Kidney retransplantation from HLA-incompatible living donors: A single-center study of 3rd/4th transplants

James C.H. Barnes | Stephen J. Goodyear | Caitlin E.A. Imray | For Tai Lam | Habib S. Kashi | Lam Chin Tan | Robert Higgins | Christopher H.E. Imray

1Department of Transplant Surgery, University Hospitals Coventry and Warwickshire NHS Trust, Coventry, UK  
2Nuffield Department of Surgical Sciences, University of Oxford, Oxford, UK  
3Department of Vascular Surgery, Worcestershire Acute Hospitals NHS Trust, Worcester, UK  
4Sheffield Medical School, University of Sheffield, Sheffield, UK  
5Warwick Medical School, University of Warwick, Coventry, UK

Correspondence  
James C.H. Barnes, Oxford Transplant Centre, Churchill Hospital, Oxford, UK.  
Email: James.Barnes@nds.ox.ac.uk

Abstract

Background: The demand for kidney retransplantation following graft failure is rising. Repeat transplantation is often associated with poorer outcomes due to both immunological and surgical challenges. The aim of this study was to compare surgical and functional outcomes of kidney retransplantation in recipients that had previously had at least two kidney transplants with a focus on those with antibody incompatibility.

Methods: We analyzed 66 patients who underwent renal transplantation at a single center between 2003 and 2011. Consecutive patients receiving their 3rd or 4th kidney were case-matched with an equal number of 1st and 2nd transplants.

Results: Twenty-two 3rd and 4th kidney transplants were matched with 22 first and 22 seconds transplants. Operative times and length of stay were equivalent between the subgroups. Surgical complication rates were similar in all groups (22.7% in 1st and 2nd transplants, and 27.2% in 3rd/4th transplants). There was no significant difference in patient or graft survival over 5 years. Graft function was similar between transplant groups at 1, 3, and 5 years.

Conclusions: Third and fourth kidney transplants can be performed safely with similar outcomes to 1st and 2nd transplants. Kidney retransplantation from antibody-incompatible donors may be appropriate for highly sensitized patients.

Keywords: complications, graft survival, HLA-incompatible transplantation, kidney retransplantation

1 INTRODUCTION

Kidney transplantation is the “gold standard” treatment for end-stage renal disease offering both improved survival and quality of life when compared to dialysis. Significant improvements have been made in graft survival over the past 30 years with current 5 year graft survival rates exceeding 80% for deceased donors and 90% for living donors. These gains in graft survival have been largely attained through advances in immunosuppression and understanding of transplant immunobiology. Nevertheless, the half-life of primary renal transplants has been estimated at 8.8 and 11.9 years for deceased and living donors, respectively. The benefits in morbidity and mortality from transplantation are thought to extend to patients following retransplantation. As a consequence, rates of retransplantation are rising as more patients find themselves back on dialysis after graft failure.

Many units have entered an era where 3rd and 4th kidney transplants are increasingly common. These patients present unique challenges from both immunological and surgical perspectives. They are often highly sensitized from previous transplants and finding appropriate donor organs can be difficult. It is not therefore surprising that an increasing proportion of these organs are from antibody-incompatible living donors. Higher levels of immunosuppression are often required for these patients.
to maintain graft function, and this in turn can increase the risk of infection and malignancy.

Surgery on previously operated iliac fossae can present additional challenges. Significant fibrosis and scarring may hamper identification of correct tissue planes necessitating more complex vascular surgery and risking inadvertent collateral damage and complications. Anastomotic and overall operative times may be extended and have been associated with a detrimental impact upon morbidity.7–11

Data for surgical and graft outcomes in 3rd and 4th renal transplants are limited, with most published series suggesting a significantly greater incidence of surgical, immunological, and infectious complications.7,11–15 This frequently translates into significantly poorer graft survival when compared with 1st or 2nd kidney transplants. Nevertheless, 3rd and 4th kidney transplants still confer a significant survival benefit over remaining on dialysis.14,16 Studies that have focused on repeat kidney transplantation predominantly consist of deceased donor transplants with very few living donor or HLA-incompatible (HLAi) transplants; therefore, it is not known whether the reported outcomes can be applied to these patients.

