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# Relationship between renal histology and later graft outcome

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**Abstract** We have created the chronic allograft damage index (CADI), which quantifies the early histopathological changes in renal allografts. In this study we showed that the CADI at 2 years after renal transplantation predicted the graft outcome 4 years later and that the CADI identified the risk group that proceeded to chronic rejection during subsequent years.

**Key words** Chronic rejection
Renal transplantation · Renal allograft · Renal histology

## Introduction

Studies with protocol core biopsies are very few. To quantify the incipient histopathological changes, we have created the chronic allograft damage index (CADI) based on numerical scoring of histological alterations. In this study, we report the relationship between renal histology at 2 years, when the graft function was still normal or near normal, and the graft outcome at 6 years after transplantation. We demonstrated that the incipient histopathological changes at 2 years predicted the later graft outcome, and that the CAD reliably identified the patients that would proceed to chronic allograft rejection 4 years later.

## Patients and methods

Based on a prospective study of 128 consecutive renal allograft recipients, we have previously demonstrated the safety of protocol biopsies using an automated biopsy device with ultrasound guidance [1]. Of 102 functioning grafts, 89 renal allograft protocol core biopsies were performed 2 years after renal transplantation. By correlating the transplant function to renal allograft histology, we have identified those incipient histological changes in the allografts that are compatible with chronic rejection [2]. To quantify these changes, we created the chronic allograft damage index (CADI) characterising the six most significant changes in chronic rejection, i.e. diffuse interstitial inflammation and fibrosis, glomelular sclerosis and mesangial matrix increase, vascular intimal proliferation and tubular atrophy [3]. A histological CADI of 2 was considered "low" and a CADI over 2 was considered "high". Of the 89 biopsies, 44 had a low CADI (under 2) and 45 had a high CADI (over 2).

Two years after transplantation, three groups were formed according to graft function (stable or deteriored) and histological changes (CADI $< 2$ or 2). In principal, four groups could have been formed but because only one patient had a low CADI and deteriorated graft function, this patient was excluded from the final analysis. At the time of biopsy, he had chronic infection complications that were later resolved and graft function returned to normal. Group 1 included grafts with a low CADI and stable graft function ($n = 43$), group 2 included grafts with a high CADI and stable graft function ($n = 31$) and group 3 included grafts with a high CADI and deteriorated graft function ($n = 14$). In the groups 1, 2 and 3, the median serum creatinine was 104 mol/l, 133 mol/l and 241 mol/l, respectively 2 years after transplantation.

Six years after transplantation, grafts were classified as chronic rejection if there was a gradual but progressive impairment in renal allograft function in the absence of other specific causes or if the deterioration in the graft function was such that the patient was on dialysis.

## Results

Of the 44 grafts with a low CADI, 3 (7%) were in chronic rejection at 6 years after transplantation. In contrast, of

the 45 grafts with a high CADI 26 (58%) were in chronic rejection. At 6 years the graft survival for the grafts with low and high CADI was 91% and 62%, respectively.

At 6 years after transplantation, 3 (7%) grafts from group 1, 13 (42%) grafts from group 2 and 13 (93%) grafts from group 4 were in chronic rejection. In groups 1, 2 and 3, two (5%), four (13%) and eight (57%) patients had returned to dialysis, respectively. Graft survival in the groups 1, 2 and 3 was 91%, 77% and 29%, respectively at 6 years after transplantation. Patient survival did not differ significantly in the three groups. In groups 1, 2 and 3, two, three and two patients succumbed, respectively. All patients in groups 1 and 2 who died had good and stable graft function at the time of death. In group 3 all patients who died had deteriorating graft function at death.

## Discussion

After transplantation many functional problems are noted that reflect graft history. In problematic situations, biopsies are performed and histological connections to clinical situations are well known. We have earlier performed the protocol biopsies with a complete clinical evaluation of the renal allograft 2 years after transplantation. In this study, we followed these patients for a further 4 years, up to 6 years after transplantation, and compared the 2-year biopsy histology to the subsequent function of the renal allograft and to graft survival. The incipient histological changes compatible to chronic rejection and expressed with the CADI were present in approximately, one-half of transplants including approximately one-third of the transplants with stable function. The grafts with good function and a low CADI were still functioning well 4 years later. In contrast, half of the grafts with good function but with a high CADI at 2 years were in chronic rejection 6 years after transplantation. Furthermore, 8 of 14 patients with histological changes expressed by a high CADI, together with clinically deteriorating graft function were back on dialysis during the next 4 years and 2 patients died with deteriorating graft function.

In conclusion, we demonstrated that the incipient histological findings quantitated as the CADI at 2 years predicted graft function at 6 years.

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