

# FOLLOW-UP OF CYTOTOXICITY NEGATIVE, FLOW CYTOMETRY POSITIVE CROSSMATCH RENAL TRANSPLANT RECIPIENTS



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## Introduction

Flow cytometry crossmatching (FCXM) is claimed to be more 'sensitive' at detecting HLA antibodies than complement dependent cytotoxicity (CDC). However, the clinical significance of a positive FCXM in renal transplant recipients with a negative CDC crossmatch remains unclear.

Here, we present our findings on a study of patients transplanted with a negative CDC crossmatch but later identified as having a positive FCXM.

## Methods

We performed retrospective FCXM, on patients' sera taken immediately prior to renal transplantation, on 343 consecutive patient/cadaveric donor pairs.

All had a pre-transplant negative CDC crossmatch using unseparated splenic lymphocytes and DTT-treated sera.

FCXM positive was set at the mean median channel value of the negative control plus 40 linear channel shifts.

## Results

A total of 17 (4.96%) of the 343 patients were FCXM positive. Of these 12 were T-cell and B-cell FCXM positive and 5 were FCXM B-cell positive only.

An analysis of gender, primary/regraft, transfusion status, and panel reactivity antibody (PRA) between the FCXM positive and negative groups identified the following:

- The gender distribution and the level of HLA-A, B, DR mismatching between the FCXM positive and negative groups did not differ ( $p > 0.1$ ).
- There were significantly more patients awaiting a regraft in the FCXM positive group ( $n=9$ , 53%) compared to the FCXM negative patients (17%) and conversely less awaiting their primary graft in the FCXM positive group (both  $p < 0.001$ ).
- 9 (53%) of the FCXM positive patients had received previous transfusions compared to 29% of the FCXM negative patients (Fisher's  $p=0.07$ ).
- 35.3% ( $n=6$ ) of the FCXM positives had a CDC DTT-treated serum PRA of  $>49\%$  compared to only 5.3% of the FCXM negative group ( $p < 0.0001$ ).

## Clinical follow-up on the FCXM positive patients

The 17 patients transplanted with a CDC negative but FCXM positive graft were followed-up from between 174 and 314 weeks. The findings were:

- Currently 9 (53%) of the 17 patients have a functioning graft with graft survival of between 123 and 360 weeks.
- Two patients died with a functioning graft.

The remaining 6 patients had graft failures - of these:

- 2 were classified as 'non-immunological'
- 1 was due to the recurrence of the original disease
- 3 were caused by apparent rejection (failure at 6, 180 and 254 weeks).

Of the 9 functioning grafts:

- 4 were primary grafts (1 with a PRA  $>10\%$ , 3 were T-cell and B-cell FCXM positive)
- 5 were regrafts (4 with a PRA  $>10\%$ , 4 were T-cell and B-cell FCXM positive).

## Summary

A retrospective study of 343 consecutive CDC crossmatch negative renal transplants identified 17 (5%) as FCXM positive.

Overall the FCXM positive group had a greater opportunity for HLA sensitisation by transfusion and transplantation compared to the crossmatch negative patients and this was reflected in their PRAs.

Of the 17 FCXM positive grafts 9 were functioning at between 174 and 314 weeks, 3 were lost due to 'rejection' at 6, 180 and 254 weeks, the remainder were lost due to non-immunological reasons or patients' death.

## Comment

Attention to a prospective positive FCXM would have denied 17 of our patients a transplant. Therefore, we recognise that, even in view of the scarcity of cadaveric donor kidneys and the large number of patients awaiting a transplant, transplanting a CDC negative FCXM positive kidney may be justified, at least for certain patients.