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Origional Research Article

The Relationship between Obesity Indicator and Gallbladder Polyps

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Abstract: **Background:** Recent studies have shown that obesity and impaired glucose tolerance are associated with gallbladder polyps (GBP), and are currently considered risk factors for gallbladder cancer. Therefore, the prevalence of GBP seems to be increasing. However, there is less studies discussing the correlation between obesity indicators and gallbladder polyps. **Purpose:** This study used adult health examination data analysis to understand the association of obesity indicators with GBP. **Methods:** This study is a cross-sectional data analysis study. The study collected the medical examinations of a regional hospital in Kaohsiung from 2011 to 2016. Gallbladder polyps were determined by abdominal ultrasound scanning. Use waist circumference (WC), body mass index (BMI), and waist-height ratio (WHR) as the obesity indicator. All statistical analysis was performed using the SPSS 20.0 software package for Windows. **Results:** The higher rate of abnormal GBP was male, less than 40 years old, normal waist circumference, normal waist-height ratio, and normal BMI. Performed a logistic regression analysis. The variables included in the regression analysis are: gender, age, BMI, WC, WHR. The results show WHR and BMI are protective factor for gallbladder polyps, odds ratio and 95% (confidence interval, CI) are (OR=0.544, 95% CI=0.442-0.670) and (OR=0.782, 95%CI=0.613-0.998) respectively. **Conclusions:** For the obesity indicators, this study found that WHR and BMI are protective factor for GBP.
Keywords: Gallbladder polyps, health examination, waist circumference, body mass index, waist-height ratio.

INTRODUCTION

Gallbladder polyps (GBP) are defined as any type of gallbladder mass, and are discovered when performing ultrasonic examinations, which are widely used for health examinations. GBP are roughly classified as true polyps and pseudo polyps. True polyps include adenomas and adenocarcinomas; pseudo polyps contain cholesterol polyps, inflammatory polyps and hyperplastic polyps (Christensen, A. H. 1970). Recent studies have shown that obesity and abnormal glucose tolerance are associated with GBP and are currently considered to be risk factors for gallbladder cancer (Shim, S. G., *et al.,* 1999; Chen, C. Y. , *et al.*, 1997; Renehan, A. G., *et al.*, 2008; Kuriyama, S., *et al.*, 2005; Larsson, S. C., & Wolk, A. 2007; Segawa, K., *et al.*, 1992; Kim, S. Y. *et al.*, 2006). Therefore, the prevalence of GBP seems to be increasing.

The prevalence of GBP estimated by abdominal ultrasonography (USG) is 3% to 12% of the total population (Lee, K. F. *et al.*, 2004; Hayashi, Y., *et al.*, 1996; Lin, W. R., *et al.*, 2008, Pandey, M.*et al.*, 1996). In pathology, cholesterol polyps are the most common and account for 46% to 70% of all GBP (Lee, K. F. *et al.*, 2004; Yang, H. L. *et al.*, 1992; Wan, Y. L. 1989). One study used visceral adipose tissue (VAT) and total adipose tissue (TAT) to measure visceral obesity associated with GBP regardless of body mass index or waist circumference (Lee, J. K. *et al.*,2016).

Another study about Koreans showed that metabolic syndrome, male, insulin resistance, and abdominal obesity are risk factors for gallbladder polyps. Therefore, it is believed that metabolic syndrome is strongly associated with gallbladder polyps in Koreans (Lim, S. H.*et al.*, 2007). Obesity (Segawa, K. *et al.*, 1992), glucose intolerance or increased BMI (Shim, S. G. et al., 1999; Kim, S. Y. *et al.*, 2006) are considered by the literature to be associated with gallbladder polyps. These reports indicate that risk factors for gallbladder polyps are probably related to lifestyle habits such as eating habits and daily activities. In addition, obesity and glucose intolerance are the main causes of metabolic syndrome, which is related to

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lifestyle. Obesity is an important risk factor for gallbladder (GB) cancer. Among more than 181,000 people in The Cancer Prevention Study II Nutrition Cohort, compared with people with normal BMI, the relative risk of GB cancer in subjects with a BMI of 30.0 to 34.9 was 1.8-fold (95% CI, 1.1 to 2.9). Particularly, obese female had a relative risk of 2.1-fold (95% CI, 1.6 to 2.9) compared with female with normal BMI (Calle, E. E. *et al.*, 2002). Larsson and Wolk concluded that obesity increases the risk of GB cancer in a meta-analysis of integrated analysis with 3,288 cases (Larsson, S. C., & Wolk, A. 2007).

