

## Correlation of Waist to Height Ratio with Leptin Serum Level in Coronary Artery Disease

Vito Damay, Alberta Claudia Undarsa

**Background:** Adiposity assessment plays an important role in coronary artery disease (CAD) prevention. One of the adiposity parameter in major CAD management guideline is waist to height ratio (WHtR). Adiposity promotes the pathogenesis of coronary atherosclerosis by involving adipokines released by adipose tissue. Leptin is obesity identic adipokine which is used as prognostic predictor of cardiovascular event. This study aims to analyze correlation between WHtR and leptin serum level.

**Method:** A cross sectional study was performed to 37 stable CAD patients undergone elective coronary angiography in Heart Catheterization Laboratory Dr Hasan Sadikin Hospital, Bandung, West java in July 2014

**Results:** Mean age of the subjects was  $56.7 \pm 9.12$  years old with mean age of men ( $n=32$ ) and women ( $n=5$ ) were  $55.9 \pm 9.47$  years old and  $62 \pm 3.54$  years old consecutively. There were 30 (81%) subjects classified as obese ( $WHtR \geq 0.5$ ) with mean WHtR  $0.54 \pm 0.06$ . Median value of leptin serum was 8599.90 pg/ml (780-36929.3 pg/ml). Based on rank-spearman correlation test, a positive moderate correlation was significantly found between WHtR and Leptin serum level (Spearman's  $\rho = 0.5$ ,  $p = 0.001$ ).

**Conclusion:** Positive correlation was found between WHtR and leptin serum level. Hence, WHtR might be useful as indicator of leptin serum level which has been used as a prognostic biomarker in CAD patients

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**Keywords:** adiposity, waist to height ratio, leptin, coronary artery disease

# Korelasi Rasio Lingkar Pinggang/Tinggi Badan dengan Kadar Leptin Serum Pada Penyakit Jantung Koroner

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**Latar belakang:** Penilaian adipositas merupakan bagian dari upaya preventif penyakit jantung koroner (PJK). Salah satu parameter antropometri adipositas yang digunakan pada panduan tatalaksana PJK adalah pengukuran rasio lingkar pinggang/tinggi badan (LP/TB). Adipositas diketahui berperan dalam patomekanisme terbentuknya aterosklerosis koroner melalui pelepasan adipositokin oleh jaringan adiposa. Leptin merupakan adipositokin identik adiposit yang digunakan sebagai biomarka indikator prognostik kejadian kardiovaskular. Penelitian ini bertujuan untuk menganalisa korelasi LP/TB dengan kadar leptin serum.

**Metode:** Studi potong lintang dengan menganalisis antropometri LP/TB dan kadar leptin serum pada 37 pasien PJK yang menjalani angiografi elektif di Laboratorium Kateterisasi Jantung RSUP Dr.Hasan Sadikin, Bandung, Jawa Barat pada bulan Juli 2014.

**Hasil:** Rerata usia subjek adalah 56.7± 9.12 tahun dengan rerata usia pria (n=32) dan wanita (n=5) secara berurutan adalah 55.9±9.47 tahun dan 62±3.54 tahun. Terdapat 30 (81%) subjek tergolong obesitas (nilai LP/TB ≥0,5) dengan rata-rata LP/TB 0.54±0,06. Nilai median leptin serum 8599.90 pg/ml (780-36929.3 pg/ml). Berdasarkan uji korelasi *rank-spearman*, terdapat korelasi positif bermakna antara LP/TB dengan kadar leptin serum (Spearman rho = 0.5, p= 0.001).

**Kesimpulan:** Terdapat korelasi positif bermakna antara pemeriksaan antropometri LP/TB dengan kadar leptin serum. Rasio lingkar pinggang/tinggi badan dapat digunakan sebagai salah satu indikator kadar leptin serum yang merupakan biomarka prognostik kardiovaskular.

