

## Original Article

# Anthropometric Measurements and Body Composition of Indonesian Patients with Type 2 Diabetes are Associated with Inflammation, Independent of Sex and Disease Duration

Perdana Samekto Tyasnugroho Suyoto\*, Adhea Fildza Pramnesti, Aprillanna Lucky Mahartie, Salsabila Aisyah, Sinthya Rasela

Department of Nutrition and Health, Faculty of Medicine, Gadjah Mada University, Yogyakarta, Indonesia

\* Correspondence to: Perdana Samekto Tyasnugroho Suyoto, Departemen Gizi Kesehatan FKMK UGM, Jl. Farmako, Sekip Utara, Sleman, Indonesia, 55281. e-mail: perdana.sts@gmail.com; Phone: +62 274 547775; Fax: +62 274 547775

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### Abstract

**Introduction:** Abnormal body composition, such as a high percentage of body fat, triggers an inflammatory reaction, which links the association between obesity and diabetes complications. Females, in general, have higher body fat, which may play a part in elevating cardiovascular disease risk. This study aimed to study the association between several anthropometric measurements and inflammatory markers in individuals with type 2 diabetes mellitus. We intended to confirm if this association is independent of sex and duration of diabetes. **Material and Methods:** People with type 2 diabetes mellitus were recruited from primary health care centers in Sleman, Indonesia. Several anthropometric measurements were performed, followed by an analysis of plasma high-sensitivity C-reactive protein. A comparison of anthropometric measurements was made between individuals with (high-sensitivity CRP < 3 mg/L) and without inflammation (high-sensitivity CRP ≥ 3 mg/L). Spearman correlation analysis was conducted to learn the association between anthropometric measurements with the high-sensitivity CRP level. Adjustments were made for sex and duration of diabetes. **Results:** Differences were found on weight, BMI, hip circumference, upper-arm circumference, and wrist circumference. Among body composition measurements, total body fat, subcutaneous fat (whole body, trunk and leg), and visceral fat were different between groups. Bodyweight, BMI, waist circumference, hip circumference, arm circumference, neck circumference, and wrist circumference were significantly correlated with high-sensitivity CRP values. **Conclusion:** Associations were found between the inflammatory marker and anthropometric measurements, independent of sex and disease duration.

**Keywords:** Diabetes, inflammation, C-reactive protein, anthropometry, body composition

### Introduction

Inflammation is a natural mechanism against infection and injury. Inflammation is initiated and intensified in a short time following the insults, which can sustain for days. In a normal condition, the inflammatory response is swiftly terminated upon clearance of infection and injurious mediators. This careful control of complex inflammatory signaling cascades minimizes tissue damage as a consequence of free radicals released during inflammation [1].

A milder and sustained version of inflammation has been extensively studied within past decades, which is linked to several conditions, including cardiovascular diseases [2], cancer [3], Alzheimer's disease [4], sarcopenia [5] and type 2 diabetes mellitus [6]. This phenomenon is commonly termed chronic, low-grade inflammation, or metabolic inflammation (metaflammation). It drifts from the classic type of inflammation, as it lacks calor, dolor, rubor, and tumor. In addition to that, there is no substantial increase in basal energy expenditure observed [7]. A higher degree of chronic



inflammation was observed with increasing age. This aging-associated chronic inflammation or inflammaging may result from genetic factors, central adiposity, leaky gut, gut dysbiosis, mitochondrial dysfunction, and chronic infection [8].

In type 2 diabetes mellitus (T2DM), inflammation may be triggered by several distinct mechanisms. Excessive adiposity increases the concentration of Interleukin-6 (IL-6) in the circulation [9, 10]. IL-6 induces an acute phase response, which is followed by the release of acute phase mediators such as serum amyloid A (SAA), haptoglobin, fibrinogen, and C-reactive protein (CRP) from the liver [11]. Poor glycemic control may lead to the formation of advanced glycation end products (AGEs), which can bind to the receptor of AGE (RAGE). RAGE ligation on vascular or immune cells triggers several signal transduction cascades leading to activation of NF- $\kappa$ B [12] and transcription of several inflammatory cytokines including IL-1, IL-2, IL-6, IL-8, IL-12 and TNF- $\alpha$  [13]. AGE formation is accelerated due to inflammation, oxidative stress, and aging [14].

There are differences between genders in terms of the risk and outcome of diabetes. These differences may be caused by organs' systemic response to a difference in sex chromosome and gender-specific expression of genes in the autosomes and sex-specific hormones [15]. These differences lead to phenotypic differences between genders, including body composition. Body fatness, which is commonly higher in females, is associated with diabetes outcomes. According to the UK Biobank Study, which investigated the differences of anthropometric adiposity measures (weight, waist and hip circumference, BMI, and body fat) between individuals with and without diabetes, the measure differences were higher in female participants [16]. Adiposity is positively correlated with chronic inflammation [17], which contributes to the sex-associated difference in inflammation state. Indeed, a previous study involving a large number of female and male participants with new-onset diabetes (13,676 and 7,809, respectively) showed that high-sensitivity C-reactive protein (hs-CRP) concentration tended to be higher in females ( $1.85 \pm 3.09$  vs.  $1.47 \pm 2.33$ ;  $p < 0.000001$ ) [18]. In a systematic review of over five-million participants, women with diabetes have a 58% higher risk of developing coronary heart disease. Compared with their male counterparts, females with diabetes also have a 30% greater risk of cardiovascular disease. In addition to that, a 13% greater all-cause mortality risk is attributable to females with diabetes [19].

