Nephrectomy of the First Failed Kidney Allograft Predisposes Kidney Transplant Recipients to Presensitization with Alloreactive T-cells and Inferior Allograft Survival After Retransplantation

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INTRODUCTION

During the last decades the number of patients being evaluated and waitlisted for a subsequent kidney transplantation has increased to almost 25% of all waitlisted patients. But, evidence for the optimal management of the failed first kidney allograft with respect to nephrectomy remains inconsistent and controversially discussed.The rate of transplant nephrectomies varies widely with respect to the local preferences. Some authors have advocated the removal of all failed grafts due to a susptected state of chronic inflammation that may be associated with further complications. On the contrary, it has been suggested that a retained kidney allograft may fix the circulating antibodies and result in lower PRA levels, thereby protecting the new allograft.

Particularly in retransplant patients, the presence of alloreactive T-cells, has been suggested as a key initiator of the alloimmune response. These alloreactive T-cells have been associated with an increased risk of acute cellular rejection early after transplantation, and with inferior allograft survival and function compared to those without preformed alloreactive T-cells.

PATIENTS AND METHODS

We examined 111 recipients of a second kidney allograft from 1998 until 2015. 60 KTRs were identified with the first kidney allograft retained in situ and 51 KTRs were identified with the first kidney allograft removed. KTRs with primary non-function or allograft loss within the first 12 months of the first kidney allograft were excluded from analysis. We monitored alloreactive T-cells pretransplantation and at +1 months by IFNγ Elispot after stimulation. We tried to address the following questions: (1) What impact does the management of the previous allograft have on allograft survival?; (2) What impact does the management of the previous allograft have on patient survival?; and (3) What impact does the management of the previous allograft have on the development of alloreactive T-cells?

	2nd KTRs with previous allograft retained *in situ* (n=60)	2nd KTRs with previous allograft removed (n=51)	*P value*
Age, yr*	46 (20-67)	43 (21-74)	*0.206*
Male sex, n (%)	35 (58)	28 (55)	*0.848*
Donor age, yr*	48 (12-72)	50 (15-76)	*0.277*
Previous allograft function, mo*	130 (18-245)	107 (23-296)	*0.203*
Total HLA mismatch, n (%) **4-6 HLA mismatch**	3 (0-6) 17 (28)	3 (0-5) 12 (24)	*0.702* *0.666*
PRAs, n (%) **<10%** **10-50%** **>50%**	 39 (65) 10 (17) 11 (18)	 36 (71) 9 (18) 6 (12)	*0.631*
Delayed Graf Function, n (%)	21 (35)	15 (29)	*0.549*
Acute rejection, n (%) **IA/IB** **IIA/IIB/III**	18 (30) 14 (23) 4 (7)	27 (53) 17 (33) 10 (20)	*0.019**
De novo DSA, n (%)	9 (15)	5 (10)	*0.568*
Septic complications, n (%)	5 (8)	6 (12)	*0.751*

