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Coronary Artery Disease Treatment in Dialysis Patients at the *Hospital das Clínicas da Faculdade de Medicina de Botucatu - UNESP*

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Summary

Background: Interventional treatment of coronary insufficiency is underemployed among dialysis patients. Studies confirming its efficacy in this set of patients are scarce.

Objective: To assess the results of interventional treatment of coronary artery disease in patients undergoing dialysis.

Methods: A total of 34 dialysis patients submitted to coronary angiography between September 1995 and October 2004 were divided according to presence or absence of coronary lesion, type of treatment and presence or absence of diabetes mellitus. The groups were compared according to their clinical and survival characteristics. Survival of patients undergoing interventional treatment was compared to overall survival of 146 dialysis patients at the institution in the same period. Interventional treatment was indicated to the same clinical conditions in the general population.

Results: Thirteen patients with no angiography coronary lesions presented a survival rate of 100% in 48 months as compared to 35% of 21 patients with coronary artery disease. Diabetic patients had a lower survival rate compared with non-diabetics. Angioplasty had a worse prognosis compared to surgery; however, 80% of patients undergoing angioplasty were diabetic. Seventeen patients submitted to interventional procedures presented a survival rate similar to that of the others 146 hemodialysis patients without clinical evidence of coronary disease.

Conclusion: This small series shows that myocardial revascularization, whenever indicated, can be performed in dialysis patients. This conclusion is corroborated by similar mortality rates in two groups of patients: coronary patients submitted to revascularization and overall dialysis patients.

Key words: Renal insufficiency, chronic; coronary artery disease, myocardial revascularization.

Introduction

Cardiovascular diseases, particularly coronary artery disease (CAD), are the major cause of death in patients with chronic renal failure (CRF) treated by dialysis[1]. Cardiovascular diseases account for over 50% of deaths of dialysis patients in the US and Europe[2,3]. In Brazil, they represent 51% of total deaths[4], if adding up the cardiac and cerebrovascular causes of deaths.

The high cardiovascular mortality rate seen in chronic renal patients is due, at least partially, to the high prevalence of traditional cardiovascular risk factors in these patients, such as high blood pressure, diabetes mellitus and hyperlipidemia. The prevalence of atherosclerosis in chronic renal patients is higher than expected and might be due to presence of other predisposing factors for coronary artery disease and related to uremia: increased levels of lipoprotein A, hyperhomocysteinemia, increased oxidative stress, inflammatory status, low serum levels of HDL, in addition to the volume overload associated with renal failure[5]. Therefore, chronic renal disease has a direct participation in the process of atherogenesis[6].

The myocardium of uremic patients is more susceptible to cell death due to ischemic insult than the myocardium of individuals with normal renal function[7]. Susceptibility to ischemia is also aggravated by the high prevalence of ventricular hypertrophy among uremic patients. Thus, appropriate perfusion of myocytes in this population is very important.

In transplanted patients, the main cause of death is also of cardiovascular nature, and CAD also stands out[8]. Perioperative mortality and renal graft failure rates in patients with uncorrected CAD are high and the transplant should be discouraged[9]. Therefore, coronary investigation is necessary in renal transplant candidates. However, coronary angiography is not indicated to all chronic renal patients since it is an invasive and high-cost procedure, not exempt form risks. Consequently, coronary angiography is reserved to patients considered as high risk for significant CAD[8].

The dialysis population has significantly increased in the past years. There were 15 thousand dialysis patients in Brazil,

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in 1995, and this number tripled in 2000. It is estimated that 70 thousand patients currently receive this type of treatment[9]. This rise reflects the increased number of chronic renal patients with coronary artery disease and highlights the importance of studying CAD in dialysis patients.

The European and North American guidelines for the treatment of CAD in individuals with CRF[10,11], as well as most specialists[12-14], suggest that the indications for myocardial revascularization in these patients should be similar to those for the general population. However, the results are considerably lower if compared with those obtained in the general population, but higher when compared to the prognosis of chronic renal patients who have not been submitted to interventional therapy[15,16]. Only one randomized controlled study[17] and few case series support this management and, to our knowledge, no series has been reported in Brazil.

The present study aims to assess the results of interventional treatments for myocardial revascularization in patients with CAD and chronic renal failure being treated with dialysis at the *HC, Faculdade de Medicina de Botucatu* (UNESP).