Increased risk of diabetes complications is also associated with a longer duration of diabetes. In a previous study, the duration of diabetes is associated with death, microvascular, and macrovascular events [20]. A Sri Lankan study showed that the duration of diabetes >10 years was associated with a doubled risk of microvascular complication and diabetic foot [21]. The risk of infectious diseases, such as infective endocarditis, is also elevated with longer duration of diabetes. A three-times higher risk of infective endocarditis is seen in individuals that have diabetes for more than 15 years compared with 0-5 years [22].

CRP, as a marker of inflammation, was shown to be associated with several diseases risk. CRP can be categorized into lower (<1 mg/L), moderate (1-3 mg/L), and higher (>3 mg/L), which represent a relative risk of heart disease [23]. In a meta-analysis using a fixed-effect model, the subjects in the highest category of hs-CRP had twice the risk of cardiovascular mortality. In the same study, cancer risk was increased by 25% for those in the highest category of hs-CRP [3].

In this study, we aimed to investigate the factors that may be related to inflammation in patients with type 2 diabetes mellitus, in this case, anthropometric measurements, muscle strength, and body composition. Associations were evaluated controlling for sex and duration of disease.

## Material and Methods

### Participants

Participants were recruited from two-state primary health care centers and one private primary care clinic in Sleman, Indonesia. At the time, they were participating in a Chronic Disease Management Program, an activity organized at primary health care level to promote health to people with chronic diseases including physical activity, health monitoring, medical consulting, psychological services, nutrition counseling, physiotherapy, and laboratory tests [24]. All male and female individuals diagnosed with type 2 diabetes were recruited to this study. Participation in this study was entirely voluntary. This study was approved by the Medical and Health Research Ethics Committee (MHREC), Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada (No. KE/FK/1253/EC/2018). All subjects gave written informed consent to participate in the study.

## Anthropometric Measurements

We measured participants' body weight, height, waist circumference, hip circumference, upper arm circumference, neck circumference, wrist circumference, handgrip strength, and triceps skinfold. All measurements were performed in compliance with the Body Measurements (Anthropometry) protocol published by the U.S. Center for Disease Control and Prevention [25]. Bioelectrical impedance analysis (BIA) was also performed to estimate whole body, trunk, arm and leg subcutaneous fat and muscle mass, visceral fat, and total body fat (Omron HBF 375, USA).

## Laboratory method

Venipuncture by a phlebotomist was carried out for all subjects after 8 hours of fasting, using vacuum extraction tube systems. The blood in the tube containing EDTA was centrifuged at 2000 x g for 15 minutes, followed by the transfer of the supernatant into microtubes. The tubes were then frozen at 20°C until further analysis. Plasma high-sensitivity C-reactive protein analysis was performed using the Enzyme-linked immunosorbent assay (ELISA) method as instructed in the provided manual (Calbiotech, USA). The concentration of hs-CRP at or above 3 mg/L was considered inflammation.

## Data analysis

Participants were divided into two groups according to inflammation status (hs-CRP <3 vs. ≥3 mg/L). Anthropometric measurement differences between groups were analyzed using the General Linear Model. Statistical significance was determined in three models: unadjusted, adjusted for sex, and adjusted for sex and duration of diabetes. Besides, partial Spearman's Correlation was used to analyze the association between anthropometric measurements with hs-CRP, adjusted for sex, and duration of diabetes. A P-value of <0.05 was considered statistically significant.

## Results

Subject characteristics are shown in Table 1. Female participants were three times as many as their male counterparts. The majority (77.9%) of the subjects were >55 years old. The number of subjects with a duration of diabetes of <5 years, 5-10 years, and >10 years

Table 1: Subject Characteristics (n=86).

Variable	n (%)
<b>Age</b>	
18-35 y	1 (1.2)
36-55 y	18 (20.9)
>55 y	67 (77.9)
<b>Sex</b>	
Male	23 (26.7)
Female	63 (73.3)
<b>Duration of Diabetes</b>	
<5y	35 (40.7)
5-10y	27 (31.4)
>10y	24 (27.9)
<b>BMI</b>	
Underweight	2 (2.3)
Normal	30 (34.9)
Overweight	36 (41.9)
Obesity	18 (20.9)
<b>hs-CRP serum concentration</b>	
<3 mg/L	36 (41.8)
≥3 mg/L	50 (58.1)

was nearly proportional (40.7% vs. 31.4% vs. 27.9%, respectively). According to BMI, most of the subjects fell into the overweight category (41.9%). Obesity was present in 20.9% of all participants. More than half (58.1%) of the subjects had an inflammation state, as indicated by hs-CRP values (≥3).

