ELSEVIER

Complications of Renal Transplantation in Patients With Amyloidosis

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ABSTRACT

Objective. Renal transplantation in patients with end-stage renal failure (ESRF) secondary to amyloidosis carries a high risk of postoperative complications. Preoperative investigations are crucial for a successful perioperative course. There are limited data studying the outcome of patients with amyloid nephropathy who undergo renal transplantation. Therefore, we undertook this retrospective review of our experience to highlight the difficulties.

Materials and methods. Thirteen patients with AA amyloid-induced ESRF underwent cadaveric renal transplantation from 1985 to 2001 in the Irish transplant population. The perioperative course of these patients was compared to an age-matched control group of 142 nonamyloid patients who had cadaveric renal transplantation during the same time period. Both groups were followed annually for 5 years.

Results. The 1- and 5-year patient survival rates were 69% and 69% in the amyloid as compared with 97% and 87% for the control group. In the amyloid group, early death was primarily due to cardiac causes followed by complications of sepsis. Graft survival at 1 and 5 years was 56% and 56% in the amyloid group as compared with 87% and 59% in the control group ($P = .0027$). Four deaths with a functioning graft contributed to the early graft losses.

Conclusion. Increased complications, especially cardiac, are noted post–renal transplantation among patients with renal amyloidosis. However, appropriate guideline, for the perioperative management of these patients has yet to be established.

AMYLOIDOSIS is a multisystem disorder characterized by extracellular deposition of fibrillar proteins disrupting normal organ structure and function. Amyloidosis can be primary or secondary. The cause of primary amyloidosis is largely unknown, but the condition is related to abnormal turnover of immunoglobulins by plasma cells. Chronic inflammatory conditions and dialysis are common important causes of secondary amyloidosis. Renal failure may result secondary to amyloid deposits and take decades to develop. One of the most important factors determining survival is the presence of cardiac involvement. Cardiac amyloidosis is classically manifested as a restrictive cardiomyopathy, also known as "stiff heart syndrome." Less frequently, cardiac amyloidosis leads to dilated cardiomyopathy. Optimal cardiac function is vital for the success of any type of major surgery resulting in less peri- and postoperative complications. Patients with cardiac amyloidosis display a decreased ejection fraction, stiffer ventricles, and sometimes coronary obstruction. There have only been a few reports of the outcome of patients with amyloidosis following renal transplantation. Therefore, we undertook this retrospective review of our experience.

MATERIALS AND METHODS

Follow-up data were available on all renal transplants performed after 1985. This retrospective study included patients transplanted from 1986 to 2001. During this time there were 1905 transplant operations performed on 1686 patients, including 13 diagnosed with end-stage renal disease (ESRD) secondary to AA-type amyloid nephropathy as confirmed by renal biopsies. Of the 13 patients with AA amyloidosis: 11 were due to rheumatoid arthritis, one was from inflammatory bowel disease, and one from hydra-adenitis

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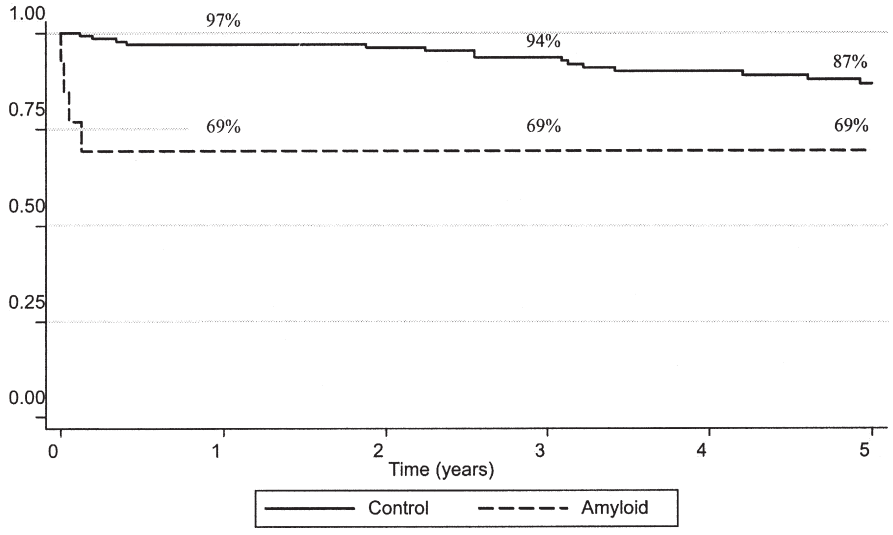

