

ORIGINAL ARTICLE

## 채식주의자에 있어서 담낭 용종의 유병률은 일반인과 차이를 보이는가?

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### Is the Prevalence of Gallbladder Polyp Different between Vegetarians and General Population?

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**Background/Aims:** Gallbladder polyps (GBP) are a common clinical finding that can express malignant potential. The aim of this study was to evaluate whether vegetarianism protects against GBP, together with other putative risk factors.

**Methods:** A retrospective, cross-sectional study was conducted with subjects who received a health check-up from July 2005 to December 2011. Korean Buddhist priests, who are obligatory vegetarians by religious belief, were identified as vegetarians (vegetarian group) and compared with a non-vegetarian control group sampled from those coming for health check-ups at the same institution.

**Results:** Out of 18,483 subjects, GBP were found in 810 (4.4%). Although GBP tended to be less common in the vegetarian group (23 [3.5%] out of 666) than in control group (787 [4.4%] out of 17,817), the difference was insignificant statistically ( $p=0.233$ ). By logistic regression, old age (OR=1.61, 95% CI=1.19-2.26 for 30-39 years; OR=1.47, 95% CI=1.08-1.98 for 40-49 years), male gender (OR=1.51, 95% CI=1.31-1.75), high BMI (OR=1.18, 95% CI=1.00-1.39 for  $\geq 23.0$  kg/m<sup>2</sup> and  $< 25.0$  kg/m<sup>2</sup>) and HBsAg positivity (OR=1.53, 95% CI=1.19-1.98) were independent risk factors of GBP.

**Conclusions:** GBP was significantly associated with old age, male gender, high BMI and HBsAg positivity, but not with vegetarianism. (Korean J Gastroenterol 2015;66:268-273)

**Key Words:** Gallbladder polyp; Vegetarian diet; Metabolic syndrome; Risk factors

### INTRODUCTION

Any mucosal projection protruding into the lumen of gallbladder is defined as a gallbladder polyp (GBP). The prevalence of GBP is observed to be 3-12%, and diagnosis is increasing due to widespread use of ultrasonography for routine health check-ups and advances in imaging technology.<sup>1-4</sup>

When GBP are classified pathologically, cholesterol polyp is the most common and comprises 46% to 70% of all GBP.<sup>1,5,6</sup>

There are also hyperplasia, leiomyoma and inflammatory polyps and adenoma. The possibility of malignancy is markedly elevated when with polyps larger than 10 mm, when cholecystectomy is recommended.<sup>5</sup>

The risk factors for GBP are not established clearly despite

Received August 15, 2015. Revised September 24, 2015. Accepted October 12, 2015.

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Financial support: None. Conflict of interest: None.

its clinical importance. Among the potential risk factors, the components of metabolic syndrome, i.e., obesity, dyslipidemia and glucose intolerance are consistently reported to be important.<sup>7-11</sup> Because diet is one of the main modifiable risk factors in the development of metabolic syndrome and vegetarianism is reported to be associated with a lower risk of the metabolic syndrome,<sup>12-19</sup> we hypothesized that vegetarianism could protect against GBP. To our knowledge, there has been no research examining the relationship between GBP and vegetarianism. In this study, we tried to evaluate the risk factors of GBP by comparing Korean Buddhist priests, who are obligatory vegetarians for religious beliefs, and a sample of non-vegetarians from the same healthcare facility.

## SUBJECTS AND METHODS

### 1. Study population

A retrospective, cross-sectional study was conducted with subjects who visited Medical Screening Center in Dongguk University Ilsan Hospital (Goyang, Korea), which was founded by the Jogye Order of Korean Buddhism, for a health check-up from July 2005 to December 2011. The Korean Buddhist priests who adhere to a vegetarian diet in accordance with Buddhist teachings were assigned to the vegetarian group, and compared with the general population (control group). The following subjects were excluded: those who became Korean Buddhist priests less than five years from the index day, those who answered "yes" to a question, "Are you a vegetarian?" in the questionnaire although not Buddhist priests, cholecystectomized subjects, and those who did not undergo ultrasonography. Subjects who received a health check-up more than once were recruited for analysis just once at the time of an index check-up.