Table 2 shows the anthropometric measurements, muscle strength, and body composition in subjects classified as being in a non-inflammation and inflammation state. Patients in the inflammation state had higher body weight in corrected models (64.56 ± 11.19 vs. 59.67 ± 12.61; p<sub>2</sub>=0.02, p<sub>3</sub>=0.03). Using BMI as a comparison, the difference was significant across all models (27.44 ± 4.17 vs. 25.24 ± 4.21; p<sub>1</sub>=0.01, p<sub>2</sub>=0.02, p<sub>3</sub>=0.01). Among all the body circumference measurements, only neck circumference had no significant difference between the groups. No significant difference in the wrist circumference was observed, only in the unadjusted model. However, after adjustment for sex or sex and disease duration, the differences between groups were significant (p<sub>2</sub>=0.02, p<sub>3</sub>=0.01). Regarding

Table 2: Comparison of anthropometric measurements between the group with and without inflammation (n=86).

Variables	hs-CRP serum concentration		p-value		
	<3 mg/L	≥3 mg/L	Model 1 <sup>b</sup>	Model 2 <sup>c</sup>	Model 3 <sup>d</sup>
Weight (kg)	59.67 ± 12.61	64.56 ± 11.19	0.06	0.02*	0.03*
Height (cm)	153.30 ± 8.06	153.31 ± 7.27	0.99	0.51	0.73
BMI (kg/m <sup>2</sup> )	25.24 ± 4.21	27.44 ± 4.17	0.01*	0.02*	0.01*
Waist circumference (cm)	86.53 ± 10.90	90.59 ± 10.0	0.07	0.05	0.03*
Hip circumference (cm)	94.14 ± 12.40	99.43 ± 9.08	0.02*	0.02*	0.05*
Upper arm circumference (cm)	27.51 ± 3.89	29.51 ± 3.95	0.02*	0.02*	0.03*
Neck circumference (cm)	34.53 ± 4.19	35.38 ± 4.12	0.35	0.13	0.08
Wrist circumference (cm)	15.16 ± 1.22	15.67 ± 1.33	0.07	0.02*	0.01*
Handgrip strength (kg)	18.48 ± 14.19	19.79 ± 11.15	0.63	0.36	0.61
Triceps skinfold (cm)	19.22 ± 6.97	21.75 ± 8.50	0.14	0.18	0.17
Total body fat (%)	32.75 ± 6.44	35.81 ± 5.34	0.01*	0.01*	0.01*
Visceral fat (%)	10.44 ± 6.02	12.86 ± 6.18	0.07	0.03*	0.02*
Whole subcutaneous fat (%)	26.61 ± 7.47	29.92 ± 6.81	0.03*	0.01*	0.02*
Trunk subcutaneous fat (%)	23.91 ± 6.64	26.95 ± 6.14	0.03*	0.01*	0.01*
Arm subcutaneous fat (%)	39.84 ± 12.39	43.42 ± 11.29	0.16	0.09	0.12
Leg subcutaneous fat (%)	34.87 ± 9.39	39.16 ± 9.09	0.03*	0.01*	0.01*
Total muscle mass (%)	23.58 ± 3.42	22.78 ± 2.99	0.25	0.34	0.23
Trunk muscle mass (%)	17.31 ± 3.30	16.54 ± 2.65	0.23	0.32	0.25
Arm muscle mass (%)	26.81 ± 5.89	25.00 ± 5.63	0.15	0.12	0.14
Leg muscle mass (%)	37.48 ± 5.52	36.96 ± 4.62	0.64	0.94	0.98

Note: a unadjusted mean ± SD; b unadjusted p-value; c p-value adjusted for sex; d p-value adjusted for sex and duration of diabetes; \* p<0.05

waist circumference, statistical significance was shown only after adjustment for sex and duration of diabetes (p=0.03). No difference was found on triceps skinfold. In body composition, whole body, trunk, arm, and leg skeletal muscle showed no significant difference between groups. However, the group with higher hs-CRP showed overall higher body fat, except for the arm subcutaneous fat.

Several anthropometric measurements were correlated with the hs-CRP level, including body weight, BMI, waist circumference, hip circumference, and arm circumference. The associations remained significant even after adjustment for sex and duration of diabetes (Figure 1). Neck and wrist circumference only become significant after being adjusted. Arm muscle mass is the only muscle mass measurement that correlated

with hs-CRP. All measures of percent body fat were correlated with hs-CRP (Figure 2).

## Discussion

Being widely used for measurement of the nutritional status, BMI should be interpreted cautiously for its lack of accuracy to predict body fatness [26]. Several efforts have been made to create an alternative of BMI with comparable practicality yet perform better in predicting body fat mass. Waist circumference was shown to be a better predictor of adiposity [27] and mortality risk [28]. Recently studied in the United States, relative fat mass (RFM), calculated from height, waist circumference, and sex, predicted whole-body fat percentage

