

Risk Factors for Cholesterol Polyp Formation In The Gallbladder - Closely Related to Lipid Metabolism

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Abstract

Objective The purpose of this study was to assess the risk factors for cholesterol polyp formation in the gallbladder.

Method This was a multicenter retrospective study based on pathology. From January 2016 to December 2019, patients receiving cholecystectomy and non-polyp participants confirmed by continuous ultrasound follow-ups were reviewed. Patients in the cholesterol polyp group were recruited from three high-volume centers with diagnosis of pathologically confirmed cholesterol polyps larger than 10mm. Population characteristics and medical data were collected within 24 hours of admission before surgery. The non-polyp group included participants from hospital physical examination center database. They had at least two ultrasound examinations with the interval longer than 180 days. Data from the final follow-up of the non-polyp group were analyzed. The risk factors for cholesterol polyp formation were analyzed by comparing the two groups.

Results A total of 4 714 participants were recruited, including 376 cholesterol polyp patients and 4 338 non-polyp participants. In univariate analysis, clinical risk factors for cholesterol polyp were age, male gender, higher body mass index (BMI), higher low-density lipoprotein (LDL), lower high-density lipoprotein (HDL), higher aspartate aminotransferase (AST), and alanine aminotransferase (ALT). In multivariate logistic analysis, independent risk factors were age>50 years (OR=3.41, 95% CI 2.61-4.47, p<0.001), LDL>2.89mmol/L (OR=1.45, 95% CI 1.13-1.87, p=0.003), AST>40IU/L (OR=3.58, 95% CI 2.03-6.31, p<0.001) and BMI>25kg/m² (OR=1.62, 95% CI 1.23-2.13, p<0.001).

Conclusion Age, LDL, AST and BMI are strong risk factors for cholesterol polyp formation. Older overweight patients with polyps, accompanied by abnormal lipid levels, are at high risk of cholesterol polyps.

Introduction

Gallbladder polyps (GBP) are tumors or tumor-like lesions with gallbladder protrusion on mucous membranes, with an annual incidence of 6.9%-7.6% in the cholecystectomy specimen.[1, 2] Cholesterol polyps account for the majority of all polyps, ranging from 63.0%-92.0%, and the remaining belong to non-cholesterol gallbladder polyps, such as adenomatous polyps, inflammatory polyps and adenocarcinoma.[1-4] Previous studies based on ultrasound have shown variable risk factors associated with GBP, including a higher body mass index (BMI), male gender, higher glucose, higher low-density lipoprotein(LDL), lower high-density lipoprotein(HDL), increased triglyceride(TG) and higher serum total cholesterol(TC).[2, 4-8] While, no consensus has been reached, and tailored evidence for cholesterol polyps is rare. Exploring the risk factors for cholesterol polyp formation, actively controlling the risk factors to reduce the incidence of cholesterol polyps, and decreases in number of patients undergoing cholecystectomy due to cholesterol polyps are desirable to reduce the surgery trauma and economic

costs caused by unnecessary surgery. Because cholesterol polyps are benign lesions, they can be treated without surgery.

Ultrasonography is used for preliminary diagnosis of GBP, but the final diagnosis requires postoperative pathology. As differences exist in the formation and pathological process between cholesterol GBP and non-cholesterol GBP, predictor investigation of cholesterol GBP based on pathological classification is more accurate and reliable. However, to our knowledge, no such researches have been conducted. Therefore, we recruited patients with cholesterol GBP, the dominant type of GBP, according to postoperative pathology from the four-year database of three high-volume centers, to investigate specific risk factors for cholesterol GBP formation and, to provide basis for its prevention and treatment.

Method

Patients and design

From January 2016 to December 2019, patients with gallbladder cholesterol polyp and admitted in three hospitals (Department of General Surgery, Xuanwu Hospital, The First Clinical Medical College, Capital Medical University; Department of General Surgery, Peking University First Hospital; Department of General Surgery, Beijing Tiantan Hospital, Capital Medical University) were retrospectively recruited and classified as the cholesterol polyp group. Participants in the non-polyp group were recruited from Health Screening Center of Xuanwu Hospital. The study protocol was ethically approved by each hospital, and all patients provided informed consent.

