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Review

Growth rate and malignant potential of small gallbladder polyps – Systematic review of evidence

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ARTICLE INFO

Article history:
Received 22 September 2013
Received in revised form
20 December 2013
Accepted 3 January 2014
Available online 4 February 2014

Keywords:
Gallbladder
Polyps
Neoplasms
Cancer
Tumour
Carcinoma
Malignant
Adenoma
Ultrasound

ABSTRACT

The background and purpose: The overall aim of this systematic review was to determine whether ultrasound (US) follow up for gallbladder polyps (GBPs) measuring less than 10 mms is necessary.

Methods: A search was performed in MEDLINE and EMBASE between January 1976 and January 2012 using keywords: gallbladder, polyps, neoplasm, cancer, tumour, carcinoma, malignant, adenoma. Included were studies involving adult patients, examined with transabdominal US at least twice. The outcomes of included studies were gallbladder polyp growth as demonstrated on US over time, followed where available by histological examination of cholecystectomy specimens.

Main findings: Ten studies met the inclusion criteria for the review. Altogether 1958 subjects with mean age between 41.5 and 59 years were followed up with US. The percentage of GBPs which showed growth over the follow up period ranged from 1% to 23%. 43 neoplastic polyps were found in total irrespective of size, 20 of which were malignant and at least 7 of those were >10 mms. At least 7 malignancies were present in polyps <10 mms but it was unknown if they had undergone growth on follow up.

Conclusions: Level II-2 and below evidence on rate of growth of small GBPs <10 mms exists in the literature. It indicates that growth does occur in a significant minority of small GBPs, but it is slow. Due to deficient reporting and small numbers of cases, the correlation between growth of GBP and development of malignancy cannot be established using currently available evidence. Malignancy can be present in polyps <10 mms although it is significantly more frequent in polyps >10 mms. Cholecystectomy for symptomatic GBPs irrespective of their size, alongside the current practice for removal of gall bladders containing asymptomatic polyps >10 mms, is proposed. No evidence based US follow up schedule can be recommended at present for asymptomatic polyps <10 mms, and in its absence an intuitive follow up with US is likely to continue.

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1479-666X/$ – see front matter
http://dx.doi.org/10.1016/j.surge.2014.01.003

Introduction

Gallbladder polyp (GBP) is a growth protruding into its lumen from the inner gall bladder wall. Standard ultrasound (US) features of a GBP are: protrusion of internal gall bladder wall of similar echogenicity as that of the gallbladder wall and hyperechoic compared with the surrounding bile, lack of mobility, and no associated acoustic shadowing.[1]

An appreciable number are actually pseudopolyps, representing focal accumulation of cholesterol or adherent calculi, but whilst US features suggestive of a pseudopolyp have been described, an overlap of pseudopolyps with both true polyps and gallstones is common, making US differentiation difficult.[2]

GBPs are reportedly diagnosed in up to 5% of the general population, with frequency increasing due to more patients having US scans and a better US technology.[3]

True GBPs can be non-neoplastic or neoplastic. Non-neoplastic polyps comprise hyperplastic and inflammatory polyps. Neoplastic polyps can be benign or malignant; the benign ones being adenomas, adenomyomas, leiomyomas, fibromas, and lipomas, whilst malignant tumours being adenocarcinoma, squamous cell carcinoma, and mucinous cystadenoma.

Although adenomas are benign, they are seen as being pre-malignant, with an adenoma-carcinoma sequence proposed.[4]

Four out of five cases of gall bladder cancer (GBC) are diagnosed at an advanced stage, with 5-year survival rates being <15% for tumours invading muscularis mucosae or beyond.[5] It is not known how many GBCs are preceded by a GBP, but clearly differentiating the non-neoplastic from malignant or premalignant polyp is extremely important. This distinction, however, constitutes a major diagnostic challenge. Malignancy is more frequent in polyps with diameters of 10 mm or greater, presence of coexisting gall stones, solitary and symptomatic polyps, congenital and some acquired biliary anomalies, in females and with increasing patient age.[6–9] Some studies have shown an increase in prevalence of GBPs in certain ethnicity.[10] Of these factors, size of at least 10 mm is the predictor of malignancy in pre-existing GBPs. Majority of incidentally detected GBPs, however, are less than 10 mm in size and are often too small to allow accurate characterisation.

Current practice regarding the management of GBPs consists of cholecystectomy for lesions with a diameter of 10 mm or greater, and US follow-up for lesions smaller than 10 mm.

However, the threshold size above which polyps should be followed, the interval of follow-up, and its overall duration remain controversial. The knowledge about the long-term natural history of smaller than 10 mms GBPs is limited and there is no evidence based guidelines.[11]

The primary aims of this systematic review were to identify, appraise and synthetise the evidence on whether:

- GBPs smaller than 10 mms grow over time when followed up
- growth of a GBP smaller than 10 mms, as identified on US, is an indicator of malignancy.

Table 1 – Inclusion and exclusion criteria.

Criteria	Details
Participants	Only studies involving adult patients were included. Papers which dealt with other than transabdominal US imaging modalities were excluded.
Intervention	Studies in which the patient has had at least one follow up US scan of the gallbladder were included.
Outcomes	Studies were included in which the outcomes were: - gallbladder polyp growth as demonstrated on US over time, or - gallbladder polyp growth as demonstrated on US followed by histological examination of cholecystectomy specimens. Studies in which patients had cholecystectomy after a single US scan (i.e. who did not undergo US follow up) were excluded.
Study design	Randomised controlled trials, cohort studies and case control studies were included. Case studies were excluded. Both retrospective and prospective studies were included.
Additional criteria	Studies were excluded if a reasonable effort to procure a copy of the paper either in print or online failed.
Language	English and Polish language papers were included.

Methods and materials

Inclusion and exclusion criteria

The inclusion and exclusion criteria used for studies is outlined below (Table 1).

Study identification

We searched Medline and Embase via the Evidence Search databases. Papers published between January 1976 and January 2012 were included. The references for all included articles were reviewed and any relevant abstracts and full text articles were obtained and included in the review. Full search strategy is available from the authors.

Study selection

The initial list of titles followed by the abstracts for those studies which met the inclusion and exclusion criteria was reviewed independently by at least two reviewers.

For those papers whose abstracts met the inclusion criteria, the full text articles were obtained.

Data extraction

Data was extracted independently by two reviewers using the Strengthening the Reporting Skills in Epidemiology (STROBE) checklist.[12]