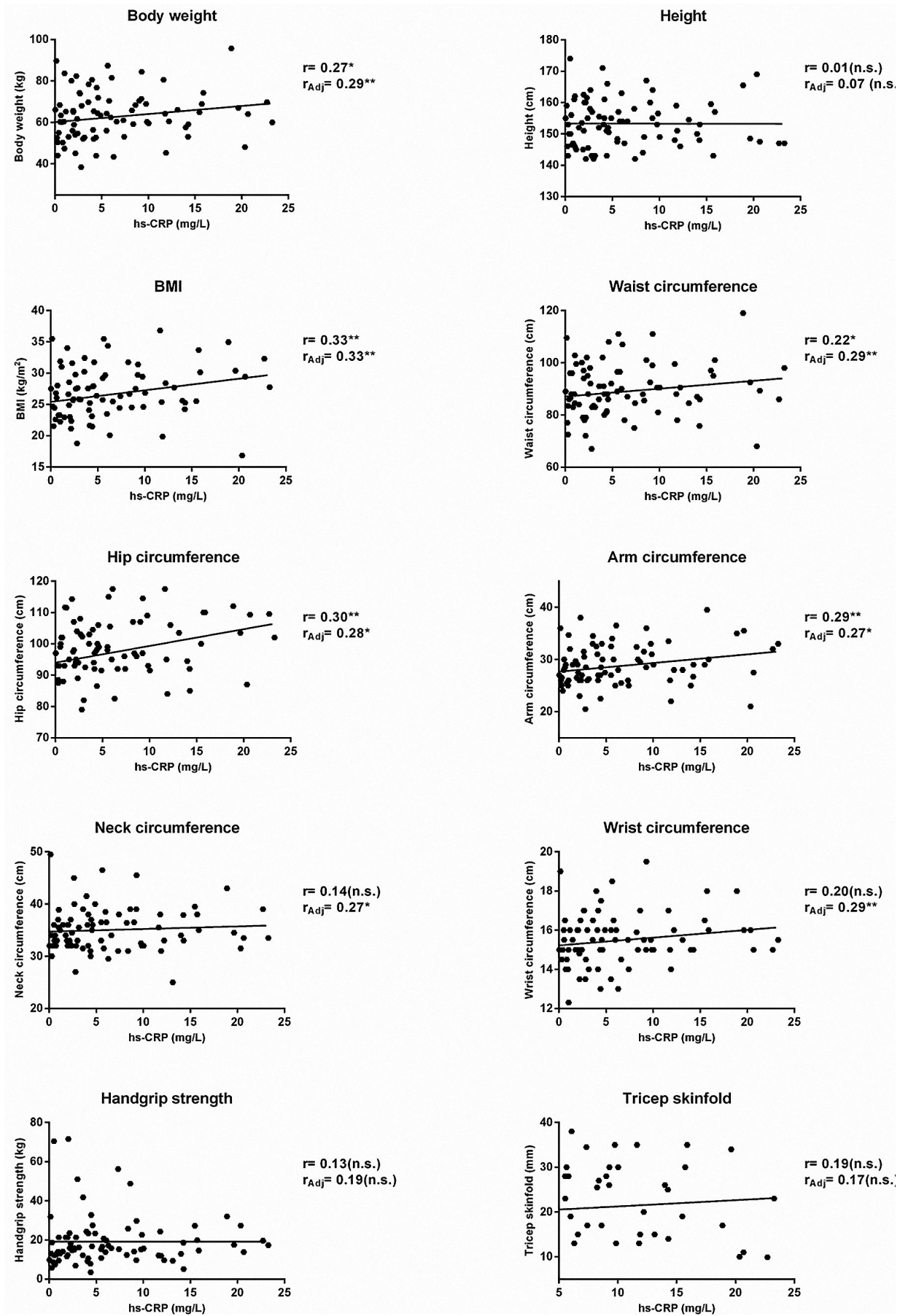


Figure 1: Correlation between anthropometric measurements and handgrip strength with hs-CRP concentration. r: Spearman's rank correlation coefficient, rAdj: correlation coefficient adjusted for sex and duration of diabetes, \* p<0.05, \*\* p<0.01, (n.s.) no statistically significant.

