Impact of Diabetes Mellitus on Survival in Patients with End-Stage Renal Disease: A Three-Year Follow-Up

Anna Tomaszuk-Kazberuk^a Hanna Bachorzewska-Gajewska^b Jolanta Malyszko^c
Jacek Malyszko^c Michal Mysliwiec^c Włodzimierz J. Musiał^a

Departments of ^aCardiology, ^bInvasive Cardiology, and ^cNephrology, Medical University, Białystok, Poland

Key Words

Diabetes mellitus • End-stage renal disease •
Atherosclerotic changes • Adverse cardiac events

Abstract

Background/Aims: To assess the impact of diabetes mellitus (DM) on clinical outcome in patients with end-stage renal disease (ESRD) on a 3-year follow-up. **Methods:** 58 ESRD patients were divided into 2 groups according to the presence of DM. We analyzed following end points: death, cardiac arrest, myocardial infarction, stroke, hospitalizations due to cardiovascular causes, revascularization, and combined end point. **Results:** Among diabetics, 14 (77.8%) had significant atherosclerotic changes, in the group without DM only 8 (38.1%), $p = 0.01$. In the group without DM, 14 (46.7%) patients reached combined end point, while in the group with DM 16 (53.3%) patients, $p = 0.0013$. There were no statistical differences in mortality ($p = 0.423$). **Conclusion:** Survival of hemodialyzed diabetic patients is not inferior to nondiabetics; however, morbidity is significantly higher due to adverse cardiac events.

Copyright © 2011 S. Karger AG, Basel

Introduction

In many countries, diabetic nephropathy has become the single most frequent cause of end-stage renal disease (ESRD) in patients undergoing hemodialysis [1]. The management of these high-risk patients has improved; however, they continue to do worse in terms of higher rates of new ischemic heart disease and new cardiac failure compared with nondiabetics [2]. In diabetics with ESRD, the risk of death has been reported as extremely high, but worse survival than in nondiabetics is a matter of discussion. The aim of the present study was to evaluate the impact of diabetes mellitus (DM) on mortality and morbidity in patients with ESRD on a 3-year follow-up.

Materials and Methods

Between January 2005 and October 2007, 58 consecutive ESRD patients (21 women; mean age 59 ± 14 years) on regular dialysis were prospectively divided into 2 groups according to the presence of DM. Chest pain was a main indication for evaluation. Thirty-nine patients out of 58 underwent coronary angiography.

We analyzed the following end points during a 3-year follow-up: death, cardiovascular complications (cardiac arrest, myocardial infarction, stroke, hospitalization due to cardiac reasons, revascularization), and combined end point which consisted of death and all adverse cardiac events mentioned above. The study complies with the declaration of Helsinki. The study protocol was approved by local ethics committee, and informed consent was obtained from all subjects participating in the study.

Transthoracic Echocardiography

Left ventricular ejection fraction (LVEF) and wall motion score index (WMSI) were obtained for all echo scans. WMSI was obtained by dividing the sum of the segment scores by the number of segments scored. LVEF was derived using the bi-plane method.

Coronary Angiography

Coronary angiography was performed by hand injection of contrast medium (low osmolality, low viscosity) via a 6-Fr catheter. Luminal stenosis more than 75% by diameter was regarded as significant (visual assessment).

Statistical Analysis

Descriptive statistics (percentages for discrete variables and mean $\pm$ SD for continuous variables) was done for baseline characteristics. Student t test was performed to reveal possible differences in data between groups. The χ^2 and NW tests were used to analyze the differences between the group with and without DM. A p value ≤ 0.05 was considered statistically significant. The statistical software NCSS 2007 was used.

Results

Overall, out of 58 ESRD patients, 20 (37.8%, 6 women and 14 men) had DM. There were no significant differences between patients with DM and those without DM in age (60.6 ± 10.6 vs. 59.0 ± 10.6 years, $p = 0.665$), EF (52.6 ± 12.8 vs. $54.2 \pm 12.8\%$, $p = 0.59$), and WMSI (1.21 ± 0.3 vs. 1.15 ± 0.3 , $p = 0.37$). The mean time from onset of diabetes to dialysis was 15.2 years.

Coronary angiographies revealed differences in the appearance of the coronary vessels in the group of patients with and without DM ($p = 0.009$; table 1). Among diabetics, 14 (77.8%) had significant atherosclerotic changes, while in the group without DM only 8 (38.1%; $p = 0.01$).