RESULTS

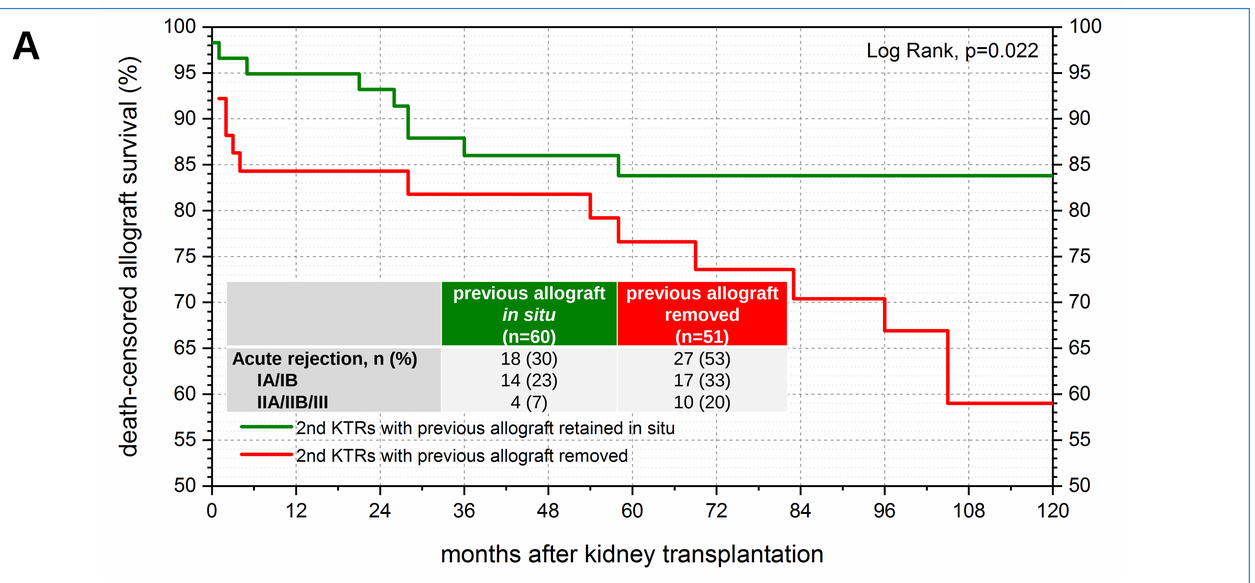

Figure 1A KTRs with the first kidney allograft removed showed significantly inferior death-censored allograft survival compared to KTRs with the first kidney allograft retained in situ. This observation is in line with the higher incidence of severe acute cellular rejections, with allograft loss due to rejection in the early-posttransplant period and shorter long-term allograft function due to the initial immunological damage.

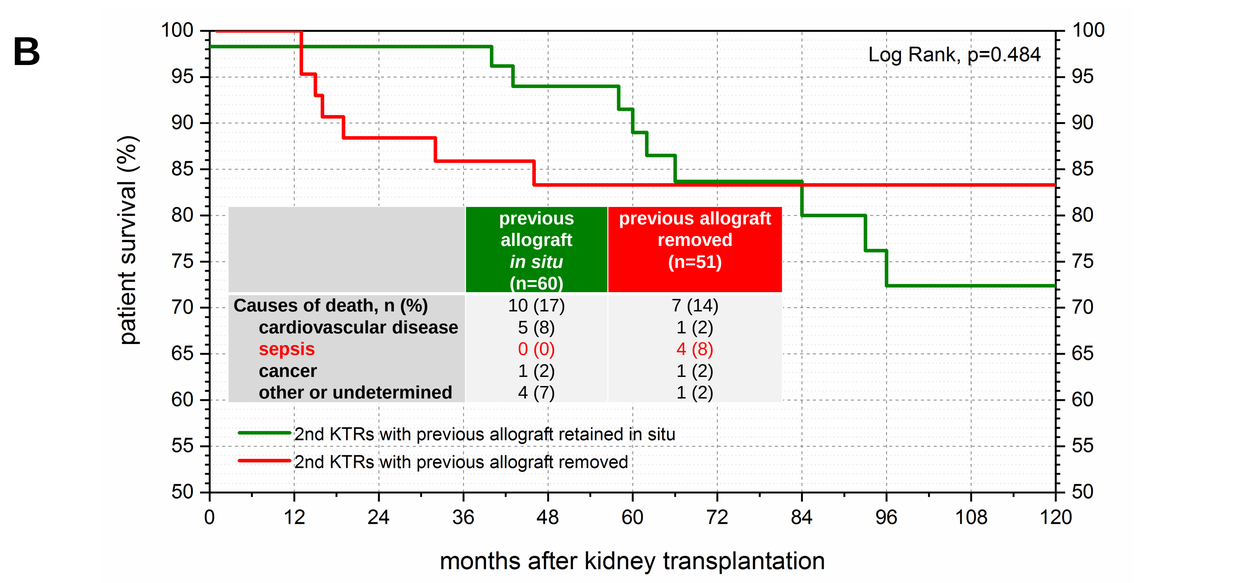

Figure 1B No differences were observed for patient survival between KTRs with the first kidney allograft removed and those with the first kidney allograft retained. However, KTRs with the first kidney allograft removed showed inferior patient survival in the first two years posttransplantation, that could be attributed to a higher number of deaths from sepsis in those KTRs who received intensive anti-rejection treatment.