For the cholesterol polyp group, inclusion criteria were as the followings: Laparoscopic cholecystectomy was performed in patients with gallbladder polyps whose maximum size was longer than 1.0 cm,[9] and cholesterol polyp group was diagnosed by postoperative pathology. Pathological analysis was independently diagnosed by two senior pathologists and confirmed by a third pathologist. The exclusion criteria were: (1) non-cholesterol polyps or mixed polyps; (2) gallbladder polyps with gallstones; (3) malignant lesions.

For the non-polyp group, the clinical data during annual physical examination in the database of the Health Screening Center of Xuanwu Hospital and recorded results of ultrasound examination were reviewed. The inclusion criteria were: (1) two or more times of ultrasonography; (2) no gallbladder lesions in any ultrasonography; (3) the interval between the first and final examination was longer than 180 days. The results of the final examination were included in the non-polyp group. The exclusion criteria were: (1) accompanied by gallstones; (2) bile duct obstructive diseases; (3) acute or chronic cholecystitis. Data from the final follow-up of the non-polyp group were collected and analyzed. The mechanism of the formation of gallstones and cholesterol polyp was unclear, so the confounding factor of gallstones was excluded in both groups.

Analysis Of Risk Factors

Data characteristics of cholesterol polyp group and non-polyp group were collected: age, gender, TG, TC, HDL, LDL, higher systolic blood pressure (SBP), diastolic blood pressure (DBP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), fasting plasma glucose (FPG) and Body mass index (BMI). BMI was deemed by dividing weight (kg) by height squared (m^2). These lab indicators were drawn as standard of care. All study participants were subjected to overnight fasting (over 12 hours) after which blood samples were drawn from an antecubital vein and the samples were used for the analysis of biochemical values. Primary data collected within 24 hours after admission in cholesterol polyp group. For non-polyp group, the data for each physical examination is recorded in real time. Both groups of patients underwent all the required exams. Overweight status was defined as BMI over $25 \text{ kg}/m^2$, according to the World Health Organization BMI criteria for an Asian population.[10]

Statistical analysis

Statistical analysis was performed using SPSS21.0 software (SPSS, Inc., Chicago, Illinois, USA). Continuous variables expressed as means \pm standard deviation(SD) were tested by Student's T-test, and skewed distribution by Mann-Whitney test which are expressed as median (interquartile range). Categorical variables were analyzed by Chi-square test or Fisher exact test. Univariate analysis was performed initially and variables with statistically significant difference were further analyzed in the multivariate logistic regression analysis. The $p < 0.05$ was considered statistically significant.

Results

This study included cholesterol polyp group and non-polyp group. In cholesterol polyp group, 664 patients with definite diagnosis of gallbladder polyps were included through postoperative pathology (**Fig. 1**). Cholesterol polyps accounted for 67.2% (446/664). Mixed polyps were defined as the presence of two or more different polyps based on postoperative pathological results, such as cholesterol polyps with adenomyosis, cholesterol polyps with adenomatous polyps, gallbladder adenomyosis with adenoma, etc. Among them, a total of 376 patients with cholesterol polyps confirmed by pathology after cholecystectomy were classified into the cholesterol polyp group after excluding polyps with gallstones or patients with cholecystitis. The mean age of patients in the cholesterol polyp group was 48.28 ± 12.81 years old, and 41.0% were female.

At the same time, in non-polyp group a total of 124 021 ultrasound results were screened. We excluded 63 192 cases of data that were not available. In the remaining 60 829 cases, the patients with at least two ultrasound records and the follow-up interval longer than 180 days were further screened out. The final 4 338 patients and their final ultrasound results were included in non-polyp group. The mean age is 40.9 ± 13.85 years old, and there were 2 049(47.2%) females.

