RELATION OF MICROALBUMINURIA AND CORONARY ARTERY DISEASE IN NON DIABETIC PATIENTS

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Abstract

INTRODUCTION: Prospective studies confirmed that microalbuminuria is a predictor of cardiovascular diseases, independent of classical risk factors and is associated with all-cause mortality in patients with diabetes or hypertension and in the general population. However, there is few data linking angiographic severity of coronary artery disease (CAD) to microalbuninuria (MA). We examined coronary angiograms for extent of severe CAD (luminal narrowing 50%) in patients without Diabetes Mellitus (DM) and general population.

METHODS: Our study comprised of 153 patients undergoing coronary angiography in Hazrat Fatemeh hospital in Iran (M/F 80/73, mean age 57 ± 11 y). Urine albumin excretion was measured in 24h urine samples by immune precipitation technique. Age-sex, distribution of coronary risk factors and MA were compared between patients with and without CAD.

RESULTS: Overall, 70.5% (108) of patients had CAD and 29.4% (45) had no coronary lesion. MA was detected in 62.9% of patients with CAD and 8.8% of those without coronary artery lesion ($P < 0.05$). The presence of 1 or 2 vessels CAD showed a linear increase from group to group without microalbuminuria ($P < 0.05$).

CONCLUSION: Patients with MA have more severe angiographic CAD compared to those without MA. This relation is independent of other risk factors.

Keywords: Coronary artery disease, diabetes, microalbuminuria

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Introduction

The risk of cardiovascular diseases (CVD) in cohort studies is predicted by traditional risk factors including age, sex, smoking, diabetes mellitus, hypertension and dyslipidemia. However, these factors don't entirely explain the variation of CVD incidence and mortality in individuals and populations.[1] This fact has led to studies on nontraditional cardiovascular risk factors and reside concentration of urinary albumin is one of these factors. Microalbuminuria is independently associated with all–cause mortality and cardiovascular morbidity and mortality in patients with Diabetes,[2,3] hypertension[4,5] and in the general population.[6-10] In diabetic patients, microalbuminuria is predictive of nephropathy.[11]

As the association between proteinuria and cardiovascular events is well described,[12] the purpose of this study is to investigate whether urinary albumin excretion is a sign of atherosclerotic involvement of coronary artery in the general population.

Materials and Methods

In the present study, we investigated the relation between extent of atherosclerosis and microalbuminuria by comparing the angiographic severity of coronary artery disease (CAD) in patient with microalbuminuria. The purpose was to document the association of MA and severe CAD. We studied 153 Patients (79 men and 74 women: mean age 57 ± 11 years) who underwent Coronary angiography in the hospitals of Mazandaran University of Medical Sciences between January 2007 and June 2007. Collected data included well-recognized cardiovascular risk factors of age, hypertension, hypercholesterolemia, DM, and smoking as well as MA and fasting glucose levels in all patients.

Microalbumin was measured by rate nephelomety using the Behring protein analyzer. Urine creatinine was measured by a Behring analyzer. Patients with albumin levels less than 30 mg/g of creatinine were defined as having normoalbuminuria, those with albumin levels > 30-300 mg/g were defined as having macroalbuminuria.

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CAD was defined significant if a diameter stenosis was ≥ 50% in ≥ 1 major coronary artery. Diagnosis of DM was based on abnormal fasting blood glucose ≥ 126 mg/dl on more than two occasions or the use of hypoglycemic agent.

Patients who received medication for hypertension or those with systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg and not on concurrent antihypertensive therapy were classified as having hypertension.

Hypertension diabetic patients were defined as systolic ≥ 130.80 mmHg. Patients who had smoked within a year before entry to the study were deemed current smokers. Patients who used cholesterol lowering medication or had a total serum cholesterol level ≥ 200 mg/dl were classified as having hypercholesterolemia.

Statistical analysis was performed using the SPSS (version 13). Chi-square or tailed test was used to examine the baseline difference between proportions or means, and P ≤ 0.05 was considered statistically significant. Because the prevalence of conventional CAD risk factors such as hypertension, hypercholesterolemia and smoking was not significantly different across groups, we did not perform multivariate analysis.

Results

The mean age of patients in both groups was similar. CAD occurred more frequent in male than female and in smokers than none smokers. The prevalence of different CAD risk factors (age, hypertension and hypercholesterolemia) was also similar across groups (table 1). Microalbuminuria was more frequent in CAD patients (62.9% vs 8.8%). Severity of CAD in different subgroups of patients is presented in table 2. Three-vessel CAD was presented in 21 of 37 patients (56.7%) with microalbuminuria and in 16 of 37 patients without microalbuminuria (43.2%).

