicion of gallstones in another, and unknown reason in the last. After FU visit five no more operative treatments were initiated, although according to guidelines 2017 and 2021 at least 12 and eight patients had an indication for cholecystectomy. Conservative treatment and set FU period varied greatly between visits and often deviated from the guidelines. Most commonly a FU period of 1 year was set, while this was often not valid according to guidelines. See table 3 for an overview of the conservative follow-up periods according to the classification of the guidelines.

Operative treatment and histopathological analysis

In total, 77 patients (27.6%) received a cholecystectomy, of which polyp size was a valid indication in 66 patients (85.7%) according to the 2017 guidelines and 65 patients (84.4%) according to the 2021 guidelines. Polyp size >10mm was the indication for 45 patients (58.4%). 75 patients received a laparoscopic cholecystectomy and an open cholecystectomy was performed in two patients. Per-operative inspection was reported in nineteen patients (24.6%), in three cases a polyp was identified and in thirteen cases a gallstone was present and in three it was not mentioned what was found upon inspection. No focal wall thickening or tumor has been found upon per-operative inspection. Per-operative complications were present in 12 patients (15.6%), namely gall spill (n=10), vascular injury (n=1), and bleeding of the liver bed (n=1). Post-operative complications within 30 days were reported in four cases (1.4%); wound infection was present in two, one patient complained of dizziness with a tendency to fall, and one had severe abdominal pain and temporary liver function disorders with spontaneous recovery. No post-operative complications were recorded within 90 days.

Table 4.

Pathology

Pathology reports were present in 76 patients, GB polyps were present in 43.4%. The mean polyp size was 6.5 mm (± 2.7mm, range 2-13mm) and the polyps were most often cholesterol polyps (26.3%). None of the polyps were malignant. Controversially, in 43 patients no polyps were identified upon pathology (PA)-analyses. Moreover, 15 and 13 of these patients had an indication based on a polyp size >10mm and 6-9mm with risk factors, respectively. In 28 patients who received cholecystectomy, pathology showed different gallbladder disease, i.e. cholecystitis or cholelithiasis, present in fourteen and twelve cases, respectively. Additionally, gallstones were present in six patients. Cholesterolosis

was present in fourteen patients. Four patients had an adenoma, of these one with high grade dysplasia, one with low grade dysplasia and two without dysplasia.

Polyp size upon pathological analysis was recorded in eighteen cases. Of these, thirteen cases had a pre-operative polyp size >10mm, ultimately, in three cases polyp-size was ≥10mm after analysis (10mm, 10mm, and 13mm, respectively). Five patients had a pre-operatively polyp size 6-9 mm with an additional risk factor and showed polyp sizes of 2mm, 6mm, and 7 mm on PA-analyses. Spearman's coefficient is 0.210 (non-normally distributed data), indicating a weak monotonic relationship between the pre-operative and post-operative polyp size (p=0.403). This implies that the initial polyp size recorded via TAUS pre-operatively does not appear to correlate with the subsequent post-operative polyp size as determined through PA-analysis.

DISCUSSION

This study unveiled substantial discrepancies in the guideline recommendations and clinical practice. Guidelines from 2017 and 2021 underscore the importance of polyp size as a valid indication for operative treatment, with 85.7% and 84.4% adherence, respectively. Nevertheless, the alignment between these guidelines and actual clinical management of patients remains suboptimal, as only 48.4% and 59.7% of patients reaching indication for cholecystectomy according to 2017 and 2021 guidelines, underwent surgical intervention. Almost 40% of patients had no symptoms and were deemed incidental findings. Ultimately, almost one in four patients underwent operative treatment for GB polyps. In 43.4% of patients GB polyps were found upon histopathological analysis, none were malignant polyps. This emphasizes the necessity for a refined approach for pre-operative assessment and identification of patients for operative treatment.

In addition, guideline adherence for conservative follow-up period is low and follow-up periods are not adequately planned. After the first visit a mere 38.9% (2017) and 42.6% (2021) experienced an appropriate follow-up duration. However, with minor polyp size changes throughout visits and the tendency for polyps to not grow throughout follow-up, changes in follow-up period may be justified in clinical practice since high follow-up rates may exert high pressure on radiology services[37, 42]. Additionally, since GB polyps that are smaller than 10mm at diagnosis are almost never associated with GBC throughout FU, and diagnostic accuracy remains poor, it is even suggested that FU of GB polyps with TAUS has no additional value [21, 36]. Polyp size change between visits was low (<1 mm), this is in accordance with other studies. Kratzer et al. found that there was no significant size change throughout 30 months of follow-up (polyp size 5.0mm± 2.1mm vs. 5mm±2.8mm) or at 84 months (4.0mm± 2.3mm)[5]. Another study showed that size growth above 3mm occurred in only 6% of

patients with a polyp <10mm at diagnosis[11]. Interestingly, in this study pre- and post-operative found polyp size showed a weak correlation (*r*=0.201), indicating that polyp size registered on TAUS does not appear to correlate to the post-operative recorded polyp size. This corresponds to previous studies, where a poor correlation is shown between ultrasonography diagnosis and final pathology[36].

