

Relation of Microalbuminuria and Coronary Artery Disease in non Diabetic Patients

V.N. Hoseini and O. Taziki

Fateme Zahra Hospital, Artesh Boulevard, Sari, Mazandaran, Iran

Abstract: Prospective studies confirm that microalbuminuria is predictive, independently of classical risk factor of cardiovascular disease events and all-cause mortality within groups of patients with diabetes or hypertension and in the general population. However, there are few data linking angiographic severity of Coronary Artery Disease (CAD) to Microalbuminuria (MA). We examined coronary angiograms for extent of severe CAD (luminal narrowing 50%) in patients without Diabetes Mellitus (DM) and general population. Our study consisted of 153 patients who undergoing coronary angiography in Hazrat Fatemeh hospital in Iran. (M/F 80/73, mean age 57±11y). Urine albumin excretion was measured in 24 h urine samples by immune precipitation technique. Age-sex, distribution of coronary risk factors and MA was compared between patient with and without CAD. 70/5% (108) of patient had CAD and 29/4% (45) had no coronary lesion. MA was detected in 62.9% in patients with CAD and 8.8% in those without coronary Artery lesion ($p < 0.05$). The presence of 1 or 2 vessel CAD showed a linear increase from group to group without microalbuminuria ($p < 0.5$). Thus, patients with MA have more severe angiographic CAD than those without MA. This relation is independent of other risk factor.

Key words: Coronary artery disease, diabetes, microalbuminuria, cardiovascular disease, patients

INTRODUCTION

The risk of Cardiovascular Diseases (CVD) in cohort studies is predicted by traditional risk factor including age, sex, smoking, diabetes mellitus, hypertension and dyslipidemia. However, these don't entirely explain the variation in CVD incidence and mortality between individuals and between populations (Kuulasmaa *et al.*, 2000), which has led to studies aimed at nontraditional cardiovascular risk factors. Reside concentration of urinary albumin is one such factor. Microalbuminuria is independently associated with all-cause mortality and cardiovascular morbidity and mortality in patients with Diabetes (Messent *et al.*, 1992; Park *et al.*, 2003), hypertension (Bigazzi *et al.*, 1998; Wachtell *et al.*, 2003) and in the general population (Gerstein *et al.*, 2001; Romundstad *et al.*, 2003; Yuyun *et al.*, 2004a, b; Klausen *et al.*, 2004). In diabetic patients, it is predictive of nephropathy (Krolewski and Warram, 1995).

As the association between proteinuria and cardiovascular events is well described (Sarnak *et al.*, 2003), the purpose of this study was to investigate whether urinary Albumin excretion was sign of atherosclerotic involvement of coronary artery in 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 of this study was to document the association between MA and severe CAD. We studied 153 Patients (79 men and 74 women: mean age 57±11 years) who under vent Coronary angiography in the University of Mazandaran medical science hospitals between January 2007 and June 2007. We collected data on the following well-recognized cardiovascular risk factor in these patient age, hypertension, hypercholesterolemia, DM and smoking. We also, collected data on MA, fasting glucose levels in all patients.

Microalbumin was measured by rate nephelometry using the Behring protein analyzer. Urine creatinine was measured by a Behring analyzer. Patients with albumin levels less than 30 mg g⁻¹ of creatinine were defined as having normoalbuminuria, those with albumin levels >30-300 mg g⁻¹ as having macroalbuminuria.

CAD was defined significant if there was = 50% diameter stenosis in = 1 major coronary artery. Diagnosis of DM was based on abnormal fasting blood glucose = 126 mg dL⁻¹ on more than 2 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 was classified as having hypertension.

Hypertension diabetic patients were defined as systolic = 130/80 mmHg. Patients who had smoked within the previous 1 year of entry in to the study were deemed current smokers. Patients who used cholesterol lowering medication or had a total serum cholesterol level = 200 mg dL⁻¹ were classified as having hypercholesterolemia.

A statistical analysis was performed with SPSS (version 13). Chi-square or tailed test was used to examine for baseline difference between two proportions or means and p value = 0.05 was considered statically significant. Because the prevalence of conventional CAD risk factor, such as hypertension, hypercholesterolemia and smoking, was not statically different across groups. We did not perform multivariate analyses.

RESULTS AND DISCUSSION

Patients mean age was similar between the 2 patients groups. CAD occurred more frequent in male than female and in smokers than none smokers. The prevalence of different CAD risk factor (age, hypertension and hypercholesterolemia) was also similar across group (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%) in group with microalbuminuria, in 16 of 37 patients without microalbuminuria (43.2%).

Two vessel CAD was founded in 36 of 54 patients (66.6%) in group with microalbuminuria and in 18 of 54 patients (33.3%) without microalbuminuria comparison between two groups this difference was significant (p<0.01).