Two vessel CAD was found in 36 of 54 patients (66.6%) with microalbuminuria and in18 of 54 patients (33.3%) without microalbuminuria. Comparing the two groups showed that this difference was significant (P < 0.01).

Table 1: Patients' demographics and prevalence of coronary artery disease risk factors

variable	CAD+	CAD-	P
N	108	45	
Age (yrs)	58 ± 11	58 ± 9.8	> 0.05
M/F	62/46	18/27	< 0.05
Smoking (n)	12 (11.1%)	2 (4.5%)	< 0.05
Hypertension (n)	42 (38.8%)	16 (35.6%)	> 0.05
Hypercholesterolemia (n)	38 (35.1%)	15 (33.3%)	> 0.05
MA* (n)	68 (62.9%)	4 (8.8%)	< 0.05

* Microalbuminuria

Table 2: Prevalence of three vessels and two or three vessel CAD in different patient groups

No. of coronary arteries narrowed	MA+	MA -	P
3 (n)	21	16	< 0.05
2 (n)	36	18	< 0.05
1 (n)	11	6	< 0.05

MA: microalbuminuria

Discussion

In the present study microalbuminuria was high in patients with CAD.

Despite extensive data linking microalbuminuria to coronary atherosclerosis,[5,6,10,13,14] few studies have examined the correlation between angiographic severity of coronary artery diseases and microalbuminuria. The aim of this study was to find whether microalbuminuria was associated with more extensive coronary atherosclerosis in nondiabetic patients. We found that patients with microalbuminuria had much greater atherosclerotic burden in the form of multivessel CAD compared to patients without MA especially nondiabetics.

Studies showed that correlation between angiographic severity and microalbuminuria was significant among diabetics.[15] The mechanism of accelerated atherosclerosis in microalbuminuria is uncertain, but abnormal vasodilatation, endothelial dysfunction, inflammation, insulin resistance or abnormal coagulation may be involved.[16-20]

Aggressive treatment of microalbuminuria in CAD patients may have salutary effects. Some study showed that decrease in baseline albuminuria, which was more pronounced with losartan than with atenolol, was associated with cardiovascular benefits.[21,22]

Another study was performed in 846 normotensive patients with normal serum cholesterol level and microalbuminuria was randomly assigned to fosinopril or placebo and to pravastin or placebo. At a follow-up of almost 4 years, Fosinopril was associated with a significant trend in lowering the rate of cardiovascular mortality and hospitalization.[23]

We used a ratio of spot trinity albumin to creatinine to detect microalbuminuria. Although a 24h urine collection is the gold standard for the detection of microalbuminuria, several studies have found that a urinary albumin to creatinin ratio is equally sensitive and specific.[24]

Conclusion: this study showed significant correlation between microalbuminuria and severity of CAD, treatment of microalbuminuria is recommended.