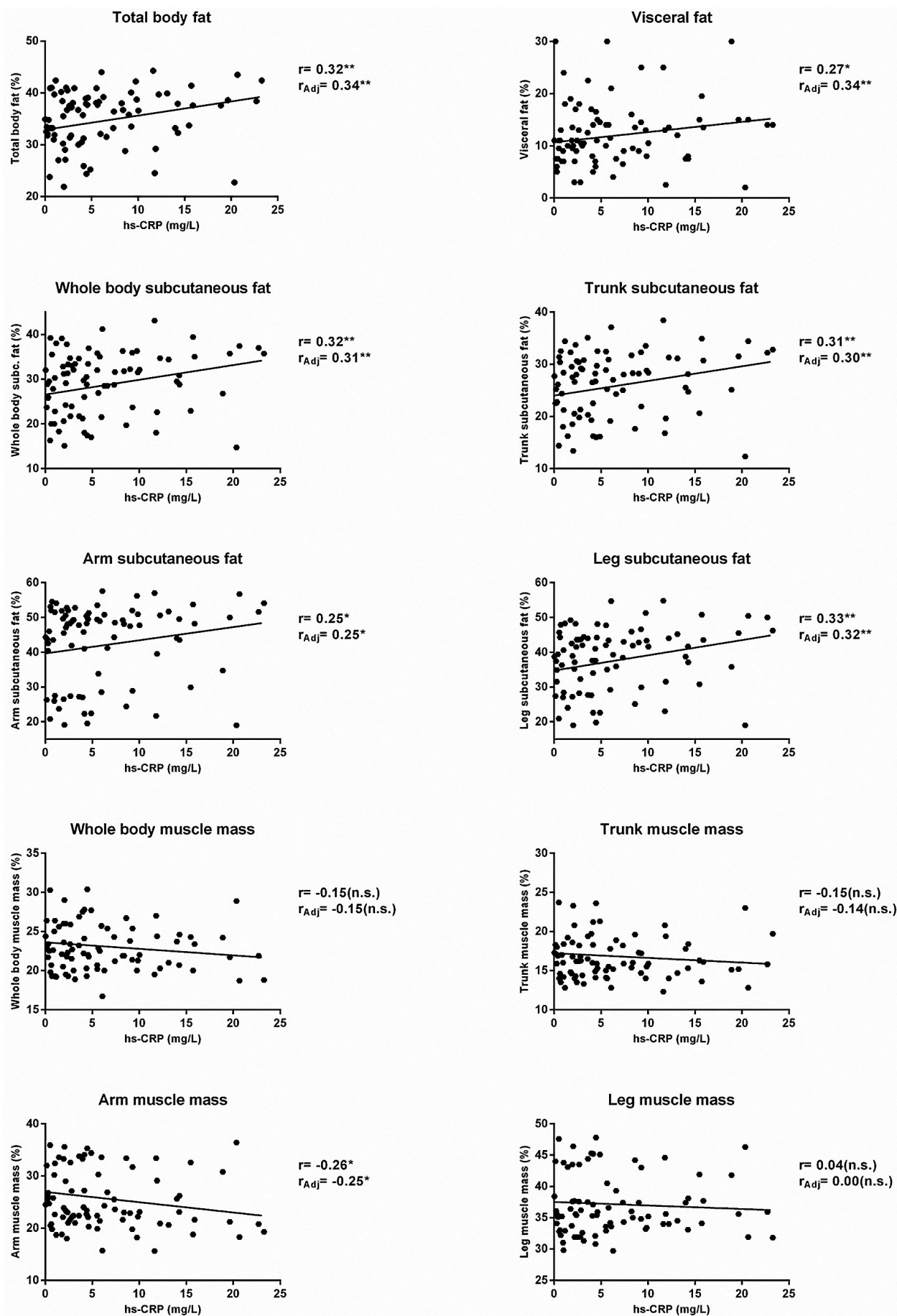


Figure 2: Correlation between body compositions with hs-CRP concentration. r: Spearman’s rank correlation coefficient, r<sub>Adj</sub>: correlation coefficient adjusted for sex and duration of diabetes, \* p<0.05, \*\* p<0.01, (n.s.) no statistically significant.

better than BMI [29]. Among non-obese individuals, abdominal obesity is related to a high level of CRP independent of BMI [30]. However, the results of our study showed that the adjusted correlation of hs-CRP with BMI is similar to that of a more reliable inflammation predictor such as total, subcutaneous, and visceral body fat. This may indicate that for a population under investigation, BMI is as powerful as other better indicators in predicting inflammation.

Obesity is more prevalent in adults with T2DM compared with the general population. Data obtained from the 1999–2002 National Health and Nutrition Examination Survey (NHANES) indicated that in the United States, 85% of adults with T2DM patients are obese or overweight. Excluding the overweight, there are 54% obese adults among them [31]. In the same survey, the prevalence of adults with overweight and obesity in the US is 35% and 30%, respectively [32]. In Saudi Arabia, the prevalence of obesity in healthy adults and adults with diabetes was 12.05 and 20.68%, respectively [33]. It seems that the prevalence of obesity in people with diabetes was double compared to the general population. The increase of year by year diabetes prevalence was associated with the increase of obesity, not overweight prevalence [34].

Body fatness is associated with diabetes complications, which may be mediated by inflammatory processes [17]. Having similar BMI, diabetes was associated with nearly three times the risk of high percentage body fat (female: >28%; male: >20%) among Iraqi people [35]. This may partially explain why inflammatory markers such as hs-CRP, IL-6, and TNF- $\alpha$  tend to increase in people with diabetes [36]. Elevated pro-inflammatory cytokines levels are associated with diseases such as atherosclerosis [37], coronary heart disease [38], colorectal, and gastric cancers [39], and chronic renal diseases [40]. While inflammation is consistently associated positively with complications, the role of obesity in these diseases is more complicated. Acting as a risk factor for de novo kidney failure, obesity is associated with a lesser mortality rate in hemodialysis patients [41]. An inverted correlation between adiposity and the risk of retinopathy was observed [42, 43]. This suggests a paradoxical situation considering that inflammation, which is linked to body fatness, was positively associated with diabetic retinopathy [44].

