

Ultrasound follow-up for gallbladder polyps less than 6 mm may not be necessary

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ABSTRACT

INTRODUCTION: The management of ultrasound (US)-detected gallbladder (GB) polyps remains a dilemma. The aim of this study was to assess the size distribution and the outcome of US follow-up of GB polyps.

MATERIAL AND METHODS: The study was approved by the Danish Data Protection Agency. US reports from patients examined with abdominal US in our department from January 2008 to the end of December 2009 were reviewed with a view to including all patients with GB polyps. Patients with GB polyps are routinely recommended a 2-year follow-up with US every six months. The GB polyp size was recorded at baseline and at subsequent US reports. Pathology reports were finally reviewed for all patients with GB polyps to check who underwent cholecystectomy and to register the histological diagnosis.

RESULTS: A total of 203 patients (median age 54 years; range 19-95 years) with GB polyps were included; 89 (44%) men and 114 (56%) women. The mean polyp size was 5 mm (range 2-40 mm). In 143 patients (70%) the GB polyp diameter was less than 6 mm. The first US follow-up was performed in 120 patients (59%), and only 31 (15%) completed the full 2-year US follow-up programme. Polyp size was stable in 100 patients, decreased in five patients, increased in eight and resolved in 15 patients. A total of 13 patients (6%) underwent cholecystectomy. Of the 203 patients, none showed neoplastic or malignant GB polyps.

CONCLUSION: We recommend that follow-up US of patients with GB polyps < 6 mm is avoided. Alternatively, the intervals between US follow-up of GB polyps < 6 mm may be extended.

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Gallbladder (GB) polyps are often detected incidentally and they are more frequently encountered with the increased use of ultrasonography (US). About 5% of the healthy population is expected to have GB polyps [1].

The majority of GB polyps are benign and when removed by cholecystectomy, the typical finding is that they consist of cholesterol and inflammatory polyps, skin folds or gallstones, but malignant transformation is a concern [1-4].

In rare cases, the resected GB polyps are malignant. In Denmark, the annual incidence of GB and bile duct

cancer is approximately 200 with a slight preponderance in women [5]. In the United States, the annual incidence is 1-2.5 cases per 100,000 for GB carcinoma alone [6], but the incidence varies widely in non-Western populations [6]. The overall prognosis for GB cancer is poor with a relative one-year survival rate of 35% for males and 29% for females, and a five-year survival rate for of 11% for males and 13% for females [5].

The risk of malignancy is increased in polyps with diameters of 10 mm or greater, age over 50 years, co-existing gallstones and rapid growth of polyps [7]. With the exception of advanced GB cancer, the US technique remains unable to differentiate between benign and malignant lesions. Polyp size greater than 10 mm is the most established predictor of malignancy [8-11]; and in polyps less than 10 mm in diameter, the risk of GB cancer is minimal [11].

GB malignancies are rare, while GB polyps are common. Almost no small polyps will therefore progress to cancer. However, the current guidelines recommend that patients with GB polyps smaller than 10 mm are followed with subsequent US to detect growth, and patients with GB polyps exceeding 10 mm are recommended a referral for cholecystectomy to ascertain the risk of malignancy [3, 4, 9, 12-14]. This strategy may result in a large number of unnecessary US examinations in patients with small GB polyps, which involves significant economic cost to the health care system and anxiety among patients.

The aim of this study was to assess the size distribution of GB polyps and the outcome of US follow-up on small GB polyps.

MATERIAL AND METHODS

The study was approved by the Danish Data Protection Agency. Retrospectively US reports from all patients examined with abdominal US in the Radiology Department in Vejle Hospital from January 2008 to the end of December 2009 were reviewed with a view to include all patients with GB polyps. A GB polyp was defined as any elevated lesion of the mucosal surface of the GB wall, with similar echogenicity as the GB wall, projected into the lumen, lack of displacement and no acoustic shadow on US. Patients with GB polyps smaller than 10 mm were routinely recommended a two-year follow-up with US

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every six months, and patients with GB polyps 10 mm or larger were recommended cholecystectomy. The patient's GB polyp size (largest diameter) was measured with an electronic ruler and recorded at baseline and in the subsequent US reports. The national electronic pathology reports (Webpatologi) were reviewed in all patients with GB polyps up to December 2011 to check who underwent cholecystectomy, which in most cases was performed as a laparoscopic procedure, and to register the histopathological diagnosis.

All US examinations and reports were performed by experienced radiologists or by an experienced sonographer in the department. All patients had been fasting at minimum of four hours before US examinations. Patients were examined in supine position and when needed in the left lateral decubitus position. All US examinations were performed on one of three different new scanners (two Siemens, one Hitachi) with abdominal, curved array transducers.

When more than one GB polyp was detected, only the largest was registered. A change in GB polyp size of 2 mm or more was considered a significant change.

Patients under eighteen years of age and patients with no recorded size of the GB polyp at baseline US were excluded. All data from the reports were entered into a computerized database designed specifically for the study.