In our center, living donor transplants represent a high proportion of the workload with a special interest in antibody-incompatible patients. Many of these patients have been referred from other transplant centers due to technical and immunological complexity.17 The aim of this study was to assess the surgical and functional outcomes of 3rd and 4th kidney transplants with a focus on living donor HLAi transplants that make up the majority of this group in our unit.

2 MATERIALS AND METHODS

All 3rd and 4th kidney transplants performed at University Hospitals Coventry and Warwickshire NHS Trust (UHCW) between 2003 and 2011 were retrospectively analyzed. Control groups of primary (n = 22) and secondary (n = 22) kidney transplant recipients were selected for comparison and matched hierarchically for antibody incompatibility, gender, age, time on dialysis, and the presence of diabetes.

Data relating to transplantation, hospital stay, and graft outcomes were collected from patient records. The parameters analyzed included recipient demographic characteristics, cause of renal disease, comorbidities, peri-operative data, and immunosuppressive therapy regimens. The occurrence, type, and management of allograft rejection were recorded. Estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease equation (MDRD).

Graft and patient survival were recorded at 1, 6, 12, 36, and 60 months.

2.1 Operative technique

The transplant team at UHCW practices synchronous laparoscopic donor nephrectomy and recipient retroperitoneal exposure in adjacent theaters for all living donor kidney transplantation, thereby minimizing ischemic times. Following nephrectomy, the retrieved kidney is immediately received by a member of the transplant team, perfused with cold histidine-tryptophan-ketoglutarate solution and packed in ice prior to workbench preparation and transfer into the adjoining theater for transplantation. Cold ischemic time was less than 2 hours for all cases of living donation.

Dual consultant operating is common practice for transplantation in this unit, with the surgeons drawn from the fields of both transplant and vascular surgery. Where possible, a vascular and transplant surgeon were present during cases of ipsilateral iliac fossa retransplantation, or where pre-operative imaging had suggested potential arterial complexity (eg severe calcification requiring endarterectomy). All patients referred for a 3rd or 4th transplant underwent duplex ultrasound and CT or MR angiography of the aorto-iliac vessels to guide the laterality of subsequent surgery. An extraperitoneal approach with vascular anastomoses to the external iliac vein and artery was performed in all cases.

2.2 HLA-incompatible transplants

HLA antibody-incompatible transplantation was defined as the presence of an HLA antibody at the time of transplantation, or immediately before pre-transplant conditioning. Antibodies were measured by microbead analysis, flow cytometric, and complement-dependent cytotoxic cellular cross-matching. An antibody was considered to be potentially clinically significant if present at a microbead level of MFI 500 or more, although most patients had levels well in excess of this. If a cellular cross-match was positive but antibodies were not detectable by microbead analysis, this was not considered to be a donor-specific HLA antibody. Plasmapheresis was performed to render the pre-transplant flow cytometric cross-match negative, although in many cases, this was not possible and many transplants proceeded in the face of a positive flow cytometric cross-match. Donor-specific antibody levels were measured daily during the early post-transplant period using microbeads. Immunosuppressive drug therapy evolved during the study so that most patients received standard immunosuppression, with escalation of therapy only "on demand" if acute antibody-mediated rejection was shown by biopsy (performed "on demand" for delayed function or rising creatinine), or if strongly suspected because of a rising creatinine level and rising donor-specific antibody levels. The primary antirejection therapy was antithymocyte globulin. More details of the procedures and outcomes are described elsewhere.17–20

2.3 Immunosuppression

The peri-operative immunosuppression regimens for antibody-incompatible transplants in our unit are tailored to individual patients and have been reported previously in the literature.18–20 Standard immunosuppression was with tacrolimus 0.15 mg/kg/day, azathioprine 1.5 mg/kg/day, or mycophenolate 1000 mg twice daily started on the day of transplant or at the start of pre-transplant plasmapheresis. Methylprednisolone 500 mg and basiliximab 20 mg were administered to all subjects intra-operatively.