In 25 patients (8.9%) the polyp could not be seen on imaging during follow-up, calling into question the original diagnosis of GB polyps. Since cholesterolosis or an adhered gallstone to the GB wall may look like a polyp, they can easily be mistaken for GB polyps[43]. These findings were also reported by other studies[5, 36]. Csendes et al. found that 11% and 10% of GB polyps disappeared on imaging at 48 and 96 months, respectively[44]. Reporting of polyp disappearance raises concerns about the diagnostic accuracy on TAUS and may have aided unnecessary follow-up and patient harm.

Current guidelines for the management of GB polyps lead to a high number of unnecessary cholecystectomies. In our cohort 43 patients did not have a GB polyp on PA-analysis, even though in 28 polyp size was an absolute indication for surgery. None of the polyps were found to be malignant. Therefore, the surgical threshold of 10mm remains a subject for debate. Relying solely on polyp size as a threshold for operative treatment and for selection of neoplastic polyps is insufficient[12]. Additionally, guidelines state that solitary polyps with additional risk factors should be considered for cholecystectomy, however, this advice is questionable and holds low-quality evidence[24, 45]. This is underlined by the fact that the current study showed three solitary polyps in which size was no indication for cholecystectomy, but with presence of additional risk factors where surgically removed, and of these none were malignant. Several studies showed that polyp size alone is insufficient as pre-operative screening, whereby nearly a third of patients reach indication for surgery due to the surgical threshold[12, 46].

Sensitivity and specificity for TAUS for detecting GB polyps varies greatly between studies, with reported sensitivity of 50%-83.1%, and a specificity of 89%-99.7%[28, 33, 34, 36, 47]. Additionally, TAUS holds a high false-positive rate (85.1%) for true GB polyps, indicating that distinguishing true polyps is difficult on TAUS[34]. This high variability probably lies within the fact that ultrasonography is operator-dependent, and polyp detection and measurement are highly susceptible for measurement or operator error. As aforementioned, since 90% of polyps do not change size throughout FU this suggests that the majority of reported size changes may be attributable to measurement error[37]. Polyp size change between visits in this cohort were on average <1 mm, however data showed extreme outliers in polyp size change between visits. Some polyps were sometimes not visible on TAUS during follow-up, but were seen on the next visit, leading to a large polyp size change and outliers. At first follow-up

a total of 30 patients had a polyp growth of >2mm in between visits, however, most are likely, at least partly, due to measurement error.

To our knowledge this is the first study to prospectively look at the guideline adherence in clinical practice within the Netherlands. One previous study reported on experiences in clinical practice in accordance with the new guideline of 2017, here surveillance uptake was suboptimal at 32.8% of patients entering established formal surveillance. However, it is argued that consensus to guidelines would ultimately be clinically cost-effective, but strict adherence would exert amplified pressure on radiology services[42]. This may not be the first study addressing the management of GB polyps, but it distinctly highlights that current guidelines contribute to overtreatment of GB polyps, manifesting as unnecessary cholecystectomies and excessive follow-up procedures. There is a necessity for improved pre-operative patient selection in GB polyps, a strategy that not only proves to be cost-effective but also leads to less patient harm.

Limitations

We acknowledge several limitations in this study. Firstly, guideline adherence is based on multi-center prospectively collected data, where reporting of GB polyps and guideline adherence may vary between study centers. Additionally, variations in physicians' knowledge of guidelines and their experiences with GB polyps may influence their adherence to guidelines.

Even though, a recent study showed that polyp size on ultrasonography is highly repeatable and reproducible[32]. However, this study was performed between two trained radiologists with the same TAUS images under the same conditions. The physician's knowledge, difference in imaging and measurement error should be taken into account as polyps tend to be overestimated between 3-4 mm[33, 35]. Furthermore, limitations in description and identification of characteristics in imaging and pathology reports were observed. In many reports, essential information such as polyp size was not consistently mentioned. Measurement error and differences in interpretation in diagnostic imaging between physicians may contribute to variances in guideline adherence. Another limitation relates to the conservative treatment follow-up period that is often not well recorded, including insufficient documentation of reasons for discontinuation of FU or changes in indications for operative treatment. In patients who received conservative treatment even though there was an indication for cholecystectomy, reasons were very poorly recorded and could therefore not be taken into account for guideline adherence. However, since this is the first Dutch study on guideline adherence and how GB polyps are managed in clinical practice, it has shed light on current shortcomings and identified areas in need of improvement.

