

The Investigation on the Correlation between Obesity Indicator and Hepatitis B and C

Abstract

Background: Obesity is an important health issue worldwide, and hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are the two major causes of liver disease that lead to Taiwan's medical health and socio-economic problems. There are currently few studies in the nation on the correlation between obesity indicators and hepatitis B and C.

Purpose: This study uses adult health check data analysis to understand the correlation of obesity indicators and hepatitis B and C.

Methods: This study is a cross-sectional research. The study collected people who did health examinations of a regional hospital in Kaohsiung from 2011 to 2016. The waist circumference (WC), body mass index (BMI), and waist-height ratio (WHR) are used as obesity indicators.

Results: A total of 16,459 cases were included in the analysis. The prevalence of abnormal WC is 20.5%, and the WHR abnormal prevalence rate is 32.1%. Underweight Body Mass Index (BMI) $BMI \leq 18.4 \text{ kg/m}^2$ (3.8%), normal BMI ranging from $18.5\text{--}23.9 \text{ kg/m}^2$ (48.1%), overweight BMI ranging from $24.0\text{--}26.9 \text{ kg/m}^2$ (26.7%), obesity $BMI \geq 27 \text{ kg/m}^2$ (21.4%). The abnormal rate of hepatitis B was 13.6%, and the abnormal rate of hepatitis C was 1.9%. Logistic regression analysis shows that WC is a risk factor for hepatitis B ($OR=1.181$, $95\%CI=1.014\text{--}1.377$), and WHR is a protective factor ($OR=0.771$, $95\%CI=0.673\text{--}0.885$). WHR is a risk factor for hepatitis C ($OR=1.571$, $95\%CI=1.246\text{--}1.981$).

Conclusions: The WC and WHR are respectively the risk factors for hepatitis B and hepatitis C, and the WHR is the protective factor for hepatitis B.

Key words: Waist circumference (WC), Waist-height ratio (WHR), Body mass index (BMI), Hepatitis B, Hepatitis C

29 **Introduction**

30 Taiwan is an area with high prevalence of hepatitis B, and the carrier rate in general
31 population is about 15% to 20%. The prevalence of hepatitis C is about 4%. Chronic hepatitis
32 B and C are the main causes of liver cancer. According to the survey, about 70% of patients
33 who die of liver cancer are those with hepatitis B and 20% are those with chronic hepatitis C
34 infection. The risk of HCC is increased by more than 100 times if carriers of hepatitis B virus
35 (HBV) or hepatitis C virus (HCV) patients also suffer from obesity and diabetes, there is a
36 multiplication effect. It is pointed out that both obesity and diabetes are risk factors for
37 predicting hepatocellular carcinoma (HCC), and with the differences of infection status of
38 HBV and HCV, it will affect the prevention of HCC (1).

39 Previous studies on chronic liver disease and obesity have shown in Mexico, the
40 prevalence of chronic liver disease is increasing (2,3) with obesity, diabetes, and metabolic
41 syndrome (MS). Weight gain and diabetes or MS were significantly associated with the
42 increased risk of alanine aminotransferase (ALT) (2). It is estimated that by 2050, 90% of
43 chronic liver disease cases in Mexico are caused by obesity and alcohol consumption
44 compared with other countries with higher rates of liver disease caused by HBV or HCV (4).

45 HBV or HCV infection and consuming alcohol are both confirmed risk factors for
46 chronic liver disease (5,6). Other risk factors include obesity (7,8), MS (9,10) and diabetes
47 (8,11,12); and the mechanism is developed through nonalcoholic fatty liver disease (NAFLD)
48 and nonalcoholic steatohepatitis (NASH) (8,13,14). The ratio of chronic liver disease
49 increases rapidly in Mexico with the prevalence of obesity, MS, and diabetes. An article on
50 patients in a teaching hospital in southern Taiwan with chronic hepatitis B (CHB), chronic
51 hepatitis C (CHC) and NAFLD, the results showed that elevated BMI is an independent risk
52 factor for LC (liver cirrhosis) in three different chronic liver diseases. Therefore, for these
53 patients, weight loss may be beneficial (15). Other studies have pointed out that obesity,
54 diabetes and hyperlipidemia have recently become potential cofactors for the development

55 of chronic HCV and HBV cases developing into fibrosis (16-18). At the same time, another
56 Hong Kong study reported that patients with CHB with metabolic syndrome had a higher
57 prevalence of liver cirrhosis than patients with CHB without metabolic syndrome. (38% vs
58 11%, $P < 0.001$) (19). Another prospective study from Taiwan, including 2,903
59 HBsAg-positive men, its median is 14.7 years; higher BMI at baseline is associated with the
60 incidence of NAFLD and liver cirrhosis (20). A previous study measured visceral obesity by
61 abdominal CT and indicated that HCV infection is a risk factor for the development of insulin
62 resistance, especially in visceral obese patients (21).