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**Kata kunci:** rasio lingkar pinggang/tinggi badan, leptin, penyakit jantung koroner

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## Introduction

Coronary artery disease (CAD) caused by atherosclerosis remains a global health issue and is leading cause of both men and women death in the United states and Europe.<sup>1</sup> Based on Indonesia Health Profile 2013, coronary heart disease belongs to the 10 most prevalent non-communicable diseases in Indonesia. Non-communicable disease itself has negative impact on the economy and productivity of the nation therefore it has become a major health public issue.<sup>2</sup>

In European Society of Cardiology (ESC) 2016, secondary prevention by controlling risk factor could

reduce up to 50% coronary mortality risk.<sup>1</sup> Therefore, secondary prevention to reduce recurrent CAD events and decrease coronary mortality in CAD patients has gained more attention as it approaches in both control of risk factors and also direct therapeutic protection of plaque eruption in coronary artery.<sup>1</sup> Obesity remains one of the important major risk factor in CAD as the adipose tissue apart from the fat storage functions, also known as endocrine releasing adipokines. These adipokines leads to pro-inflammatory and pro-thrombotic states contributing to endothelial dysfunction in coronary atherosclerotic pathomechanism.<sup>3</sup> Leptin is an adipocyte identic adipokine which involved in diverse physiological processes such as induces atherogenesis, angiogenesis and thrombosis by enhancing the secretion of inflammatory cytokines includes C-reactive protein, TNF and IL- 6 and also by inducing oxidative stress. These direct vascular effect of leptin shows leptin as a conjunction between obesity and CAD. A significant association found between circulating plasma leptin and inflammatory markers suggests leptin as a prognostic factor of CAD and coronary artery restenosis.<sup>3,4</sup>

Body mass index (BMI) and waist circumference (WC) are routine parameters to assess adiposity in various CAD guidelines.<sup>1,5</sup> Waist to height ratio (WHtR) is also another proxy for central obesity anthropometric parameter which offers the advantage of a universal boundary value that may be useful in different ethnic, age, sex, body posture groups, while WC and BMI requires population-specific boundary values.<sup>6</sup> Ashwell and Gelber et al shows that WHtR is a better adiposity anthropometric parameter events compared with BMI and WC as a predictor of cardiovascular events ( $p < 0.01$ ).<sup>7,8</sup> Adiposity showed by BMI and WC parameter both showed positive correlation with circulating plasma leptin which links obesity and CAD.<sup>9,10,11</sup> However, it is not known whether WHtR likewise shows correlation with leptin serum. Hence, this study aims to analyze correlation between WHtR and leptin serum level as prognostic predictor of cardiovascular event.

## Methods

This study was a clinical epidemiological cross sectional study. All patients undergone elective angiography in Heart Catheterization Laboratory Dr Hasan Sadikin Hospital, Bandung, West java in July 2014 participated as the study population.

## Participant recruitment and data collection

All patients undergone elective angiography in Heart Catheterization Laboratory Dr Hasan Sadikin Hospital, Bandung, West java in July 2014 which fulfilled inclusion and exclusion criteria were consecutively recruited as participants. Inclusion criteria were subjects undergone elective coronary angiography and stenosis was found  $\geq 50\%$  in at least one major coronary artery. Exclusion criteria were as follows: 1) steroid user patients; 2) acute coronary syndrome (ACS) patients; 3) patients with chronic kidney failure. Data of the patients was collected through patients' medical record such as anthropometric measurement (waist circumference and height) and other cardiovascular risk factors. Fasting serum was collected for the measurement of leptin.

## Statistical Analysis

The statistical analysis was performed using the SPSS software. Descriptive followed by Saphiro-wilk test for normality test were done. Mean values were used for normally distributed data and median values were used if a skewed distribution existed. Spearman correlation test were used to analyze correlation between WHtR and serum leptin. Leptin serum levels based on subjects' characteristics were analyzed using unpaired-t test and Mann-whitney test while another confounding variable was analyzed using linier regression analysis. Differences were considered significant when P-values were 0.05 or less.

## Results

A total of 64 CAD patients undergone elective angiography and had serum leptin analyzed in July 2014; 6 patients with history ACS and 21 patients with incomplete angiography report and documentation were excluded, allowing a total of 37 stable (32 men and 5 women) CAD patients were suitable as subjects to this study.