Recommendations

There is a need for improved imaging techniques and patient selection for operative treatment. Predictive models for identification of neoplastic polyps have been proposed and results are promising, however, none have yet found their way into clinical practice or guidelines[48, 49]. New imaging techniques have been proposed, such as high-resolution ultrasound (HRUS), MRI, and endoscopic ultrasound (endo-US). Although HRUS showed to accurately identify hypoechoic foci in neoplastic polyps which is a strong predictive factor for neoplastic GB polyps, strong evidence for advantages of HRUS are lacking[4]. Other imaging modalities such as MRI, endo-US, and positron-emission tomography have been studies in single-center studies with small cohorts, even though alternative imaging modalities seem promising, further research is needed in order to accurately differentiate true- and pseudo polyps[24, 28, 50]. These imaging modalities are insufficient for pre-operative selection and are associated with high costs and patient burden[24].

Currently, there is a pressing need for improved reporting and description of imaging findings. Additionally, investigating the interobserver variability is essential as measurement errors can lead to inappropriate indications for operative treatment. Alternatively, analysis of specific neoplastic polyp characteristics on TAUS may ultimately be cost-effective and of sufficient discriminatory capacity to provide adequate indications for cholecystectomy.

CONCLUSION

This study shows the discordance between current guidelines and clinical practice pose in the management of GB polyps, leading to unnecessary cholecystectomies and patient harm. Additionally, the aggressive conservative management of small polyps leads to increased costs and unnecessary follow-up imaging whereas the malignant potential of these polyps remains very small. While guideline adherence remains sub-optimal, strict adherence to the guideline may paradoxically result in further overtreatment and futile cholecystectomies. Our findings advocate towards a new approach and improved imaging diagnostics for GB polyps, specifically with more dedicated imaging and reporting, in order to improve pre-operative patient selection and identification for potential malignant polyps.

Conflicts of interest

There are no conflicts of interest.

TABLES AND FIGURES

Table 1. Baseline characteristics

	Number (%)	
Age in years (mean +/- SD)	60	13.0
Gender		
Male	113	40.5
Female	166	59.5
Incidental finding	111	39.8
ASA		
I	87	31.2
II	131	47.0
III	46	16.5
Unknown	15	5.4
Ethnicity		
European/North American	176	63.1
Indian	3	1.1
Asian	4	1.8
Other/ unknown	95	34
Medical history		
No	106	38.0
Cardiac	35	12.5
Pulmonary	39	14.0
Endocrine	36	12.9
Gastro-intestinal	76	27.2
Malignancy	57	20.4
Colon carcinoma	21	36.8
Other *	36	63.2
Hepatobiliary history		
Gallstones	19	6.8
Hepatitis BC	4	1.4
PSC	-	-
Other, not specified	34	12.2
Symptoms		
No symptoms	111	39.8
Abdominal pain, aspecific	140	50.2
Nausea / vomiting	42	15.1
Dyspepsia	23	8.2
Weight loss	25	9.0
Icterus	-	-
Colic pain	30	10.8
Reason for referral		
Abdominal pain, aspecific	103	36.9
GB polyp on earlier imaging	40	14.3
Gallstones	37	13.3
Cholecystitis	2	0.7
Other	97	34.8
Imaging diagnostics		
TAUS	275	98.6
CT	2	0.7
MRI	1	0.4
Not specified*	1	0.4
Reason for diagnostic imaging, suspicion for:		
Cholecystolithiasis	68	24.4
Cholecystitis	8	2.9
Abdominal infection	23	8.2
Abdominal malignancy	26	9.3
Abdominal pain, aspecific	97	34.8
Other	110	39.4

Figure 1. Baseline characteristics Numbers are presented as n (percentage of group). Means are presented as mean (+/- standard deviation). TAUS = Transabdominal ultasonography. *Not specified imaging included: imaging was performed elsewhere, type of imaging not specified in referral letter.

TABLE 2. Polyp number and sizes, classification according to guidelines 2017 and 2021.