The correlation between obesity indicators and gallbladder polyps is rarely discussed domestically and abroad. Therefore, this study uses adult health examination data analysis to understand the correlation of obesity indicators to gallbladder polyps.

METHODS

Study design

This study uses cross-sectional study design, the medical examinations were collected from a regional hospital in Kaohsiung from 2011 to 2016, using physical examinations and blood test data as analytical data. All participants were above 20 years of age and met fasting for the examinations.

Inclusion criteria: Using the people who participated in adult health examination from 2011 to 2016 as subjects.

Exclusion criteria: Age < 20 years old and deducted the incomplete blood test data and repeated screening.

Definition of Variables：

Height and weight data were obtained using standardized techniques and equipment.

1. Definition of obesity indicators (Shiao, W. C. *et al.*, 2019)
   - Abnormal waist circumference: Male: ≧ 90 cm, female: ≧ 80 cm. WC was measured at the midpoint between the bottom of the rib cage and the top of the iliac crest.
   - Waist-height ratio: Normal (< 0.5), abnormal (≧0.5)。
   - WHtR was calculated as WC divided by height.
   - Body Mass Index: Categorize body mass index according to the criteria of the Ministry of Health and Welfare in 2004.

   Underweight: BMI≤18.4kg/m2
   Normal: BMI between 18.5-23.9kg/m2
   Overweight: BMI between 24.0-26.9kg/m2
   Obese: BMI≥27kg/m2
   BMI was calculated by dividing the weight in kilos on the square of the height in meters.
2. Gallbladder polyps:

   When required to be diagnosed as gallbladder polyp by a gastro-intestinal specialist through abdominal ultrasound and is recorded in the health examination data file, it is seen as individual case in this study.

Ethical Considerations

This study began the data collection after approval by the hospital's Institutional Review Board (IRB). Any identifiable information had been through unlinking process.

Data processing and statistical analysis

All statistical analysis was performed using the SPSS 20.0 software package for Windows (SPSS Taiwan Corp.). Statistical methods include: descriptive statistics (frequency distributions, percentage, mean and standard deviation), analytical statistics: chi-square test, logistic regression. These are used to analyze the effects of obesity indicators on gallbladder polyps. The statistically significant level is α=0.05, and the confidence interval (CI) is 95%.

RESULTS

16,459 cases were included in the analysis from 2011-2016.Table 1 shows the definition of obesity index (Christensen, A. H.1970). 1.Abnormal prevalence of WC (male: ≧90 cm, female: ≧80 cm) 20.5%. (Shim, S. G.*et al.*, 1999). 2. The prevalence rate for abnormal WHR (≧0.5) is 32.1%. 3. Categorize Body Mass Index (BMI) according to the criteria of the Ministry of Health and Welfare in 2004. Underweight BMI≤18.4kg/m^2(3.8%); normal BMI from 18.5-23.9kg/m^2(48.1%); overweight BMI from 24.0-26.9kg/m^2(26.7%), obesity BMI≥27kg/m^2(21.4%). The abnormal rate of gallbladder polyps was 5.6%.

Table 2 shows that there was a higher prevalence of gallbladder polyps among men, those who are younger than 40 years old, normal WC, normal WHR, and normal BMI, which all reach statistically significant difference. Logistic regression analysis was performed for whether there are gallbladder polyps or not in Table 3. The variables included in the regression analysis are: gender, age, BMI, WC, WHR. It is shown that WHR and BMI are protective factors for gallbladder polyps; the odds ratio (OR) and 95% CI are respectively (OR=0.544, 95% CI=0.442-0.670), (OR=0.782, 95% CI=0.613-0.998).