Univariate Analysis Of Cholesterol Polyps Formation

Compared with the non-polyp group, patients in cholesterol polyp group had older age[48.28 ± 12.81 versus(vs). 40.9 ± 13.85, p < 0.001], a lower percentage of female gender[154(41.0%) vs. 2049(47.2%), p = 0.019], higher BMI(25.04 ± 4.09 vs. 23.88 ± 3.95, p < 0.001), higher SBP (125.44 ± 15.67 vs. 120.86 ± 15.99, p < 0.001), higher DBP(78.26 ± 10.34 vs. 74.38 ± 10.48, p < 0.001), higher LDL(2.91 ± 0.91vs. 2.81 ± 0.78, p = 0.037), lower HDL(1.29 ± 0.75 vs. 1.46 ± 0.37, p < 0.001), lower TC[4.30(1.38) vs. 4.58(1.14), p < 0.001], higher ALT[23.00(22.00) vs. 17.00(14.00), p < 0.001], higher AST[24.00(15.00) vs. 21.00(7.00), p < 0.001]. FPG, hypertension and TG were not statistically significant between the two groups (Table 1).

Table 1
Univariate analysis of cholesterol polyp group and non-polyp group

	Cholesterol polyp group (n = 376)	Non-polyp group (n = 4338)	P value
Age(years old)	48.28 ± 12.81	40.9 ± 13.85	< 0.001*
Age > 50 years old	240(63.8%)	1298(29.9%)	< 0.001*
Female gender	154(41.0%)	2049(47.2%)	0.019*
BMI(kg/m ²)	25.04 ± 4.09	23.88 ± 3.95	< 0.001*
BMI > 25 kg/m ²	188(49.9%)	1692(39.0%)	< 0.001*
SBP(mmHg)	125.44 ± 15.67	120.86 ± 15.99	< 0.001*
DBP(mmHg)	78.26 ± 10.34	74.38 ± 10.48	< 0.001*
Hypertension	68(18.0%)	737(17.0%)	0.588
LDL(mmol/L)	2.91 ± 0.91	2.81 ± 0.78	0.037*
LDL > 2.89 mmol/L	186(49.5%)	1822(42.0%)	0.005*
HDL(mmol/L)	1.29 ± 0.75	1.46 ± 0.37	< 0.001*
HDL < 0.90 mmol/L	44(11.7%)	694(16.0%)	0.028*
FPG(mmol/L)	5.10(1.13)	5.11(0.64)	0.971
TC(mmol/L)	4.30(1.38)	4.58(1.14)	< 0.001*
TC > 5.70 mmol/L	41(13.0%)	521(12.0%)	0.526
TG(mmol/L)	1.13(0.76)	1.08(0.91)	0.736
ALT(IU/L)	23.00(22.00)	17.00(14.00)	< 0.001*
ALT > 40 IU/L	68(18.0%)	521(12.0%)	0.001*
AST(IU/L)	24.00(15.00)	21.00(7.00)	< 0.001*
AST > 40 IU/L	49(13.0%)	304(7.0%)	< 0.001*
Values are mean ± SD, n(%) or median (interquartile range), BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; Hypertension, SBP ≥ 140 mmHg or DBP ≥ 90 mmHg; LDL, low-density lipoprotein; HDL, high-density lipoprotein; FPG, fasting plasma glucose; TC, total cholesterol; TG, triglyceride; ALT, alanine aminotransferase; AST, aspartate aminotransferase.			
* p < 0.05			

Logistic Regression Analysis Of Cholesterol Polyps Formation

The comparison between the two groups showed that age > 50 years old [odds ratio (OR) = 3.41, 95% confidence interval (CI) 2.61–4.47, $p < 0.001$], LDL > 2.89 mmol/L (OR = 1.45, 95% CI 1.13–1.87, $p = 0.003$), AST > 40 IU/L (OR = 3.58, 95% CI 2.03–6.31, $p < 0.001$) and BMI > 25 kg/m² (OR = 1.62, 95% CI 1.23–2.13, $p < 0.001$) were risk factors for cholesterol polyps. Gender, HDL, ALT were not statistically significant factors (Table 2).