Table 1: Patient's demographics and prevalence of coronary artery disease risk factor

Variable	CAD+	CAD-	p-value
N	108	45	
Age (years)	58±11	58±9.8	p>0.5
M/F	62/46	18/27	p<0.5
Smokers (n)	12 (11.1%)	2 (4.5%)	p<0.5
Hypertension (n)	42 (38.8%)	16 (35.6%)	p>0.5
Hypercholesterolemia (n)	38 (35.1%)	15 (33.3%)	p>0.5
MA (n)	68 (62.9%)	4 (8.8%)	p<0.5

MA- 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-value
3 (n)	21	16	p<0.5
2 (n)	36	18	p<0.5
1 (n)	11	06	p<0.5

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

Despite extensive data linking microalbuminuria to coronary atherosclerosis (Gerstein *et al.*, 2001; Wachtell *et al.*, 2003; Hillege *et al.*, 2002; Klausen *et al.*, 2004; Wang *et al.*, 2005) few studies have examined the correlation of angiographic severity of coronary artery disease with microalbuminuria. In nondiabetic patients, the aim of our study was to demonstrate the microalbuminuria is associated with more extensive coronary atherosclerosis. We found that patients with microalbuminuria had much greater atherosclerotic burden in the form of multivessel CAD than patients without it and this was especially in patients without diabetes.

Study in diabetic showed correlation between angiographic severity and microalbuminuria was significant (Sukhija *et al.*, 2006). The mechanism of accelerated atherosclerosis in microalbuminuria is uncertain. Abnormal vasodilatation, endothelial dysfunction, inflammation, insulin resistance or abnormal coagulation maybe involved (Clausen *et al.*, 2001; Pedrinelli *et al.*, 1994; Festa *et al.*, 2000; Mykkanen *et al.*, 1998; Meeking *et al.*, 1999).

Aggressive treatment of microalbuminuria in CAD patients may have salutary affects. other study showed decrease in baseline albuminuria, which were more pronounce with losartan than with atenolol, were associated with cardiovascular benefits (Ibsen *et al.*, 2004, 2005).

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 to ward a lower rate of cardiovascular mortality and has pitalization (Asselbergs *et al.*, 2004).

We used a ratio of spot trinity albumin to creatinine to detect microalbuminuria. Although, a 24-h urine collection is the gold standard for detection of microalbuminuria, several studies have found that a ratio untimed avinavy albumin to creatinin is equally sensitive and specific (Eknoyan *et al.*, 2003).

CONCLUSION

This study showed significant correlation between microalbuminuria and severity of CAD, treatment of microalbuminuria is recommend is recommend.