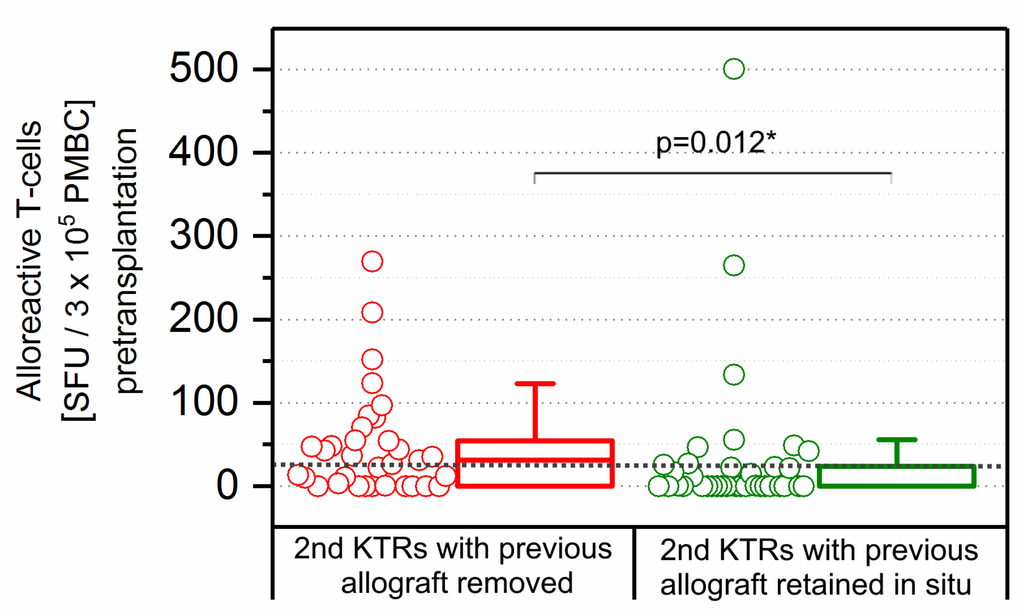

Figure 2AB: KTRs with the first kidney allograft removed showed significantly higher alloreactive T-cells pretransplantation and at +1 month posttransplantation compared to KTRs with the first kidney allograft retained in situ.

CONCLUSIONS

1. **Our data suggest a higher incidence of acute cellular rejection episodes among 2nd KTRs with the previous allograft removed compared to those with previous allograft retained *in situ.* This particularly includes mores severe acute cellular rejections.**

2. **Our data suggest inferior death-censored allograft survival among 2nd KTRs with the previous allograft removed compared to those with previous allograft retained *in situ.* These inferior outcomes are strongly associated with the higher incidence of acute cellular rejections.**

3. **Our data suggest higher frequencies of alloreactive T-cells among 2nd KTRs with the previous allograft removed.**

The immunological mechanisms that account for these differences remain unclear. On the one hand, the reasons that lead to allograft nephrectomy itself, acute cellular rejection of the retained allograft with pain and inflammation, may select those patients with cellular presensitization. On the other hand, prolonged maintenance immunosuppression to safe urine output in KTRs with the first kidney allograft retained in situ may contribute in less cellular presensitization.

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There are no relevant conflicts of interest to disclose.

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Renal transplantation - Epidemiology & outcome I
Thomas Schachtner
DOI: 10.3252/pso.eu.54ERA.2017
ePosters supported by F. Hoffmann- La Roche Ltd.
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