Association Between Coronary Artery Lesion Severity and Erectile Dysfunction in Stable Coronary Heart Disease Patients

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Abstract

Background: Atherosclerosis is the underlying process of coronary heart disease. Atherosclerosis is preceded by endothelial dysfunction caused by systemic mechanical and chemical stressors that may occur throughout the blood vessels. Recent studies have found the link incidence of atherosclerosis in the coronary arteries and other arteries as well. Erectile dysfunction (ED) is a clinical manifestation might be caused by atherosclerosis in iliac or pudendal artery. Previous studies have established the relationship between coronary artery involvement and the incidence of ED, but the odds of risk has not been well established.

Methods: This was an age matched-paired case-control study. Erectile dysfunction in CHD patients who had undergone coronary angiography was checked by IIEF - 5 questionnaire. The severity of coronary artery lesion was assessed with a Syntax score from coronary angiography results. Moreover these results were assessed by a single experienced observer, blind method and were shown consistency test. Then, the risk of coronary artery lesion severity of the ED was analyzed by chi square test using SPSS version 20.

Result: There were 86 subjects consist of 57 subjects in the case group and 29 subjects in the control group. Stable CHD patients with high Syntax scores had 2.75 times risk for development of ED compare with low Syntax scores patients (OR : 2.75, 95 % CI : 1.08 to 6.95, p = 0.03). The severity of coronary artery lesions assessed with Syntax scores were not statistically significant as an independent factor as the incidence of ED.

Conclusion: Stable CHD patients with higher severity of lesions in coronary artery have a higher risk of erectile dysfunction than patients with lower severity of the lesion but was not statistically significant as an independent factor on the incidence of ED.

Keywords: Severity of coronary artery lesions, erectile dysfunction, stable coronary heart disease

Introduction

Atherosclerosis is a process underlies the occurrence of various diseases that have an increasing prevalence from year to year, such as coronary heart disease and stroke. Atherosclerosis is based on disruption of the balance that called homeostasis in endothelial cells that was defined as endothelial dysfunction. Endothel of blood vessels is a major regulator for vascular homeostasis in the artery. Endothelial layer has the ability to maintain a balance between vasodilation and vasoconstriction of blood vessels, prevent and stimulate proliferation and migration of smooth muscle cells, thrombogenesis and fibrinolysis. Mechanical and chemical stressors can disrupt the balance caused endothelial dysfunction that can initiate the process of atherosclerosis such as an increase in endothelial permeability, platelet aggregation, leukocyte adhesion, and release sitokin.[1] The existence of several mechanical and chemical stressors include the traditional cardiovascular risk factors would cause oxidative stressors that cause endothelial dysfunction occured in whole body artery.[2]

Coronary heart disease (CHD) is a disease that largely associated with atherosclerosis process in the coronary arteries. Atherosclerosis is a chronic, progressive and multifactorial process involving the blood vessels artery with the presence of atheroma plaque that causes narrowing of the lumen of blood vessels arteria.[3]

Several studies have shown the correlation of the plaque existence in coronary artery with other arteries. In addition, atherosclerosis in other arteries can also cause comorbidities for CHD patients and add patient's burden. In the study conducted by Kablak-Ziembicka et al. (2004)[4], Coskun et al. (2009)[5] and Geeta et al. (2014)[6], the relationship between the increase in carotid

intima-media thickness with the presence and extent of atherosclerosis in the coronary arteries was described. Study from Khoury et al. (1997)[7] showed a significant difference of atherosclerosis in the aorta, carotid artery and femoral artery in patients with significant lesions in coronary artery as compared to patients with normal coronary arteries.

Atherosclerosis in hypogastric pudendal artery is considered as one of the erectile dysfunction (ED) pathophysiology due to decreased blood flow to the corpus area cavernosus.[8] Endothelial dysfunction cause thickening of the intima and media layer, obstruction of vascular and reduction of flow due to stenosis. Severeal studies showed that the prevalence of erectile dysfunction among CHD patients is 42-75%.[9,10,11] Other studies showed the relationship between severity of ED with the number of blood vessel stenosis in CHD patients that were performed coronary angiography.[12,13]

Differences in blood vessels size, the amount of branching and the composition of the blood vessels between the arteries coronary artery to artery pudendal is the local factors that affect the incidence of atherosclerosis in the arteries so that the occurrence of endothelial dysfunction and atherosclerosis in artery pudendal are different in timing as theoretically. Shamlaul et al. (2004)[14] states that ED is a predictor for CHD in asymptomatic patients. However, in a study conducted by Montorsi et al. (2006)[15] showed that three coronary vessel stenosis was an independent predictor for ED incidence diagnosed with International Index of Erectile Function (IIEF) questionnaires in CHD patients.

