



Review

Can gallbladder polyps predict colorectal adenoma or even neoplasia? A systematic review



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HIGHLIGHTS

- A potential association of gallbladder polyps with colorectal adenomas and neoplasia is evident.
- Current evidence does not suffice to strongly support this hypothesis.
- Future studies are needed to shed more light to this association.

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ABSTRACT

Objective: The purpose of the present systematic review is to identify whether an association between gallbladder polyps and colorectal adenoma or neoplasia exists.

Data sources: We conducted a systematic review searching the Medline (1966–2016), Scopus (2004–2016), ClinicalTrials.gov (2008–2016) and Cochrane Central Register of Controlled Trials CENTRAL (1999–2016) databases together with reference lists from included studies.

Study eligibility criteria: All prospective and retrospective observational cohort studies were included.

Results: Four studies were finally included which included 17,437 patients. The association between gallbladder polyps and colorectal adenoma or even neoplasia is not unanimously supported. However, a possible association is clearly depicted. According to one study it seems that this correlation seems to become significant only when the gallbladder polyps exceed the size of 5 mm. However, the impact of size of gallbladder polyps was not investigated in the remaining studies.

Conclusion: According to the results of our systematic review there is some evidence to support the hypothesis that gallbladder polyps might adequately predict future risk of colorectal neoplasia. At present, however, current knowledge is very limited and the available data scarce. In this context further studies are necessary to be carried out, before the presence of gallbladder polyps on ultrasound can be recommended as an indication to perform a screening colonoscopy on the same patient.

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1. Introduction

Colorectal neoplasia (CRN), including both significant adenomas and carcinomas, has become one of the most frequent malignancies in western societies, especially during the last few decades. Progression to an invasive cancer is potentially preventable with screening colonoscopy. The risk factors for developing CRN have

been broadly studied and the results show a clear relationship between CRN and older age, glucose intolerance, metabolic syndrome, hyperlipidaemia and obesity [1–5].

The same factors that increase CRN risk are responsible for gallbladder disease as well. Several studies have shown a strong positive association between cholecystectomy and colorectal carcinoma [6–8].

Gallbladder polyps (GBPs) are found in 5% of the adult population, although true GBPs are relatively rare [9]. In most cases, other pathological lesions appear in similar form to GBPs on commonly used imaging tools, such as ultrasound or CT scan. GBPs are usually

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accidental findings, as they frequently exist for a period of time without causing any symptoms to patients [9]. In the 1970s, Christensen and Ishak examined a number of gallbladder specimens and classified their findings into different types of GBPs [10]. Although the majority of GBPs are classified as benign of cholesterol type, in everyday clinical practice the most important concern is true GBPs with malignant potential, as the latter have a poor 5-year survival when gallbladder cancer is diagnosed, ranging from 60% to 1% for patients presenting with stage 0 and IV, respectively [11]. To date, the natural history in developing gallbladder cancer from GBPs is not known. In order to minimize the cancer risk, early diagnosis, follow-up and appropriate management of GBPs are necessary. Current guidelines recommended polyps larger than 1 cm should lead to, cholecystectomy [12]. GBPs smaller than 1 cm are usually subjected to different regimes of surveillance and the therapeutic modality of choice have not been clearly defined.

Colonic polyps are overgrowths of the large bowel mucosa carrying a risk of less than 1% of becoming malignant. Colonic polyps are highly prevalent in the general population and related to age over 40 years [13]. Black race and male gender are associated with higher risk of developing colonic polyps, and in some cases people with family history of polyps [13]. Apart from familial syndromes, obesity and diet factors play a significant role on developing colonic polyps and colonic neoplasia. A known predisposition of polyps developing colon cancer exists and therefore all polyps should be removed upon diagnosis. Usually colonic polyps are asymptomatic, but occult bleeding, anemia and diarrhea can be manifestations of polyps. Stryker et al. report that the risk of cancer development from sporadic 1-cm colonic polyps is 8% and 24% at 10 years and 20 years, respectively [14]. The risk of developing cancer from colonic polyps depends on the size of the polyp, histology, and whether an association with polyposis syndromes exists.