63 In Western countries, 75 to 90% of primary HCC are associated with chronic liver
64 disease (22). The most common chronic liver disease that causes HCC is hepatitis B or C
65 virus infection and excessive alcohol consumption. Whether the development of HCC is
66 associated with obesity and diabetes or changes in NAFLD is still unclear (23).

67 There are currently few studies in Taiwan on the correlation between obesity indicator
68 (WC, WHR, BMI) and hepatitis B and C. Therefore, this study uses adult health examination
69 data analysis to understand the correlation between obesity indicator and hepatitis B and C.

70 **Methods**

71 **Study design**

72 This study is designed as a cross-sectional study, collecting physical examination and blood
73 test data as analytical data from people who had health examination from 2011 to 2016 in a
74 regional hospital in Kaohsiung. All participants were above 20 years of age and met fasting
75 for the examinations.

76 Inclusion criteria : Those who participated in adult health examination from 2011 to 2016 as
77 subjects.

78 Exclusion criteria : Age <20 years old and those who had incomplete blood test data and
79 repeated screening are deducted.

80 **Definition of Variables :**

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

82 1. Definition of obesity indicator

83 (1) Waist circumference (WC) outlier: Male ≥ 90 cm, female ≥ 80 cm. WC was measured at
84 the midpoint between the bottom of the rib cage and the top of the iliac crest.

85 (2) Waist-height ratio (WHR): Normal (< 0.5), abnormal (≥ 0.5).

86 WHR was calculated as WC divided by height.

87 (3) Body Mass Index (BMI): Taiwan Ministry of Health and Welfare's Standard
88 Classification BMI for 2004

89 Underweight: BMI $\leq 18.4 \text{ kg/m}^2$

90 Normal: BMI between $18.5\text{-}23.9 \text{ kg/m}^2$

91 Overweight: BMI between $24.0\text{-}26.9 \text{ kg/m}^2$

92 Obesity: BMI $\geq 27 \text{ kg/m}^2$

93 2. Chronic hepatitis B, C:

94 After blood biochemical tests, the gastrointestinal specialist judged that it is the
95 asymptomatic carrier of hepatitis B and C.

96 **Ethical Considerations**

97 Data collection of this study began after approval by the hospital's Institutional Review Board
98 (IRB).

99 **Data processing and statistical analysis**

100 All statistical analyses were performed using SPSS software (IBM SPSS Statistics 20; Asia
101 Analytics Taiwan Ltd., Taipei, Taiwan). Statistical methods include: Descriptive statistics
102 (number of frequencies, percentage, mean and standard deviation), analytical statistics:
103 logistic regression. The above are used to analyze the effects of obesity indicators on hepatitis
104 B and C. Statistically significant level with $\alpha=0.05$, and with 95% confidence interval (CI).

Results

This study includes the analysis from year 2011 to 2016, with 16,459 cases included in the analysis. The result of table 1 shows that: obesity indicator defines (1) the prevalence of abnormal waist circumference (male: ≥ 90 cm, female: ≥ 80 cm) 20.5%. (2) Prevalence of abnormal waist-height ratio is 32.1%. (3) Body Mass Index: according to the Health and Welfare Department's standards for Body Mass Index (BMI) in 2004, underweight BMI $\leq 18.4\text{kg/m}^2$ (3.8%), normal: BMI between $18.5\text{-}23.9\text{kg/m}^2$ (48.1%), overweight: BMI between $24.0\text{-}26.9\text{kg/m}^2$ (26.7%), obesity: BMI $\geq 27\text{kg/m}^2$ (21.4%). The abnormal rate of hepatitis B was 13.6%, and the abnormal rate of hepatitis C was 1.9%.