2.4 Statistical analysis

All data were tabulated, and statistical analyses were performed using Graphpad Prism 7® (Graphpad, CA, USA) and SPSS Statistics 22
The normality of data was assessed with the D’Agostino and Pearson Omnibus normality test. Nonparametric unpaired data were analyzed using the Mann-Whitney U-test or Kruskal-Wallis analysis of variance, whilst categorical variables were analyzed using the chi-squared test or Fisher’s exact test. Parametric data were assessed with a Student’s t-test or one-way ANOVA. Survival data were evaluated by Kaplan-Meier and log-rank analysis. A P-value of less than .05 was considered significant.

### RESULTS

#### 3.1 Demographics

No significant differences were seen between the studied 3rd/4th kidney transplant group and the 1st and 2nd transplant groups matched for antibody incompatibility, age at the time of transplant, gender, BMI, smoking status, and prevalence of diabetes (Table 1). Within each group, there were 15 living donor HLAi and seven deceased donor kidney transplants.

#### 3.2 Renal replacement therapy

Individuals undergoing primary kidney transplantation at an equivalent age to those receiving their second, third, or fourth organs demonstrated a significantly greater age at 1st dialysis. No significant difference was shown between the 3rd/4th and secondary groups in this regard (Table 2).

Similarly, individuals receiving their first kidney transplant in their early 40s had experienced a significantly shorter term of dialysis than those in the second transplant and the 3rd/4th transplant groups (1-way ANOVA, $P < .001$). Post-testing demonstrated no statistical difference in duration of dialysis for the secondary and 3rd/4th transplant groups (Tukey’s post-test, $P = .285$).

#### 3.3 Operative data

Total operative time for patients undergoing transplantation was analyzed using 1-way ANOVA and found to be equivalent for the primary, secondary, and 3rd/4th transplant cohorts ($F = 1.98, P = .149$; Figure 1). No significant difference could be demonstrated for recipient anastomotic time between 3rd/4th transplants and the control primary and secondary groups ($F = 1.65, P = .202$). Within the 3rd/4th transplants group, there was no significant difference in operative times between those patients requiring a concurrent graft nephrectomy and those that did not ($220.83$ minutes SE $16.01$ vs $272.5$ minutes SE $38.12$; $t = 1.485, P = .157$).
3.4 | Peri-operative complications

Total peri-operative complication rates observed for primary, secondary, and 3rd/4th transplants were 22.7%, 22.7%, and 27.2%, respectively (P = 1.0 between all cohorts by Fisher’s exact test). In total, five patients required a return to theater for complications (7.6%). Specific complications and their treatment are described in Table 3.

3.5 | Graft survival

Five-year allograft survival is seen in 83.1% of primary transplant cases, 85.6% of secondary, and 95% of 3rd/4th transplant cases (P = .339; Figure 2). There were two graft nephrectomies in the primary transplant group.

Five-year rejection-free survival for recipients could be seen in 59.6% of primary transplants, 43.3% for secondary, and 67.0% of 3rd/4th kidney transplants (P = .208). Cellular-mediated rejection was mainly seen in the 3rd/4th transplants (71%), whereas in the 1st/2nd transplants, antibody-mediated and vascular rejection predominated (65%) (Figure 3).

3.6 | Patient survival

Overall transplant recipient 5-year survival was 82.5% for primary, 100% for secondary, and 95% for 3rd/4th kidney transplants (P = .091; Figure 4). Of the five patient deaths, four died with a functioning renal allograft. One patient died 32 months after graft failure and return to hemodialysis.
3.7 | Functional outcome

Estimated glomerular filtration rate (eGFR) derived using the MDRD equation was considered representative of kidney transplant function. Table 4 displays mean eGFR between 1 month and 5 years postoperatively for patients receiving either a 1st, 2nd, or 3rd/4th kidney transplant. There was no significant difference between the 3rd/4th group and the 1st or 2nd at any time point. This was also confirmed by further analysis of 3rd/4th transplants compared with a larger group consisting of both 1st and 2nd transplants combined.

