

Clinical Outcome of Renal Transplant Patients after Coronary Stenting

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Summary

Objective: To assess the clinical outcome of renal transplant patients who developed coronary artery disease and were treated with coronary stenting (TCA-ST).

Methods: A total of 3,334 renal transplants were performed in our service – *Hospital do Rim e Hipertensão – HRH* (Kidney and Hypertension Hospital) from July, 1998 to November, 2004. During this period, 33 of the renal transplant patients underwent TCA-ST to treat 62 severe stenoses in 54 coronary arteries. A retrospective analysis was performed with renal transplant patients undergoing TCA-ST at HRH. The clinical events were registered using medical charts, medical visits and phone calls.

Results: During the 30-month clinical follow-up after TCA-ST, 67% of the patients remained asymptomatic, 18% presented stable angina, 6% presented acute coronary syndrome without ST-segment elevation (ACSWSTE), and 3% presented acute coronary syndrome with ST-segment elevation (ACSSTE). No strokes, CHF or cardiac deaths were observed. Three non-cardiac deaths occurred. A restenosis rate of 9% was observed, which is comparable to those found in studies on drug-eluting stents.

Conclusion: In conclusion, renal transplant patients who developed CAD and were treated with coronary stenting had a low rate of in-stent restenosis, probably related to the immunosuppressive regimen given to prevent kidney rejection.

Key words: Renal transplant, coronary angioplasty, in-stent restenosis.

Introduction

Two hundred seventy five thousand patients with chronic renal failure (CRF) undergoing dialysis were registered in the United States, from 1997 to 1999, with 239 deaths/1000 patients/year. Cardiovascular diseases were the cause of death in 44% of the cases. In the same period, 107 thousand renal transplant patients were registered. Mortality in this population was 34 deaths/1000 patients/year, of which 41% resulted from cardiovascular diseases. The lower mortality in transplant patients is related to factors such as selection of patients at a lower risk for transplantation and risk reduction resulting from the transplantation itself. It is important to observe that despite the lower mortality of transplant patients when compared to that of patients undergoing dialysis, cardiovascular diseases remain the main cause of death¹⁻⁵.

Patients with CRF associated with diabetes mellitus have a higher risk of death of 70% in 7 years⁵⁻⁷. It is worth pointing out that the majority of patients with CRF present associated diabetes mellitus.

CRF patients undergoing stent angioplasty present a 2.2-fold higher need for repeated target vessel revascularization

when compared to non-CRF patients (35% versus 16%)^{8,9}.

CRF is a predictor of in-stent restenosis, with an angiographic restenosis rate after balloon angioplasty of approximately 60 to 81%^{10,11} and clinical restenosis rate after stent implantation of approximately 10 to 50%^{12,13,14}.

The use of cyclosporine in experimental studies has demonstrated inhibition of smooth muscle cell proliferation in response to vascular injury^{15,16}. The use of prednisone in patients undergoing angioplasty and who had high CRP levels demonstrated a reduction of clinical events and of angiographic restenosis¹⁷.

Using intracoronary ultrasound, we have previously demonstrated a minimal in-stent intimal hyperplasia in the group of renal transplant patients using routine immunosuppressive regimen¹⁸.

Data on the clinical course, clinical restenosis rates, and progression of the coronary artery disease (CAD) in this population of renal transplant patients undergoing coronary angioplasty with stenting (TCA-ST) are not available in the literature.

The objective of this study was to assess the clinical course of renal transplant patients with CAD, undergoing TCA-ST. The following cardiovascular events were considered in the clinical course: clinical restenosis, acute coronary syndrome with ST-segment elevation (ACSSTE), acute coronary syndrome without ST-segment elevation (ACSWSTE), stroke, congestive

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heart failure (CHF), and death.

Methods

A total of 3,334 renal transplants were performed in our service, *Hospital do Rim e Hipertensão* (HRH) from July, 1998 to November, 2004 (Figure 1). During this period, 33 of the renal transplant patients underwent TCA-ST to treat 62 severe stenoses in 54 coronary arteries.