This study aims to investigate whether the severity of coronary artery lesions assessed by a Syntax score is a risk to develop ED in patients with stable CHD. Syntax score was developed to characterize the coronary vascular lesions that include depiction of number, location, complexity of the lesion and the functional lesion effect.[16] The severity of DE was obtained through measurement of International Index of Erectile Function (IIEF) questionnaires.

Methods

In a case-control study performed between September and October 2015, We evaluated patients of who had been diagnosed as CHD with coronary angiography examinations that were examined in outpatient heart clinic Sardjito General Hospital. This study included 30-80 years aged men with CHD. Patients with sexual inactivity, history of trauma or surgery in the pelvic region, a history of stroke, Parkinson's or epilepsy were excluded from the study. Erectile dysfunction was checked by the validated Indonesian language version of IIEF-5 questionnaire. Depression and anxiety examined by the validated Indonesian language version of HADS questionnaire. Assessment of severity of coronary artery lesions in coronary angiography examination was performed by single observer blinded to the study group. Syntax score was assessed by an interventional cardiologist that had been performed consistency test or Kappa test. Kappa test results was 0.815, p = 0.001.

The presence of traditional cardiovascular risk factors such as diabetes mellitus, hypertension, dyslipidemia and smoker were assessed. The case group study was ED patients and the control group was patients who did not meet the criteria of DE. Each group will be matched by age. The ethics committee of the Faculty of Medicine Universitas Gadjah Mada approved this study.

The association between coronary artery lesion severity with ED was analyzed by chi-square test. Multivariate analysis with logistic regression for confounding factors was performed after univariate analysis. The p value < 0.05 was considered significant.

Results

Baseline characteristic

There were 244 patients with stable CHD who visit the heart outpatient clinic of Sardjito General Hospital, 34 patients refused to participate in the study and 12 patients were over 80 years age, therefore 198 stable CHD patients were enrolled in this study and 54 patients were excluded during the study. Of the 144 patients then do matching based on age and grouping samples in case and control groups with a ratio of 2 : 1, so that there were 86 patients as study subjects. Allocation for cases were 57 patients and for control were 29 patients.

Of 86 patients there were 28 diabetes mellitus patients (32.5 %) with 23 patients (40.3 %) in cases and 5 patients (18.5 %) in control group (p = 0.03). Fourty seven hypertensive patients (54.6 %) with 32 patients (56.1 %) in cases and 15 patients (51.7 %) in control group, 50 patients (58.1

Table 1. Baseline characteristics

Variables	Cases (n=57)	Control (n=29)	P value
Age, mean ± SD	55.7±6.3	53.1±6.9	0.28
BMI, mean ± SD	24.7± 3.4	25.2± 3.5	0.34
Traditional Risk Factor			
Diabetes mellitus, n(%)	23 (40.3)	5(18.5)	0.03
Hypertension, n(%)	32 (56.1)	15 (51.7)	0.69
Dyslipidemia, n(%)	32 (56.1)	18 (62.0)	0.59
Smoker, n(%)	40 (70.1)	23 (79.3)	0.37
Medication			
Beta blocker, n(%)	53 (92.9)	27 (93.1)	0.68
Diuretic, n(%)	7 (12.3)	2 (6.7)	0.36
Psychogenic factor			
Depression, n(%)	5 (8.7)	1 (3.4)	0.34
Anxiety, n(%)	11 (19.3)	3 (10.3)	0.28
History of AMI	42(73.6)	22(75.8)	0.83

ED : Erectile Dysfuctioni, BMI : Body Mass Index, SD : standard deviation, AMI : acute myocardial infarction

Table 2. Bivariate analysis of Syntax score with incidence of ED

Characteristics	Cases (n=57)	Control (n=29)	OR	95% CI	p
High Syntax score, n(%)	41(71.9)	14(48.3)	2.75	1.08-6.95	0.03
Low Syntax score, n(%)	16(28.1)	15(51.7)			

ED : Erectile Dysfunction, OR : odds ratio, CI : Confidence Interval

%) had dyslipidemia with 32 patients (56.1 %) in cases and 18 patients (62 %) in control group. Smoking history was found in 63 patients (73.2 %) with 40 patients (70.1 %) in cases and 23 patients (79.3 %) in control group. Study subjects suffering from hypertension, dyslipidemia and smoking in case and control groups was not significantly difference (p > 0.05) .