### 2. Analysis of possible risk factors

All of the subjects answered a questionnaire for dietary pattern, life styles, medications, and chronic disorders, received thorough physical examinations including anthropometric measurements, and underwent a series of biochemical tests including HBsAg, anti-HCV, hemoglobin A1c (HbA1c), total cholesterol, HDL cholesterol (HDL-C), triglyceride (TG), AST, ALT, GGT, CA 19-9 and CEA after fasting for at least 12 hours.

BMI was grouped into five categories<sup>20</sup>; BMI < 18.5 kg/m<sup>2</sup>

as underweight,  $\geq 18.5$  kg/m<sup>2</sup> but < 23 kg/m<sup>2</sup> as normal weight,  $\geq 23$  kg/m<sup>2</sup> but < 25 kg/m<sup>2</sup> as overweight,  $\geq 25$  kg/m<sup>2</sup> but < 30 kg/m<sup>2</sup> as moderate obesity and  $\geq 30$  kg/m<sup>2</sup> as severe obesity. Age was also categorized into five groups; < 30 years, 30-39 years, 40-49 years, 50-59 years and  $\geq 60$  years. Total cholesterol was categorized using the NCEPATPIII (National Cholesterol Education Program, ATP III) criteria into three groups<sup>21</sup>; < 200 mg/dL, 200 mg/dL, but < 240 mg/dL and  $\geq 240$  mg/dL. For HDL-C, 2 categories were made; < 40 mg/dL and  $\geq 40$  mg/dL in men and < 50 mg/dL and  $\geq 50$  mg/dL in women. TG was also categorized into two groups; < 150 mg/dL and  $\geq 150$  mg/dL.

### 3. Statistical analysis

The chi square test was used to analyze categorical differences, while continuous variables were compared between groups with Student's t-test. The results of univariate analysis were expressed by OR and 95% CI. To identify risk factors for GBP, a backward stepwise logistic regression was performed. All variables associated with GBP ( $p=0.05$ ) in the univariate analysis were entered in the multivariate analysis. Data were analyzed using R (<http://www.R-project.org>).

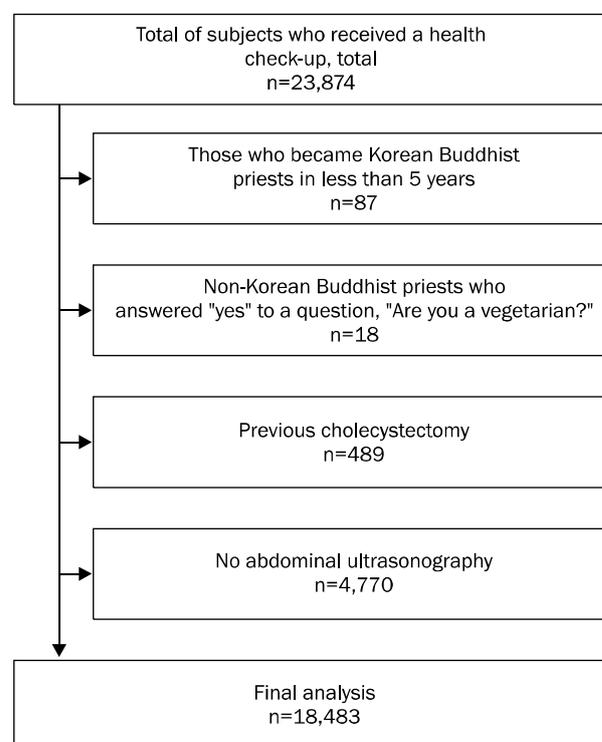


Fig. 1. Subject selection process.

## RESULTS

Altogether, 23,847 subjects received a health check-up during the study period and 5,364 ineligible subjects were excluded (Fig. 1). The final analysis was performed with 18,483 subjects and GBP were found in 810 (4.4%). There were 666 subjects in vegetarian group and 17,817 in control group. The mean age was higher and there were more females in the vegetarian group than in the control group ( $p < 0.001$  in both comparisons) (Table 1). Smoking and alcohol consumption

was less frequent in the vegetarian group (both  $p < 0.001$ ). In contrast, systolic blood pressure ( $p=0.012$ ) and the levels of serum HbA1c, TG, AST, ALT, GGT was higher ( $p=0.020$ , 0.037, 0.022 and 0.004, respectively) and the level of HDL-C was lower ( $p=0.002$ ) in vegetarian group.