Methods

We carried out a prospective, non-concurrent study of all dialysis patients undergoing coronary angiography between September1995 and October 2004 (34 patients). All data necessary to this study were collected through analysis of medical charts.

Inclusion criteria - Chronic renal patients submitted to coronary angiography presenting or not coronary atherosclerotic lesion, who were submitted or not to interventional treatment for coronary insufficiency. Interventional treatment included coronary angioplasty and coronary artery bypass graft. The indications for myocardial revascularization followed those proposed by the National Kidney Foundation (NKF)[11] and European Dialysis and Transplantation Association (EDTA)[12], for the management of coronary artery disease in chronic renal patients, which recommend interventional treatment in the same conditions indicated for chronic non-renal patients.

Groups - The individuals were divided into different groups according to the following criteria: presence or absence of coronary artery lesion and performance or not of interventional treatment. In patients undergoing interventional treatment, the presence or absence of diabetes mellitus and the type of procedure performed were also considered. The number of patients was determined by the total number of cases who met the inclusion criteria and whose data were available for analysis.

Of 34 patients undergoing coronary examination, 21 presented positive results for CAD and they were called group **GCO** (group of patients with coronary occlusion). The remaining 13 patients, characterized by absence of coronary lesion were named group **GNO** (group of patients with no coronary occlusion). In group **GCO**, 17 patients underwent interventional treatment and they were grouped as **G1**. This group was, in turn, subdivided as to presence of diabetes mellitus, as follows: **G1a** composed of diabetic patients (n=10) and **G1b** of non-diabetic patients (n=7). The survival rates in these different groups were calculated and compared.

Group **G1** was further subdivided according to the interventional procedure used. The group of patients undergoing surgical treatment was called **Group Sur** (n=10) and **Group Angio** comprised patients who underwent angioplasty (n=7); all patients undergoing angioplasty received a stent implantation.

The survival rate of patients undergoing interventional treatment was also compared to the overall survival of 146 dialysis patients (41 diabetic and 105 non-diabetic patients) at the institution during the same period (control group).

The study was carried out according to Resolution 169/96 of the *Conselho Nacional de Saúde* [National Council of Health] and it was approved by the Research Ethics Committee of the *Faculdade de Medicina de Botucatu* - UNESP.

Variables assessed - The following variables were obtained through analyses of medical charts and transcribed into a standardized form: medical chart number, gender, age, race, dialysis method (hemodialysis or peritoneal dialysis), cause of renal failure, date of first dialysis, date of coronary angiography, date of intervention (when performed), date of last follow-up and status at this moment (death or censure; censure includes recovery of renal function, transference to another service, renal transplantation or a live patient still undergoing dialysis), symptoms (compatible with congestive heart failure), past history of smoking habit, diabetes mellitus, high blood pressure and complementary exams (total cholesterol, HDL-cholesterol and triglycerides).

The parametric data were expressed as mean ± standard deviation, while non-parametric data were expressed as median and interquartile interval. Survival was expressed as percentage throughout years. Inferences in continuous variables were carried out by a "t" test for independent samples and by the chi-square (χ^2) test for discreet variables. The survival curves were traced taking into account survival as from performance of an interventional method until death or censure, as well as from the beginning of dialysis treatment, in order to correct this data for previous period in dialysis program.

Survival was compared among patients in the different groups and also with the control group by using the statistical method of a survival table. The statistical inference was calculated through the method proposed by Greenwod[18].

Results

There was a statistically significant difference regarding survival of patients in groups **GCO** (patients with coronary artery occlusion) and **GNO** (patients with no coronary artery occlusion). After coronary angiography, survival of 100% was observed at 48 months in group **GNO** and 71% (confidence interval - CI: 62%-80%), 35 % (CI: 23%-47%) and 23% (CI: 10%-36%) at 12, 48 and 60 months, respectively, for group **GCO** (p< 0.05). Survival of these groups is expressed in Figure 1. No statistical difference was found in terms of age, race and cause of renal failure between these 2 groups; there was a higher percentage of male patients in the group with coronary artery disease (Table 1). As to clinical variables, these groups did not present statistically significant differences (Tables 1

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and 2). Concerning plasma lipids, there was a statistical trend towards higher cholesterol levels in group **GCO** (Table3).

Group **GNO** had no fatal events. The causes of 17 deaths in group **GCO** were seven cases of myocardial infarction, with three deaths during the peri-revascularization procedure period, one death due to stroke, one death due to acute pulmonary edema, one death due to a neoplasm and four deaths caused by infections.