Fourteen (46.7%) patients without DM and 16 (53.3%) with DM reached combined end point. The difference was statistically significant ($p = 0.0013$). Cardiac arrest occurred 4 times (20%) in the group with DM and once (2.6%) in the group without DM, which was also statistically significant ($p = 0.028$). Six (30%) diabetics and 3 (7.9%) nondiabetics were hospitalized due to cardiovascular causes ($p = 0.031$).

Table 1. Differences in the appearance of the coronary vessels in patients with and without DM ($p = 0.009$)

Coronary angiography results	Patients without DM who had coronary angiography (n = 21)	Patients with DM who had coronary angiography (n = 18)
No significant narrowings	13 (61.9%)	4 (22.2%)
One-vessel disease	1 (4.8%)	8 (44.4%)
Two-vessel disease	5 (23.8%)	3 (16.7%)
Three-vessel disease	2 (9.5%)	3 (16.7%)

There were 9 (40%) procedures (PCI and CABG) in the group with DM, whereas in the group without DM there were only 2 (5.3%; $p = 0.0003$).

There were no statistical differences between the groups in all cause mortality [9 (45%) vs. 13 (34.2%), $p = 0.423$], acute myocardial infarction [1 (5%) vs. 4 (10.5%), $p = 0.458$] and stroke ($p = 0.672$).

Discussion

Survival among nondiabetics who require dialysis due to a chronic glomerular disease or hypertensive nephrosclerosis is significantly better than in diabetics [3]. According to Batista et al. [4], mortality relative risk was 27% lower in patients with polycystic kidney disease ($p < 0.0001$); 29% lower in patients with glomerulonephritis ($p < 0.0001$), and 100% greater in DM patients ($p < 0.0001$). Still, the data on mortality according to the literature are contradictory. Pieringer and Biesenbach [5] observed patients on dialysis older than 65 years. The 3-year survival was 20.0% in nondiabetic and 17.0% in diabetic patients (NS). The difference was not statistically significant. In our group, mortality in patients with DM was 45%, while in the group without DM 34.2%. The difference was not statistically significant either. Opposite results come from the nationwide Australian representative cohort which included over 4,000 patients with ESRD and type 2 DM and over 13,000 patients without diabetes. ESRD was associated with a greater relative increase in mortality in the nondiabetic study population [6].

The frequency of cardiac arrest on dialysis increases with time, almost doubling within 4 years [7]. In our group, cardiac arrest occurred in 20% of the patients in the group with DM and in 2.6% in the patients with-

out DM, which was also statistically significant. Recently published data revealed 24% mortality attributed to sudden cardiac death in 230 ESRD patients in a 5-year study [8].

Hospital admissions for diabetic ESRD patients are 26% more frequent compared with others, particularly for cardiovascular (27%) causes [9]. More diabetics were hospitalized due to cardiovascular causes in our group ($p = 0.031$). We also observed differences in revascularization rate. There were 9 (40%) procedures (PCI and CABG) in the group with DM, whereas in the group without DM only 2 (5.3%; $p = 0.0003$), which reflects increased risk of coronary atherosclerosis in diabetes.

We have found no significant difference in mortality between nondiabetic and diabetic patients, despite more advanced changes in coronary vessels, more cardiac arrests and more frequent hospitalizations due to cardiovascular causes in the latter. The reasons for these findings are not clear. The diagnostics and treatment of diabetes and its complications has significantly improved over the last few years. Glucose control is stricter than it was years ago; this is why life expectancy might have improved.

Moreover, in the recent paper by Hoffmann et al. [10], it has been shown that the impact of diabetes on mortality was time dependent. Diabetics had an increased mortality risk after the first year. The fixed baseline effect of diabetes in these models was non-significant. This corroborates with the results of our study. Therefore, we might not see differences in mortality in our study with 3 years of follow-up.

We did not investigate asymptomatic patients, but Koch et al. [11] proved that sensitivity of angina pectoris to detect CAD was very low (43%) in ESRD diabetic patients. However, they even suggested that coronary angiography should be performed in all diabetic patients prior to renal transplantation. According to K/DOQI [12] and Canadian Guidelines (level of evidence B – data de-

rived from a single randomized clinical trial or large randomized studies) [13], asymptomatic renal transplant candidates with diabetes should have noninvasive stress tests as a screening test for the cardiological evaluation. Echocardiographic dobutamine test enables to select high-risk patients and avoids performing other investigations like a treadmill test and isotope scintigraphy [14]. In the population of asymptomatic renal transplant candidates, dobutamine test reveals silent ischemia [15].