DISCUSSIONS

The World Health Organization officially listed obesity as a chronic disease in 1996. Among the top five causes of death, cancer, stroke, heart disease, diabetes, and many other chronic diseases and obesity are closely related. Obesity is also the second cause of early death in adults, second only to the effects of smoking. With the increase in the prevalence of obesity globally, and the complications and the huge medical expenditures that comes along with it, obesity has become a public health issue that compatriot must pay attention to.

In the "2013-2014 Nutrition and Health Survey in Taiwan(NAHSIT)" in Taiwan, the prevalence of overweight and obesity in adults is 43%, of which the ratio for male is 48.9%, and the ratio for female is 38.3%. (Note: Adult BMI cut-off weight is 24≦BMI<27kg/m^2, obesity is BMI≧27kg/m^2). This study includes 16,459 cases in the analysis from 2011-2016. The results showed that the definition of obesity indicators (Christensen, A. H. 1970). 1.The prevalence of abnormal waist circumference (male: ≧90 cm, female: ≧80 cm) 20.5%. (Shim, S. G. *et al.,* 1999) 2.Abnormal waist-height ratio (≧0.5). The prevalence is 32.1%. (Chen, C. Y. *et al.*, 1997). 3. Body mass index (BMI) ≤ 18.4 kg/m^2 (3.8%), 18.5-23.9 kg/m^2 (48.1%), 24.0-26.9 kg/m^2 (26.7%), and BMI ≥ 27 kg/m^2 (21.4%). Among them, subjects with excessive BMI and obesity were lower than domestic surveys. It may be that the study subjects were from a single hospital, due to regional differences.

Ultrasound is the first choice of methods for screening gallbladder and biliary tract diseases with a diagnostic rate of 95%. Gallbladder polyps refer to benign neoplastic tissue that grow from the gallbladder wall. Gallbladder polyps are not uncommon, with an incidence rate of about 4%.

The prevalence of gallbladder polyps varies from country to country (Lin, W. R. *et al.*, 2008) and may vary from urban to agricultural/rural districts (Hayashi, Y., *et al.*, 1996). Reports from countries other than South Korea show that the prevalence of gallbladder polyps is about 5% (Jørgensen, T., & Jensen, K. H. 1990). The prevalence rate in Korea is 3% (Shim, S. G. *et al.*, 1999). The prevalence rate in a single institution was 2.2% (Kuriyama, S. *et al.,* 2005), and the prevalence of gallbladder polyps in this study was 5.6%, slightly higher than domestic. It shows that there is a higher prevalence of gallbladder polyps in the southern region.

In addition, logistic regression analysis was performed for whether there are GBP or not. The variables included in the regression analysis are: gender, age, BMI, WC, WHR. It is shown that men suffering from GBP are 1.591 times higher than females (95% CI = 1.384-1.830). Most of the current studies have shown that the prevalence of male GBP is higher than that of females (Chen, C. Y. *et al.*, 1997; Segawa, K., *et al.*, 1992; Jørgensen, T., & Jensen, K. H. 1990). This study also showed the same results. Therefore, being a male is considered a risk factor for GBP. In this study, the WHR and BMI were the protective factors of GBP. The OR and 95% CI were (OR=0.544, 95% CI=0.442-0.670), (OR=0.782, 95%CI=0.613-0.998). However, the risk factor for GBP has not been clearly established, despite its clinical importance. Although older age, male, and metabolic syndrome are more likely to be associated with GBP, their results are not always consistent (Shim, S. G., *et al*., 1999; Segawa, K., *et al.*, 1992; Kim, S. Y. *et al.*, 2006; Lim, S. H. *et al.,* 2007). Especially that there are conflicting reports on obesity (Chen, C. Y. *et al.*, 1997; Jørgensen, T., & Jensen, K. H., 1990; Canturk, Z. *et al.*, 2007). Some studies also shown that no association between obesity and GBP were found (Chen, C. Y. *et al.*,1997; Jørgensen, T., & Jensen, K. H.1990). In particular, there are few literatures on WC, WHR and BMI as the main subject of discussion. Therefore, it is difficult to compare this study with previous studies, but it can be used as a reference for follow-up researchers.