Although GBP tended to be less common in vegetarian group (23 [3.5%] out of 666) than in control group (787 [4.4%] out of 17,817), the difference was not significant statistically ( $p=0.233$ ). There was no difference in the characteristics of GBP between the two groups (Table 2).

**Table 1.** Comparison of Baseline Characteristics between Vegetarian and Control Group

Characteristic	Vegetarian group (n=666)	Control group (n=17,817)	p-value
Age (yr)	49.3±10.0	43.4±10.7	< 0.001
Gender (male:female)	366:300	10,023:7,794	< 0.001
BMI (kg/m <sup>2</sup> )	24.3±3.3	23.4±3.2	0.021
Current smoking	0 (0)	3,214 (18.0)	< 0.001
Alcohol consumption	0 (0)	6,542 (36.7)	< 0.001
Systolic blood pressure (mmHg)	122.4±17.7	119.6±15.7	0.012
Diastolic blood pressure (mmHg)	78.4±12.5	77.7±12.2	0.112
HBsAg positivity	26 (3.9)	998 (5.6)	0.614
Anti-HCV positivity	5 (0.8)	152 (0.9)	0.765
HbA1c (%)	5.6±0.8	5.5±0.7	0.020
Total cholesterol (mg/dL)	196.2±38.8	194.4±35.8	0.229
HDL-C (mg/dL)	53.0±13.2	56.3±14.4	0.002
TG (mg/dL)	144.3±58.4	134.2±67.4	0.037
AST (IU/L)	28.8±18.5	24.3±19.8	0.022
ALT (IU/L)	29.9±15.6	24.9±14.2	0.015
GGT (IU/L)	34.8±24.3	30.0±20.5	0.004
CEA (ng/mL)	1.9±1.3	1.9±1.4	0.552
CA 19-9 (IU/mL)	10.9±5.3	10.5±8.5	0.552
No gallbladder polyp	23 (3.5)	787 (4.4)	0.233

Values are presented as mean±SD or n (%).

HbA1c, hemoglobin A1c; HDL-C, HDL cholesterol; TG, triglyceride.

**Table 2.** Characteristics of Gallbladder Polyps

Characteristic	Vegetarian group (n=23)	Control group (n=787)	p-value
Mean size (mm)	4.6±2.6	4.8±2.3	0.999
Size classification (mm)			
< 5	15 (65.2)	511 (64.9)	0.862
5-10	7 (30.5)	239 (30.4)	0.999
≥ 10	1 (4.3)	37 (4.7)	0.901
Mean number	1.7±1.3	1.8±1.2	0.780
Multiplicity			0.865
Single	16 (69.6)	556 (70.6)	
Multiple	7 (30.4)	231 (29.4)	
Cholecystectomy	0 (0)	32 (4.1)	NA
Cholesterol polyp	0 (0)	28 (87.4)	
Adenoma	0 (0)	2 (6.3)	
Miscellaneous	0 (0)	2 (6.3)	

Values are presented as mean±SD or n (%).

NA, not available.

By univariate analyses, old age (OR=1.81, 95% CI=1.35-2.43 for 30-39 years; OR=1.78, 95% CI=1.32-2.39 for 40-49 years), male gender (OR=1.69, 95% CI=1.48-1.92), high BMI (OR=0.50, 95% CI=0.33-0.74 for < 18.5 kg/m<sup>2</sup>; OR=1.32, 95% CI: 1.13, 1.54 for ≥ 23.0 kg/m<sup>2</sup> and < 25.0 kg/m<sup>2</sup>) and HBsAg positivity (OR=1.59, 95% CI=1.23-2.05), low HDL-C (OR=1.34, 95% CI=0.73-1.96) and high TG (OR=1.16, 95% CI=1.02-1.33) were statistically associated with GBP. However, vegetarianism was not associated with GBP in this study (OR=0.78, 95% CI=0.51-1.18) (Table 3).

Finally, old age (OR=1.61, 95% CI=1.19-2.26 for 30-39 years; OR=1.47, 95% CI=1.08-1.98 for 40-49 years), male gender

(OR=1.51, 95% CI=1.31-1.75), high BMI (OR=1.18, 95% CI=1.00-1.39 for ≥ 23.0 kg/m<sup>2</sup> and < 25.0 kg/m<sup>2</sup>) and HBsAg positivity (OR=1.53, 95% CI=1.19-1.98) were found to be independent risk factors of GBP by multivariate analyses (Table 4).