Logistic regression analysis was performed respectively for the positive or negative of hepatitis B and hepatitis C. The variables included in regression analysis are: gender, age, BMI, waist circumference, waist-height ratio. Table 2 shows that waist circumference is a risk factor for hepatitis B (OR=1.181, 95%CI=1.014-1.377), and waist-height ratio is protective factor (OR=0.771, 95%CI=0.673-0.885). Table 3 shows that waist-height ratio is the risk factor of hepatitis C (OR=1.571, 95%CI=1.246-1.981).

Discussions

Hepatitis virus infection is a progressive disease that leads to the development of cirrhosis and even hepatocellular carcinoma (HCC); there are about 20 ± 30% of patients worldwide (24,25). HBV and HCV infection are the two major causes of liver disease that leads to health and socio-economic problems in Taiwan (26,27). Seventy-five percent of all chronic HBV infections occur in Asia. The prevalence in Taiwan is 15%-20%, and >90% of adults have been infected with hepatitis B virus in the past. It is estimated that there are two million to three million HBV carriers in Taiwan today (28).

According to data from the Liver Disease Prevention and Treatment Research Foundation, among adults over the age of 20, the prevalence of HCV in Taiwan is estimated at 4.4% (or 423,283 anti-HCV positive carriers) (27). The study analyzed 157,720 patients between 1996 and 2005, the infection rates were similar between males and females, with significant increases in age and geographic differences. Although the prevalence in most countries is between 1% and 2%, the prevalence in some countries is relatively high, including Egypt (15%), Pakistan (4.7%) and Taiwan (4.4%). The global prevalence of hepatitis C virus (HCV) is about 2% -3%. Between 1990 and 2005, the prevalence of positive anti-HCV antibodies increased from 2.3% to 2.8% (29). HCV infection causes 60%-80% of those who were infected to develop chronic hepatitis (30) and it is associated with liver steatosis, fibrosis, cirrhosis and hepatocellular carcinoma (31). The abnormal rate of hepatitis B in the study was 13.6%, and the abnormal rate of hepatitis C was 1.9%, both are lower than the average domestic populace. It may be different because this is a non-national sample survey that it only shows the results of health examination data in a regional hospital.

Previous studies have highlighted the important role of hepatitis virus infection in interacting with obesity. Hepatitis virus infections such as HCV, HBV and HCV/HBV co-infection are positively correlated with the increase in percent body fat (PBF), especially for male (32). Logistic regression analysis was performed in this study, on whether or not

patients have hepatitis B and whether or not they have hepatitis C. The variables included in the regression analysis model are: gender, age, BMI, WC, WHR. It shows that WC is a risk factor for hepatitis B (OR=1.181, 95%CI=1.014-1.377), and WHR is protective factor (OR=0.771, 95%CI=0.673-0.885). The WHR is a risk factor for hepatitis C (OR=1.571, 95%CI=1.246-1.981). Previous studies show that elevated BMI was an independent risk factor associated with possible liver cirrhosis (LC) across the three different etiologies of chronic liver disease. Therefore, weight loss can be beneficial for the patients (15). Another study points out that WHR may be a better obesity indicator on identifying the individual risk for non-alcoholic fatty liver disease in Korean women (33). Since previous studies used less of the three obesity indicators: WC, WHR, and BMI respectively on the effects on hepatitis B and C, therefore, it is difficult to compare directly in the literature comparison. However, some studies have shown that obesity is indeed associated with chronic hepatitis B and C and is associated with nonalcoholic fatty liver disease and metabolic diseases. As previous literature has shown, obesity is significantly associated with NAFLD, and visceral fat is more directly related to the onset of NAFLD (34). Compared with BMI, abdominal obesity is considered a better predictor of CVD and metabolic diseases. WC has become a widely used measurement method for quantifying abdominal fat accumulation. Epidemiological studies have shown that WHR appears to be more strongly associated with obesity-related diseases and metabolic risk factors than other obesity indicators (35,36). Since obesity is associated with many diseases and the deterioration of the disease, this study hopes to prevent obesity by finding the correlation between obesity indicators and HBV and HCV, which may help to reduce the progressive deterioration of HBV and HCV. There is also literature (15) pointed out that weight loss can help with the progression of chronic liver disease. We look forward to the future follow-up study to assess the effectiveness of weight loss to help us understand.