3.8 | 3rd and 4th kidney transplants: living donor HLAi vs deceased donor antibody compatible

Further analysis of the 3rd and 4th allograft group was performed to identify differences between the living donor HLAi and deceased donor HLA-compatible transplants. Five-year allograft survival was seen in 92.9% of the living donor HLAi transplants and 100% of the deceased donor transplants within the 3rd and 4th group (1 graft loss in the HLAi group).

There was no significant difference observed in the eGFR at any time point between the HLAi and deceased donor allografts of the 3rd/4th retransplant group (Table 5).

TABLE 4  Post-operative eGFR values for 1st, 2nd, and 3rd/4th kidney transplants

| Month | 1st Transplants eGFR | 2nd Transplants eGFR | 3rd/4th Transplants eGFR | P value 3rd/4th vs 1st | P value 3rd/4th vs 2nd | P value 3rd/4th vs 1st/2nd |
|-------|-----------------------|-----------------------|--------------------------|------------------------|------------------------|--------------------------|
| 1     | 52.3 (3.9)            | 50.8 (4.2)            | 56.0 (4.5)               | .559                   | .406                   | .381                     |
| 3     | 54.7 (3.5)            | 49.3 (3.8)            | 52.1 (4.6)               | .660                   | .643                   | .935                     |
| 6     | 51.9 (4.3)            | 48.5 (4.4)            | 50.7 (4.3)               | .840                   | .729                   | .670                     |
| 12    | 56.0 (5.3)            | 47.8 (3.6)            | 47.6 (4.4)               | .226                   | .970                   | .475                     |
| 36    | 58.8 (5.8)            | 48.7 (4.9)            | 41.0 (3.7)               | .011                   | .211                   | .315                     |
| 60    | 47.7 (3.6)            | 47.9 (6.6)            | 42.5 (5.0)               | .513                   | .512                   | .042                     |

GFR values are mean (standard error).

4 | DISCUSSION

Despite significant improvements in renal allograft survival, many patients will experience graft loss and return to dialysis in the long term. Repeat transplantation improves patient survival and quality of life, even when extended to three or more transplants. However, most published series of these patients report worse graft outcomes and higher complication rates. In this study, we have focused on living donor antibody-incompatible retransplantation—which represents a cohort with the most complex immunological and surgical challenges. Nevertheless, our results compare favorably with published series of both 3rd/4th transplants and also 1st/2nd antibody-incompatible transplants. This is timely given the increasing evidence that supports the use of living donor antibody-incompatible kidneys as primary or secondary transplants rather than waiting for a deceased donor kidney. However, only very small numbers have been reported as 3rd or more retransplants, and the 15 living donor HLAi 3rd and 4th transplants described in this study are currently the largest series reported with specific graft outcomes.

Repeat surgery to the iliac fossa is technically challenging. This is demonstrated in several studies that have shown increased operative times, blood loss, and vascular and ureteric complications. In the biggest series to date, Ooms et al describe 99 patients that received ipsilateral iliac fossa retransplantation. Mean operative time was significantly increased from 180 to 241 minutes, and median blood loss was increased from 300 to 500 mLs. Vascular complications were increased from 2% to 8% but urological and other surgical

FIGURE 4  Patient survival for 1st, 2nd, and 3rd/4th kidney transplant cohorts (P = .091, log-rank test)
complications were not significantly increased. A study by Kienzl-Wagner et al.\(^7\) analyzed 56 third or more kidney transplants and also reported higher rates of surgical complications, although blood loss and anastomotic times were not specifically described.