	First visit		Follow-up 1		Follow-up 2		Follow-up 3		Follow-up 4		Follow-up 5		Follow-up 6		Follow-up 7		Follow-up 8		Follow-up 9	
Patients (counts)	**N=279 (%)**		**N=189 (%)**		**N=105 (%)**		**N=66 (%)**		**N=45 (%)**		**N=29 (%)**		**N= 18 (%)**		**N=11 (%)**		**N=5 (%)**		**N=3 (%)**	
Polyp size																				
≥ 10 mm	56 (20.1)		24 (12.7)		13 (12.4)		7 (10.6)		6 (13.0)		3 (10.3)		1 (5.6)		1 (9.1)		-		-	
6-9 mm	85 (30.5)		95 (50.0)		59 (56.2)		33 (50.0)		20 (45.7)		13 (44.8)		12 (66.7)		6 (54.5)		4 (80)		2 (66.7)	
< 6 mm	138 (49.5)		61 (32.2)		27 (25.7)		21 (31.8)		16 (34.8)		12 (41.4)		4 (22.2)		4 (36.4)		1 (20)		1 (33.3)	
0 mm	N/A		9 (4.8)		6 (5.7)		5 (7.6)		3 (6.5)		1 (3.4)		1 (5.6)		-		-		-	
Mean (SD)	7.0 (2.8)		6.4 (2.8)		6.6(3.0)		6.1(2.8)		6.5(2.6)		6.9(2.3)		7.1(1.8)		6.5(2.1)		6.8(1.6)		6.7(2.0)	
Number of polyps																				
0	-		5 (2.6)		3 (2.9)		3 (4.5)		3 (6.7)		1 (3.4)		-		-		-		-	
1	130 (46.6)		89 (47.0)		49 (46.7)		22 (33.3)		19 (42.2)		11 (37.9)		6 (33.3)		2 (18.1)		3 (60)		2 (66.7)	
2	35 (12.5)		20 (10.6)		14 (13.3)		9 (13.6)		4 (8.9)		6 (20.7)		2 (11.1)		2 (18.1)		1 (20)		-	
3	22 (7.9)		14 (7.4)		6 (5.7)		6 (9.0)		3 (6.7)		-		2 (11.1)		2 (18.1)		1 (20)		-	
4	5 (1.8)		9 (4.7)		3 (2.9)		2 (3.0)		-		1 (3.4)		1 (5.5)		-		-		-	
≥ 5	8 (2.9)		7 (3.7)		4 (3.8)		3 (4.5)		4 (8.9)		2 (6.9)		3 (16.7)		-		-		-	
Multiple	79 (28.3)		45 (23.8)		26(24.5)		21 (31.8)		12 (26.7)		8 (27.6)		4 (22.2)		5 (45.5)		-		1 (33.3)	
Polyp size change																				
Mean (SD)	N/A		0.002 (2.69)		0.360 (2.62)		-0.577 (2.56)		0.419 (1.57)		0.068 (1.61)		-0.294 (1.35)		0.091 (1.81)		0.400 (1.14)		0.333 (1.15)	
Range	N/A		-15 – 9		-8 – 11		-11 – 4		-3 – 6		-4 – 3		-3 – 3		-4 – 2		-1 – 2		-1 – 1	
Growth >2 mm (total count)[a]	N/A		30		16		8		5		4		1		3		1		0	
Classification guideline 2017	**279**		**189**		**105**		**66**		**45**		**29**		**18**		**11**		**5**		**3**	
Indication cholecystectomy																				
Polyp ≥10mm	56	(20.1)	24	(12.7)	13	(12.4)	7	(10.6)	6	(13.3)	3	(10.9)	1	(5.6)	1	(9.1)	-	-	-	-
Growth >2mm[d]	N/A	N/A	1	(0.5)	4	(2.9)	2	(3.0)	4	(8.8)	0	-	0	-	-	-	-	-	-	-
Polyp ≥6 with risk factors[b]	100	(35.8)	74	(39.4)	46	(43.8)	27	(40.9)	16	(35.6)	11	(37.9)	11	(61.1)	7	(63.6)	4	(80)	2	(66.7)
Indication conservative treatment																				
Polyp < 6mm no risk factors	22	(7.9)	12	(6.4)	3	(2.9)	4	(6.0)	4	(8.8)	2	(6.9)	-	-	-	-	-	-	-	-
Polyp 6-9, no risk factors	30	(10.8)	20	(10.6)	(11)	(10.4)	5	(7.6)	3	(6.7)	2	(6.9)	1	(5.6)	-	-	-	-	-	-
Polyp <6 mm with risk factors[b]	71	(25.4)	49	(25.9)	(22)	(20.9)	16	(24.2)	9	(20.0)	10	(34.5)	4	(22.2)	3	(27.3)	1	(20)	1	(33.3)
Disappearance	N/A	N/A	9	(4.8)	6	(5.7)	5	(7.6)	3	(6.7)	1	(3.4)	1	(5.6)	-	-	-	-	-	-
Classification guideline 2021																				
Indication cholecystectomy																				
Polyp ≥10mm	56	(20.1)	24	(12.7)	13	(12.4)	7	(10.6)	6	(13.3)	3	(10.9)	1	(5.6)	1	(9.1)	-	-	-	-
Growth >2mm[c]	N/A	N/A	3	(1.6)	4	(2.9)	4	(6.0)	4	(8.8)	0		0	-	1	(9.1)	-	-	-	-
Polyp ≥6 with risk factors[d]	73	(26.2)	55	(29.7)	34	(32.4)	16	(24.2)	10	(22.2)	7	(24.1)	7	(38.9)	4	(36.4)	3	(60)	1	(33.3)
Indication conservative treatment																				
Polyp < 6mm no risk factors	45	(16.1)	27	(14.3)	10	(9.5)	8	(12.1)	6	(13.3)	6	(20.7)	1	(5.6)	1	(9.1)	-	-	-	-
Polyp 6-9, no risk factors	57	(20.4)	39	(20.6)	21	(20)	13	(19.7)	9	(20)	6	(20.7)	5	(27.8)	2	(18.1)	1	(20)	1	(33.3)
Polyp <6 mm with risk factors[d]	48	(17.2)	32	(16.9)	17	(16.2)	13	(19.7)	7	(15.5)	6	(20.7)	3	(16.6)	2	(18.1)	1	(20)	1	(33.3)
Disappearance	N/A	N/A	9	(4.8)	6	(5.7)	5	(7.6)	3	(6.6)	1	(3.4)	1	(5.6)	-	-	-	-	-	-

