ORIGINAL PAPER

Prevalence of erectile dysfunction and relationship between high sensitivity C-reactive protein, albuminuria, and cardiovascular risk factors with erectile dysfunction in coronary artery disease patients

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Summary ***Introduction:** It is estimated that more than 150 million men worldwide have erectile dysfunction (ED) and this number will reach more than 300 million by 2025. There is strong evidence that ED increases the risk of future cardiovascular events. ED and CAD share common risk factors. High sensitivity C-Reactive Protein (hs-CRP) is an important inflammatory biomarker in subclinical atherosclerosis. Albuminuria is also a marker of widespread endothelial dysfunction and is thought to be associated with ED. This study was conducted to analyze the prevalence of ED and the relationship between hs-CRP, albuminuria, and cardiovascular risk factors with the occurrence of ED in CAD patients.*

***Materials and methods:** From July 2024 to October 2024, 288 CAD cases from Saiful Anwar general hospital heart clinic met the inclusion criteria. Data on hs-CRP, albuminuria, and cardiovascular risk factors such as age, hypertension, diabetes mellitus, dyslipidemia, obesity, and smoking were observed in relation to incidence of erectile dysfunction in CAD patients. Then logistic regression analysis was performed.*

***Results:** There were 255 CAD patients (88.5%) who experienced ED. There was no significant relationship between hs-CRP and albuminuria with ED in CAD patients ($p > 0.05$). Significant risk factors for ED in CAD patients were age (OR = 15.92; 95% CI = 4.67-54.22; $p = 0.000$), triglycerides (OR = 2.52; 95% CI = 1.12-5.66; $p = 0.024$), and smoking (OR = 0.29; 95% CI = 0.09-0.89; $p = 0.031$).*

***Conclusions:** The prevalence of erectile dysfunction was 88.5% in patients with coronary artery disease. Hs-CRP and albuminuria did not have a significant relationship with the incidence of ED in patients with CAD. Risk factors that independently affect incidence of ED in patients with CAD are age, smoking, and hypertriglyceridemia.*

KEY WORDS: *Erectile dysfunction; Hs-CRP; Albuminuria; Coronary artery disease.*

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INTRODUCTION

It is estimated that more than 150 million men worldwide have *erectile dysfunction* (ED) and this number will reach more than 300 million by 2025 (1). There is strong evidence that ED increases the risk of future cardiovascular events (2). ED and CAD share common risk factors. *High-sensitivity C-Reactive Protein* (hs-CRP) is an important inflammatory biomarker in subclinical atherosclerosis (3). Albuminuria is also a marker of widespread endothelial dysfunction and is thought to be associated with ED (4). This study was conducted to analyze the prevalence of ED and the relationship of hs-CRP, albuminuria, and cardiovascular risk factors with ED in CAD patients.

METHODS

From July 2024 to October 2024, 288 cases from Saiful Anwar general hospital heart clinic met the inclusion criteria. The sample inclusion criteria used were being male patients diagnosed with stable coronary heart disease, detected by coronary angiography. The exclusion criteria used were: 1. Patients with diseases that interfere with sexual activity such as liver cirrhosis, kidney failure, thyroid disease, stroke, Parkinson's, and epilepsy; 2. Patients with a history of surgery on the pelvic organs, penis, urethra and prostate; 3. Patients with chronic infectious or inflammatory diseases; 4. Patients who are taking steroids, antidepressants (eg, selective serotonin reuptake inhibitors, tricyclics), antipsychotics, and antiandrogens (GnRH analogs and antagonists; 5-alpha reductase inhibitors); 5. Patients with psychogenic erectile dysfunction.

Patients were evaluated by assessing The *International Index of Erectile Function* (IIEF-5) questionnaire for evaluating patient erectile dysfunction and *Erection Hardness Score* (EHS) scoring to measure erectile hardness, C-Reactive Protein test to measure serum CRP levels, *urinary albumin to creatinine ratio* (UACR) test and cardiovascular risk factors, as hypertension, diabetes mellitus, dyslipidemia, obesity, smoking, and age.