Muscle mass was associated with a lower risk of developing T2DM [45]. Low muscle mass was found to increase the risk of all-cause mortality in the 11,687 participants of the 1999–2004 NHANES. Among people with obesity, those with low muscle mass have a 2.5

times higher risk of mortality than those with preserved muscle mass [46]. There is a high prevalence of low muscle mass among patients with T2DM. A Korean study conducted in newly diagnosed and drug-naïve T2DM subjects showed that 12% had low muscle mass, and 8% had low muscle mass with abdominal obesity. Low muscle mass in this study was defined as appendicular skeletal muscle mass (ASM)  $\div$  height<sup>2</sup> of 2 SD below the mean value of the young reference group [47]. Among people with T2DM, low muscle mass is associated with insulin resistance [48, 49]. Low muscle mass was also associated with hyperglycemia in diabetes mellitus [50]. Inflammation contributes to muscle atrophy, possibly via impaired insulin signaling, which subsequently blunts Akt kinase activity [51]. It was observed that Akt activity in response to insulin was suppressed by 34% [52]. Reduced Akt activation results in phosphorylation of the FoxO transcription factors and transcription of MuRF1 and Atrogin-1, which result in muscle protein degradation [51]. In our study, inflammation is negatively correlated with arm muscle mass.

Measurements of wrist circumference were found to be correlated with inflammation in our study. Wrist circumference is used as a measurement to determine body frame size.

A recent study conducted in obese children suggested that wrist circumference is a biomarker of adipose tissue dysfunction and is a cardiovascular risk factor. Wrist circumference was shown to independently associated with the adiponectin-leptin ratio [53]. In a different study, wrist circumference was significantly correlated with metabolic syndrome by IDF ( $r=0.158$ ), NCEP-ATPIII ( $r=0.184$ ), Cook's ( $r=0.197$ ), and De Ferranti's ( $r=0.237$ ) definition [54]. Most of the studies evaluating wrist circumference only involved children; therefore, more studies in the adult population should be conducted [55]. Among Ghanaian female patients with T2DM, wrist circumference was an independent predictor of metabolic syndrome [56]. The association between wrist circumference and the risk of cardiovascular disease may be related to anatomical anomalies in the heart. Wrist circumference is positively correlated with left ventricular dimensions and mass and epicardial adipose tissue in overweight children. The strongest association was found between wrist circumference and left ventricular end-diastolic dimension ( $r=0.73$ ;  $p<0.0001$ ). The association of left ventricular end-diastolic dimension with wrist circumference was markedly better than that with BMI ( $r=-0.04$ ,  $p=NS$ ) [57].

## Conclusion

We found that sex and duration of diabetes had a limited impact on the association between anthropometric measurements and inflammation.

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## Conflict of Interest

The authors declare no conflict of interest.