TABLE 2. Polyp number and sizes, classification according to guidelines 2017 and 2021. Numbers are presented as n (percentage of group). Means are presented as mean (+/- SD). N/A = Not Applicable. *(a)* Total count of patients with polyp growth >2mm between visits. This includes patients with polyp >10mm or patients with 6-9 mm with risk factors. *(b)* Risk factors guideline 2017: age> 50, PSC, Indian ethnicity, sessile polyp (incl. focal wall thickening>4mm). *(c)* Includes patients which had an indication for conservative treatment according to records, but retrospective analysis showed polyp growth >2mm. These are cases were solely polyp growth >2 mm was an indication, if patients had either a polyp > 10mm or 6-9 mm with risk factors there were classified in the latter categories. *(d)* Risk factors of guideline 2021: age>60, PSC, Asian ethnicity, sessile polyp (incl. focal wall thickening >4mm). *(e)* Other reasons include: FU with imaging without reason why, imaging elsewhere, polyp around 10 mm therefore follow-up.

Table 3. Classification according to guidelines with patient trajectory throughout FU.

	First visit		FU 1		FU 2		FU 3		FU 4		FU 5		FU 6		FU 7		FU 8		FU 9	
	GL 2017	GL 2021	GL 2017	GL 2021	GL 2017	GL 2021	GL 2017	GL 2021	GL 2017	GL 2021	GL 2017	GL 2021	GL 2017	GL 2021	GL 2017	GL 2021	GL 2017	GL 2021	GL 2017	GL 2021
OPERATIVE TREATMENT	**43**		**19**		**7**		**2**		**5**		**1**		**-**		**-**		**-**		**-**	
Polyp >10mm	26	26	11	11	4	4	1	1	3	3	-	-	-	-	-	-	-	-	-	-
Polyp 6-9 mm + risk	11	11	5	4	1	1	1	1	-	-	1	1	-	-	-	-	-	-	-	-
Polyp < 6 + risk	3	2	1	0	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Polyp 6-9 no risk	1	1	0	1	0	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-
Polyp <6 no risk	2	3	0	1	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Polyp >2mm growth	-	-	1	1	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-
Polyp disappeared	-	-	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Valid indication	**37**	**37**	**17**	**16**	**5**	**5**	**2**	**2**	**4**	**4**	**1**	**1**								
No valid indication	6		2	3	2	-	-	-	1	-	-	-	-	-	-	-	-	-	-	-
Wish of patient	1		-	-	-	-	-	-	1	-	-	-	-	-	-	-	-	-	-	-
Suspicion of gallstones	2		-	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Abdominal pain	2		2	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Other / unknown	1		-	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
CONSERVATIVE TREATMENT	**190**		**133**		**76**		**50**		**31**		**19**		**14**		**7**		**4**		**2**	
Missing cases	46		37		22		14		9		9		4		4		1		1	
Follow-up after 1 year	80		76		44		32		19		17		12		5		2		1	
Polyp >10	3	3	2	2	0	0	0	0	0	0	-	-	-							
Polyp 6-9 + risk	26	17	26	21	23	16	12	7	8	5	6	4	7	4	4	3	1	1		
Polyp <6 + risk	34	22	27	15	12	8	11	8	7	4	9	5	4	3	1	1	1	1	1	1
Polyp 6-9 no risk	8	17	13	17	7	14	4	9	2	5	1	3	1	4		1				
Polyp <6 no risk	9	21	6	18	1	5	3	6	1	4	1	5	-	1						
Polyp disappeared		-	1	1	1	1	2	2	1	1	-	-	-	0						
Valid indication	**9**	**21**	**6**	**18**	**1**	**5**	**3**	**6**	**1**	**4**	**1**	**5**	**0**	**1**	**0**	**0**	**0**	**0**	**0**	**0**
Follow-up after 6 months	74		25		15		7		3						1		-		-	
Polyp >10	2	2	0	0	1	1	0	0	0	0	-	-	-	-			-	-	-	-
Polyp 6-9 + risk	39	31	16	16	6	4	3	3	2	2	-	-	-	-			-	-	-	-
Polyp <6 + risk	18	10	5	5	5	4	2	2	1	1	-	-	-	-	1	1	-	-	-	-
Polyp 6-9 no risk	11	19	2	2	2	4	0	0	0	0	-	-	-	-			-	-	-	-
Polyp <6 no risk	4	12	1	0	1	2	1	1	0	0	-	-	-	-			-	-	-	-
Polyp disappeared			1	1	0	0	1	1	0	0	-	-	-	-			-	-	-	-
Valid indication	**68**	**60**	**23**	**23**	**13**	**12**	**5**	**5**	**3**	**3**					**1**	**1**				
Discontinued from follow-up	3		14		8		7		5		1		2		1		1			
Polyp >10	-	-	0	0	0	0	0	0	0	0	-	-	0	0	-	-	-	-	-	-
Polyp 6-9 + risk	-	-	5	5	4	3	2	0	1	1	-	-	1	1	1	-	1	1	-	-
Polyp <6 + risk	1	1	5	5	1	1	0	0	2	2	-	-	0	0	-	-	-	-	-	-
Polyp 6-9 no risk	-	-	1	1	0	1	0	2	0	0	-	-	0	0	-	1	-	-	-	-
Polyp <6 no risk	2	2	1	1	1	1	1	1	2	2	-	-	0	0	-	-	-	-	-	-
Polyp disappeared	-	-	2	2	2	2	1	1	0	0	1	1	1	1	-	-	-	-	-	-
Other conservative treatment	**33**		18		**9**		7		4		1						1		1	
Polyp >10	2	2	0	0	0	0	0	0	0	0	-	-	-	-	-	-	-	-	-	-
Polyp 6-9 + risk	11	4	7	4	5	3	4	3	2	1	-	-	-	-	-	-	1	1	1	1
Polyp <6 + risk	11	10	4	3	2	0	2	2	1	1	1	1	-	-	-	-	-	-	-	-
Polyp 6-9 no risk	6	13	1	4	0	1	0	1	0	1	-	-	-	-	-	-	-	-	-	-
Polyp <6 no risk	3	4	3	4	1	2	0	0	0	0	-	-	-	-	-	-	-	-	-	-
Polyp disappeared	-	-	3	3	2	2	1	1	1	1	-	-	-	-	-	-	-	-	-	-