This study had several limitations. First, the study was cross-sectional in design, and hence causal relationships cannot be inferred. Second, this study can only present

demographic characteristics, obesity indicators, biochemical blood tests and the correlation between hepatitis B and C. Due to the use of health examination data to perform analysis, the potential impact factors affecting the above results cannot be fully collected, so it is also necessary to be conservative in inference.

Conclusion

HBV and HCV is an important health issue in Taiwan. In particular, hepatitis virus infection is a progressive disease that leads to the development of cirrhosis and even HCC. And liver cancer has been ranked second in the top ten cancers. Obesity is highly associated with many chronic diseases, and is even one of the risk factors for some cancers, such as colorectal cancer, endometrial cancer, and breast cancer. Therefore, if we can find out the correlation between obesity indicators and HBV, HCV, prevention of obesity may help reduce the progressive deterioration of HBV and HCV.

This study shows that waist circumference is a risk factor for hepatitis B, while waist-height ratio is a protective factor. The waist-height ratio is a risk factor for hepatitis C.

Consent Disclaimer:

As per international standard or university standard, patient's consent has been collected and preserved by the authors.

Ethical Considerations

Data collection of this study began after approval by the hospital's Institutional Review Board (IRB).

195 **Table 1 Descriptive statistics of demographic characteristics, obesity indicators and**

196 **Hepatitis B ,C (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
Male<90 cm, female<80 cm	13092	79.5	
Male≥ 90 cm, female≥ 80 cm	3367	20.5	
BMI			24.3±3.9
< 27kg/m ²	12940	78.6	
≥ 27kg/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	
≥ 27kg/m ²	3519	21.4	
Waist-height ratio			
Normal<0.5	11170	67.9	
Abnormal≥0.5	5289	32.1	
Hepatitis B			
Negative	14220	86.4	
Positive	2239	13.6	
Hepatitis C			
Negative	16140	98.1	
Positive	319	1.9	

197 **Table 2 Regression analysis of obesity indicators on hepatitis B (n=16459)**

Variables [#]	β	wald	OR(95%CI)	<i>P</i> value
Gender(female)	0.193	16.363	1.213(1.105-1.332)	<.001
Age(< 40 years old)	0.096	3.872	1.101(1.000-1.211)	0.049
WC(normal)	0.167	4.548	1.181(1.014-1.377)	0.033
WHR(normal)	-0.260	13.795	0.771(0.673-0.885)	<.001

198 Note 1: Stepwise regression method, the variables included in the regression analysis are:
 199 gender, age, BMI, WC, WHR.

200 Note 2: Dependent variable (1) with hepatitis B, (0) without hepatitis B.

201 [#]() is indicated as the reference group.

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207 **Table 3 Regression analysis of obesity indicators on hepatitis C (n=16459)**

Variables [#]	β	wald	OR(95%CI)	<i>P</i> value
Gender(female)	-0.254	4.765	0.776(0.618-0.974)	0.029
Age(< 40 years old)	0.568	17.336	1.766(1.351-2.307)	<.001
WHR(normal)	0.452	14.567	1.571(1.246-1.981)	<.001

208 Note 1: Stepwise regression method, the variables included in the regression analysis are:
 209 gender, age, BMI, WC, WHR.

210 Note 2: Dependent variable (1) with hepatitis C, (0) without hepatitis C.

211 [#]() is indicated as the reference group.