## References

- Zhong J, Shi G. Editorial: Regulation of Inflammation in Chronic Disease. *Front Immunol* 10: 737, 2019
- Yousuf O, Mohanty BD, Martin SS *et al.* High-Sensitivity C-Reactive Protein and Cardiovascular Disease: A Resolute Belief or an Elusive Link? *J Am Coll Cardiol* 62: 397–408, 2013
- Li Y, Zhong X, Cheng G, *et al.* Hs-CRP and all-cause, cardiovascular, and cancer mortality risk: A meta-analysis. *Atherosclerosis* 259:75–82, 2017
- Newcombe EA, Camats-Perna J, Silva ML, Valmas N, Huat TJ, Medeiros R. Inflammation: the link between comorbidities, genetics, and Alzheimer's disease. *J. Neuroinflammation* 15: 276, 2018
- Wang J, Leung K-S, Chow SK-H, Cheung W-H. Inflammation and age-associated skeletal muscle deterioration (sarcopaenia). *J Orthop Transl* 10: 94–101, 2017
- Wang X, Bao W, Liu J *et al.* Inflammatory Markers and Risk of Type 2 Diabetes: A systematic review and meta-analysis. *Diabetes Care* 36: 166–75, 2013
- Calay ES, Hotamisligil GS. Turning off the inflammatory, but not the metabolic, flames. *Nat Med* 19: 265–7, 2013
- Ferrucci L, Fabbri E. Inflammageing: chronic inflammation in ageing, cardiovascular disease, and frailty. *Nat Rev Cardiol* 15: 505–22, 2018
- Vojarova B, Weyer C, Hanson K, Tataranni PA, Bogardus C, Pratley RE. Circulating Interleukin-6 in Relation to Adiposity, Insulin Action, and Insulin Secretion. *Obes Res* 9: 414–7, 2001
- Sindhu S, Thomas R, Shihab P, Sriraman D, Behbehani K, Ahmad R. Obesity Is a Positive Modulator of IL-6R and IL-6 Expression in the Subcutaneous Adipose Tissue: Significance for Metabolic Inflammation. *PLoS One* 10: e0133494, 2015
- Schmidt-Arras D, Rose-John S. IL-6 pathway in the liver: From physiopathology to therapy. *J Hepatol* 64: 1403–15, 2016
- Chavakis T, Bierhaus A, Nawroth PP. RAGE (receptor for advanced glycation end products): a central player in the inflammatory response. *Microbes Infect* 6: 1219–25, 2004
- Liu T, Zhang L, Joo D, Sun S-C. NF- $\kappa$ B signaling in inflammation. *Signal Transduct Target Ther* 2: 17023, 2017
- Senatus LM, Schmidt AM. The AGE-RAGE Axis: Implications for Age-Associated Arterial Diseases. *Front Genet* 8: 187, 2017
- Kautzky-Willer A, Harreiter J, Pacini G. Sex and Gender Differences in Risk, Pathophysiology and Complications of Type 2 Diabetes Mellitus. *Endocr Rev* 37: 278–316, 2016
- Peters SAE, Huxley RR, Woodward M. Sex differences in body anthropometry and composition in individuals with and without diabetes in the UK Biobank. *BMJ Open* 6: e010007, 2016
- Ellulu MS, Patimah I, Khaza'ai H, Rahmat A, Abed Y. Obesity and inflammation: the linking mechanism and the complications. *Arch Med Sci* 13: 851–63, 2017
- Tutuncu Y, Satman I, Celik S *et al.* A Comparison of hs-CRP Levels in New Diabetes Groups Diagnosed Based on FPG, 2-hPG, or HbA1c Criteria. *J Diabetes Res* 2016: 1–9, 2016
- Wang Y, O'Neil A, Jiao Y *et al.* Sex differences in the association between diabetes and risk of cardiovascular disease, cancer, and all-cause and cause-specific mortality: a systematic review and meta-analysis of 5,162,654 participants. *BMC Med* 17: 136, 2019
- Zoungas S, Woodward M, Li Q *et al.* Impact of age, age at diagnosis and duration of diabetes on the risk of macrovascular and microvascular complications and death in type 2 diabetes. *Diabetologia* 57(12): 2465–74, 2014
- Arambewela MH, Somasundaram NP, Ranjan Jayasekara HBP *et al.* Prevalence of Chronic Complications, Their Risk Factors, and the Cardiovascular Risk Factors among Patients with Type 2 Diabetes Attending the Diabetic Clinic at a Tertiary Care Hospital in Sri Lanka. *J Diabetes Res* 2018: 1–10, 2018
- Østergaard L, Mogensen UM, Bundgaard JS *et al.* Duration and complications of diabetes mellitus and the associated risk of infective endocarditis. *Int J Cardiol* 278: 280–4, 2019
- McCormack JP, Allan GM. Measuring hsCRP—an important part of a comprehensive risk profile or a clinically redundant practice? *PLoS Med* 7: e1000196, 2010
- Sleman Health Office. Permudah Layanan Kesehatan Bagi Pro-lanis, Puskesmas Mlati II Luncurkan Inovasi Kreatif “Lapis Kenyal”. Accessed at: <https://dinkes.slemankab.go.id/permudah-layanan-kesehatan-bagi-prolanis-puskesmas-mlati-ii-luncurkan-inovasi-kreatif-lapis-kenyal.html> 2019
- CDC. Body Measurements (Anthropometry) - NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY III. Accessed at: <https://www.cdc.gov/nchs/data/nhanes3/manuals/anthro.pdf> Rockville, MD: Westat, Inc.; 1988.
- Rothman KJ. BMI-related errors in the measurement of obesity. *Int J Obes* 32(3): S56–9, 2008
- Ashtary-Larky D, Daneghian S, Alipour M *et al.* Waist circumference to height ratio: Better correlation with fat mass than other anthropometric indices during dietary weight loss in different rates. *Int J Endocrinol Metab* 16(4), 2018