Other conservative treatment [A]										
No FU planned or executed	19	1	3	1	2	-	-	-	-	-
Different FU time/treatment	14	15	6	6	2	1	-	-	1	1

TABLE 3. Size classification according to guidelines 2017 and 2021 combined with patient trajectory. Numbers are presented as counts. GL 2017/GL 2021 = Guideline 2017 / Guideline 2021. Cases are classified according to guidelines 2017 and 2021 after each visit. Cases are classified according to guidelines and compared against the received operative/conservative treatment. If classification and initiated treatment were adequate according to guidelines, this was counted as valid. (A) Other conservative treatment shows the actual reported other conservative treatment; 'different treatment' was not specified in records; missing cases are not included; 'different time' includes all patient with a FU time different from guidelines (3 months up to 3 years).

Table 4. Surgical details and post-operative findings

	Operative treatment (n=77)
Cholecystectomy	
Laparoscopic	75 (97.4%)
Open	2 (2.6%)
Per-operative findings	
Polyp	3 (3.8%)
Gallstones	13 (16.9%)
Per-operative complications	
Gall spill	10 (13%)
Vascular injury	1 (1.3%)
Other	1 (1.3%)
Post-operative complications	
< 30 days	4 (5.2%)
< 90 days	0 (-)
Clavien-Dindo	
I	3 (3.8%)
II	-
III a/ b	1 (1.3%)
IV	-
V	-
Pathology report present	76 (98%)
Polyp characteristics after PA	
Polyp present	33 (43.4%)
Polyp size	6.5 (+/- 2.7)
Number of polyps	
1	2
2	1
3	1
4	-
>5	2
Multiple, number not specified	6
Polyp classification	
Neoplastic	0 (-)
Non-neoplastic	76 (100%)
Diagnosis after PA	
Adenomatosis	2 (2.6)
Adenoma[a]	4 (5.2)
Cholecystitis	14 (18.4)
Cholelithiasis	12 (15.8)
Cholecystitis + cholelithiasis	2 (2.6)
Cholesterol polyp	20 (26.3)
Cholesterolosis	14 (18.4)
Other[b]	8 (10.5)
Gallstones present	6 (7.9)

TABLE 4. Surgical details and post-operative findings. Numbers are presented as n (percentage %). (a) Adenoma: one with high grade dysplasia, one with low grade dysplasia, two without dysplasia. (b) Other includes: pseudopolyps (n=3), hyperplasia (n=1), wall hypertrophy (n=1), chronic inflammation (n=1), adenomyosis and cholelithiasis (n=1), no abnormalities (n=1).

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APPENDIX

Appendix 1.A – Flowcharts of Joint Guidelines on management of GB polyps: Guideline 2017 and updated Guideline 2021.

Figure 1.A. Joint Guideline: Management and follow-up of GB polyps, 2017 [2].