Data were described and analyzed using the *Statistical Package for Social Science* (SPSS) version 22. Data were presented as values and percentages for categorical variables. Chi-Square analysis was applied to categorical data. Then multivariate analysis was performed using logistic regression test. The level of significant difference was defined as $p < 0.05$ with a 95% confidence interval.

RESULTS

In this study, 255 patients (88.5%) had ED and 33 patients (11.5%) did not experience ED. Of the 288 subjects, 56 (19.4%) of them suffered from DM, 100 (34.7%) suffered from hypertension, and 267 (92.7%) smoked (Table 1).

In univariate analysis, there was a significant relationship between age, smoking and triglycerides with ED in CAD patients ($p < 0.05$). Meanwhile, for other risk factors, there was no significant relationship with ED. *Body mass index* (BMI) ($p = 0.834$), smoking history ($p = 0.773$), hypertension ($p = 0.833$), diabetes mellitus ($p = 0.459$), total cholesterol levels ($p = 0.082$), LDL ($p = 0.501$), and HDL ($p = 0.076$) were also not associated with ED in CAD patients. Similarly, number of affected coronary vessels in coronary angiography, hs-CRP and UACR were not associated with ED in CAD patients ($p > 0.05$) (Table 2).

Table 1.
Characteristics of CAD patients with and without ED.

Characteristics	CAD with ED (n, %)	CAD without ED (n, %)
Age (year)		
< 50	19 (7.5)	12 (36.4)
50-59	70 (27.5)	18 (54.5)
60-69	124 (48.6)	2 (6.1)
≥ 70	42 (16.5)	1 (3.0)
Body mass index (kg/m^2)		
Normal (18.5-24.9)	144 (56.5)	18 (54.5)
Overweight (25.0-29.9)	81 (31.8)	10 (30.3)
Obesitas (≥ 30)	30 (11.8)	5 (15.2)
Smoking history		
Yes	241 (94.5)	26 (78.8)
No	14 (5.5)	7 (21.2)
Hs-CRP (mg/dL)		
Low (< 1)	195 (76.5)	27 (81.8)
Intermediate (1-3)	19 (7.5)	4 (12.1)
High (> 3)	41 (16.1)	2 (6.1)
UACR (mg/g)		
Normal (< 30)	236 (92.5)	31 (93.9)
Microalbuminuria (30-300)	13 (5.1)	1 (3.0)
Macroalbuminuria (> 300)	6 (2.4)	1 (3.0)
Blood pressure (mmHg)		
Normal	167 (65.5)	21 (63.6)
140-159	51 (20.0)	7 (21.2)
≥ 160	37 (14.5)	5 (15.2)
Diabetes melitus		
Yes	48 (18.8)	8 (24.2)
No	207 (81.2)	25 (75.8)
Hypertension + DM		
Yes	16 (6.3)	5 (15.2)
No	239 (93.7)	28 (84.8)
Coronary angiography (Vessel Disease)		
1	80 (31.4)	6 (18.2)
2-3	175 (68.6)	27 (81.8)
> 3	0 (0.0)	0 (0.0)
Total cholesterol (mg/dL)		
> 200	39 (15.3)	9 (27.3)
≤ 200	216 (84.7)	24 (72.7)
LDL (mg/dL)		
> 130	78 (30.6)	12 (36.4)
≤ 130	177 (69.4)	21 (63.6)
HDL (mg/dL)		
< 40	161 (63.1)	26 (78.8)
≥ 40	94 (36.9)	7 (21.2)
Triglycerides (mg/dL)		
> 150	72 (28.2)	18 (54.5)
≤ 150	183 (71.8)	15 (45.5)

Table 2.
Univariate analysis of risk factors for ED in CAD patients.