The subjects of the study were also given questionnaires to assess the HADS depression and anxiety. There were no significant differences between two goups on depression, anxiety, history of treatment with a beta blocker or diuretic drugs, and history of acute myocardial infarction (p > 0.05).

In the cases there were 41 patients (71.9%) with a high Syntax score and 16 patients (28.1%) with a low Syntax score. Whereas in the control group there were 14 patients (48.3%) with a high Syntax score and 15 patients (51.7%) with a low Syntax score. Results of bivariate analysis with chi-square test showed an odds ratio (OR) of 2.75 with a 95% CI 1.08 to 6.95 (p = 0.03).

There are several factors that can affect the incidence of ED among stabil CHD patients. These factors include traditional risk factors such as diabetes, hypertension, dyslipidemia and smoking, psychogenic factors such as depression and anxiety and medication such as diuretics and beta blockers. Bivariate analysis concluded that diabetes mellitus and Syntax score as factors that had significance risk for DE.

Multivariate analysis with logistic regression was performed to analyze whether the incidence of ED among CHD patients were affected by Syntax score and diabetes mellitus. The result of the multivariate analysis inclued diabetes mellitus and Syntax score was not statistically significant.

Tabel 3. Multivariate analysis between diabetes mellitus and Syntax score as independent predictor for DE

Variables	OR	95% CI	p
Syntax score	2.46	0.95-6.37	0.07
Diabetes mellitus	2.90	0.95-8.89	0.06

OR : Odds Ratio, CI : Confidence Interval

Discussion

This study showed that the severity of CHD increased to risk to develop ED in patients with

stable CHD. Higher Syntax score was associated with 2.75 time the risk of ED as compared to those with low Syntax score. However, multivariate analysis included diabetes mellitus as covariate showed that the high Syntax score did not predict ED independently.

In some studies mentioned that age was one of the factors that affect the incidence of ED.[17,18] Age played a role on ED incidence in which the prevalence of ED increases with age and there was a significant mean age difference on the group of patients who have severe ED. In this research, matching to the age factor was to control the effects on outcomes to be studied, it is evidenced by no significant difference in the mean age of cases and controls (p = 0.28) .

The study by Fung et al. (2004)[18] also concluded the increased severity of ED affected by BMI. In this study, the mean BMI of the two groups studied did not have a significant difference (p = 0.342) so that this factor does not affect the outcome studied. In this study there were also no significant differences in mean patients who have experienced of MI between the case group and the control group. Montorsi et al. (2003)[19] investigated the incidence of ED in patients with acute chest pain who was performed coronography and showed that 67% prevalence of ED in the study subjects. However previous study conducted showed there was no significant difference in the group that had history of MI. Furthermore the incidence of ED in patients with a history of MI associated with the severity of coronary artery lesions.[15]

Traditional risk factors such as diabetes mellitus, hypertension, dyslipidemia and smoking were analyzed in this study and was only diabetes mellitus that has a higher proportion of the cases and has a significant difference to the control group. The use of beta blockers and diuretics medications in this study did not differ significantly between the two groups. This was likely to occur because the study population homogeneous in patients who have been diagnosed with CHD so exposure to drugs such as beta blockers or diuretics do not have significant differences in proportions. Depression and anxiety were also not significantly different between two group. The assessment of depression in patients with CHD will be more apparent in patients with acute myocardial infarction, so that the low proportion of depression and anxiety in this study due to the possibility of having different coping mechanisms.[20]

The severity of coronary artery lesions in this study was assessed by Syntax scores. It is a scoring system that in general as an unification of various scoring systems already exist include Leaman scoring system, the ACC / AHA classification, segments classification of the AHA that have been modified on an ARTS study, Duke classification and ICPS about lesions bifurcation, and total occlusion lesion scoring system. Lesions were assessed in each segment that caused obstruction > 50 % of the blood vessels with a diameter ≥1,5 mm. Syntax score assessment carried out by a interventional cardiologistthat was previously tested the validity assessment with consistency test. It performed intraobserver assessment and the result was good with kappa value of 0.815 (p = 0.001).[16]