Survival of patients in group **G1** (all patients submitted to coronary intervention) and in its subgroups was calculated as from the date of the interventional procedure and the following values were found: group **G1**, 59% (CI: 36%-82%) at 12 months, 35% (CI: 21%-49%) between 24 and 60 months, with group age at 59 (57-68) (Table 1). In the same period, group **G1a** (a subdivision comprising diabetic patients in group G1) presented a survival rate of 50% (CI: 29%-61%) at 12 months *versus* 78% (CI: 65%-91%) in **G1b** ($p < 0.05$). At 24 months, **G1a** and **G1b** presented a survival rate of 33% (CI: 12%-54%) and 41% (CI: 16%-66%), respectively. As to clinical and demographic variables, these groups did not present any statistically significant differences (Tables 1 and 2). Concerning plasma lipids, the

triglyceride mean level was significantly higher in **G1a,** with a trend towards lower levels of HDL-cholesterol ($0.05 < p < 0.1$). The values of plasma lipids are shown in Table 3.
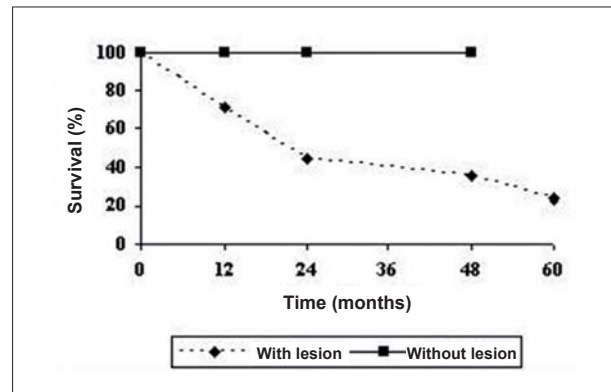

Fig. 1 - *Survival of 21 dialysis patients with coronary artery disease, compared to 13 patients with normal coronary angiography (as from the date of coronary angiography).*

Table 1 - Demographic variables of different groups

Variables	Total (n=34)	GOC (n=21)	GNO (n=13)	Angio (n=10)	Sur (n=7)	G1a (n=10)	G1b (n=7)
Sex (% males)	47	62#	23	50	51	50	71
Race (% white)	74	62	92	60	57	50	71
Age (years)	56(52-59)	58(55-61)	53(49-56)	58(52-59)	57(56-62)	59(57-68)	56(55-59)
Cause of RF (%)							
AH	24	19	31	10	14	0	29
DM	47	43	54	80*	0	80*	0
Other	29	38	15	10	86	20	71

GCO - patients with coronary artery occlusion; GNO - patients with no coronary artery occlusion; G1a - diabetic patients undergoing intervention; G1b - non-diabetic patients undergoing intervention; RF - renal failure; AH - arterial hypertension; DM - diabetes mellitus; Angio - angioplasty; Sur - surgery; # - $0.05 < p < 0.10$; * - $p < 0.05$.

Table 2 - Clinical features of different groups

Variables	Total (n=34)	GOC (n=21)	GNO (n=13)	Angio (n=10)	Sur (n=7)	G1a (n=10)	G1b (n=7)
Smoking habit (%)	62	67	54	60	86	50	100
AH (years)	14 (8-18)	15 (10-20)	10 (8-17)	15.5 (7-20)	23 (16-30)	16 (7-20)	21 (16-24)
DM (%)	62	57	69	90*	14	100*	0
CHF (%)	47	52	38	50	57	40	57
CHF – IV (%)	29	43	15	40	57	40	57
Beginning until coronary angiography (months)	22 (9-43)	22 (9-40)	27 (8-48)	18 (10-27)	25 (15-42)	22 (10-27)	22 (14-42)

GCO - patients with coronary artery occlusion; GNO - patients with no coronary artery occlusion; G1a - diabetic patients undergoing intervention; G1b - non-diabetic patients undergoing intervention; RF - renal failure; AH - arterial hypertension; DM - diabetes mellitus; Angio - angioplasty; Sur - surgery; # - $0.05 < p < 0.10$; * - $p < 0.05$.