Finally, cholesterol polyps, adenomatous polyps, and inflammatory polyps were considered GBP in this study. In fact, all polyps are included in the group of polyps, regardless of the size and form of the polyps, which may affect the results of the study. However, unless confirmed by histopathology after surgery, it is very difficult to make a clear pathological diagnosis of GBP, and therefore all polyps must be classified in the same category. Future research can classify polyps base on size and quantity and the results of pathological examinations, and then perform a more detailed analysis of obesity indicators, perhaps there will be a clearer finding.

Study limitations

Although our study is unique, there are still many limitations. First, the study subjects were patients who went to the health examination center of the hospital, and therefore did not represent the entire community. Moreover, using the physical examination data analysis could not fully collect the potential impact factors that affect GBP, such as the absence of body fat and muscle mass measurement subjects excluded, may underestimate the risk factors of GBP. Furthermore, the study was retrospective and cross-sectional designed, the duration of obesity was not estimated, and the temporal association between obesity and GBP could not be assessed.

Table-1 Demographic characteristics, obesity indicators and gallbladder polyps of the subjects descriptive statistics (n=16459)

Variables	Number of people	Percentage	Mean ± standard deviation
Gender			
Male	8987	54.6	
Female	7472	45.4	
Age			45.4±11.4
＜40 years old	5735	34.8	
40 years old and above	10724	65.2	
Waist circumference			77.7±10.9
Normal	13092	79.5	
Abnormal	3367	20.5	
BMI			24.3±3.9
BMI＜27 kg/m^2	12940	78.6	
BMI≥27 kg/m^2	3519	21.4	
BMI			
≤18.4kg/m^2	627	3.8	
18.5-23.9kg/m^2	7918	48.1	
24.0-26.9kg/m^2	4395	26.7	
≥27 kg/m^2	3519	21.4	
Waist-height ratio			
Normal	11170	67.9	
Abnormal	5289	32.1	
Gallbladder polyps			
Without	15541	94.4	
With	918	5.6	

Abnormal waist circumference: Male: ≧90 cm, female: ≧80cm
Waist-height ratio: Normal (＜0.5), abnormal (≧0.5)

Table -2 Correlation analysis between gallbladder polyps, demographic characteristics and obesity indicators (n=16459)

Variables	Without gallbladder polyps (n=15541)		With gallbladder polyps (n=918)		*P* value
	Number of people	Percentage	Number of people	Percentage	
Gender					<.001
Male	8416	93.6	571	6.4	
Female	7125	95.4	347	4.6	
Age					0.014
＜40 years old	5380	93.8	355	6.2	
40 years old and above	10161	94.8	563	5.2	
Waist circumference					<.001
Normal	12288	93.9	804	6.1	
Abnormal	3253	96.6	114	3.4	
Waist-height ratio					<.001
Normal	10440	93.5	730	6.5	
Abnormal	5101	96.4	188	3.6	
BMI					<.001
BMI<27 kg/m^2	12145	93.9	795	6.1	
BMI≥27 kg/m^2	3396	96.5	123	3.5	
BMI					<.001
≤18.4kg/m^2	604	96.3	23	3.7	
18.5-23.9kg/m^2	7428	93.8	490	6.2	
24.0-26.9kg/m^2	4113	93.6	282	6.4	
≥27 kg/m^2	3396	96.5	123	3.5	

Note: Using chi-square statistical analysis, and using two-tailed test, significant level α=.05.
Abnormal waist circumference: Male: ≧90 cm, female: ≧80cm
Waist-height ratio: Normal (＜0.5), abnormal (≧0.5)

Table-3 Regression analysis of obesity indicators on gallbladder polyps (n=16459)

Item	β	wald	OR(95%CI)	*P value*
Gender (female)	0.465	42.563	1.591(1.384-1.830)	<.001
WHR (normal)	-0.609	33.095	0.544(0.442-0.670)	<.001
BMI (<27kg/m^2)	-0.246	3.894	0.782(0.613-0.998)	0.048

Note 1: The method is stepwise logistic regression, the variables included in this regression analysis model are: gender, age, BMI, WC, WHR.
() those in parentheses are reference groups.

Note 2: According to the variables: 1 With gallbladder polyps, 0 Without gallbladder polyps.

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