28. Staiano AE, Reeder BA, Elliott S et al. Body mass index versus waist circumference as predictors of mortality in Canadian adults. *Int J Obes* 36(11): 1450-4, 2012
29. Woolcott OO, Bergman RN. Relative fat mass (RFM) as a new estimator of whole-body fat percentage - A cross-sectional study in American adult individuals. *Sci Rep* 8: 10980, 2018
30. Lapice E, Maione S, Patti L et al. Abdominal adiposity is associated with elevated C-reactive protein independent of BMI in healthy nonobese people. *Diabetes Care* 32(9): 1734-6, 2009
31. CDC. Prevalence of overweight and obesity among adults with diagnosed diabetes -United States, 1988-1994 and 1999-2002. *Morb Mortal Wkly Rep* 53(45): 1066-8, 2004
32. Hedley AA, Ogden CL, Johnson CL, Carroll MD, Curtin LR, Flegal KM. Prevalence of overweight and obesity among US children, adolescents, and adults, 1999-2002. *J Am Med Assoc* 291(23): 2847-50, 2004
33. El-Hazmi MAF, Warsy AS. Prevalence of overweight and obesity in diabetic and non-diabetic Saudis. *East Mediterr Heal J* 6(2-3): 276-8, 2000
34. Menke A, Casagrande S, Geiss L, Cowie CC. Prevalence of and Trends in Diabetes among Adults in the United States, 1988-2012. *JAMA - J Am Med Assoc* 314(10): 1021-9 2015
35. Mohammed SJ. Association between Percentage of Body Fat in Normal Body Mass Index Subjects and Type 2 Diabetes Mellitus in Iraqi Population: Case Control Study. *J Diabetes Metab* 8, 2017
36. Phosat C, Panprathip P, Chumpathat N et al. Elevated C-reactive protein, interleukin 6, tumor necrosis factor alpha and glycemic load associated with type 2 diabetes mellitus in rural Thais: A cross-sectional study. *BMC Endocr Disord* 17(1): 44, 2017
37. Adar SD, D'Souza J, Mendelsohn-Victor K et al. Markers of inflammation and coagulation after long-term exposure to coarse particulate matter: A cross-sectional analysis from the multi-ethnic study of atherosclerosis. *Environ Health Perspect* 123(6), 2015
38. Danesh J, Kaptoge S, Mann AG et al. Long-term interleukin-6 levels and subsequent risk of coronary heart disease: Two new prospective studies and a systematic review. *PLoS Med* 5(4): e78, 2008
39. Taniguchi K, Karin M. IL-6 and related cytokines as the critical lymphins between inflammation and cancer. *Semin Immunol* 26(1): 54-74, 2014
40. Gluba A, Mikhailidis DP, Lip GYH, Hannam S, Rysz J, Banach M. Metabolic syndrome and renal disease. *Int J Cardiol* 164(2): 141-50, 2013
41. Rhee CM, Ahmadi SF, Kalantar-Zadeh K. The dual roles of obesity in chronic kidney disease: A review of the current literature. *Curr Opin Nephrol Hypertens* 25(3): 208-16, 2016
42. Chan JCY, Chee ML, Tan NYQ, Cheng CY, Wong TY, Sabanayagam C. Differential effect of body mass index on the incidence of diabetes and diabetic retinopathy in two Asian populations. *Nutr Diabetes* 8(1): 16, 2018
43. Man REK, Sabanayagam C, Chiang PPC et al. Differential association of generalized and abdominal obesity with diabetic retinopathy in Asian patients with type 2 diabetes. *JAMA Ophthalmol* 134(3): 251-7, 2016
44. Al-Kharashi AS. Role of oxidative stress, inflammation, hypoxia and angiogenesis in the development of diabetic retinopathy. *Saudi J Ophthalmol* 32(4): 318-323, 2018
45. Hong S, Chang Y, Jung H-S, Yun KE, Shin H, Ryu S. Relative muscle mass and the risk of incident type 2 diabetes: A cohort study. *PLoS One* 12: e0188650, 2017
46. Abramowitz MK, Hall CB, Amodu A, Sharma D, Androga L, Hawkins M. Muscle mass, BMI, and mortality among adults in the United States: A population-based cohort study. *PLoS One* 13(4): e0194697, 2018
47. Kim JA, Hwang SY, Chung HS et al. Proportion and Characteristics of the Subjects with Low Muscle Mass and Abdominal Obesity among the Newly Diagnosed and Drug-Naive Type 2 Diabetes Mellitus Patients. *Diabetes Metab J* 43(1): 105-113, 2018
48. Han SJ, Boyko EJ, Kim SK, Fujimoto WY, Kahn SE, Leonetti DL. Association of Thigh Muscle Mass with Insulin Resistance and Incident Type 2 Diabetes Mellitus in Japanese Americans. *Diabetes Metab J* 42(6): 488-495, 2018
49. Srikanthan P, Karlamangla AS. Relative muscle mass is inversely associated with insulin resistance and prediabetes. Findings from the third National Health and Nutrition Examination Survey. *J Clin Endocrinol Metab* 96: 2898-903, 2011
50. Sugimoto K, Tabara Y, Ikegami H et al. Hyperglycemia in non-obese patients with type 2 diabetes is associated with low muscle mass: The Multicenter Study for Clarifying Evidence for Sarcopenia in Patients with Diabetes Mellitus. *J Diabetes Investig* 10(6): 1471-1479, 2019
51. Perry BD, Caldwell MK, Brennan-Speranza TC et al. Muscle atrophy in patients with Type 2 Diabetes Mellitus: Roles of inflammatory pathways, physical activity and exercise. *Exerc Immunol Rev* 22: 94-109, 2016
52. Krook A, Roth RA, Jiang XJ, Zierath JR, Wallberg-Henriksson H. Insulin-stimulated Akt kinase activity is reduced in skeletal muscle from NIDDM subjects. *Diabetes* 47(8): 1281-6, 1998
53. Luordi C, Maddaloni E, Bizzarri C et al. Wrist circumference is a biomarker of adipose tissue dysfunction and cardiovascular risk in children with obesity. *J Endocrinol Invest* 43(1): 101-107, 2019
54. Fazeli M, Mohammad-Zadeh M, Darroudi S et al. New anthropometric indices in the definition of metabolic syndrome in pediatric patients. *Diabetes Metab Syndr Clin Res Rev* 13(3): 1779-1784, 2019
55. Namazi N, Djalalinia S, Mahdavi-Gorabi A et al. Association of wrist circumference with cardio-metabolic risk factors: a systematic review and meta-analysis. *Eat Weight Disord* 25(1): 151-161, 2018
56. Obirikorang C, Obirikorang Y, Acheampong E et al. Association of wrist circumference and waist-to-height ratio with cardio-metabolic risk factors among type II diabetics in a Ghanaian population. *J Diabetes Res*, 2018
57. Zampetti S, Campagna G, Leto G et al. Relation Between Wrist Circumference and Left Ventricular Structure in Overweight Children. *Am J Cardiol* 121(12): 1624-1628, 2018