## DISCUSSION

GBP is a common clinical finding that can possess malignant potential. Although its pathogenesis and risk factors are not established, most epidemiological studies find that GBP is associated with the components of the metabolic syndrome.<sup>7-11</sup> Cholesterol polyps, the most common histological

**Table 3.** Univariate Analysis for Possible Risk Factors for Gallbladder Polyp

Variable	Gallbladder polyp		OR (95% CI)	p-value
	Yes (n=810)	No (n=17,673)		
Age (yr)				
< 30	39 (4.8)	1,381 (7.8)	1.00	
30-39	346 (42.7)	6,689 (37.8)	1.81 (1.35-2.43)	< 0.001
40-49	280 (34.6)	5,566 (31.5)	1.78 (1.32-2.39)	< 0.001
50-59	101 (12.5)	2,485 (14.1)	1.41 (1.01-1.95)	0.042
≥ 60	44 (5.4)	1,401 (7.8)	0.97 (0.66-1.42)	0.867
Gender				
Male	542 (66.9)	9,638 (54.5)	1.69 (1.48-1.92)	< 0.001
Female	268 (33.1)	8,035 (45.5)	1.00	
BMI (kg/m <sup>2</sup> )				
< 18.5	20 (2.5)	992 (5.6)	0.50 (0.33-0.74)	< 0.001
≥ 18.5, < 23.0	304 (37.5)	7,416 (42.0)	1.00	
≥ 23.0, < 25.0	222 (27.4)	4,116 (23.3)	1.32 (1.13-1.54)	< 0.001
≥ 25.0, < 30.0	242 (29.9)	4,679 (26.5)	1.26 (1.08-1.47)	0.003
≥ 30.0	22 (2.7)	470 (2.6)	1.18 (0.80-1.73)	0.411
Systolic blood pressure (mmHg)	122.4±17.7	119.6±15.7	1.80 (0.90-3.59)	0.095
Diastolic blood pressure (mmHg)	78.4±12.5	77.7±12.2	1.63 (1.19-2.24)	0.002
HBsAg positivity	53 (6.5)	741 (4.2)	1.59 (1.23-2.05)	< 0.001
Anti-HCV positivity	6 (0.7)	115 (0.6)	1.17 (0.57-2.39)	0.664
HbA1c (%)	5.6±0.8	5.5±0.7	0.94 (0.80-1.11)	0.470
Total cholesterol (mg/dL)				
< 200	482 (59.5)	10,581 (59.9)	1.00	
≥ 200, < 240	239 (29.4)	5,298 (30.0)	0.99 (0.86-1.14)	0.912
≥ 240	89 (11.1)	1,803 (10.1)	1.09 (0.89-1.34)	0.396
HDL-C (mg/dL)				
< 40 (M), < 50 (F)	224 (27.7)	4,304 (24.4)	1.34 (0.73-1.96)	0.013
≥ 40 (M), ≥ 50 (F)	586 (72.3)	13,369 (75.6)	1.00	
TG (mg/dL)				
< 150	552 (68.1)	12,611 (71.4)	1.00	0.026
≥ 150	258 (31.9)	5,062 (28.6)	1.16 (1.02-1.33)	
AST (IU/L)	27.6±15.5	27.5±14.1	1.00 (0.99-1.01)	0.546
ALT (IU/L)	28.1±13.6	25.8±13.4	1.26 (0.85-1.86)	0.210
GGT (IU/L)	32.1±19.5	33.8±20.3	1.01 (0.84-1.22)	0.388
CEA (ng/mL)	1.9±1.3	2.0±1.5	1.12 (0.85-1.48)	0.434
CA19-9 (IU/mL)	10.9±5.3	11.2±8.5	0.96 (0.64-1.43)	0.835
Vegetarianism	23 (2.8)	643 (3.6)	0.78 (0.51-1.18)	0.233

Values are presented as n (%) or mean±SD.

HbA1c, hemoglobin A1c; HDL-C, HDL cholesterol; TG, triglyceride.