References

1. Kuulasmaa K, Tunstall-Pedoe H, Dobson A, Fortmann S, Sans S, Tolonen H, et al. Estimation of contribution of changes in classic risk factors to trends in coronary-event rates across the WHO MONICA Project populations. Lancet 2000; 355(9205): 675-87.
2. Messent JW, Elliott TG, Hill RD, Jarrett RJ, Keen H, Viberti GC. Prognostic significance of microalbuminuria in insulin-dependent diabetes mellitus: a twenty-three year follow-up study. Kidney Int 1992; 41(4): 836-9.
3. Park HY, Schumock GT, Pickard AS, Akhras K. A structured review of the relationship between microalbuminuria and cardiovascular events in patients with diabetes mellitus and hypertension. Pharmacotherapy 2003; 23(12): 1611-6.
4. Bigazzi R, Bianchi S, Baldari D, Campese VM. Microalbuminuria predicts cardiovascular events and renal insufficiency in patients with essential hypertension. J Hypertens 1998; 16(9): 1325-33.
5. Wachtell K, Ibsen H, Olsen MH, Borch-Johnsen K, Lindholm LH, Mogensen CE, et al. Albuminuria and cardiovascular risk in hypertensive patients with left ventricular hypertrophy: the LIFE study. Ann Intern Med 2003; 139(11): 901-6.
6. Gerstein HC, Mann JF, Yi Q, Zinman B, Dinneen SF, Hoogwerf B, et al. Albuminuria and risk of cardiovascular events, death, and heart failure in diabetic and nondiabetic individuals. JAMA 2001; 286(4): 421-6.
7. Romundstad S, Holmen J, Kvenild K, Hallan H, Ellekjaer H. Microalbuminuria and all-cause mortality in 2,089 apparently healthy individuals: a 4.4-year follow-up study. The Nord-Trøndelag Health Study (HUNT), Norway. Am J Kidney Dis. 2003; 42(3): 466-73.
8. Yuyun MF, Khaw KT, Luben R, Welch A, Bingham S, Day NE, et al. Microalbuminuria independently predicts all-cause and cardiovascular mortality in a British population: The European Prospective Investigation into Cancer in Norfolk (EPIC-Norfolk) population study. Int J Epidemiol 2004; 33(1): 189-98.
9. Yuyun MF, Khaw KT, Luben R, Welch A, Bingham S, Day NE, et al. Microalbuminuria and stroke in a British population: the European Prospective Investigation into Cancer in Norfolk (EPIC-Norfolk) population study. J Intern Med 2004; 255(2): 247-56.
10. Klausen K, Borch-Johnsen K, Feldt-Rasmussen B, Jensen G, Clausen P, Scharling H, et al. Very low levels of microalbuminuria are associated with increased risk of coronary heart disease and death independently of renal function, hypertension, and diabetes. Circulation 2004; 110(1): 32-5.
11. .Krolewski AS, Warram JH, Natural history of diabetic nephropathy: how much can it be changed? Diabetes Rev 1995; 3(3): 446-59.
12. Sarnak MJ; Levey AS; Schoolwerth AC; Coresh J; Culleton B; Hamm LL, et al. Kidney disease as a risk factor for development of cardiovascular disease: a statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. Circulation 2003; 108(17): 2154-69.
13. Hillege HL, Fidler V, Diercks GF, van Gilst WH, de Zeeuw D, van Veldhuisen DJ, et al. Urinary albumin excretion predicts cardiovascular and noncardiovascular mortality in general population. Circulation 2002; 106(14): 1777-82.
14. Wang TJ, Evans JC, Meigs JB, Rifai N, Fox CS, D'Agostino RB, Levy D, Vasan RS. Low-grade albuminuria and the risks of hypertension and blood pressure progression. Circulation 2005; 111(11): 1370-6.
15. Sukhija R, Aronow WS, Kakar P, Garza L, Sachdeva R, Sinha A, et al. Relation of microalbuminuria and coronary artery disease in patients with and without diabetes mellitus. Am J Cardiol 2006; 98(3): 279-81.
16. Clausen P, Jensen JS, Jensen G, Borch-Johnsen K, Feldt-Rasmussen B. Elevated urinary albumin excretion is associated with impaired arterial dilatory capacity in clinically healthy subjects. Circulation 2001; 103(14): 1869-74.
17. Pedrinelli R, Giampietro O, Carmassi F, Melillo E, Dell'Omo G, Catapano G, et al. Microalbuminuria and endothelial dysfunction in essential hypertension. Lancet 1994; 344(8914): 14-8.
18. Festa A, D'Agostino R, Howard G, Mykkänen L, Tracy RP, Haffner SM. Inflammation and microalbuminuria in nondiabetic and type 2 diabetic subjects: The Insulin Resistance Atherosclerosis Study. Kidney Int 2000; 58(4): 1703-10.
19. Mykkänen L, Zaccaro DJ, Wagenknecht LE, Robbins DC, Gabriel M, Haffner SM. Microalbuminuria is associated with insulin resistance in nondiabetic subjects: the insulin resistance atherosclerosis study. Diabetes 1998; 47(5): 793-800.
20. Meeking DR, Cummings MH, Thorne S, Donald A, Clarkson P, Crook JR, et al. Endothelial dysfunction in Type 2 diabetic subjects with and without microalbuminuria. Diabet Med 1999; 16(10): 841-7.
21. Ibsen H, Wachtell K, Olsen MH, Borch-Johnsen K, Lindholm LH, Mogensen CE, et al. Does albuminuria

predict cardiovascular outcome on treatment with losartan versus atenolol in hypertension with left ventricular hypertrophy? A LIFE substudy. J Hypertens 2004; 22(9): 1805-11.

22. Ibsen H, Olsen MH, Wachtell K, Borch-Johnsen K, Lindholm LH, Mogensen CE, et al. Reduction in albuminuria translates to reduction in cardiovascular events in hypertensive patients: losartan intervention for endpoint reduction in hypertension study. Hypertension 2005;45(2): 198-202.

23. Asselbergs FW, Diercks GF, Hillege HL, van Boven AJ, Janssen WM, Voors AA, et al. Effects of fosinopril and pravastatin on cardiovascular events in subjects with microalbuminuria. Circulation 2004; 110(18): 2809-16.

24. Eknoyan G, Hostetter T, Bakris GL, Hebert L, Levey AS, Parving HH, et al. Proteinuria and other markers of chronic kidney disease: a position statement of the national kidney foundation (NKF) and the national institute of diabetes and digestive and kidney diseases (NIDDK). Am J Kidney Dis 2003; 42(4): 617-22.