

Albuminuria/Proteinuria in Cardiology Practice: Do Cardiologists Ask For Urine Testing?

Kardiyoloji Pratiğinde Albüminüri/Proteinüri: Kardiyologlar İdrar Testi İstiyorlar mı?

ABSTRACT

OBJECTIVE: Even a small amount of albumin in urine is predictive of cardiovascular morbidity and mortality, not only in patients with diabetes or hypertension but also in the general population. We hypothesized that determination of urinary protein excretion is usually not included in the laboratory work-up of most patients in cardiology practice.

MATERIAL and METHODS: One thousand forty two patients who underwent coronary angiography during a one-year period were included. The total number of urine tests for evaluating albuminuria/proteinuria ordered for the patients during the 12 months preceding angiography was recorded. Types of urine tests were recorded as routine dipstick urinalysis, 24 hour urine collection for albuminuria or proteinuria, and protein/creatinine or albumin/creatinine ratios.

RESULTS: No urine tests were ordered in 642 (61.6%) patients. Spot urinalysis for dipstick proteinuria was the most common test for proteinuria evaluation (35.7% of the patients). 24-hour urine collection for albuminuria/proteinuria was ordered in 56 (5.4%) patients and spot urine albumin or protein/creatinine ratio in 56 (5.4%) patients.

CONCLUSION: This study has shown that urine testing is rarely ordered in a high-risk population who had coronary angiography. Omission of such an important, but easy to measure parameter in assessing risk status may jeopardize the overall care of these patients.

KEY WORDS: Albuminuria, Cardiology, Cardiovascular risk factors, Coronary angiography, Proteinuria

ÖZ

AMAÇ: Çok sayıda çalışmada, idrarda az miktarda albümin atılımının bile kardiyovasküler olayların ve tüm nedenlere ve kardiyovasküler olaylara bağlı mortalitenin önemli bir belirteci olduğu gösterilmiştir. İdrarda albüminüri incelemesi, yüksek riskli durumlarda standart bakımın bir kalite belirteci olarak kabul edilebilir. Bu çalışmada, koroner anjiyografi yapılan hastalarda idrar testinin istenme sıklığı incelendi.

GEREÇ ve YÖNTEMLER: Bir yıllık süre içinde koroner anjiyografi yapılan 1044 hasta çalışmaya dahil edildi. İşlem tarihinden önceki on iki aylık dönemde proteinüri saptamak için yapılmış olan idrar tetkikleri hastanenin bilgisayarlı tıbbi kayıt sistemi kullanılarak kaydedildi. İdrar tetkikleri; spot idrarda dipstick testi, spot idrar albümin/kreatinin veya protein/kreatinin oranı ve yirmidört saatlik idrarda albüminüri veya proteinüri olarak sınıflandırıldı.

BULGULAR: Çalışmaya alınan hastaların 642 sinde (%61,6) herhangi bir yöntemle proteinüri incelenmemiştir. Proteinüri incelemek için kullanılan en sık yöntem spot idrar dipstick testiydi. (%35,7). 24 saatlik idrarda albümin veya protein 56 hastada (%5,4) ve spot idrarda albümin/kreatinin oranı veya protein/kreatinin oranı 56 hastada (%5,4) incelenmişti.

SONUÇ: Bu çalışmada, koroner anjiyografi yapılan yüksek riskli hastalarda idrar testinin nadiren kullanıldığı gösterilmiştir. Risk değerlendirmesinde bu kadar önemli ve aynı zamanda kolay ölçülebilir bir parametrenin kullanılmaması, bu hastaların tedavi yönetiminde eksikliğe sebep olabilir.

ANAHTAR SÖZCÜKLER: Albüminüri, Kardiyoloji, Kardiyovasküler risk faktörleri, Koroner anjiyografi, Proteinüri

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INTRODUCTION

Cardiovascular diseases are the leading cause of death all over the world. Beside the well-known traditional risk factors such as male gender, age, diabetes, hypertension, hyperlipidemia and smoking; proteinuria and reduced glomerular filtration rate are regarded as novel and significant risk factors for cardiovascular disorders (1). Many studies indicated that even small amounts of albumin in urine were predictive of all-cause and cardiovascular mortality and cardiovascular events, not only in patients with diabetes or hypertension, but also in the general population. Guidelines from the American Heart Association recommend that individuals with proteinuria should be considered to be at similar cardiovascular risk to people with established coronary heart disease (2). Even small amounts of albumin excretion which is a manifestation of general endothelial damage, may also be considered as a prognostic parameter that may determine the intensity of strategies for preventive measures. Treatment strategies aiming to reduce urinary albumin excretion rate, such as drugs blocking renin angiotensin aldosterone system had been shown to slow down the progression of cardiovascular diseases and commonly used by both cardiologists and nephrologists for organ protection. Although determination of urinary protein excretion should be routine in general practice and in nephrology; we hypothesize that it is usually not included in the laboratory work-up of most patients in cardiology practice. Patients undergoing coronary angiography usually have many comorbidities and thus represent a high-risk condition. Urine testing for albuminuria/proteinuria in this high-risk setting may be accepted as a quality indicator of standard care. This study was planned to assess the frequency of urine testing in patients who underwent coronary angiography in a cardiology unit.