Little is known regarding the correlation of gallbladder polyps and colorectal neoplasia. The purpose of the present systematic review is to investigate the potential association between the two pathologies. If such an association exists, the presence of gallbladder polyps on ultrasound or CT could act as an indication for screening colonoscopy.

2. Methods

2.1. Study design

The present study was designed according to the PRISMA guidelines [15]. Eligibility criteria were predetermined by the authors. No language or date restrictions were applied during the literature search. All observational studies, prospective and retrospective were held eligible for inclusion. Case reports were excluded. KS and MF abstracted and tabulated predetermined data to a structured form, while the rest reviewed them independently. Discrepancies between the authors during data collection were resolved by the consensus of all authors.

2.2. Literature search and data collection

We used Medline (1966–2016), Scopus (2004–2016), ClinicalTrials.gov (2008–2016), Cochrane Central Register of Controlled Trials CENTRAL (1999–2016) and Google Scholar (2004–2016) search engines in our primary search, together with reference lists from included studies. We restricted our search strategy to a minimum number of keywords in order to assess an eligible number that could be hand searched, minimizing the loss of articles. All the articles which met or were presumed to meet the inclusion criteria were retrieved in full text.

We searched the literature using the words “gallbladder,

colorectal, polyps”. We specifically searched PubMed using the MeSH terms (“gallbladder” [MeSH Terms] OR “gallbladder” [All Fields]) AND colorectal [All Fields] AND (“polyps” [MeSH Terms] OR “polyps” [All Fields] OR “polyp” [All Fields]). The PRISMA flow diagram summarizes the process of article retrieval (Fig. 1).

2.3. Quality assessment

We assessed the methodological quality of all included studies using the Oxford Level of Evidence criteria [16,17].

2.4. Definitions

The existence of gallbladder polyps was evaluated with ultrasonography. Gallstones were diagnosed when immobile echoes were present and protruding inside the gallbladder wall. Colorectal polyps, on the other hand, were assessed via colonoscopy.

3. Results

Two studies were excluded after retrieving the full texts because they did not study the relation of gallbladder polyps to colorectal polyps [18,19]. Four studies were finally included in our review which presented direct and indirect evidence of the studied association. Meta-analysis of pooled results was not possible due to the significant heterogeneity of included studies. Their methodological characteristics and the inclusion criteria of patients are summarized in Table 1. Their results are briefly presented in Table 2.

Specifically, in 1998, Kahn et al. suggested that the presence of gallbladder disease (polyps and/or stones) was significantly associated with colorectal polyps ($p < .001$) [20]. However, this was a retrospective study based on a questionnaire filled by patients themselves. In 2014, Jeun et al. published a prospective study on consecutive asymptomatic patients undergoing health screening tests and found that gallbladder polyps were associated with colorectal adenoma (Odds ratio = 1.796 $p = .055$) [21]. More recently, Hong et al. retrospectively studied 4626 asymptomatic individuals and reported that gallbladder polyps were associated with an increased risk of developing colorectal neoplasia ($p = .032$) [22]. However, the association was significant only when the gallbladder polyps exceeded a size of 5 mm. Contradictive evidence were presented by Lee et al. in their retrospective analysis of 44,220 participants [23]. These researchers observed that gallbladder polyps were not associated with colorectal neoplasia when they performed a multivariate analysis which included the co-assessment of age, sex, smoking status, family history of colorectal neoplasia, BMI, aspirin use, diabetes mellitus and arterial hypertension ($p = .304$).

4. Discussion

Colorectal cancer is a major health problem and today is the 2nd most common cause of cancer death in the UK. It is the 4th most common cancer following breast, prostate and lung cancer accounting for more than 33,000 diagnoses of cancer (Cancer Research UK) every year. The lifetime risk of developing the disease in the UK is 5%. Identification of risk factors, inheritance and early detection of colorectal polyps is vital and great efforts have been implicated in the past in order to diagnose and treat at a favorable stage the disease.

Based on the results of our systematic review there is evidence to support the hypothesis that the presence of gallbladder polyps is associated with a higher incidence of colorectal adenomas, which in turn may develop colorectal cancer. Exposure to the same risk factors seems to be the base of the association between gallbladder

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