Table 3 - Plasma lipids in different groups							
Variables	**Total (n=34)**	**GOC (n=21)**	**GNO (n=13)**	**Angio (n=10)**	**Sur (n=7)**	**G1a (n=10)**	**G1b (n=7)**
Cholesterol (mg/dl)	234±37	232±70#	188±59	247±56*	185±37	229±28	213±88
HDL-cholesterol (mg/dl)	40±12	38±12	40±16	39±9	36±11	41±9 #	32±8
Triglycerides (mg/dl)	263±133	272±128	209±145	332±103*	189±115	337±105*	181±8

GCO - patients with coronary artery occlusion; GNO - patients with no coronary artery occlusion; G1a - diabetic patients undergoing intervention; G1b - non-diabetic patients undergoing intervention; RF - renal failure; AH: arterial hypertension; DM - diabetes mellitus; Angio - angioplasty; Sur - surgery; # - $0.05 < p < 0.10$; * - $p < 0.05$.

The overall survival of 41 diabetic patients undergoing dialysis during the same period (control group) was respectively, 64% (CI: 55%-73%) at 12 months, 54% (CI: 43%-65%) at 24 months, 54 % (CI: 43%-65%) at 36 months and 39% (CI: 26%-52%) at 48 months. These results were comparable to the survival curves in G1a patients. This comparison was carried out after an adjustment that included – in the calculation of survival in subgroups – the time of dialysis before the intervention period. Therefore, in this same period, the survival evaluated as from the beginning of dialysis in diabetic patients undergoing revascularization procedures was 65% (CI: 51%-79%) at 12 months, 54% (CI: 36% -72%) at 24 months, 41% (CI: 20%-62%) at 36 months and 41% (CI: 20%-62%) at 48 months, respectively.

The overall survival of 105 non-diabetic patients treated with dialysis in the same period (control group) was 79% (CI: 74%-84%) at 12 months, 70% (CI: 63%-77%) at 24 months, 66% (CI: 57%-75%) at 36 months and 62% (CI: 52%-62%) at 48 months, respectively. These results were comparable to the survival curves in group G1b. This comparison was performed after an adjustment that included – in the calculation of survival in subgroups – the time of dialysis before the intervention period. Therefore, in this same period, the survival of non-diabetic patients undergoing revascularization procedures was was 81% (CI: 67%-95%) at 12 months, 58% (CI: 37%-79%) at 24, 36 and 48 months.

Of 21 patients who presented epicardial abnormalities at coronary angiography, four did not undergo interventional treatment despite having a clinical indication. One patient refused the procedure and, in the other patients, the procedure was considered unfeasible and they received only medical treatment. Two patients died before one year of treatment and one patient has been followed up for 9 months.

Considering the revascularization procedure adopted (surgery or angioplasty), the survival rate in group Sur was 71% (CI: 63%-79%) at 12 months, 37% (CI: 22%-52%) between 24 months and 60 months. The survival rates in group Angio were 51% (CI: 40%-62%) at 12 months and 34% (CI: 17%-51%) at 24 months (p<0.05 at 12 months). Therefore, individuals who underwent a surgical procedure presented a higher survival rate than patients submitted to angioplasty. We should emphasize that 80% of patients in group Angio had renal failure due to diabetes mellitus, whereas no patients in group Sur were on

dialysis due to diabetic nephropathy (Table 1), which resulted in a statistical difference. The same applies to the higher rate of diabetes mellitus in group Angio (Table 2). As to mean plasma lipids, group Angio presented significantly higher levels of cholesterol and triglycerides than group Sur (Table 3).

Discussion

In this group comprising chronic renal patients undergoing dialysis treatment, the survival of coronary artery disease patients submitted to myocardial revascularization was similar that of overall chronic renal patients at this institution, which corroborates the interventional management in the same indications for the general population.

Some studies comparing case series of chronic renal patients submitted to myocardial revascularization and series of non-chronic renal patients undergoing the same procedures suggest that the presence of renal failure implies a poor prognosis. These findings led some authors to discourage these procedures among chronic renal patients with coronary artery disease. However, in these studies there were no comparisons of groups composed of chronic renal patients with CAD with indication for revascularization who, in fact, underwent myocardial revascularization and patients with similar characteristics who did not undergo any intervention. There is only one study with a small sample that carried out this comparison with a randomized control which, despite showing perioperative mortality rate of 20%, also presented a survival rate of 80%, at one year, in the intervention group, and of 20%, in the same period, in the group undergoing medical treatment[16].