Table 2
Logistic regression analysis of cholesterol polyp group and non-polyp group

	OR	95% CI	P value
Age > 50 years old	3.41	2.61–4.47	< 0.001*
Female gender	0.98	0.76–1.27	0.891
HDL < 0.90 mmol/L	0.78	0.51–1.17	0.237
LDL > 2.89 mmol/L	1.45	1.13–1.87	0.003*
ALT > 40 IU/L	0.92	0.56–1.50	0.756
AST > 40 IU/L	3.58	2.03–6.31	< 0.001*
BMI > 25 kg/m ²	1.62	1.23–2.13	< 0.001*
Hypertension, SBP \geq 140 mmHg or DBP \geq 90 mmHg; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index.			
* $p < 0.05$			

Discussion

GBPs are one of the most common diseases worldwide. Cholesterol polyps accounted dominantly in GBP patients, and was 67.2% in our study. Few previous studies have indicated that cholesterol polyps have the potential to become malignant, and surgical removal of cholesterol polyps may not be necessary. Non-surgical treatment and prevention can bring more benefits to patients because of the trauma and cost associated with unnecessary surgery. Thus, identifying the risk factors for cholesterol polyps formation is important for its prevention as well as individualized treatment. However, previous etiological studies investigating risk factors for gallbladder polyps formation failed to separate cholesterol polyps from other types, such as inflammatory polyps and adenomatous polyps.[4, 6, 8] Also, false positive results are inevitable in the diagnosis of cholesterol polyps by abdominal ultrasound, a diagnostic method widely used in previous studies.[11, 12] Thus, we recruited cholesterol polyps patients based on

pathology to avoid biases from the above confounding factor, trying to specify appropriate preventive as well as intervention measures for cholesterol polyp.

Age is an independent risk factor for cholesterol polyps. Our previous studies have found that the mean age of GBP patients is 48 years. This is consistent with our findings[13, 14] While, it is worth noting that aging may be related to changes of body's metabolism, and our previous studies have found that gallbladder polyps may disappear during long-term follow-up.[3] Self-regulation of bile metabolism may affect changes in the gallbladder mucosa. At the same time, in the cholesterol polyp group, we found a higher proportion of male, which may be related to the influence of female sex hormones on the body metabolism. But more evidence is needed.

The LDL could also contribute to cholesterol gallbladder polyp formation, and this is supported by our previous meta-analysis not specifying GBP type.[13] LDL stands for liver anabolism and cholesterol transport. High LDL can promote the formation of cholesterol polyps by lowering the sensitivity of gallbladder to cholecystokinin, which subsequent decreased gallbladder contraction, cholestasis and relative deficiency of cholic acid.[15–17] These physiological changes could promote cholesterol crystallization and polyp formation. While, Wu et al[8] found that TG, TC, HDL, and LDL showed no statistical differences between the cholesterol polyp group and the non-cholesterol polyp group, indicating that lipid levels may only play a partial role in the formation of cholesterol polyps. Thus, more potential serum indicators are needed to support our conjecture.

Liver function status had a certain influence on the formation of cholesterol polyps. The specific mechanism of the relationship between liver function status and cholesterol polyps is unclear, and the poor liver function may be related to hypermetabolic syndrome, including obesity, hyperglycemia, hyperlipidemia and hypertension.[18] Lipid metabolism, together with abnormal liver function, may interacts closely and simultaneously contribute to the formation of cholesterol polyps. The mechanisms need to be further discussed in the future. Additionally, BMI was an independent risk factor for cholesterol polyps, which is consistent with previous research. [7] Previous studies found that the formation of GBP was closely related to overweight status of patients.[18–20] Thus, weight control may help reduce the risk of cholesterol polyps formation. We suspect that both liver function metabolism and BMI may be related to abnormal lipid metabolism, which, of course, need further studies to confirm.