MATERIALS and METHODS

One thousand forty two patients who underwent coronary angiography at Hacettepe University Medical Faculty Hospital during one calendar year from 1st of January to 31st of December were included. There were no exclusion criteria. Total number of complete blood count tests, lipid profile tests, biochemical analysis and urine tests for evaluating albuminuria/proteinuria that have been ordered to patients during preceding 12 months to coronary angiography were recorded. Types of urine tests were routine dipstick urinalysis, 24 hour urine collection for albuminuria or proteinuria, and protein/creatinine ratio or albumin/creatinine ratio in first morning urine samples. Data about comorbidities of patients including diabetes, hypertension, chronic kidney disease and congestive heart failure were collected from computerized medical recording system of the hospital. Indications for coronary angiography were recorded as elective or urgent. Frequency and types of urine testing in diabetic patients, hypertensive patients and in patients with acute coronary syndrome were determined and compared with frequency and types of urine testing in whole study population. Amount of protein excretion was also recorded for the patients

that underwent testing for proteinuria. SPSS (Statistical Package for the Social Sciences, Inc., Chicago, IL) version 16 is used for statistical analysis. Descriptive statistics is used to determine patient characteristics, frequencies of each test utilized and mean proteinuria levels. Categorical variables are compared with the chi-square test.

RESULTS

One thousand forty two patients (676 male, 366 female) were included in the study. The mean age of the study population was 60.2±11.9 years. Acute coronary syndrome was the indication for coronary angiography for 102 patients. All other patients had undergone elective coronary angiographies for evaluation of coronary heart disease. Table I shows demographic characteristics and comorbidities of the patients.

Four hundred patients (38.4%) had been evaluated for albuminuria/proteinuria. Spot urinalysis was the most common test for proteinuria evaluation. This test had been ordered in 372 (35.7%) patients; 24-hour urine collection for albuminuria/proteinuria in 56 (5.4%) patients and spot urine albumin or protein/creatinine ratio in 56 (5.4%) patients. No urine tests had been ordered in 642 (61.6%) patients in preceding 12 months.

Rates of urine analysis were higher for diabetic patients. There were 204 diabetic patients (117 male, 87 female). Proteinuria had been evaluated in 106 (52.0%) diabetic patients. Spot urinalysis for proteinuria was the most common test and had been ordered in 97 (47.5%) patients, spot urine albumin or protein/creatinine ratio in 23 (11.3%) patients, 24 hour urine collection for albuminuria/proteinuria in 18 (8.8%) patients. No urine tests had been ordered in 98 (48.0%) patients in preceding 12 months. There were 562 hypertensive patients (310 male, 252 female). Proteinuria had been evaluated in 240 (42.7%) hypertensive patients. Spot urinalysis for proteinuria was the most common test and had been ordered in 226 (40.2%) patients, 24 hour urine collection for albuminuria/proteinuria in 37 (6.6%) patients, spot urine albumin or protein/creatinine ratio in 31 (5.5%) patients.

Table I: Demographic characteristics and comorbidities of the patients.

	(n=1042)
Age	60.2±11.9
Sex	
Male	676 (64.9%)
Female	366 (35.1%)
Comorbidities	
Hypertension	562 (53.9%)
Diabetes mellitus	204 (19.6%)
Coronary heart disease	366 (35.1%)
Congestive heart failure	51 (4.9%)
Chronic kidney disease	21 (2.0%)

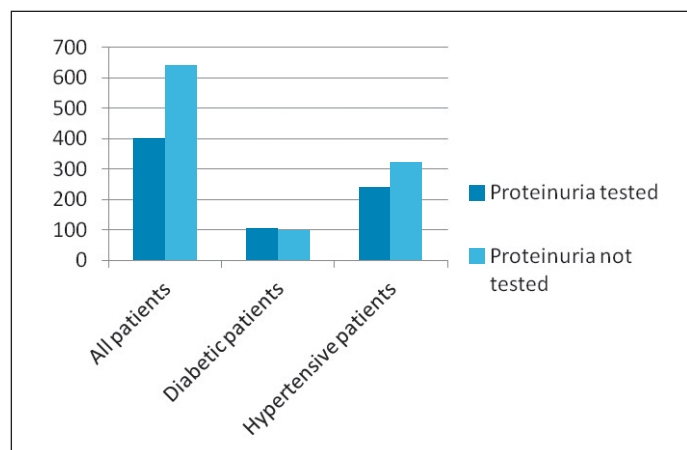


Figure 1: Number of patients evaluated for proteinuria.