The baseline characteristics of all of the participants, including age, sex, anthropometry are shown in table 1. Average age of the patients undergone elective coronary angiography which meet up the criteria for this study was  $56.73 \pm 9.12$  years, average age for men and women consecutively were  $55.9 \pm 9.47$  years and  $62 \pm 3.54$  years. Risk factors of CAD of all the participants were presented in table 2, we found that dyslipidemia and

**Table 1.** Participants characteristics

Characteristics	Mean (SD)
Age, years	56,73 (9,12)
Men	55,91 (9,47)
Women	62,00 (3,54)
Body height, cm	163,62 (6,43)
Men	165,19 (5,14)
Women	153,60 (4,72)
Waist circumference, cm	88,19 (10,18)
Men	89,00 (10,24)
Women	83,00 (8,94)
BMI, kg/cm <sup>2</sup>	24,57 (3,31)

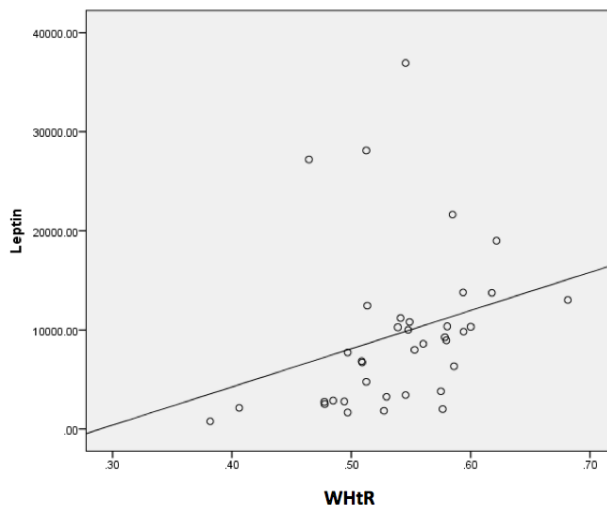
cigarette smoking were the most common risk factor for coronary heart disease in this study followed by hypertension, diabetes mellitus, and family history.

Anthropometry classification were made based on BMI, WC and WHtR. Two CAD patients were categorized as obese based on BMI parameter; 22 subjects were having central obesity based on WC parameter, and 30 subjects were obese based on WHtR parameter (**Table 3**).

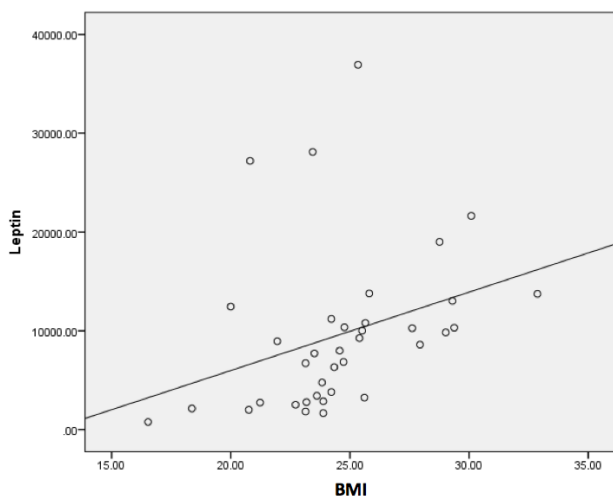
WHtR data was normally distributed while leptin serum level was not; Mean WHtR is 0.54±0.06 and median leptin serum level is 8599.90 pg/ml (range

780-36929.3 pg/ml). Spearman correlation test was performed and showed a positive moderate correlation between WHtR and leptin serum (Spearman's rho = 0.51; p = 0.001). Positive correlations were also found between both leptin serum and other anthropometry parameters such as BMI (Spearman's rho = 0,54, p <0,001) and WC (Spearman's rho = 0.41, p=0.01). These results are presented graphically in **Figure 1**, **Figure 2**, and **Figure 3**.

