Management of paediatric patients with a failing kidney transplant: a survey of UK-based renal units

Running title: Failing transplant practice survey

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Abbreviations:

CNI – calcineurin inhibitor

eGFR – estimated glomerular filtration rate

KRT – kidney replacement therapy

Kidney transplantation is the gold standard treatment for children with kidney failure, offering better life expectancy, quality of life, and growth compared to dialysis[1]. Graft failure is defined by the start of another kidney replacement therapy (KRT) (dialysis or re-transplantation) but there is no international consensus on what GFR defines graft failure for those who do not pursue further KRT. Given their young age at receipt of transplant, paediatric kidney recipients are likely to experience graft failure in their lifetime: in the UK, 20 years post transplantation, 58% of child recipients have experienced graft failure[2].

A 2022 KDIGO Controversies Conference highlighted the lack of evidence to inform management of transplant failure[3], with a paucity of paediatric research noted. We aimed to describe UK practice patterns regarding the management of children with a failing kidney transplant, and investigate variation in practice.

Between March and November 2022, a structured survey was sent to Paediatric Nephrologist and Transplant Surgeon representatives at the 13 UK paediatric kidney units via NHS Blood and Transplant's Kidney Advisory Group and the UK Kidney Association. Summary statistics were used to describe the data (Freeman-Halton extension, Fisher's exact test). Data were analysed using R v4.2.1[4]

We received responses from 11/13 (85%) units, of which nine were transplanting centres. Results are presented in Table 1. No centre had a protocol for the management of failing kidney transplants. Patients were managed in different clinic settings, with transplant clinic or other clinical settings being most common (36.4%, 4/11, respectively). At centres where children were transferred to a low-clearance clinic (27.2%, 3/11), the threshold eGFR was <20mls/min/1.73m^2 at two, and <15mls/min/1.73m^2 for the other. Over half (54.6%, 6/11) of centres routinely adjusted immunosuppression for children with failing transplants: 36.4% (4/11) reduced the calcineurin

inhibitor (CNI), 9.1% (1/11) reduced the anti-proliferative agent, and 9.1% (1/11) reduced both. If a re-transplantable child required dialysis then 27.3% (3/11) of centres stated they would not alter immunosuppression. The majority, 72.7% (8/11), would stop the anti-proliferative, with 45.5% (5/11) also reducing the CNI, and 27.3% (3/11) leaving the CNI dose unchanged. No centres discontinued all immunosuppression at graft failure.

No centre performed transplant nephrectomy routinely; 36.4% (4/11) performed it for specific indications only.

Practice patterns did not differ (p-value >0.09) according to whether the centre was a transplanting centre (n=9) or not (n=2), nor with the volume of transplants the centre carried out.

This brief cross-sectional survey of UK practice patterns for failing paediatric kidney has identified heterogeneity in all aspects of care, as has been observed for adults[5]. Whilst some adult centres had a failing transplant protocol to standardise management, no paediatric centres reported having such a protocol. As described in adult care, paediatric centre practice varies with respect to immunosuppression management when transplants fail. No paediatric centres reported stopping immunosuppression, as is practiced at 6% of adult centres.

Our findings demonstrate equipoise within the transplant community regarding the best way to manage children with failing transplants: evidence-based guidance is needed. Research is needed to investigate whether the observed variation in UK-centre practice is associated with variable patient outcomes. With the information provided by this study, we are undertaking a linked analysis with UK Renal Registry data to allow these associations to be explored.

References

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Table 1. Responses to survey questions

Survey Question	Overall (n = 11)
Does your unit have a protocol for managing children with failing kidney transplants? n (%)	
No	11 (100.0)
Yes	0 (0.0)
Where are children with failing transplants managed? n (%)	
General low clearance clinic	3 (27.3)
General transplant clinic	4 (36.4)
Other	4 (36.4)
Do you modify immunosuppression prior to graft failure? n (%)	
No	1 (9.1)
Only if toxicity	4 (36.4)
Yes, reduce CNI	4 (36.4)
Yes, reduce anti-proliferative	1 (9.1)
Yes, reduce both CNI and anti-proliferative	1 (9.1)
Yes, stop all	0 (0.0)
Do you modify immunosuppression if a re-transplantable child receives dialysis prior to re-transplantation? n (%)	
No	3 (27.3)
Yes, stop anti-proliferative and continue usual dose CNI	3 (27.3)
Yes, stop anti-proliferative and reduce CNI	5 (45.5)
Yes, stop all	0 (0.0)
When is a transplant nephrectomy considered? n (%)	
Occasionally for specific indications	4 (36.4)
Rarely (<5% failed grafts in unit)	7 (63.6)
How is immunosuppression managed post-nephrectomy? n (%)	
Reduction	2 (18.2)
Complete withdrawal	4 (36.4)
Dependent on nephrectomy	2 (18.2)
Patients do not undergo nephrectomy	3 (27.3)