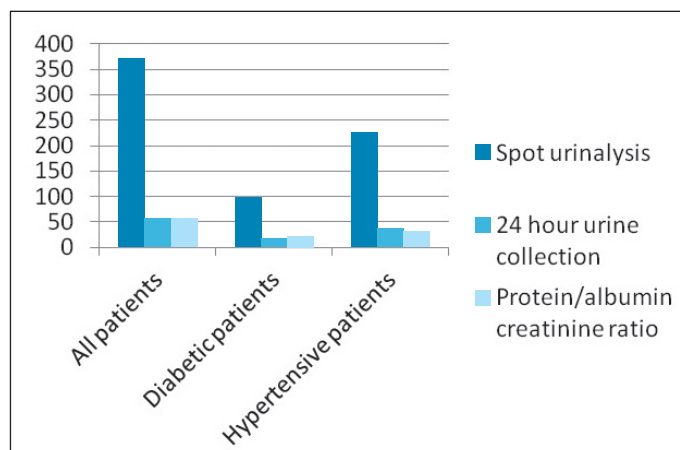


Figure 2: Distribution of different tests for proteinuria evaluation.

No urine tests had been ordered in 322 (57.3%) hypertensive patients in preceding 12 months.

Figure 1 shows the frequency of proteinuria testing in all patients and also in diabetic and hypertensive subgroups. Figure 2 shows the distribution of each test for proteinuria evaluation in patients.

Urine testing for proteinuria had been ordered in 37 of 102 patients in whom coronary angiography was performed emergently for acute coronary syndrome and in 363 of 940 patients in whom coronary angiography was performed electively. There was no statistical significant difference between two groups (36.3% vs. 38.6%, $p > 0.05$ respectively).

Forty four of 372 (11.8%) patients that had been ordered spot urinalysis had 30 mg/dl or more proteinuria. 14.4% of diabetic patients (14/97) and 13.3% hypertensive patients (30/226) had 30 mg/dl or more proteinuria. Mean daily protein excretion of patients that collected 24 hour urine was 271.7 ± 522.3 mg. Diabetic patients had higher daily protein excretion (444.7 ± 871.3 mg/day). Hypertensive patients' daily protein excretion was 319.7 ± 596.9 mg/day.

We also investigated how frequently other common laboratory tests (blood counts, lipid profiles and biochemical tests which include blood glucose, serum creatinine and electrolytes) had been utilized in 642 patients that had not been ordered urinalysis. When these 642 patients were evaluated, we observed that biochemical tests had been ordered in 567 patients (88.3%), complete blood count had been ordered in 558 patients (86.9%) and lipid profiles had been ordered in 525 patients (81.8%). In 290 of 567 patients (51.1%) biochemical tests had been ordered more than once. This percentage was 40.7 (227 of 558 patients) for blood count and 26.3 (138 of 525 patients) for lipid profile.

We evaluated whether the urine testing had been performed by cardiology outpatient service during the preceding 12 months for cardiac risk stratification or had been done coincidentally in another department for possible other indications. 58.3% of urine

dipstick tests and 36.3% of the other methods for proteinuria evaluation (24 hour urine collection for albuminuria/proteinuria, determination of spot urine albumin or protein/creatinine ratios) had been performed by cardiologists.

DISCUSSION

Proteinuria is an important and emerging risk factor for coronary artery diseases. Although serum creatinine levels are checked as a part of routine evaluation of patients we observed that evaluation of urine for proteinuria is not a common practice in patients undergoing coronary angiography. Nearly two thirds of the patients had not been evaluated for proteinuria (61.6%).