A retrospective analysis of the renal transplant patients routinely using conventional immunosuppression with cyclosporine, azathioprine, prednisone, mycophenolate mofetil, or tacrolimus, and who had undergone TCA-ST was performed at HRH.

Patients using oral rapamycin, patients who used drug-eluting stents, patients undergoing TCA-ST prior to renal transplantation, and those with unavailable clinical follow-up were not included.

The clinical events were registered using medical charts, medical visits and phone calls.

Demographic characteristics, risk factors for cardiovascular diseases, immunosuppressive drugs used, cardiovascular drugs used by the time of angioplasty, dialysis time prior to transplantation, the type of donor, number of stented coronary arteries, number of stents implanted, and the clinical course for at least six months after TCA-ST were analyzed.

Patients underwent repeat cardiac catheterization when presenting symptoms of CAD, or when presenting a non-invasive test positive for myocardial ischemia.

Results

A total of 33 patients with a median time between renal

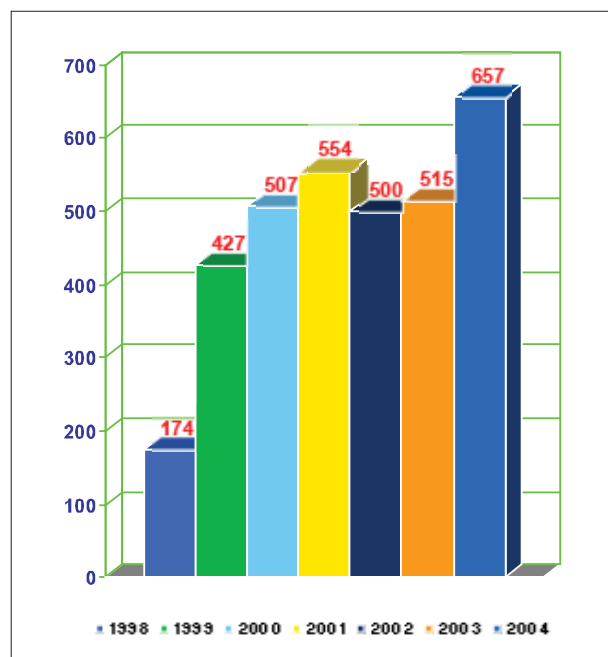


Fig. 1 - Number of renal transplants per year at HRH.

transplantation and coronary stenting of 37 months (ranging from three days to 121 months) were included. Demographic characteristics of these patients are shown in Table 1.

All patients were using aspirin and thienopyridine derivatives routinely for at least three days prior to stent implantation. Aspirin was maintained continuously, and thienopyridine derivatives for at least 30 days after TCA-ST (Table 2).

The median dialysis time until renal transplantation was 12 months, ranging from patients who did not undergo dialysis to those who underwent dialysis for 84 months.

Fifty five percent of the patients received renal transplants from living donors.

Immunosuppression regimen was distributed as follows: 90% prednisone, 70% cyclosporine, 64% azathioprine, 33% mycophenolate mofetil, and 12% tacrolimus.

Indications for coronary angioplasty were: ACSWSTE in 67%, ACSSTE in 18%, and stable angina in 15%.

All stents were successfully implanted and all patients were discharged with no complications within 48 hours of the procedure. A mean of 1.88 ± 1.11 stents/patient were implanted.

The median clinical follow-up period was 30 months (ranging from six months to 82 months).

A favorable clinical outcome was observed, with 67% of the patients remaining asymptomatic, 18% remaining with stable angina, 6% presenting ACSWSTE, and 3% presenting ACSSTE.

No patients with stroke were observed after the procedure.

Table 1- Clinical characteristics of the population

Mean age	56 ± 10.5 years
Male gender	88%
Systemic hypertension	96%
Diabetes mellitus*	45%
Smoking	42%
Dyslipidemia	58%
Family history of cardiovascular disease	45%

*73% were taking insulin.