Trial registration: not relevant.

RESULTS

A total of 231 patients with GB polyps were identified in the inclusion period. We excluded 28 patients; one patient was less than 18 years of age and 27 patients did not have a baseline measurement of polyp size. The primary causes why patients with GB polyps were referred to abdominal US were non-specific abdominal pain (127 patients, 62%) and elevated liver enzymes (21 patients, 10%). Indications for the first US are shown in **Figure 1**.

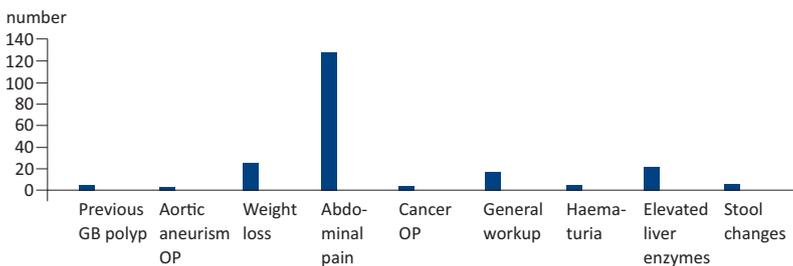
A total of 203 patients with GB polyps were included. The median age was 54 years (range of 19-95 years). There were 89 men (44%) and 114 women (56%). At baseline, 103 patients (50.7%) had one GB polyp, 29 patients (14.3%) had two GB polyps and 60 patients (29.5%) had five or more GB polyps. Simultaneously, co-existing gallstones were detected in ten patients (5%). The mean polyp size at baseline was 5 mm, with a standard deviation ± 3.9 and a range of 2-40 mm (**Figure 2**). In 175 patients (86%), GB polyp diameter was ≤ 6 mm, and in 143 patients (70%) the GB polyp was ≤ 5 mm. In nine patients, the GB polyp size at baseline was 10 mm or larger (**Figure 3**).

The first US follow-up was performed in 120 patients (59%) and only 31 (15%) completed the full two-year US follow-up programme. In the patients participating in the subsequent US follow-up, the GB polyp size was stable in 100 patients, decreased in five patients, increased in eight patients and resolved in 15 patients.

Of the 203 patients with GB polyps, 27 patients were referred to the department of surgery for cholecystectomy due to right upper quadrant abdominal pain with or without coexisting gallstones (ten patients), GB polyps measuring 10 mm or more (nine patients) or increasing polyp size (eight patients) in US follow-up. Even though the patients were informed of the risk of GB cancer, 13 of the 27 patients refused to undergo cholecystectomy. In one patient, the cholecystectomy was cancelled due to elevated age and co-morbidity. None of these 14 patients underwent cholecystectomy later during the observation period. The remaining 13 patients underwent cholecystectomy. Of the nine patients with GB polyps at baseline measuring 10 mm or more, six patients underwent cholecystectomy which revealed no neoplastic or malignant GB polyps. Of the eight patients with increasing GB polyps, four polyps increased 3 mm, three polyps increased 2 mm and one polyp in-

FIGURE 1

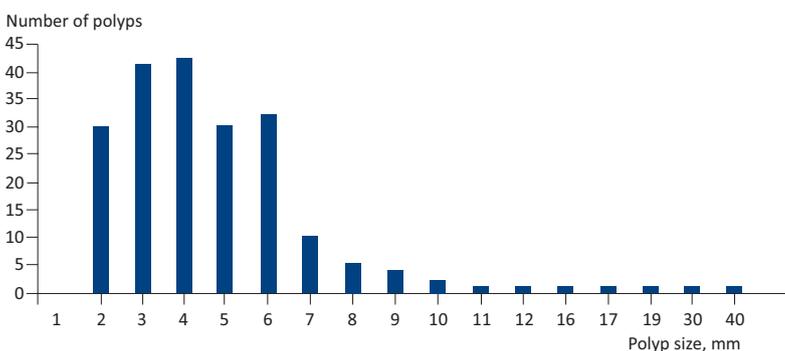
Clinical indications for referral to the first (baseline) ultrasound.



GB = gallbladder; OP = observatio pro.

FIGURE 2

Number of gallbladder polyps at baseline ultrasound versus polyp diameter.



creased 6 mm. Only the last patient, whose GB polyp increased from 4 mm to 10 mm, underwent cholecystectomy which revealed a cholesterol polyp in the GB. The remaining seven patients with increasing polyps were not operated for GB cancer. In total, the histopathological diagnosis of the GB polyps in the 13 patients who underwent cholecystectomy showed five patients with cholesterol polyps, five patients with gall stones, two patients with inflammatory polyps, one patient with a normal GB and none with neoplastic or malignant GB polyps.