References

1. Chen CL, Yang HI, Yang WS, Liu CJ, Chen PJ, You SL, Wang LY, Sun CA, Lu SN, Chen DS, Chen CJ. Metabolic factors and risk of hepatocellular carcinoma by chronic hepatitis B/C infection: a follow-up study in Taiwan. *Gastroenterology*. 2008 Jul; 135(1): 111-21. doi: 10.1053/j.gastro.2008.03.073. Epub 2008 Apr 4.
2. Yvonne N. FLORES, Allyn AUSLANDER, Catherine M. CRESPI, Michael RODRIGUEZ, Zuo-Feng ZHANG, Francisco DURAZO & Jorge SALMERÓN. Longitudinal association of obesity, metabolic syndrome and diabetes with risk of elevated aminotransferase levels in a cohort of Mexican health workers. *Journal of Digestive Diseases* 2016; 17; 304–312doi: 10.1111/1751-2980.12341
3. Rivera JA, Barquera S, González-Cossío T, Olaiz G, Sepúlveda J. Nutrition transition in Mexico and in other Latin American countries. *Nutr Rev* 2004; 62: S149–57.
4. Méndez-Sánchez N, Villa AR, Chávez-Tapia NC et al. Trends in liver disease prevalence in Mexico from 2005 to 2050 through mortality data. *Ann Hepatol* 2005; 4: 52–5.
5. World Health Organization. Hepatitis. (2013). Cited: 22 March 2016. Available from URL: <http://www.who.int/immunization/topics/hepatitis/en/>
6. Rehm J, Samokhvalov AV, Shield KD. Global burden of alcoholic liver diseases. *J Hepatol* 2013; 59: 160–8.
7. Zheng RD, Chen ZR, Chen JN, Lu YH, Chen J. Role of body mass index, waist-to-height and waist-to-hip ratio in prediction of nonalcoholic fatty liver disease. *Gastroenterol Res Pract* 2012; 2012: 362147.
8. Regimbeau JM, Colombat M, Mognol P et al. Obesity and diabetes as a risk factor for hepatocellular carcinoma. *Liver Transpl* 2004; 10 (2 Suppl 1): S69–73.
9. Watanabe S, Yaginuma R, Ikejima K, Miyazaki A. Liver diseases and metabolic syndrome. *J Gastroenterol* 2008; 43: 509–18.
10. Smits MM, Ioannou GN, Boyko EJ, Utzschneider KM. Nonalcoholic fatty liver disease as an independent manifestation of the metabolic syndrome: Results of a US national survey

239 in three ethnic groups. *J Gastroenterol Hepatol* 2013; 28: 664–70.

240 11. Firneisz G. Non-alcoholic fatty liver disease and type 2 diabetes mellitus: the liver disease
241 of our age? *World J Gastroenterol* 2014; 20: 9072–89.

242 12. Davila JA, Morgan RO, Shaib Y, McGlynn KA, El-Serag HB. Diabetes increases the risk
243 of hepatocellular carcinoma in the United States: a population based case control study.
244 *Gut* 2005; 54: 533–9.

245 13. Ascha MS, Hanouneh IA, Lopez R, Tamini TA, Feldstein AF, Zein NN. The incidence
246 and risk factors of hepatocellular carcinoma in patients with nonalcoholic steatohepatitis.
247 *Hepatology* 2010; 51: 1972–8.

248 14. Clark JM. The epidemiology of nonalcoholic fatty liver disease in adults. *J Clin*
249 *Gastroenterol* 2006; 40 Suppl 1: S5–10.

250 15. Yen YH, Chang KC, Tsai MC, Tseng PL, Lin MT, Wu CK, Lin JT, Hu TH, Wang
251 JH, Chen CH. Elevated body mass index is a risk factor associated with possible liver
252 cirrhosis across different etiologies of chronic liver disease. *J Formos Med*
253 *Assoc.* 2018;117(4):268-275. doi: 10.1016/j.jfma.2017.09.002.

254 16. Hourigan LF, Macdonald GA, Purdie D, Whitehall VH, Shorthouse C, Clouston A, et al.
255 Fibrosis in chronic hepatitis C correlates significantly with body mass index and steatosis.
256 *Hepatology* 1999;29:1215e9.

257 17. Mena A', Pedreira JD, Castro A', Lo'pez S, Va'zquez P, Poveda E. Metabolic syndrome
258 association with fibrosis development in chronic hepatitis B virus inactive carriers. *J*
259 *Gastroenterol Hepatol* 2014;29:173e8.

260 18. Wong GL, Chan HL, Yu Z, Chan AW, Choi PC, Chim AM, et al. Coincidental metabolic
261 syndrome increases the risk of liver fibrosis progression in patients with chronic hepatitis
262 B-a prospective cohort study with paired transient elastography examinations. *Aliment*
263 *Pharmacol Ther* 2014;39:883e93.

264 19. Wong GL, Wong VW, Choi PC, Chan AW, Chim AM, Yiu KK, et al. Metabolic syndrome

265 increases the risk of liver cirrhosis in chronic hepatitis B. *Gut* 2009;58:111e7.

266 20. Yu MW, Shih WL, Lin CL, Liu CJ, Jian JW, Tsai KS, et al. Body mass index and
 267 progression of hepatitis B: a population based cohort study in men. *J Clin Oncol*
 268 2008;26:5576e82.