Risk factors	CAD Patients		P-value	OR (95% CI)
	ED (n, %)	No ED (n, %)		
Age (Year)				
≤ 60	89 (34.9)	30 (90.9)	0.000	0.054
> 60	166 (65.1)	3 (9.1)		0.016-0.181
Body mass index				
Normal	144 (56.5)	18 (54.5)	0.834	1.081
Overweight-obesity	111 (43.5)	15 (45.5)		0.522-2.240
Smoking				
Yes	241 (94.5)	26 (78.8)	0.001	4.635
No	14 (5.5)	7 (21.2%)		1.716-12.515
Hypertension				
No	167 (65.5)	21 (63.6)	0.833	1.084
Yes	88 (34.5)	12 (36.4)		0.510-2.307
Diabetes mellitus				
Yes	48 (18.8)	8 (24.2)	0.459	0.725
No	207 (81.2)	25 (75.8)		0.308-1.705
Hypertension + DM				
Yes	16 (6.3)	5 (15.2)	0.065	2.667
No	239 (93.7)	28 (84.8)		0.908-7.837
Total cholesterol (mg/dL)				
> 200	39 (15.3)	9 (27.3)	0.082	0.481
≤ 200	216 (84.7)	24 (72.7)		0.208-1.114
LDL (mg/dL)				
> 130	78 (30.6)	12 (36.4)	0.501	0.771
≤ 130	177 (69.4)	21 (63.6)		0.362-1.645
HDL (mg/dL)				
< 40	161 (63.1)	26 (78.8)	0.076	0.461
≥ 40	94 (36.9)	7 (21.2)		0.193-1.103
Triglycerides (mg/dL)				
> 150	72 (28.2)	18 (54.5)	0.002	0.328
≤ 150	183 (71.8)	15 (45.5)		0.157-0.685
Coronary angiography (VD)				
1	80 (31.4)	6 (18.2)	0.119	2.057
2-3	175 (68.6)	27 (81.8)		0.817-5.179
Hs-CRP (mg/dL)				
< 1	195 (76.5)	27 (81.8)	0.492	0.722
≥ 1	60 (23.5)	6 (18.2)		0.285-1.832
UACR				
Normal	236 (92.5)	31 (93.9)	0.773	0.801
Albuminuria	19 (7.5)	2 (6.1)		0.178-3.607

** Significance value (p < 0.05); OR: Odds ratio; CI: Confidence interval.*

Table 3.
Multivariate analysis of risk factors for ED in CAD patients.

Risk factors	P-value	OR (95% CI)
Age	0.000	15.92 (4.67-54.22)
Smoking	0.031	0.29 (0.09-0.89)
Triglycerides	0.024	2.52 (1.12-5.66)

** Significance value (p < 0.05); OR: Odds ratio; CI: Confidence interval.*

At multivariate logistic regression it was found that age, triglyceride levels, and smoking were correlated with ED in CAD patients. Age (OR = 15.92; 95% CI = 4.67-54.22; p = 0.000), smoking (OR = 0.29; 95% CI = 0.09-0.89; p = 0.031) and triglycerides were significantly related to ED in CAD patients (OR = 2.52; 95% CI = 1.12 - 5.66; p = 0.024) (Table 3).