In this study, there was no significant difference in operative or anastomotic times between those patients having repeat iliac fossa surgery for 3rd or 4th transplants and those having 1st or 2nd transplants. This is surprising given that 36% of patients required concurrent transplant nephrectomy prior to implantation of the new organ. Although not statistically significant, the mean operative time within the 3rd/4th group was actually longer for those that did not have a concurrent nephrectomy than those that did. Whilst this may be an artifact of the small numbers involved, it may also reflect the amount of scarring and fibrosis involved. Most patients that did not require a concurrent nephrectomy had previously had a graft nephrectomy and therefore had undergone two previous operations on that iliac fossa increasing the difficulty of the dissection on the 3rd entry to that iliac fossa to transplant the 3rd/4th kidney. In contrast, those that did have concurrent nephrectomy had only had a single procedure for the original transplant in that iliac fossa; the presence of the existing graft can even aid in the identification of landmarks, and subcapsular dissection to remove this kidney can guide the surgeon through an otherwise hostile surgical field. All transplants were performed via the extraperitoneal approach which can be particularly challenging due to extensive scarring from previous surgery. Other approaches such as transperitoneal and orthotopic transplantation have been described to avoid this problem although we have not found it necessary to use these in our practice so far.\(^8,10,23\) The use of standardized pre-operative vascular imaging may have contributed to this—in many cases, severe iliac disease was identified that became important in the subsequent planning of operative strategy. Our rate of surgical complications was comparable to other studies with 22.7% in both 1st and 2nd transplants, and 27.2% in the 3rd/4th transplant group. These data suggest that the technical problems with retransplantation can be managed, and therefore, the subsequent issues influencing graft outcomes are more down to patient comorbidity and immunological factors.

Graft survival for 3rd/4th transplants in this study was 95% at 5 years compared with 83.1% in primary transplants and 85.6% for secondary transplants (\(P = .35\)). This compares favorably with other studies which report 5-year graft survival in three or more transplants of 42.9%-78.1%, although many of these have a high number of deceased rather than living donors.\(^7,11-13,15,23,26-28\) As with other studies, the majority of graft loss was caused by rejection (5 of the 6), with one caused by early renal artery thrombosis; 50% of these graft losses required graft nephrectomy. Rejection-free survival was much lower with 59.6%/43.3%/67% of 1st/2nd/3rd and 4th transplants remaining rejection-free at 5 years (no statistical difference between groups). Rescue therapy is decided on a case-by-case basis for these complex patients, and this is reflected in the heterogeneity of treatment given (steroids 19×, ATG 8×, OKT3 9×; Table 6).

All the current published series of three or more kidney transplants are limited by retrospective analysis of small numbers over the last 10-20 years. This study suffers the same limitations due to small sample size, and there is a significant risk of type 2 error. To reduce this bias and allow for the varying types of immunosuppression used over the study period, we have tried to match our 3rd/4th transplant group with appropriate controls in an attempt to delineate any factors that may be associated with worse outcomes. However, we acknowledge that case-control introduces its own biases and the small sample size has limited our ability to perform meaningful subgroup analyses (such as donor variables). Retrospective collection of data always introduces bias to studies like this. For example, blood loss was not routinely recorded, and whilst we can use blood transfusion as a surrogate for significant blood loss, it prevents useful comparison with other studies that have reported actual volumes lost. Our antibody incompatible cohort includes patients referred from across the UK and as such many patients return to follow-up at their base hospital soon after transplantation. This makes the long-term collection of outcome data

### Table 6

| Cohort          | Rejection type | Antirejection therapy |
|-----------------|----------------|-----------------------|
| 1st Transplants | Cellular (Ia)  | Steroids              |
|                 | Cellular (Ia)  | ATG                   |
| Antibody        | Steroids, OKT3 |                       |
| Antibody        | Nephrectomy    |                       |
| Antibody        | Steroids, OKT3 |                       |
| PP              | ATG            |                       |
| Antibody        | Steroids, ATG  |                       |
| Vascular        | Steroids, OKT3 |                       |