This paper has several limitations. Selection bias may occur in the surgeon's decision and more samples may be needed in future studies. But no previous studies have explored the risk factors of cholesterol polyps formation on a pathologic basis, and this study was performed based on multicenter data to achieve better evaluation effect. Although serum lipids are closely related to the formation of gallbladder cholesterol polyps and cholesterol calculus, other potential factors, such as bile acid and bile bacteria types may be needed to be further studied to illustrate the specific mechanism of cholesterol polyps formation.[21]

In conclusion, this study is to analyze the risk factors of cholesterol polyps on a pathological basis. Age, LDL, AST, and BMI were independent risk factors for cholesterol polyps. Active control of risk factors

affecting cholesterol polyps may reduce the incidence of cholesterol polyps, and there may be a new mechanism of cholesterol polyps in gallbladder. Lipid metabolism disorders may play an important role, which is worth further exploration in the future.

Abbreviations

BMI, higher body mass index; SBP, higher systolic blood pressure; DBP, diastolic blood pressure; LDL, higher low-density lipoprotein; HDL, lower high-density lipoprotein; TG, higher total cholesterol; TC, total cholesterol; AST, higher aspartate aminotransferase; ALT, alanine aminotransferase; GBP, Gallbladder polyps; FPG, fasting plasma glucose; OR, odds ratio; CI, confidence interval; SD, standard deviation; vs, versus.

Declarations

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Conflict of Interests

No Conflict of Interests.

Financial disclosure

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Authors' contributions

ZH YM, and XS contributed to the conception and design of the study. ZH and CL drafted the manuscript. XS, GB, and XQ performed statistical analysis and verification of the data. GW provided pathological diagnostic evidence and pathological pictures. HY retrieved and curated the data in the database. YM, XD, and SC provided valuable data resources. Each author participated in the final review.

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Availability of data and materials

The data in this article is dependable. The original data is available from the corresponding authors.

Ethics approval and consent to participate

The study protocol was ethically approved by the institutional research ethics committee of each hospital and all patients provided informed consent.

Consent for publication

Written informed consent for publication was obtained from all participants.

Competing interests

There are no competing interests in this article.

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References

1. Chen CY, Lu CL, Chang FY, Lee SD. Risk Factors for Gallbladder Polyps in the Chinese Population. *Am J Gastroenterol.* 1997;11:2066–8.
2. Zheng Y, Bai X, Yao G, Lliu L, Fei L. Risk Factors of Gallbladder Polyps Formation in East Asian Population: A Meta-Analysis and Systematic Review. *Asian J Surg.* 2020;1:52–9.
3. Guibin Y, Xuesong B, Yang C, Liu L, Zhou Z, Huang Y, et al. Analysis of Risk Factors for Gallbladder Polyp Formation - a Retrospective Study Based On Serial Ultrasounds. *Eur J Gastroen Hepat.* 2020.
4. Xu A, Zhang Y, Hu H, Zhao G, Cai J, Huang A. Gallbladder Polypoid-Lesions: What are they and How Should they be Treated? A Single-Center Experience Based On 1446 Cholecystectomy Patients. *Journal of gastrointestinal surgery: official journal of the Society for Surgery of the Alimentary Tract.* 2017;11:1804–12.
5. Shin SR, Lee JK, Lee KH, Lee KT, Rhee JC, Jang KT, et al. Can the Growth Rate of a Gallbladder Polyp Predict a Neoplastic Polyp? *J Clin Gastroenterol.* 2009;9:865–8.
6. Lee H, Kim K, Park I, Cho H, Gwak G, Yang K, et al. Preoperative Predictive Factors for Gallbladder Cholesterol Polyp Diagnosed After Laparoscopic Cholecystectomy for Polypoid Lesions of Gallbladder. *Annals of hepato-biliary-pancreatic surgery.* 2016; 4: 180–6.