Moreover, in the recent review published in 2010, Wang and Kasiske [16] pointed out that the best algorithm of cardiac assessment in asymptomatic patients prior to renal transplantation is unknown. In their opinion, symptomatic candidates for kidney transplantation should undergo screening with noninvasive stress testing followed by coronary angiography and revascularization, if indicated. On the other hand, they recommend that asymptomatic patients be cleared for transplantation and treated with beta-blockers and statin perioperatively.

Our study has some limitations. The sample size was rather small; however, it consisted of more than 60% of our hemodialyzed population (all symptomatic patients) coming from a single dialysis center at our Medical University. We did not investigate asymptomatic patients.

Conclusions

Survival of hemodialyzed diabetic patients is not inferior to that of nondiabetics; however, morbidity among diabetics is significantly higher due to major adverse cardiac events.

Disclosure Statement

None.

References

- 1 Broumand B: Diabetes: changing the fate of diabetics in the dialysis unit. *Blood Purif* 2007;25:39–47.
- 2 Locatelli F, Del Vecchio L, Cavalli A: How can prognosis for diabetic ESRD be improved? *Sem Dial* 2010;23:214–219.
- 3 United States Renal Data System: USRDS 2009 annual data report: atlas of end-stage renal disease in the United States. <http://www.usrds.org/adr>.
- 4 Batista PB, Lopes AA, Costa FA: Association between attributed cause of end-stage renal disease and risk of death in Brazilian patients receiving renal replacement therapy. *Ren Fail* 2005;27:651–656.
- 5 Pieringer H, Biesenbach G: Hemodialysis in patients older than 65 years with end-stage renal failure-comparison of outcome in patients with and without diabetes. *Z Gerontol Geriatr* 2008;41:139–145.

- 6 Villar E, Polkinghorne KR, Chang SH, Chadban SJ, McDonald SP: Effect of type 2 diabetes on mortality risk associated with end-stage kidney disease. *Diabetologia* 2009; 52:2536–2541.
- 7 Karamé A, Labeeuw M, Trollet P, Caillette-Beaudoin A, Cahen R, Ecochard R, Galland R, Hallonet P, Pouteil-Noble C, Villar E: The impact of type 2 diabetes on mortality in end-stage renal disease patients differs between genders. *Nephron Clin Pract* 2009; 112:c268–c275.
- 8 Wang AY, Lam CW, Chan IH, Wang M, Lui SF, Sanderson JE: Sudden cardiac death in end-stage renal disease patients: a 5-year prospective analysis. *Hypertension* 2010;56: 210–216.
- 9 Mahnensmith RL, Zorzanello M, Hsu YH, Williams ME: Quality improvement model for optimizing care of the diabetic end-stage renal disease patient. *Semin Dial* 2010;23: 206–213.
- 10 Hoffmann F, Haastert B, Koch M, Giani G, Glaeske G, Icks A: The effect of diabetes on incidence and mortality in end-stage renal disease in Germany. *Nephrol Dial Transplant* 2010, Epub ahead of print.
- 11 Koch M, Gradaus F, Schoebel FC, Leschke M, Grabensee B: Relevance of conventional cardiovascular risk factors for the prediction of coronary artery disease in diabetic patients on renal replacement therapy. *Nephrol Dial Transplant* 1997;12:1187–1191.
- 12 K/DOQI clinical practice guidelines for cardiovascular disease in dialysis patients. *Am J Kidney Dis* 2005;45(suppl 3):S1.
- 13 Knoll G, Cockfield S, Blydt-Hansen T, Baran D, Kiberd B, Landsberg D, Rush D, Cole E: Canadian Society of Transplantation Consensus guidelines on eligibility for kidney transplantation. *CMAJ* 2005;173:S1–S25.
- 14 Rakhit DJ, Armstrong KA, Beller E, Isbel NM, Marwick TH: Risk stratification of patients with chronic kidney disease: results of screening strategies incorporating clinical risk scoring and dobutamine stress echocardiography. *Am Heart J* 2006;152:363–370.
- 15 Sharma R, Pellerin D, Gaze DC, Gregson H, Streather CP, Collinson PO, Brecker SJ: Dobutamine stress echocardiography and the resting but not exercise electrocardiograph predict severe coronary artery disease in renal transplant candidates. *Nephrol Dial Transplant* 2005;20:2207–2214.
- 16 Wang JH, Kasiske BL: Screening and management of pretransplant cardiovascular disease. *Curr Opin Nephrol Hypertens* 2010; 19:586–591.