| 2nd Transplants | Cellular (Ia) | Steroids              |
|-----------------|---------------|-----------------------|
| Antibody        | Steroids, PP  |                       |
| Vascular        | OKT3          |                       |
| Antibody/Vascular | Steroids, OKT3 |                       |
| Cellular        | ATG           |                       |
| Vascular        | Steroids, PP  |                       |
| Cellular (Ia)   | Steroids, OKT3|                       |
| Vascular        | Steroids, OKT3|                       |
| Vascular        | ATG           |                       |
| Cellular (III)  | Steroids      |                       |
| Antibody        | Steroids      |                       |

| 3rd/4th Transplants | Antibody | Steroids              |
|---------------------|----------|-----------------------|
| Cellular (Ia)       | Steroids |                       |
| Antibody            | ATG      |                       |
| Cellular (Ia)       | Steroids, ATG |               |
| Cellular            | Steroids |                       |

ATG, antithymocyte globulin; Steroids, methylprednisolone/prednisolone; OKT3, muromonab-CD3; PP, plasmapheresis.
challenging, and the data are therefore biased by the early censoring of some patients (seen in the Kaplan-Meier analysis). We had not expected equivocal outcomes between transplant groups, and therefore, this may be a result of the biases described or actually an effect that is restricted to the living donor antibody-incompatible transplants.

In conclusion, our data suggest that acceptable outcomes can be achieved in living donor antibody-incompatible repeat kidney transplantation. Indeed, graft and patient survival in this study are similar to primary antibody-incompatible transplants and better than those reported for repeat transplants from deceased donors. Highly sensitized patients waiting for a 3rd or 4th kidney often face a prolonged wait for a deceased donor and therefore should also be considered for repeat transplantation from antibody-incompatible living donors.

CONFLICT OF INTEREST
None.

AUTHORS’ CONTRIBUTIONS
J.B., F.L., H.K., L.T., R.H., and C.H.E.I.: Participated in research design; J.B., C.E.A.I., and R.H.: Collected the data; J.B., S.G., R.H., and C.H.E.I.: Drafted the article; S.G., F.L., S.K., L.T., R.H., and C.H.E.I.: Participated in research design; J.B., C.E.A.I., and R.H.: Collected the data; J.B., S.G., R.H., J.B., F.L., S.K., L.T., R.H., and C.H.E.I.: Performed critical revision.

ACKNOWLEDGEMENTS
The Coventry and Oxford Transplant Network (COxTNet).

ORCID
J.C.H. Barnes [http://orcid.org/0000-0002-9351-6377]