Proteinuria at the time of percutaneous coronary intervention has been shown to be related to the severity of coronary heart disease (3,4). It is also a prognostic marker for mortality in this population. In a study performed on nearly 6000 patients, the association between urinary dipstick proteinuria with mortality and cardiovascular events was investigated. In that study, evidence of proteinuria detected by urinary dipstick method was associated with a nearly 3-fold increased risk of all-cause mortality in patients with established coronary heart disease at the time of percutaneous coronary intervention (5). In accordance with these reports the American Heart Association recommended that individuals with proteinuria should be considered to be at similar risk to people with established coronary heart disease (2) and 2013 European Society of Cardiology/European Society of Hypertension (ESC/ESH) guideline on management of arterial hypertension recommended using albuminuria in the evaluation of cardiac risk in hypertensive patients (6). The albumin/creatinine ratio can also predict development of new heart failure (7) and proteinuria at the time of coronary angiography also had been shown to be an independent predictor of contrast nephropathy (8).

Renal dysfunction is more common among patients with coronary heart disease and evidence of chronic kidney disease should be actively investigated in this population (9,10). Proteinuria along

with chronic kidney disease may be an important risk factor for stent thrombosis in patients with myocardial infarction who received intracoronary stenting (11).

24 hour urine collection is not practical in outpatient clinics, and patients often under collect or over collect urine sample that causes wrong interpretation of the amount of proteinuria. Proteinuria can also be determined by spot urinalysis or protein/creatinine ratio in a random urine sample and these are more practical. All methods have advantages and disadvantages. Patient compliance, comorbidities, financial concerns and infrastructure of medical institutions are the main factors for deciding the best method. However evaluation of proteinuria should be done for every patient undergoing coronary angiography at least once in a year.

Spot urinalysis was the most common test for evaluation of proteinuria in our patients. Although spot urinalysis was probably performed for other indications than proteinuria (fever, hematuria, hyperglycemia, etc.) in some patients, ease of this test is another reason for high utilization. Result of less than trace protein in spot urinalysis had been shown to have high negative predictive value for microalbuminuria. However, high false positive rates in these tests mandate laboratory confirmation of positive results (12). 24 hour urine proteinuria is rarely used probably due to difficulty of the procedure; amount of protein in urine can also easily be estimated by spot albumin/creatinine ratio or protein/creatinine ratio.

Microalbuminuria is the first sign of renal dysfunction in diabetic patients, and testing these patients regularly for albumin excretion is recommended by guidelines. Although we observed that diabetic patients were tested more widely for proteinuria, still nearly half of the patients had not been tested (48.0%). This shows a missed opportunity for detection and appropriate treatment of albuminuria. Evaluation of albuminuria is regarded as one of the best methods for detection of end organ damage in hypertensive patients by 2013 ESC/ESH guideline on management of arterial hypertension (6). However testing for proteinuria were also not performed in more than half of hypertensive patients.

It can be speculated that testing for proteinuria is not practical in emergent situations. However rates for proteinuria testing were not statistically different between patients undergoing emergent versus elective coronary angiography (36.3% vs. 38.6%, respectively). Moreover patients in this study had generally been hospitalized longer than 24 hours. This shows that main factor in omitting urine testing was not time constraint.

We evaluated the patients for whom urine testing were not ordered, for rates of other common tests. We observed that serum biochemical analysis, complete blood count and serum lipid profiles were commonly ordered in these patients. These tests were ordered more than once in an important percentage of patients (51.1% for biochemical analysis, 40.7% for blood count

and 26.3% for lipid profile). This is evidence that there were opportunity for urine testing in these patients. When we consider that no laboratory evaluation was performed in our hospital in a small percentage of patients it is possible that these evaluations including urine testing were performed at another hospital prior to coronary angiography.

In conclusion, this study has shown that urine testing is rarely ordered in a high-risk population that underwent coronary angiography. Omission of such an important, but easy to measure parameter in assessing risk status may jeopardize the overall care of these patients. Measures to increase the testing of patients with possible coronary heart disease for proteinuria should be undertaken.