Risk factors associated CAD need to be included in the analysis as confounding variables. Therefore, Mann-Whitney test was performed to analyze the



**Figure 1.** Correlations between WHtR and leptin serum level



**Figure 2.** Correlations between BMI and leptin serum level

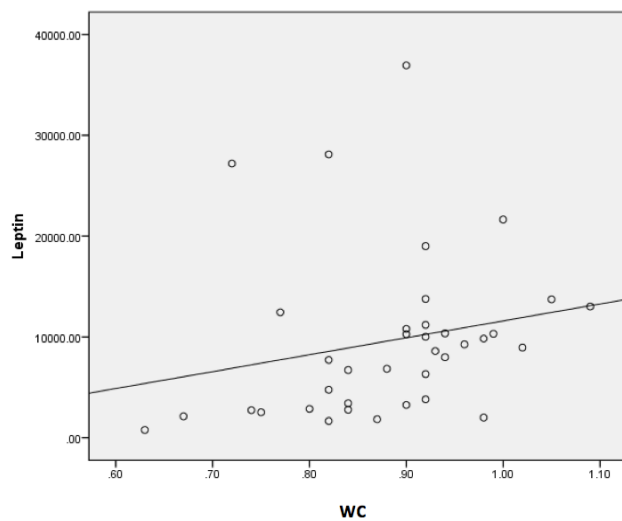
**Table 2.** Subject's risk factor associated coronary heart disease

Risk Factor	N (%)
Dyslipidemia	28 (75.7%)
Diabetes mellitus	8 (21.6%)
Cigarette smoking	26 (70.3%)
Hypertension	18 (48.6 %)
Family history	6 (16.2%)

**Table 3.** Subject's adiposity anthropometry distribution

Characteristic	N
BMI	
Underweight(<18,5 kg/m <sup>2</sup> )	2
Normal (18.5-22.9 kg/m <sup>2</sup> )	6
Overweight (22.9-24.9 kg/m <sup>2</sup> )	14
Obese (≥25 kg/m <sup>2</sup> )	15
Waist circumference	
Men	19
Women	3
WHtR	
<0,5	7
≥0,5	30

BMI: Body Mass Index; WHtR: waist to height ratio



**Figure 3.** Correlations between WC and leptin serum level

confounding factors such as dyslipidemia, diabetes mellitus, smoking history, family history, age and gender. We found no significant difference of leptin serum levels between the risk factor groups except in gender as seen on table 5. Leptin serum levels in women were significantly higher in women than in men. Median leptin serum levels for women (n=5) was 19002.5 pg/ml (range: 12445.5-28115.8 pg/ml) while lower in men (n=37) which was 7286.3 pg/ml (range: 780-36929.3 pg/ml).

**Table 4.** Analysis of confounding variables and serum leptin level

Variables	Groups	P Value
Age		0.062*
Gender	Male (n=32) Female (n=5)	0.002**
Diabetes mellitus	Yes (n=8) No (n=29)	0.84**
Dyslipidemia	Yes (n=28) No (n=9)	0.88**
Cigarette smoking	Yes (n=26) No (n=11)	0.19**
Family history	Yes (n=6) No (n=31)	0.79**
Hypertension	Yes (n=18) No (n=19)	0.134**

\*Spearman's rho, \*\*Mann-whitney test

## Discussion

Mean age of 37 CAD patients in this study was  $56.7 \pm 9.12$  years and men proportion (32 subjects) were larger than women. A similar result was found in Sonmez et al, subjects' mean age was  $57 \pm 9.12$  years with men showed a larger proportion (83%) than women.<sup>12</sup> NCEO/ATP III stated that men aged  $\geq 45$  years and women aged  $\geq 55$  years were at higher risk to develop CAD than younger ones while mean age for men and women in this study were  $55.91 \pm SD 9.47$  years and  $62 \pm 3.54$  years respectively.