Discussion

In the present study, the prevalence of ED was 88.5% in patients with CAD with a total of 255 patients experiencing ED and 33 patients (11.5%) not experiencing ED out of 288 study subjects. According to *Biernikiewicz et al.*, the prevalence of ED in men with coronary artery disease exceeded 90% (5). Other studies reported prevalence of ED in male patients with CAD between 46% and 75%. ED was associated with age, risk factors for atherosclerosis, and CAD (6). *Eardley et al*. stated that prevalence of ED varies from 1-29% in men aged 40-49 years to 26-76% in men over 70 years (7).
The majority of CAD patients with ED in the present study were in the age range 60-69 years (48.6%), while the rest were aged 50-59 years (27.5%), > 70 years (16.5%) and 7.5% were under 50 years. Logistic regression analysis conducted in the present study showed that age independently influenced the incidence of ED in CAD patients with an odds ratio for age of 15.9. The *Massachusetts Male Aging Study* (MMAS) showed that around 40% of men in their 40s will suffer from ED and this prevalence will increase by around 10% per decade so that men in their 50s will suffer from ED around 50%, and men in their 60s have a 60% chance of experiencing ED. Prevalence data from the MMAS and other data intuitively suggest that physiological processes that cause 40% of men in their 40s to experience ED have begun at an earlier age (8).
In the present study, CAD patients with ED experienced various conditions of dyslipidemia: 5.3% had total cholesterol > 200mg/dL, 30.6% LDL >130 mg/dL, 63.1% HDL < 40 mg/dL, and 28.2% TG > 150 mg/dL. Meanwhile, *Montorsi et al.* found that 57% of a total of 147 CAD patients with ED experienced hypercholesterolemia (9). In a prospective study involving 315 men aged 35-75 years (215 with ED), a higher prevalence of hypercholesterolemia (total cholesterol > 200 mg/dL) was found in men with ED (70.6%) compared to men who did not experience erectile dysfunction (52%) (10). Hypertriglyceridemia was significantly associated with ED in CAD patients with an odds ratio of 2.5 in the present study. An epidemiological study found risk factors and pathogenesis in common between ED and cardiovascular disease with TG being a common risk factor for both (11). Higher TG levels are also associated with arteriogenic ED (12). In the present study, other lipid profiles such as total cholesterol, HDL, and LDL levels were not significantly associated with ED in CAD patients. *Montorsi et al.* also showed in a study of 300 CAD patients no significant difference of hypercholesterolemia in the CAD group with and without ED (9).
Diabetes mellitus (DM) is one of the most common chronic diseases. In the present study, in the CAD group with ED, 18.8% of subjects with comorbid DM were found. In the *Montorsi et al.'s* study on 300 CAD patients, 8 subjects had comorbid type 1 DM (11%) and 22 subjects had type 2 DM (34%) in the CAD group with ED (9). CAD patients with comorbid DM were not associated with the incidence of ED in CAD patients in the present study. *Montorsi et al.'s* study also found no significant difference in type 2 DM in CAD patients with and without ED, although there was a significant difference for type 1 DM (9). *Zedan et al.* showed an odds ratio of 5.4 for DM (13). Insulin in euglycemic men is associated with the production of endothelial relaxant factor, while increased blood glucose levels decrease the release of endothelial nitric oxide. The occurrence of ED is associated with glycemic control in DM patients. Similarly, in CAD patients, good blood sugar control will reduce the number of cardiovascular events (14). The limitation of present study is that the duration of DM in our patients is unknown. This can affect the results of the study because duration of type 2 DM increases the risk of ED almost twofold compared to men without diabetes (15).
Hypertension is considered as one of risk factors for cardiovascular disease and is a common comorbidity in men with ED. In the present study, 20% of CAD patients with ED experienced hypertension stage 1 and 14.5% experienced hypertension stage 2. *Montorsi et al.* showed that 56% of subjects in CAD group with ED had comorbid hypertension. In the present study, comorbid hypertension was not associated with ED in CAD patients. In *Montorsi et al.'s* study, there was also no significant difference in hypertension in CAD patients with and without ED.9 Several previous studies have proven the presence of endothelial dysfunction in patients with hypertension. Hypertension will interfere with endothelial-mediated arterial vasodilation by damaging the NO-cGMP pathway. The limitation of present study is that some CAD patients also consume beta blocker drugs that affect blood pressure and ED, so this can affect the results of the study. Likewise, duration of hypertension was not recorded in present study.
Obesity is a major public health problem due to its rapidly increasing prevalence. In the present study, 31.8% patients of CAD group with ED, were overweight and 11.8% were obese. In another study, 73% of a total of 147 CAD patients with ED were obese (9). In a study from Slovakia, 73% of men older than 40 years of age with abdominal obesity had some degree of ED. In a further study, 79% of men with ED had a BMI ≥ 25 kg/m^2 (16). In present study, there was no significant relationship between BMI and incidence of ED in CAD patients. *Montorsi et al.* in their study also found no significant dif-