REFERENCES

1. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ; Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. National Heart, Lung, and Blood Institute; National High Blood Pressure Education Program Coordinating Committee: Seventh report of the Joint National Committee on Prevention, Detection, evaluation, and treatment of high blood pressure. *Hypertension* 2003; 42: 1206-1252
2. Mosca L, Banka CL, Benjamin EJ, Berra K, Bushnell C, Dolor RJ, Ganiats TG, Gomes AS, Gornik HL, Gracia C, Gulati M, Haan CK, Judelson DR, Keenan N, Kelepouris E, Michos ED, Newby LK, Oparil S, Ouyang P, Oz MC, Petitti D, Pinn VW, Redberg RF, Scott R, Sherif K, Smith SC Jr, Sopko G, Steinhorn RH, Stone NJ, Taubert KA, Todd BA, Urbina E, Wenger NK; Expert Panel/Writing Group; American Heart Association; American Academy of Family Physicians; American College of Obstetricians and Gynecologists; American College of Cardiology Foundation; Society of Thoracic Surgeons; American Medical Women's Association; Centers for Disease Control and Prevention; Office of Research on Women's Health; Association of Black Cardiologists; American College of Physicians; World Heart Federation; National Heart, Lung, and Blood Institute; American College of Nurse Practitioners: Evidence based guidelines for cardiovascular disease prevention in women. *Circulation* 2007; 115: 1481-1501
3. Deveci OS, Kabakci G, Tulumen E, Okutucu S, Aksoy H, Kaya EB, Canpolat U, Aytimir K, Tokgozoglu L, Oto A: The relationship between microalbuminuria and the presence and extent of coronary atherosclerosis. *Angiology* 2010; 61: 184-191
4. Hoseini VN, Rasouli M: Microalbuminuria correlates with the prevalence and severity of coronary artery disease in non-diabetic patients. *Cardiol J* 2009; 16: 142-145
5. Mercado N, Brugts JJ, Ix JH, Shlipak MG, Dixon SR, Gersh BJ, Lemos PA, Guarneri M, Teirstein PS, Wijns W, Serruys PW, Boersma E, O'Neill WW: Usefulness of proteinuria as a prognostic marker of mortality and cardiovascular events among patients undergoing percutaneous coronary intervention (Data from the evaluation of oral xemilofiban in controlling thrombotic events [EXCITE] trial). *Am J Cardiol* 2008; 102: 1151-1155

6. Mancia G, Fagard R, Narkiewicz K, Redón J, Zanchetti A, Böhm M, Christiaens T, Cifkova R, De Backer G, Dominiczak A, Galderisi M, Grobbee DE, Jaarsma T, Kirchhof P, Kjeldsen SE, Laurent S, Manolis AJ, Nilsson PM, Ruilope LM, Schmieder RE, Sirnes PA, Sleight P, Viigimaa M, Waeber B, Zannad F; List of authors Task Force Members: 2013 ESH/ESC Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens* 2013; 31(7): 1281-1357
7. Velagaleti RS, Gona P, Larson MG, Wang TJ, Levy D, Benjamin EJ, Selhub J, Jacques PF, Meigs JB, Tofler GH, Vasan RS: Multimarker approach for the prediction of heart failure incidence in the community. *Circulation* 2010; 122: 1700-1706
8. Piskinpasa S, Altun B, Akoglu H, Yildirim T, Agbaht K, Yilmaz R, Peynircioglu B, Cil B, Aytemir K, Turgan C: An uninvestigated risk factor for contrast-induced nephropathy in chronic kidney disease: Proteinuria. *Ren Fail* 2013; 35(1): 62-65
9. Anavekar NS, McMurray JJ, Velazquez EJ, Solomon SD, Kober L, Rouleau JL, White HD, Nordlander R, Maggioni A, Dickstein K, Zelenkofske S, Leimberger JD, Califf RM, Pfeffer MA: Relation between renal dysfunction and cardiovascular outcomes after myocardial infarction. *N Engl J Med* 2004; 351: 1285-1295
10. Brosius FC 3rd, Hostetter TH, Kelepouris E, Mitsnefes MM, Moe SM, Moore MA, Pennathur S, Smith GL, Wilson PW; American Heart Association Kidney and Cardiovascular Disease Council; Council on High Blood Pressure Research; Council on Cardiovascular Disease in the Young; Council on Epidemiology and Prevention; Quality of Care and Outcomes Research Interdisciplinary Working Group: Detection of chronic kidney disease in patients with or at increased risk of cardiovascular disease: A science advisory from the American Heart Association Kidney And Cardiovascular Disease Council; The Councils on High Blood Pressure Research, Cardiovascular Disease in the Young, and Epidemiology and Prevention; and the Quality of Care and Outcomes Research Interdisciplinary Working Group: Developed in collaboration with the National Kidney Foundation. *Circulation* 2006; 114: 1083-1087
11. Lambert ND, Sacrinty MT, Ketch TR, Turner SJ, Santos RM, Daniel KR, Applegate RJ, Kutcher MA, Sane DC: Chronic kidney disease and dipstick proteinuria are risk factors for stent thrombosis in patients with myocardial infarction. *Am Heart J* 2009; 157: 688-694
12. White SL, Yu R, Craig JC, Polkinghorne KR, Atkins RC, Chadban SJ: Diagnostic accuracy of urine dipsticks for detection of albuminuria in the general community. *Am J Kidney Dis* 2011; 58: 19-28