REFERENCES
1. Wolfe RA, Ashby VB, Milford EL, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. N Engl J Med. 1999;341:1725-1730.
2. Bradbury L. Annual Report on Kidney Transplantation. 2015; http://www.odt.nhs.uk/pdf/organ_specific_report_kidney_2015.pdf. Accessed January 10, 2015.
3. Meier-Kriesche HU, Schold JD, Kaplan B. Long-term renal allograft survival: have we made significant progress or is it time to rethink our analytic and therapeutic strategies? Am J Transplant. 2004;4:1289-1295.
4. Lamb KE, Lodhi S, Meier-Kriesche HU. Long-term renal allograft survival in the United States: a critical reappraisal. Am J Transplant. 2011;11:450-462.
5. Ojo A, Wolfe RA, Agodoa LY, et al. Prognosis after primary renal transplant failure and the beneficial effects of repeat transplantation: multivariate analyses from the United States Renal Data System. Transplantation. 1998;66:1651-1659.
6. Rao PS, Schaubel DE, Wei G, Fenton SS. Evaluating the survival benefit of kidney retransplantation. Transplantation. 2006;82:669-674.
7. Kienzl-Wagner K, Mark W, Maglione M, et al. Single-center experience with third and fourth kidney transplants. Transpl Int. 2011;24:780-786.
8. Halawa A. The third and fourth renal transplant: technically challenging, but still a valid option. Ann Transplant. 2012;17:125-132.
9. Mazzucchi E, Danilovic A, Antonopoulos JM, et al. Surgical aspects of third and subsequent renal transplants performed by the extraperitoneal access. Transplantation. 2006;81:840-844.
10. Nourbala MH, Ghaheri H, Kardavani B. Our experience with third renal transplantation: results, surgical techniques and complications. Int J Urol. 2007;14:1057-1059. discussion 1059.
11. Ooms LS, Roednat JI, Dor FJ, et al. Kidney retransplantation in the ipsilateral iliac fossa: a surgical challenge. Am J Transplant. 2015;15:2947-2954.
12. Horovitz D, Caumartin Y, Warren J, et al. Outcome of third renal allograft retransplants versus primary transplants from paired donors. Transplantation. 2009;87:1214-1220.
13. Izquierdo L, Peri L, Piqueras M, et al. Third and fourth kidney transplant: still a reasonable option. Transplant Proc. 2010;42:2498-2502.
14. Redfield RR, Gupta M, Rodriguez E, Wood A, Abt PL, Levine MH. Graft and patient survival outcomes of a third kidney transplant. Transplantation. 2015;99:416-423.
15. Ahmed K, Ahmad N, Khan MS, et al. Influence of number of retransplants on renal graft outcome. Transplant Proc. 2008;40:1349-1352.
16. Reboux AH, Kamar N, Fort M, et al. A third renal transplantation: is it relevant and is it worth it? Transplant Proc. 2005;37:4199-4202.
17. Higgins R, Lowe D, Hathaway M, et al. Human leukocyte antigen antibody-incompatible renal transplantation: excellent medium-term outcomes with negative cytotoxic crossmatch. Transplantation. 2011;92:900-906.
18. Higgins R, Hathaway M, Lowe D, et al. Blood levels of donor-specific human leukocyte antigen antibodies after renal transplantation: resolution of rejection in the presence of circulating donor-specific antibody. Transplantation. 2007;84:876-884.
19. Higgins R, Lowe D, Hathaway M, et al. Rises and falls in donor-specific and third-party HLA antibody levels after antibody incompatible transplantation. Transplantation. 2009;87:882-888.
20. Higgins R, Lowe D, Hathaway M, et al. Double filtration plasmapheresis in antibody-incompatible kidney transplantation. Ther Apher Dial. 2010;14:392-399.
21. Higgins RM, Daga S, Mitchell DA. Antibody-incompatible kidney transplantation in 2015 and beyond. Nephrol Dial Transplant. 2015;30:1972-1978.
22. Orandi BJ, Luo X, Massie AB, et al. Survival benefit with kidney transplants from HLA-incompatible living donors: A single-center study of 3rd/4th transplants. N Engl J Med. 2016;374:940-950.
23. Blanco M, Medina J, Gonzalez E, et al. Kidney transplantation: results, surgical techniques and complications on outcomes of third and subsequent kidney transplants. Transplantation. 2007;83:385-391.
24. Loupy A, Angelicheau D, Timsit MO, et al. Impact of surgical procedures and complications on outcomes of third and subsequent kidney transplants. Transplantation. 2007;83:385-391.
25. Musquera M, Peri LL, Alvarez-Vijande R, Oppenheimer F, Gil-Vernet JM, Alcaraz A. Orthotopic kidney transplantation: an alternative surgical technique in selected patients. Eur Urol. 2010;58:927-933.
26. Kousoulas L, Vondran FW, Srycza P, Klemplnauer J, Schrem H, Lehner F. Risk-adjusted analysis of relevant outcome drivers for patients after more than two kidney transplants. J Transplant. 2015;2015:712049.
27. Loupy A, Angelicheau D, Suberbielle C, et al. Long-term outcome of third kidney transplants. Nephrol Dial Transplant. 2007;22:2693-2700.
28. Ott U, Busch M, Steiner T, Schubert J, Wolf G. Renal retransplantation: a retrospective monocentric study. Transplant Proc. 2008;40:1345-1348.

How to cite this article: Barnes JCH, Goodyear SJ, Imray CEA, et al. Kidney retransplantation from HLA-incompatible living donors: A single-center study of 3rd/4th transplants. Clin Transplant. 2017;31:e13104. https://doi.org/10.1111/ctr.13104