ferences in BMI or obesity in CAD patients with and without ED (9). In the study by *Biernikiewicz et al.*, there was no significant relationship between BMI and ED in patients with CAD although they found that waist circumference significantly influenced ED in patients with CAD (5). In the present study, waist circumference measurements were not carried out in patients with CAD. This is a limitation of the present study because waist circumference itself may act as a potential predictor for ED.

Smoking can cause cardiovascular disease and is now established as an independent risk factor for development of ED. In the present study, most CAD patients with ED had a history of smoking (94.5%). Meanwhile, other studies found that as many as 75% of subjects had a history of smoking in the group of CAD patients with ED.9 In the group of young men < 40 years, smoking is a significant risk factor for ED and has a strong role in the pathogenesis of ED (17). In the present study, smoking was significantly associated with a risk of ED in CAD patients. These results are supported by research by *Nicolosi et al.* where the odds ratio of smoking to the incidence of ED was 2.3 (18). Similarly, the results of a study conducted on 2,010 Italian men showed that smoking had an odds ratio of 2.4 to the incidence of ED (19). Therefore, smoking is a proven risk factor for the development of atherosclerosis and cardiovascular disease.

In the present study, there was no significant relationship between hs-CRP and ED in CAD patients. This result is in line with the study of *Lee et al.* where hs-CRP levels were not associated with ED in elderly men (20). From their analysis, no statistically significant relationship was found between hs-CRP levels and IIEF-5 ($p > 0.05$). In addition, in an analysis that included covariates such as age, body mass index, hypertension, diabetes mellitus, hyperlipidemia, alcohol, smoking, and IPSS index, serum hs-CRP levels were not a significant risk factor (20). The high-sensitivity CRP test can measure lower CRP levels with a sensitivity of 0.1 mg/dl, and is a useful marker for detecting low-grade chronic inflammation. However, the use of this test as a biomarker to detect ED itself needs to be further proven.

In present study, albuminuria was not associated with ED in patients with CAD. This result is in line with the study of *Barassi et al.* which stated that microalbuminuria, defined as the *urinary albumin/creatinine ratio* (UACR), did not differ significantly ($p > 0.05$) between patients with arteriogenic and non-arteriogenic ED. The study concluded that microalbuminuria cannot predict the etiology of penile arteriogenic disease (21). Albuminuria (microalbuminuria or macroalbuminuria) is a marker of extensive endothelial dysfunction. Microalbuminuria has also been associated with an increased risk of cardiovascular disease (4), although its use as a test to predict ED has not been proven.

In the present study, the number of coronary blood vessels involved in CAD did not differ significantly between the two groups with and without ED. *Montorsi et al.* in their study examining 300 CAD patients with angiography, also found no significant difference in the number of coronary arteries involved on angiography between CAD patients with and without ED (9).

Erectile dysfunction occurs due to the interaction of many factors including vasculogenic, neurological, psychological, and endocrinological ones. The limitation of the present study is that endocrinological factors such as testosterone levels and other hormones that play a role in the occurrence of ED were not studied. In addition, waist circumference was not measured in addition to BMI.

Conclusions

The prevalence of erectile dysfunction was 88.5% in patients with coronary artery disease. Hs-CRP and albuminuria did not have a significant relationship with the incidence of ED in patients with CAD. Risk factors that independently affect ED in patients with CAD are age, smoking, and hypertriglyceridemia.

Declarations

Ethical approval and consent for participate: *The author has ethical clearance No. 400/198/K.3/102.7/2024 from Health Research Ethics Committee, Saiful Anwar General Hospital, Malang, Indonesia.*

Availability of data and material: *All data underlying the results are available as part of the article and no additional source of data are required.*

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