Table 2- Medication used by the time of TCA-ST

Aspirin	100%
Thienopyridine derivatives	100%
Beta blocker	79%
Diuretics	36%
Calcium channel blocker	30%
Angiotensin converting enzyme inhibitor	39%
Statin	36%

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No cardiac deaths occurred. Three non-cardiac deaths occurred: two deaths due to urinary sepsis, and one death due to colon adenocarcinoma.

Three patients presented clinical restenosis, defined as an in-stent stenosis of more than 50% in a patient undergoing repeat coronary angiography, and obtaining a rate of 9%. In the analysis of restenosis by stent implanted, five stents with restenosis in 62 stents implanted were observed, with a rate of 8%.

Ten patients presented coronary artery disease progression, defined as stenosis > 50% in another site not approached by coronary angioplasty, and obtaining a rate of 30% (Figure 2).

Discussion

A low rate of 9% clinical restenosis was found for this population at a high risk for restenosis: renal transplant patients, 45% of whom with diabetes mellitus, most of them taking insulin, and a high mean of 1.88 ± 1.11 stents per patient. These results are similar to the clinical restenosis rates of studies on drug-eluting stents in diabetic patients¹⁹. The use of a great number of stents per patient is similar to the use of approximately two stents per patient demonstrated in recent studies with drug-eluting stents in multivessel disease²⁰.

Most of the patients undergoing TCA-ST remained asymptomatic, and few major cardiovascular events occurred. A low percentage of coronary disease progression was observed, probably because of the short follow-up period of some patients in this case series of 33 patients.

The study limitations were:

- Not all patients underwent coronary angiography, because it would not be ethical to make asymptomatic patients undergo a repeat invasive procedure.

- Serum level of immunosuppressors is not available for all patients, thus not allowing for a correlation with restenosis rates.

- Due to the small number of patients, statistical power was not achieved to determine which immunosuppressor had the highest impact on the reduction of clinical restenosis.

- This is an observational retrospective study whose objective was to perform a clinical analysis of the patients, and other mechanism and surrogate variables, such as reference vessel diameter, stenosis length, stent length per patient,

Table 3 - Clinical course following stent implantation

Asymptomatic	64%
Stable angina	18%
ACSWSTE	6%
ACSSTE	3%
Death	9%*

* Two patients with urinary sepsis and one with sigmoid adenocarcinoma.

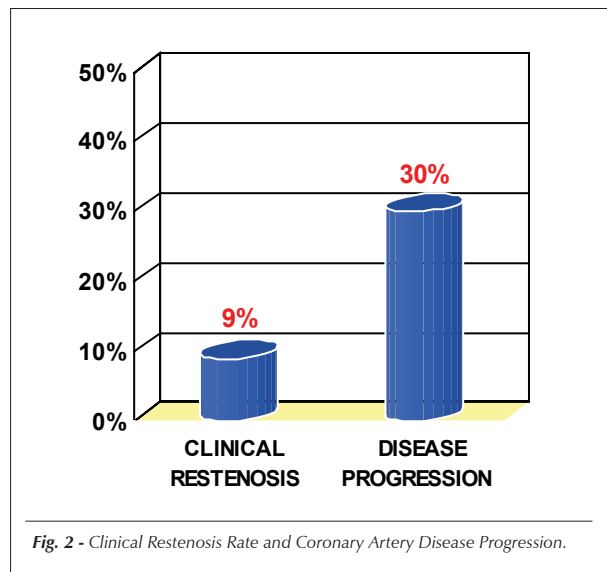


Fig. 2 - Clinical Restenosis Rate and Coronary Artery Disease Progression.

minimum lumen diameter, and acute lumen gain or late lumen loss were not assessed.

Conclusion

Renal transplant patients who developed coronary artery disease and were treated with stent implantation presented a low percentage of clinical restenosis, probably related to the immunosuppressive regimen used to prevent kidney rejection.

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