7. Kim HS, Cho SK, Kim CS, Park JS. Big Data and Analysis of Risk Factors for Gallbladder Disease in the Young Generation of Korea. *Plos One*. 2019;2:e211480.
8. Wu T, Sun Z, Jiang Y, Yu J, Chang C, Dong X, et al. Strategy for Discriminating Cholesterol and Premalignancy in Polypoid Lesions of the Gallbladder: A Single-Centre, Retrospective Cohort Study. *Anz J Surg*. 2019;4:388–92.
9. Wiles R, Thoeni RF, Barbu ST, Vashist YK, Rafaelsen SR, Dewhurst C, et al. Management and Follow-Up of Gallbladder Polyps: Joint Guidelines Between the European Society of Gastrointestinal and Abdominal Radiology (ESGAR), European Association for Endoscopic Surgery and Other Interventional Techniques (EAES), International Society of Digestive Surgery - European Federation (EFISDS) and European Society of Gastrointestinal Endoscopy (ESGE). *Eur Radiol*. 2017;9:3856–66.
10. Consultation WHOExpert. Appropriate Body-Mass Index for Asian Populations and its Implications for Policy and Intervention Strategies. *Lancet*. 2004;9403:157–63.
11. Li Y, Tejirian T, Collins JC. Gallbladder Polyps: Real Or Imagined? *The American surgeon*. 2018; 10: 1670–4.
12. Yu MH, Kim YJ, Park HS, Jung SI. Benign Gallbladder Diseases: Imaging Techniques and Tips for Differentiating with Malignant Gallbladder Diseases. *World J Gastroentero*. 2020;22:2967–86.
13. Yamin Z, Xuesong B, Zhen Z, Yue H, Liwei L, Fei L. Correlation of Dyslipidemias and Gallbladder polyps-A Large Retrospective Study Among Chinese Population. *Asian J Surg*. 2020;1:181–5.
14. Zhao X, Zheng H, Shan S, Wang K, Zhang M, Xie S, et al. Association Between the non-HDL-cholesterol-to-HDL-cholesterol Ratio and the Risk of Gallbladder Polyp Formation Among Men: A Retrospective Cohort Study. *Lipids Health Dis*. 2020;1:146.
15. Kakimoto T, Kanemoto H, Fukushima K, Ohno K, Tsujimoto H. Effect of a High-Fat-High-Cholesterol Diet On Gallbladder Bile Acid Composition and Gallbladder Motility in Dogs. *Am J Vet Res*. 2017;12:1406–13.
16. Gao Y, Liu C, Li J, Zhai Y, Lin M, Wu Q, et al. Efficacy of Lidan Tang On High-Fat-Diet Induced Hepatolithiasis in Mice and Possible Mechanism. *Journal of traditional Chinese medicine = Chung i tsa chih ying wen pan*. 2020;4:584–92.
17. Evans M, Guthrie N, El-khodor BF, Metzger B, Varadharaj S. A Whole-Food-Based Health Product (A-F Betafood) Improves Gallbladder Function in Humans at Risk of Gallbladder Insufficiency: A Randomized, Placebo-Controlled Clinical Trial. *Nutrients*. 2020; 2.
18. Lim SH, Kim D, Kang JH, Song JH, Yang SY, Yim JY, et al. Hepatic Fat, Not Visceral Fat, is Associated with Gallbladder Polyps: A Study of 2643 Healthy Subjects. *J Gastroen Hepatol*. 2015;4:767–74.
19. Lee JK, Hahn SJ, Kang HW, Jung JG, Choi HS, Lee JH, et al. Visceral Obesity is Associated with Gallbladder Polyps. *Gut Liver*. 2016;1:133–9.
20. Yoon JH, Kim YJ, Baik GH, Kim YS, Suk KT, Kim JB, et al. The Impact of Body Mass Index as a Predictive Factor of Steatocholecystitis. *Hepato-gastroenterology*. 2014;132:902–7.
21. Zhao MF, Huang P, Ge CL, Sun T, Ma ZG, Ye FF. Conjugated Bile Acids in Gallbladder Bile and Serum as Potential Biomarkers for Cholesterol Polyps and Adenomatous Polyps. *Int J Biol Mark*.