DISCUSSION

The size distribution showed that a major part of small GB polyps (86%) were 6 mm or less, which is comparable to the findings made in other studies [15, 16]. In line with other studies [11, 15], we detected very few patients with increasing GB polyps. As expected owing to the low incidence of GB carcinoma and only nine GB polyps (4%) measuring 10 mm or more, we detected no GB malignancy. Nor did we register any adenoma within the polyps. Other studies found a small number of adenomas in GB polyps measuring 7-9 mm [11, 15, 16], but none in GB polyps measuring 6 mm or less. Since it remains unclear if GB adenomas are precursors to GB cancer [17], and only 19 of our 203 patients had GB polyps measuring 7-9 mm, it is difficult to make definitive conclusions for GB polyps of this size. Overall, all malignant GB polyps reported to date have been 6 mm or larger [18]. On the basis of the current evidence, we therefore recommend that small GB polyps measuring 6-9 mm be routinely followed with US every six months over a two-year period to detect any growth. A limitation to our study is the large dropout of/lack of referred patients through the follow-up period. Many patients and referring general practitioners were probably already aware of the benign character of small GB polyps, especially in cases in which no GB polyp growth was observed at the first follow-up. Another explanation may be the fact that patients who gradually become asymptomatic or treated for their primary condition do not perceive a need for follow-up ultrasound. More focus on patients with GB polyps ≥ 6 mm may increase the referral rate of patients to follow-up ultrasound. None of the dropout patients were examined with US in other hospitals in the local area. All pathology reports of the 203 patients were subsequently reviewed. All resected gall bladders undergo routine pathological examination regardless of the tentative diagnosis. Besides the 13 patients who underwent cholecystectomy, no additional patients from this study underwent cholecystectomy in Denmark up to December 2011 according to the shared national pathology reports (Webpatologi). Although it is reasonable to assume that none of the dropout patients developed GB

cancer, it is a weakness of the present study that the exact outcome of these patients remains unknown. Because all 203 patients with GB polyps only were cross-checked in the national Webpatologi, we were not able to register patients operated outside Denmark, if any.

We did not observe any GB malignancies in our cholecystectomized patients. Given the small number of large polyps and cholecystectomized patients, the correlation between polyps measuring 10 mm or more and an increased risk of malignancy cannot be shown. A GB cancer will, theoretically, develop from a small focal GB change. This study cannot discern any correlation between small GB polyps and later transformation to GB cancer. The lack of GB polyp transformation into GB cancer indicates that the presence of malignant GB polyps is extremely low. This is in concordance with findings from other studies [11, 14-16], e.g. Corwin et al found no malignancy among the 346 patients whose GB polyps they observed. Especially the lack of malignancy in frequent small GB polyps and the minimal change in GB polyp size observed in this and other studies [9, 14-16, 19] may result in a large number of unnecessary follow-up US examinations. Another weakness of this study may be the small number of cholecystectomized patients used as a gold standard to the US-diagnosed GB polyps. Many US-diagnosed GB polyps are shown to be skin folds, gallstones or inflammation in the histopathological examination [14, 15]. This fact, however, strengthens the argument that US follow-up should not be performed on small US-defined GB polyps.

Another limitation is the relatively short observation period. Furthermore, it may be considered a limitation of this retrospective study that US reports were reviewed without the archived images. On the other hand, images from US examinations are often subopti-

 FIGURE 3

Ultrasound image of the liver and gallbladder of a 61-year-old male showing a 9-mm gallbladder polyp. Cholecystectomy showed inflammation.



mal compared to live imaging and all US examinations and reports were performed by a small group of experienced observers.

The risk of malignancy is increased in GB polyps with diameters of 10 mm or greater. Current recommendations are influenced by concern for the presence of GB carcinoma and recommend cholecystectomy for lesions with a diameter of 10 mm or greater and US follow-up for lesions smaller than 10 mm. We suggest a more detailed discrimination in the management of US-defined GB polypoid lesions based on polyp size. In concordance with the literature, the majority of US-defined GB polyps detected in this study (143 of 203) were < 6 mm, and none of the polyps progressed to malignancy. The literature also fails to show a progression of small GB polyps (< 6 mm) to cancer. A recent review from Karolinska University Hospital in Sweden of the studies of GB polyps from the past 12 years recommends that GB polyps < 6 mm are not subject to follow-up [20]. In our context, we could potentially save four follow-up US per patient in 143 patients in whom small GB polyps were detected during the two-year inclusion period. This is equivalent to 286 US examinations per year in our department. In addition, patient anxiety could potentially be reduced.

In conclusion, to reduce the unnecessary follow-up US of patients with small US-defined GB polyps, we propose a revision in current guidelines. Instead of performing follow-up US of all GB polyps measuring less than 10 mm, it should be considered to avoid follow-up US of asymptomatic polyps measuring < 6 mm. Data are inconclusive for GB polyps \geq 6 mm and these are still to be followed by US or cholecystectomized. Alternatively, it should be considered if the intervals between US follow-ups of small GB polyps should be extended.

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CONFLICTS OF INTEREST: none

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