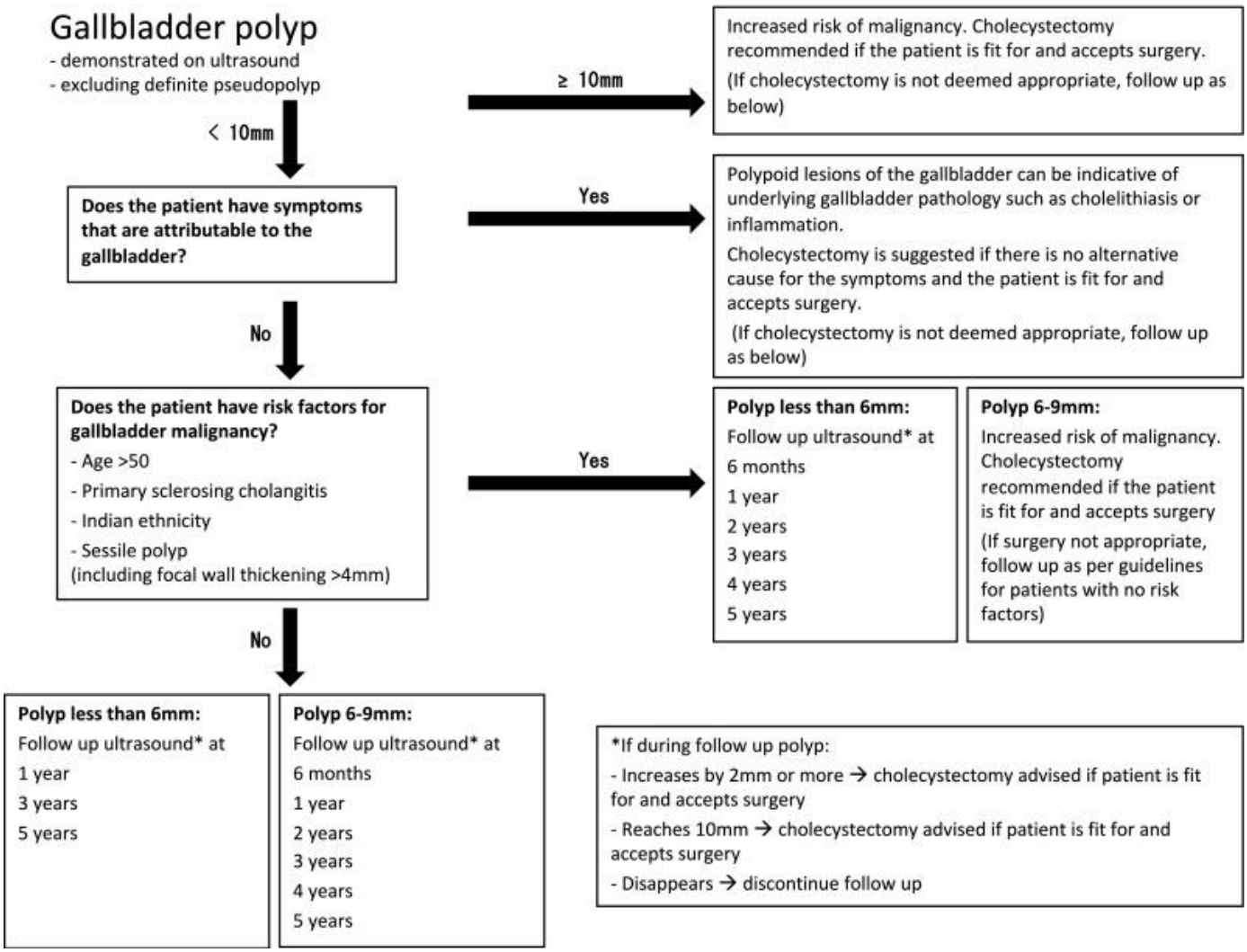
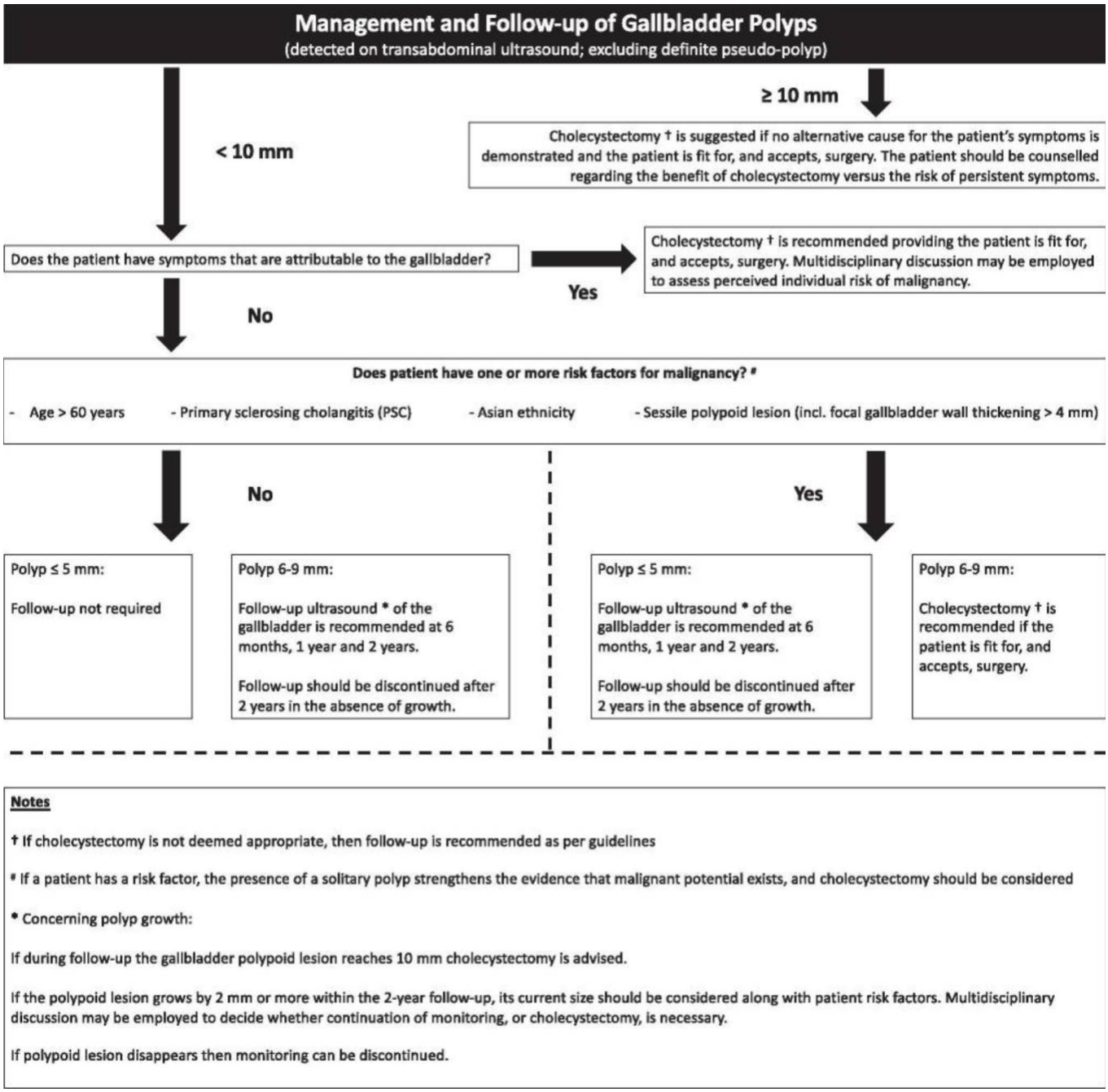