In the present series, the comparison of survival rates of diabetic and non-diabetic patients showed a statistical difference at 12 months after the interventional procedure (50% and 78%, respectively). Therefore, diabetes mellitus was an important negative prognostic factor in chronic renal patients undergoing coronary artery bypass graft.

Comparing the survival of diabetic patients undergoing dialysis at this service with the survival of diabetic patients with CAD who underwent intervention in the present study (**G1a**), corrected for the previous time of dialysis, we obtained similar survival results. The correlation of coronary lesion made the curves of these two groups closer since it was expected that patients with CAD would have shorter survival. On the other hand, survival of non-diabetic chronic renal patients with

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DAC who underwent myocardial revascularization was slightly lower than when compared with that of non-diabetic chronic renal patients from this service. However, this difference did not reach statistical significance and it leads us to an analogous conclusion in non-diabetic patients.

The causes of death in patients with coronary artery disease were not solely of cardiovascular nature. Five out of 17 deaths were due to other causes (one was due to a neoplasm and four due to infections). To explain this observation, one could speculate that the patients with heart disease are less resistant to an infectious event than those with a preserved cardiovascular system.

Previous studies[18] suggested that dialysis patients undergoing surgical treatment present longer survival than those undergoing percutaneous coronary intervention. The results of the present study were in accordance with the literature. However, we have to consider that, in the group undergoing angioplasty, 90% of patients were diabetic while only 14% had diabetes mellitus in the group treated with surgery. Therefore, diabetes mellitus may be regarded as a probable cause of higher mortality rates seen in the group undergoing angioplasty. Moreover, the lipid profile of diabetic patients was worse than that of non-diabetic patients.

A multicenter cohort study conducted in the US enrolled 15,784 dialysis patients undergoing invasive procedures of myocardial revascularization[19] and showed survival of 65.7 to 71.5% at 12 months, 48.2 to 56.4% at 24 months, and 28.6 to 37.0% at 42 months. Data from the present study are similar to those reported in the cohort study, which had 44.7% to 47.6% diabetic patients. Our caseload presents 58.8% diabetic patients, which may justify a slightly lower survival rate.

Two Japanese studies[20,21] demonstrated survival of dialysis patients undergoing revascularization as 74.5%, at 40 months, and 45%, at 70 months, in the first study and 89%, 84% and 71% at 1, 3 and 5 years, respectively, in the second study. These values are higher than those found both in the present study and in another carried out in the US. However, it should be emphasized that the survival of dialysis patients in Japan is higher than in the US. These results are similar to those found in our study since the survival of dialysis patients with coronary artery disease undergoing revascularization in the Japanese literature follows the survival rate of dialysis patients in that country.

An Italian study[22] showed a survival rate of 52.9% at one year and 47% at two years in chronic renal patients treated with dialysis and undergoing coronary revascularization procedures. These results were similar to those obtained in the present study, but the latter has 58.8% diabetic patients as compared to 35% in the Italian series. The results of the Italian study show the high risk of myocardial revascularization in dialysis patients; hence, the authors suggest an early assessment and treatment of coronary artery disease in this population; the authors of the present study share this idea.

A study on survival in chronic renal patients treated with dialysis undergoing cardiac surgery (75% coronary revascularization and 25% valvuloplasty) showed that, in elective conditions, the risk of the procedure is acceptable. The patients showed a life expectancy similar to the dialysis population with no cardiac diseases. Although that author[23] did not study coronary revascularization procedure separately, his results support findings of this study.

Our study has some limitations. The sample evaluated has a restricted number of patients and it corresponds to the dialysis population at a single site. In addition, the small sample does not allow multiple analyses; however, by and large, the clinical features were homogeneous in the different groups. The occasional differences were highlighted and the possible impact of comorbidities on the results were discussed. On the other hand, despite the limited size, it is interesting to note that the results are similar to those of few large cohort studies published in other countries, and no Brazilian cohort in this subgroup of patients has been reported. The data presented here foster carrying out multicenter studies which could also assess survival in this specific group of patients, so that, in the future, we can obtain national data with a higher number of patients.

Conclusion

The presence of CAD in chronic renal patients seems to be associated with a worse prognosis, particularly when associated with diabetes mellitus. The results presented here showing a complication rate similar to that found in overall dialysis patients suggest that myocardial revascularization can be performed by a team with experience in this specific group of patients, based on the same conditions as it would be indicated to the general population. These results support the guidelines proposed by the National Kidney Foundation[11] and European Dialysis and Transplantation Association[12].

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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