**Table 4.** Multivariate Analysis for Possible Risk Factors for Gallbladder Polyp

	OR (95% CI)	p-value
Age (yr)		
< 30	1.00	
30-39	1.61 (1.19-2.26)	0.002
40-49	1.47 (1.08-1.98)	0.013
50-59	1.15 (0.83-1.61)	0.405
≥ 60	0.83 (0.56-1.22)	0.343
Gender		
Male	1.51 (1.31-1.75)	< 0.001
Female	1.00	
BMI (kg/m <sup>2</sup> )		
< 18.5	0.55 (0.37-0.82)	0.004
≥ 18.5, < 23.0	1.00	
≥ 23.0, < 25.0	1.18 (1.00-1.39)	0.047
≥ 25.0, < 30.0	1.11 (0.70-1.55)	0.239
≥ 30.0	1.05 (0.70-1.55)	0.828
Diastolic blood pressure (mmHg)	1.25 (0.89-1.74)	0.195
HBsAg positivity	1.53 (1.19-1.98)	< 0.001
HDL-C (mg/dL)		
< 40 (M), < 50 (F)	0.97 (0.84-1.14)	0.736
≥ 40 (M), ≥ 50 (F)	1	
TG (mg/dL)		
< 150	0.94 (0.81-1.10)	0.433
≥ 150	1	

Values are presented as n (%) or mean±SD.  
HDL-C, HDL cholesterol; TG, triglyceride.

type, are thought to be related with absorption and excretion of cholesterol by gallbladder mucosa.<sup>22</sup> Gallbladder cancer, to which an adenomatous polyp may progress, is associated with obesity.<sup>23</sup> As vegetarianism is an established and practical methods of alleviating the metabolic syndrome,<sup>13,24,25</sup> we assessed the possible association between vegetarianism and GBP.

Interestingly, the Korean Buddhist priests, who are among the most historied and conservative vegetarian groups, were found to be more obese than the control group in this study, unlike the results of vegetarian studies from Western countries.<sup>26</sup> This observation, however, was consistent with other Korean Buddhist vegetarian studies.<sup>27-29</sup> The Korean Buddhist priests lead a monastic and communal life in a temple, ordinarily in rural seclusion. Traditionally, they avoid the following foods in accordance with Buddhist teaching: 1) food of animal origin, except milk products; 2) five pungent vegetables (osinchaе): garlic (*Allium sativum*), welsh onion (*Allium fistulosum*), wild garlic (*Allium monathum*), garlic chives (*Allium tuberosum*) and asafetida (*Ferula asafoetida*); 3) al-

cohol; and 4) high amounts of processed food.<sup>30</sup> Therefore, their diet is characterized by a very low fat and sugar content with rich crude fiber. However, as South Korea has become more westernized, the modern Korean Buddhist priests occasionally consume milk, yoghurt, cheese or breads, cookies, and cakes, which often contain eggs or butter, though they eat mainly so called "Temple Food".<sup>27</sup> Snacks rich in cholesterol and animal fat may contribute to obesity of the modern Korean Buddhist priests. In addition, they do not get enough exercise because they practice still asceticism, as contrasted with vegetarians in Western countries who tend to have health-related motivation and take active exercise. The higher levels of BMI, systolic blood pressure, HbA1c, TG, and liver enzymes in the vegetarian group might be interpreted in a similar way. Besides, it should not be overlooked that the mean age was lower in control group than in vegetarian group because we included only those who had been the Korean Buddhist priests at least five years before enrollment to observe the effects of chronic exposure. A protective effect of vegetarianism on GBP was not found in this study. If adjustment for such factors had been possible, however, the results might have been different. Prospective, controlled studies can compare vegetarian and non-vegetarian groups with similar life styles.

HBV positivity was a risk factor for GBP according to our data. This is not surprising since many studies from endemic regions of HBV infection report the same finding.<sup>3,22,31</sup> Although the role of HBV in formation of GBP needs further investigations, Yang et al.<sup>22</sup> suggested inflammatory reactions and alteration in bile composition as possible mechanisms.

Despite its uniqueness, this study has a few limitations in addition to uncontrolled life style mentioned above. First, there were no models and photographs of food for portion sizes and detailed information for ingredients was unavailable. Second, there may be a selection bias since the subjects were self-motivated for a health check-up. Third, this was a retrospective, single center study with a limited number of vegetarians.

In conclusion, when comparisons were made between the Korean Buddhist priests and the control sample, GBP was significantly associated with old age, male gender, high BMI and HBsAg positivity, but not with vegetarianism.

## ACKNOWLEDGEMENTS

The authors thank Mr. Ho Jung Lee for providing English proofreading of the manuscript.

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