Figure 1.B. Joint Guidelines: Management and follow-up of GB polyps, updated 2021[24].



Appendix 2 – Participating study centers

- Alrijne Hospital,
- Amsterdam Medical Center (AMC), Amsterdam, the Netherlands
- Amphia Hospital, the Netherlands
- Antonius Schweitzer Hospital (ASZ), Dordrecht, the Netherlands
- Bernhoven Hospital, Uden, the Netherlands
- BovenIJ Hospital, Amsterdam, the Netherlands
- Bravis Hospital, Roosendaal, the Netherlands
- Catharina Hospital, Eindhoven, the Netherlands
- Deventer Hospital, Deventer, the Netherlands
- Elizabeth Tweesteden Hospital (ETZ), Tilburg, the Netherlands
- Flevo Hospital, Lelystad, the Netherlands
- Isala, Zwolle, the Netherlands
- Jeroen Bosch Hospital (JBZ), ‘s Hertogenbosch, the Netherlands
- Leids University Medical Center (LUMC), Leiden, the Netherlands
- Maasstad Hospital, Rotterdam, the Netherlands
- Maastricht University Medical Center (MUMC), Maastricht, the Netherlands
- Maxima Medical Center (MMC), Eindhoven, the Netherlands
- Medisch Spectrum Twente (MST), Enschede, the Netherlands
- OLVG Hospital, Amsterdam, the Netherlands
- Pantein Hospital, Boxmeer, the Netherlands
- Reinier de Graaf Hospital, Delft, the Netherlands
- Rijnstate Hospital, Arnhem, the Netherlands
- Radboud University Medical Center, Nijmegen, the Netherlands (coordinating study center)
- St. Antonius Hospital, Nieuwegein, the Netherlands
- Tergooi Hospital, Gooi- en Vechtstreek, the Netherlands
- University Medical Center Groningen (UMCG), Groningen, the Netherlands
- VU Medical Center (VUMC), Amsterdam, the Netherlands
- Hospital Gelderse Vallei (ZGV), the Netherlands
- Zuyderland Hospital, the Netherlands