In this study, patients with stable CHD with high Syntax score had 2.75 times higher risk compare with stable CHD patients who had low Syntax score (95% CI 1.08 to 6.95, p = 0.031). It consistence with recent studies that was conducted by Montorsi et al. (2006)[15] and Shanker et al. (2013)[20] which yield an increase in the prevalence of ED among patients in the study group who had involvement of more blood vessels, higher Gensini score and the risk of vascular involvement of three coronary arteries. There is a relationship between the number of blood vessel involvement with the incidence of ED in patients with CHD.[13] All of three studies showed the relationship of the burden of atherosclerosis in coronary artery blood vessel with the incidence of ED. Assessment of atherosclerosis burden of the coronary arteries in previous studies only used the amount of blood vessels invovement and Gensini score, but in this study by using Syntax scores that assess the severity of coronary artery lesions more completely than any other score system. This study also used case control method that is more robust methodology than the cross sectional method, as was done in the three previous studies.

This study also performed a risk assessment of several pathophysiological factors for ED incidence. These factors are traditional risk factors such as diabetes mellitus, hypertension, dyslipidemia and smoking, psychological factors namely depression and anxiety as well as medicinal drugs included beta-blockers and diuretics. Baseline characteristics of these factors showed that only diabetes mellitus has a statistically significant difference between case and

control groups. Other factors have no statistically significant differences in the basic characteristics of this study .

Another study assessing traditional risk factors on the incidence of ED was the study conducted by Fung et al. (2004)[18] that examined the relationship between all the traditional risk factors with incidence of ED in the future with the result of age, BMI and hypercholesterolemia as an independent predictor of the ED incidence, while research by Martin-Morales et al. (2001)[21] obtained higher incidence of DE among diabetes mellitus, hypertension, dyslipidemia and smoker. This study has consistency of the results with previous study [21] in where diabetes mellitus is the traditional risk factors that have the highest risk for the occurrence of ED, however the results of this study differ from other study.[18] Studies with larger sample and more powerful research methodologies needed to identify risk factors that have the highest risk of ED incidence.

Multivariate logistic regression analysis showed that Syntax scores were not statistically significant as independent factors on the incidence of ED in patients with CHD. It also showed no significant independent factors for ED incidence. Diabetes mellitus also showed no statistically significant results as independent factors on the incidence of ED. At the COBRA study [15] concluded chronic symptoms, age and more extensive coronary artery lesion was an independent factors on the ED incidence but diabetes mellitus is not. In the study, multivessel lesions and chronic lesions in three arteries was an independent factor that proved to be statistically significant on the incidence of ED. This study had different results with previous study in which the severity of coronary artery lesions were assessed by a Syntax score not proven statistically as independent factors on the incidence of ED. This is likely due to differences in atherosclerosis burden assessment conducted in research by Montorsi et al. (2006)[15] with this study. Another difference was in previous study subject was chronic symptoms of CHD with three branches atherosclerotic of coronary artery and with acute coronary syndrome, whereas in this study population is stable CHD patients with or without a history of myocardial infarction. The same result is the effect of diabetes mellitus on the incidence of ED which in this study did not prove significant as a factor independent predictor of the incidence of ED in patients with CHD.

Study Limitations

Endocrinology factors are the factors that can cause erectile dysfunction other than vasculogenic, psychological, neurological factor and related anatomical fibroelastisity. In this study, testosterone hormone as endocrinologic factors which also is one of the things that can affect the incidence of ED was not investigated.

Conclusion

Stable CHD patients with higher severity of lesions in coronary artery assessed by Syntax score have a higher risk of ED than patients with lower severity of the lesion but was not statistically significant as an independent factor on the incidence of ED.