REFERENCES

- Asselbergs, F.W., G.F. Diercks, H.L. Hillege, A.J. Van Boven, W.M. Janssen, A.A. Voors, D. de Zeeuw, P.E. de Jong, D.J. Van Veldhuisen and W.H. Van Gilst, 2004. Effects of fosinopril and pravastatin on cardiovascular events in subjects with microalbuminuria. *Circulation*, 110: 2809-2816.
- Bigazzi, R., S. Bianchi and D. Baldari *et al.*, 1998. Microalbuminuria predict cardiovascular events and renal insufficiency in patients with essential hypertension. *J. Hypertense*, 16: 1325-1333.
- Clausen, P., J.S. Jensen, G. Jensen, K. Borch-Johnsen and B. Feldt-Rasmussen, 2001. Elevated urinary albumin excretion is associated with impaired arterial dilatatory capacity in clinically healthy subjects. *Circulation*, 103: 1869-1874.
- Eknoyan, G., T. Hostetter, G.L. Bakris, L. Hebert, A.S. Levey, H.H. Parving, M.W. Steffes and R. Toto, 2003. 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.*, 42: 617-622.
- Festa, A., R. D'Agostino, G. Howard, L. Mykkanen, R.P. Tracy and S.M. Haffner, 2000. Inflammation and microalbuminuria in nondiabetic and type 2 diabetic subjects the Insulin Resistance Atherosclerosis Study. *Kidney Int.*, 58: 1703-1710.
- Gerstein, H.C., J.F. Mann and O. Yi *et al.*, 2001. Albuminuria and risk of cardiovascular events, death and heart failure in diabetes and non diabetes individuals. *JAMA*, 266: 421-426.
- Hillege, H.L., V. Fidler, G.F. Diercks, W.H. Van Gilst, D. de Zeeuw, D.J. Van Velhuisen, R. Gans, W.M. Janssen, D.E. Grobbee and P.E. de Jong, 2002. Urinary albumin excretion predicts cardiovascular and non-cardiovascular mortality in general population. *Circulation*, 106: 1777-1782.
- Ibsen, H., Olsen M.H., Wachtell K., Borch-Johnsen K., Lindholm L.H., Mogensen C.E., Dahlöf B., Devereux R.B., de Faire U. and Fyhrquist, F. *et al.*, 2005. Reduction in albuminuria translates to reduction in cardiovascular events in hypertensive patient-slosartan intervention for endpoint reduction in hypertension study. *Hypertension*, 45: 198-202.
- Ibsen, H., K. Wachtell, M.H. Olsen, K. Borch-Johnsen, L.H. Lindholm, C.E. Mogensen, B. Dahlöf, R.B. Devereux, U. de Faire and F. Fyhrquist *et al.*, 2004. Does albuminuria predict cardiovascular outcome on treatment with losartan versus atenolol in hypertension with left ventricular hypertrophy? A LIFE sub-study. *J Hypertens.*, 22: 1805-1811.
- Klausen, K., K. Borch-Johnsen and B. Feldt-Rasmussen *et al.*, 2004. Very low level of microalbuminuria are associated with increased risk of coronary heart disease and deaths independently of renal function, hypertension and diabetes. *Circulation*, 110: 32-35.
- Krolewski, A.S. and J.H. Warram, 1995. Natural history of diabetic nephropathy: How much can it be changed? *Diabetes Rev.*, 3: 446-459.
- Kuulasmaa, K., H. Tunstall-Pedoe and A. Dobson *et al.*, 2000. Estimation of contribution of changes in classic risk factor to trends in coronary event rates across the WHO MONICA Project population. *Lancet*, 355: 675-678.
- Meeking, D.R., M.H. Cummings, S. Thorne, A. Donald, P. Clarkson, J.R. Crook, G.F. Watts and K.M. Shaw, 1999. Endothelial dysfunction in type 2 diabetic subjects with and without microalbuminuria. *Diabet. Med.*, 16: 841-847.
- Messent, J.W., T.G. Elliott and R.D. Hill *et al.*, 1992. prognostic significance of microalbuminuria in insulin depended diabetes mellitus; A 23 years follow up study. *Kidney Int.*, 41: 836-839.
- Mykkanen, L., D.J. Zaccaro, L.E. Wagenknecht, D.C. Robbins, M. Gabriel and S.M. Haffner, 1998. Microalbuminuria is associated with insulin resistance in nondiabetic subjectsthe Insulin Resistance Atherosclerosis Study. *Diabetes*, 47: 793-800.
- Park, H.Y., G.T. Schumock and A.S. Pickard *et al.*, 2003. A structured review of the relationship between microalbuminuria and cardiovascular events in patients with diabetes and hypertension. *Pharmacotherapy*, 23: 1611-1616.
- Pedrinelli, R., O. Giampietro, F. Carmassi, E. Melillo, G. Dell'Omo, G. Catapano, E. Matteucci, L. Talarico, M. Morale and F. De Negri, 1994. Microalbuminuria and endothelial dysfunction in essential hypertension. *Lancet*, 344: 14-18.
- Romundstad, S., J. Holmen and K. Kvenild *et al.*, 2003. Microalbuminuria and all cause mortality in 2089 apparently healthy individuals: A 4.4 years follow- up study. *Am. J. Kidney Dis.*, 42: 466-473.
- Sarnak, M.J., A.S. Levey and A.C. Schoolwerth *et al.*, 2003. Kidney disease as a risk factors 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*, 108: 2154-2169.

- Sukhija, R., W.S. Aronow, P. Kakar, L. Garza, R. Sachdeva, A. Sinha and J.L. Mehta, 2006. Relation of microalbuminuria and coronary artery disease in patients with and without diabetes mellitus. *Am. J. Cardiol.*, 98: 279-281.
- Wachtell, K., H. Ibsen and M.H. Olsen *et al.*, 2003. Albuminuria and cardiovascular risk in hypertensive patients with left ventricular hypertrophy. The LIFE study. *Ann. Int. Med.*, 139: 901-906.
- Wang, T.J., J.C. Evans, J.B. Meigs, N. Rifai, C.S. Fox, R.B. D'Agostino, D. Levy and R.S. Vasan, 2005. Low-grade albuminuria and the risks of hypertension and blood pressure progression. *Circulation*, 111: 1370-1376.
- Yuyun, M.F., K.T. Khaw and R. Luben *et al.*, 2004. Microalbuminuria independently predicts all-cause and cardiovascular mortality in British population: the European Prospective Investigation into Cancer in Norfolk (EPIC-Norfolk) population study. *Int. J. Epidemiol.*, 33: 189-198.
- Yuyun, M.F., K.T. Khaw and R. Luben *et al.*, 2004. Microalbuminuria and stroke in a British population: the European Prospective Investigation into Cancer in Norfolk (EPIC-Norfolk) population study. *J. Int. Med.*, 255: 247-256.