Hypertension was found in 51.4% subjects in this study, while 75.7% subjects had and 21.6% subjects had diabetes mellitus as risk factors for coronary heart disease. Profile distribution of CAD risk factor will vary in different research locations, however risk factor profile in this study was in accordance to study by Ueshima et al, which showed that hypertension prevalence in CAD patients in Asian countries (Taiwan, Japan, South Korea, Singapore and Thailand) is 60%. While cigarette smoking prevalence were about 40-60% in men with CAD in those countries.<sup>13</sup> In a study done by Hasan-Ali et al, diabetes mellitus was found in 31% subject with CAD while in Kaulgud et al study, diabetes mellitus prevalence in CAD patients is 48.8%.<sup>14,15</sup>

Based on BMI, we found 12 overweight subjects and 2 obese subjects while 22 subjects were classified for having central obesity based on WC parameter. More subjects (n=30) were classified as obese by using WHtR parameter; showed that some of non-obese subjects based on WC parameter were actually classified as obese by using WHtR parameter. In 2013, Zhao et al published a survey study of cardiovascular diseases risk factors in China and stated that WHtR was more sensitive than WC as central obesity indicator for both men and women with height either below or above the average.<sup>16</sup> Ashwell et al reported that WHtR was more sensitive than WC in assessing adiposity because it encompasses the adjustment to different statures and WHtR also allows the same boundary values for men and women for different age and ethnics.<sup>7</sup> WHtR is also an easier educating tool for secondary prevention of CAD owing to its simplicity to understand; 'waist circumference is supposedly not more than half of body height' as  $WHtR \geq 0.5$  is classified as central obesity.<sup>7</sup>

Anthropometry parameters of adiposity are often associated with leptin serum level, knowing that

leptin is produced by adipocyte and there were various adiposity anthropometry parameters available. Smith et al, found a positive correlation between BMI and serum leptin level ( $r=0.72$ ,  $p < 0.0001$  for men;  $r=0.54$ ,  $p=0.003$  in women). Zimmet et al also found a positive correlation between leptin serum level and WC in both men and women (Spearman's  $\rho = 0,8$  for men and Spearman's  $\rho = 0,7$  for women).<sup>10</sup> Significantly higher leptin serum levels in women than in men ( $p=0.002$ ) was presented in this study which was in accordance with study done by Olstad et al. Greater percentage of adipose tissue in women than in men attributes to higher leptin serum levels in women.<sup>17</sup>

This study aims to analyze correlation between the other adiposity anthropometric parameter, WHtR and leptin serum level and positive correlation was found between WHtR and leptin serum level (Spearman's  $\rho = 0.51$ ;  $p = 0.001$ ). Therefore, this study aligned with previous study by Smith and Zimmet which show a positive correlation between adiposity anthropometry parameter and leptin serum level.<sup>9,10</sup>

In previous prospective studies, BMI, WC and WHtR as adiposity anthropometries were known to correlate with CAD prognosis.<sup>1,8</sup> Ashwell and Gelber et al shows that WHtR is a better adiposity anthropometric parameter events compared with BMI and WC as a predictor of cardiovascular events such as fatal and non-fatal primary myocard infarct, fatal and non-fatal ischemic stroke, sudden death associated with ischemic heart disease ( $p<0.01$ ).<sup>7,8,18</sup>

Aside from adiposity anthropometries, leptin serum levels nowadays are also subsumed as cardiovascular prognostic biomarker. Wallace et al and Wolk et al reported an increase in leptin serum levels is associated with CAD prognosis.<sup>4,19</sup> These were supported by Qasim et al study which showed association of plasma level of leptin and coronary artery calcification.<sup>20</sup>

Although leptin serum level is valuable CAD prognostic biomarker, however practically it is not yet available widely as routine assessment in CAD management. Therefore, a significant correlation between leptin serum level and WHtR parameter as an easy and cheap anthropometry evaluation will facilitate an easier assessment of CAD prognosis.

## Conclusion

Our data confirm that there is positive correlation between WHtR and leptin serum level as well as other

adiposity anthropometries such as BMI and WC. We hope this correlation will lead WHtR as a cheap and easy adiposity assessment to be an indicator of leptin serum level in CAD patients and can be used as new reference for further studies.

## List of abbreviations

ACS: Acute coronary syndrome  
 BMI: Body mass index  
 CAD: Coronary artery disease  
 WC: Waist circumference  
 WHtR: Weight to height ratio

## Study Ethics

This study had been approved by Ethical Committee on Health Research, Faculty of Medicine, Hasan Sadikin University with reference numbers LB.04.01/A05/EC/308/VIII/2014.

## Publication approval

*The publication of this article has been approved by every party.*

## Conflict of interest

None

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