REFERENCES

1. Davignon J, Ganz P. 2004. Role of endothelial dysfunction in atherosclerosis. Circulation. 109:27-32.
2. Esper RJ, Nordaby RA, Vilarino JO, Paragano A. 2006. Endothelial dysfunction: comprehensive appraisal. Cardiovasc Diabet. 5: 1-18.
3. Lilly SL. 2011. Pathophysiology of Heart Diseases 5th ed. Philadelphia: Lippincott Williams and Wilkins.
4. Kablak-Ziembicka A, Tracz W, Przewlocki T, Pieniazek P, Sokolowsky A, Konieczynska M. 2004. Association of increased carotid intima-media thickness with the extent of coronary artery disease. Heart. 90:1286-1290
5. Coskun U, Yildiz A, Esen OB, Baskurt M, Cakar MA, Kilickesmez KO, Orhan LA, Yildiz S. 2009. Relationship between carotid intima-media thickness and coronary angiographic findings: a prospective study. Cardiovasc Ultrasound. 9:1-5.
6. Geeta-Khatri JK., Singh M, Pahuja K, Singh J. 2014. The usefull of B-mode ultrasound scan and correlation of carotid intimal media thickness with extent and severity of coronary artery disease. J Anat Soci India. 63:21-25.
7. Khoury Z, Schwartz R, Gottlieb S, Chenzbraun A, Stern S, Keren A. 1997. Relation of coronary artery disease to atherosclerotic disease in the aorta, carotid and femoral artery evaluated by ultrasound. Am J Cardiol. 80:1429-1433.
8. Azadzoi KM. 2006. Vasculogenic erectile dysfunction: beyond the hemodunamic changes. BJU International. 97:11-16.

9. Hodges LD, Kirby M, Solanki J, O'Donnel J, Brodie DA. 2007. The temporal relationship between erectyle dysfunction and cardiovascular disease. Int J Clin Pract. 61:2019-2025.

10. Feldman HA,Goldstein I, Hatzichristou D, Krane RJ, McKinley JB. 1994. Impotence and its medical and psychological correlates: results of the massachusetts male aging study. J Urol.151:54-61.

11. Kloner RA, Mullin SH, Shook T. 2003. Erectile dysfunction in the cardiac patients: how common and should we treat. J Urol. 170:46-50.

12. Solomon H, Msn JW, Wierzbicky AS, Jackson G. 2003. Relation of erectyle dysfunction to angiographic coronary artery disease. Am J Cardiol. 91:230-231.

13. Foroutan SK, Rajabi M. 2007. Erectile dysfunction in men with angiographically documented coronary artery disease. Urol J. 4:28-32.

14. Shamlaul R, Ghanem HM, Salem A. 2004. Correlation between penile duplex findings and stress echocardiography in men with erectile dysfunction. Internal Journal of Impot Res. 76:235-237.

15. Montorsi P, Ravagnani PM, Galli S, Rotatori F, Veglia F, Briganti A, Salonia A, Deho F, Rigatti P, Montorsi F, Fiorentini C. 2006. Association between erectile dysfunction and coronary artery disease. role of coronary clinical presentation and extent of coronary vessels involvement: The COBRA Trial. Eur Heart J. 27:2632-2639.

16. Sianos G, Morel MA, Kappetein AP, Morice MC, Colombo A , Colombo A, Dawkins K, Van den Brand M. 2005. The Syntax score: an angiographic tool grading the complexity of coronary artery disease. Euro Intervention J. 1:219-227.

17. Johaness CB, Feldman HA, Derby CA, Kleman KP, McKinley JB. 2000. Incidence of erectyle dysfunction in men 40-69 years old: longitudinal results from massachussets male aging study. J Urol. 170:546-550.

18. Fung MM, Bettencourt R, Berret-Connor E. 2004. Heart disease risk factors predicts erectyle dysfunction 25 years later: The Rancho Bernardo Study. J Am Coll Cardiol. 43(8):1405-1411.

19. Montorsi F, Briganti A, Salonia A, Rigatti P, Margonato A. 2003. Erectyle Diysfunction Prevalence, Time of Onset and Association with Risk Factors in 300 Consecutive Patients with Acute Chest Pain and Angiographically Documented Coronary Artery Disease. Eur Urol. 44:360-364.

20. Shanker SR, Panikhrisna B, Reddy CB. 2013. Association Between Erectyle Dysfunction and Coronary Artery Disease and Its Severity. Ind Heart J. 65:180-186.

21. Martin-Morales A, Sanchez-Cruz JJ, Saenz de Tejada I, Rodriguez-Vela L, Jimenez-Cruz JF, Burgos-Rodriguez R. 2001. Prevalence and independent risk factors for erectile dysfunction in Spain: results of the Epidemiologia de la Disfuncion Erectil Masculina Study. J Urol. 166(2) : 569-574.