Fig 1. Patient survival.

suppuritiva. Three of the 13 patients received a second transplant yielding a total of 16 grafts. We compared patient survival and renal graft outcome for the amyloidosis patients versus an age-matched control group of 142 patients with ESRD secondary to nonamyloid causes who received cadaveric renal transplants within the same period. Within the control group of 142 patients, 18 had two transplants making a total of 160 grafts. A multiple of 10 times the amyloid graft numbers was used to derive an age-matched control group. This number allowed us to randomly sample a control cohort to give sufficient power and with an age distribution similar to the amyloid patients.

Graft survival was analyzed for all recipients, which included second and subsequent grafts. Death with a functioning graft was included as an endpoint for graft survival outcome. All functioning grafts were censored at the last date of follow-up.

Patient survival was analyzed from the time of the first transplant to death or last date of follow-up in the amyloidosis and control groups. This analysis included patient death after graft failure in the amyloidosis and control groups. The amyloid group included five women and eight men of mean age at transplantation of 48.44 years (range 22 to 66). The entire study group received renal replacement therapy prior to transplantation with 12 receiving haemodialysis and one, continuous ambulatory peritoneal dialysis. Of the patients receiving hemodialysis, the average durations of treatment in the amyloidosis and control groups were 18.49 and 22.12 months, respectively. Each patient underwent an extensive cardiac preoperative evaluation, which included an electrocardiogram (ECG) and echocardiogram (ECHO). Left ventricular hypertrophy was noted in all patients with less than 10% of them displaying valvular lesions, and a mean ejection fraction of 50% (range 40% to 60%). The kidneys were transplanted extraperitoneally onto the iliac vessels and the ureter implanted into the fundus of the bladder. Out of the 16 total grafts in the amyloid group: one patient received a zero mismatched kidney, three had one mismatch, five had two mismatches, five had three mismatches, and two had four mismatches. The patients received immunosuppression according to a protocol that included methylprednisolone, azathioprine, cyclosporine (blood levels maintained between 150 and 300 ng/mL), and FK506 (blood levels maintained between 8 and 15). The two main parameters of comparison were patient survival and graft survival between amyloid patients versus the control group (Figs 1 and 2).

RESULTS

Demographic details were similar between the two groups (Table 1). The results were compiled according to complications and events that may have led to graft failure and patient death. It is important to note that, consistent with previous similar studies, patient death was reported as a cause of graft failure. There were a total of seven deaths recorded among the amyloidosis group, including three who died after graft failure. Out of the seven patient deaths: four were from pure cardiac complications (myocardial infarction, complete heart block, cardiogenic shock), one from sepsis, one from graft hemorrhage, and one from trauma. Of note, two of the four cardiac deaths occurred within 1 year of transplantation. In the amyloid group, these events contributed to 1-, 3-, and 5-year patient survival rates of 69%, 69%, and 69%, respectively. This result compared to 1-, 3-, and 5-year survivals in the nonamyloid control group of 97%, 94%, and 87%, respectively. Overall, patient survival was significantly worse for the amyloidosis group versus the control group (Fig 1), a difference that was especially marked at 1 year following transplantation, mainly due to cardiovascular deaths within that year.

There were nine graft failures attributed to four deaths, two rejections, two graft thromboses, and one primary nonfunction. A high proportion of graft failures occurred within the first month posttransplantation in the amyloidosis group (Fig 2). It was of interest that two out of the four deaths that contributed to graft failure were cardiac in origin. Graft survivals at 1, 3, and 5 years posttransplant for the amyloid group were 56%, 56%, and 56%, compared with 87%, 79%, and 59%, for the control group respectively.