269 21. Eguchi Y, Mizuta T, Ishibashi E, *et al.* Hepatitis C virus infection enhances insulin
 270 resistance induced by visceral fat accumulation. *Liver Int* 2009;29:213–20.

271 22. Colombo M. The natural history of hepatocellular carcinoma in Western countries.
 272 *Hepatogastroenterology* 1998;45:1221–1225.

273 23. Yang S, Lin HZ, Hwang H, Chacko VP, Diel AM. Hepatic hyperplasia in noncirrhotic
 274 fatty livers: obesity steatosis, a premalignant condition? *Cancer Res* 2001; 61:
 275 5016–5023.

276 24. Poynard T, Bedossa P, Opolon P. Natural history of liver fibrosis progression in patients
 277 with chronic hepatitis C. The OBSVIRC, METAVIR, CLINIVIR, and DOSVIRC groups.
 278 *Lancet* (London, England).1997; 349(9055):825±32.

279 25. Fattovich G, Brollo L, Giustina G, Noventa F, Pontisso P, Alberti A, et al. Natural history
 280 and prognostic factors for chronic hepatitis type B. *Gut*. 1991; 32(3):294±8. PMID:
 281 2013423.

282 26. Chen CJ, Yu MW, Liaw YF. Epidemiological characteristics and risk factors of
 283 hepatocellular carcinoma. *Journal of gastroenterology and hepatology*. 1997; 12(9±10):
 284 S294±308. PMID: 9407350.

285 27. Chen CH, Yang PM, Huang GT, *et al.* Estimation of sero prevalence of hepatitis B virus
 286 and hepatitis C virus in Taiwan from a large-scale survey of free hepatitis screening
 287 participants. *J Formos Med Assoc* 2007;106(2):148–55. [https://doi.org/10.](https://doi.org/10.1016/S0929-6646(09)60231-X)
 288 1016/S0929-6646(09)60231-X PMID: 17339159.

289 28. Department of Health, Executive Yuan, Taiwan, ROC. Public health report. Available
 290 from: http://www.doh.gov.tw/ufile/doc/Taiwan_Public_Health_Report2008.pdf; 2008.

- 291 29. Mohd Hanafiah K, Groeger J, Flaxman AD, *et al.* Global epidemiology of hepatitis C
292 virus infection: new estimates of age-specific antibody to HCV seroprevalence.
293 *Hepatology* 2013;57:1333–42.
- 294 30. Shepard CW, Finelli L, Alter MJ. Global epidemiology of hepatitis C virus infection.
295 *Lancet Infect Dis* 2005;5:558–67.
- 296 31. Negro F, Sanyal AJ. Hepatitis C virus, steatosis and lipid abnormalities: clinical and
297 pathogenic data. *Liver Int* 2009;29(Suppl 2):26–37.
- 298 32. Chen YY, Fang WH, Wang CC, Kao TW, Chang YW, Yang HF, Wu CJ, Sun YS, Chen
299 WL. Increased body fat percentage in patients with hepatitis B and C virus infection.
300 *PLOS ONE | <https://doi.org/10.1371/journal.pone.0200164> July 2, 2018
- 301 33. Lim HJ, Seo MS, Lee HR, Shim JY, Kang HT, Lee YJ. Waist-to-Height Ratio as a
302 Simple and Useful Indicator for Non-alcoholic Fatty Liver Disease in Korean Women.
303 *Korean J Obes* 2016 March;25(1):19-23. <http://dx.doi.org/10.7570/kjo.2016.25.1.19>
- 304 34. van der Poorten D, Milner KL, Hui J, Hodge A, Trenell MI, Kench JG, et al. Visceral fat:
305 a key mediator of steatohepatitis in metabolic liver disease. *Hepatology* 2008;48:449-57.
- 306 35. Ashwell M, Gunn P, Gibson S. Waist-to-height ratio is a better screening tool than waist
307 circumference and BMI for adult cardiometabolic risk factors: systematic review and
308 meta-analysis. *Obes Rev* 2012;13:275-86.
- 309 36. Hsieh SD, Yoshinaga H, Muto T. Waist-to-height ratio, a simple and practical index for
310 assessing central fat distribution and metabolic risk in Japanese men and women. *Int J*
311 *Obes Relat Metab Disord* 2003;27:610-6.