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Original Article

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ORIGINAL ARTICLE

Kidney re-transplantation in the ipsilateral iliac fossa: a surgeon's perspective on perioperative outcome

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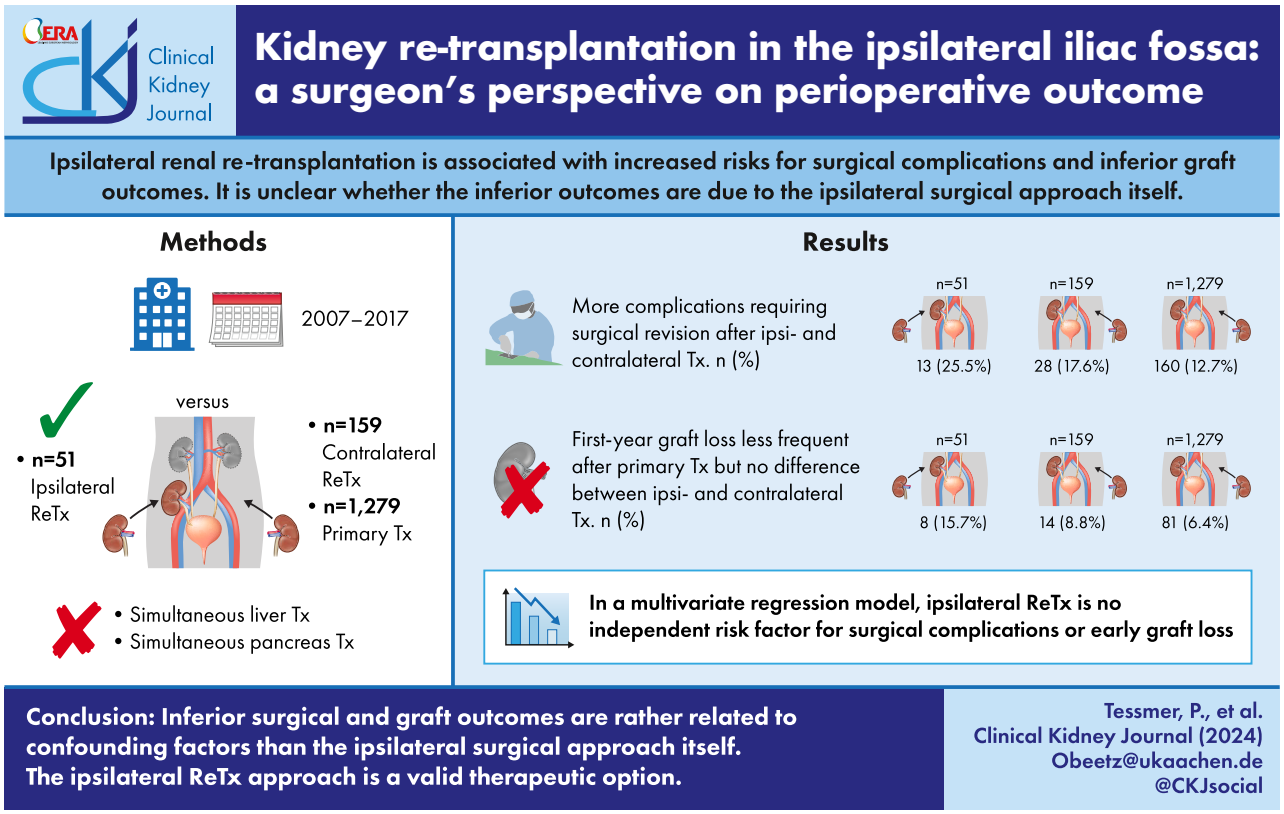
ABSTRACT

Background. Compared with primary transplantation, ipsilateral renal re-transplantation is associated with an increased risk of surgical complications and inferior graft outcomes. This study investigates whether an ipsilateral re-transplantation approach *per se* is an independent risk factor for surgical complications and early graft loss.
Methods. In this retrospective, single-centre analysis, surgical complications and early graft outcomes of ipsilateral kidney re-transplantations from January 2007 to December 2017 were compared with primary transplantations and contralateral re-transplantations. Univariate and multivariate binary logistic regression analyses were performed to identify risk factors for surgical complications requiring surgical revision and graft loss within the first year after transplantation.
Results. Of the 1489 kidney transplantations, 51 were ipsilateral, 159 were contralateral re-transplantations and 1279 were primary transplantations. Baseline characteristics did not differ between the ipsilateral and contralateral re-transplant recipients except for current and highest panel reactive antibody levels. Major complications requiring surgical revision were significantly more frequent in ipsilateral re-transplantations ($P = .010$) than in primary transplantations but did not differ between ipsilateral and contralateral re-transplantations ($P = .217$). Graft loss within the first year after transplant was 15.7% in the ipsilateral versus 8.8% in the contralateral re-transplant group ($P = .163$) versus 6.4% in the primary transplantation group ($P = .009$). In a multivariate regression model, ipsilateral re-transplantation was not identified as an independent risk factor for complications requiring surgical revision or first-year graft loss.
Conclusions. Ipsilateral renal re-transplantation is not a risk factor for inferior outcomes. Graft implantation into a pre-transplanted iliac fossa is a feasible and valid therapeutic option.

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GRAPHICAL ABSTRACT



Keywords: graft failure, ipsilateral renal re-transplantation, iterative kidney transplantation, kidney re-transplantation, surgical complications in kidney re-transplantation

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KEY LEARNING POINTS

What was known:

- Ipsilateral renal re-transplantation is associated with an increased risk for surgical complications such as venous vascular thrombosis and perioperative haemorrhage.
- In ipsilateral kidney re-transplantation, inferior graft and patient outcomes are reported compared with primary transplantation. Whether these inferior outcomes are due to the ipsilateral surgical approach or confounding factors such as immunological events and patient comorbidities is unclear.
- Most studies analysing graft outcomes after renal re-transplantation do not investigate whether ipsilateral re-transplantation is an independent risk factor for surgical complications and early graft loss.

This study adds:

- Ipsilateral renal re-transplantation is not an independent risk factor for major complications requiring surgical revision or early graft loss. The increased risks for surgical complications and early graft loss are rather related to higher immunization and deceased donor transplantations.
- Postoperative haemorrhage requiring surgical revision as the most frequent complication is more common after ipsilateral and contralateral re-transplantation than after primary transplantation and is possibly associated with the adverse effects of increased immunosuppressive therapy.
- Compared with primary and contralateral transplantations, we did not find an increased risk of vascular complications requiring surgical revision in our cohort of ipsilateral re-transplanted patients, providing further evidence that ipsilateral re-transplantations are feasible.

Potential impact:

- Renal re-transplantation to the ipsilateral iliac fossa is a valid therapeutic option. It should therefore not be withheld from patients after graft failure, even if the outcome is inferior to primary transplantation.
- In the future, the number of kidney transplantations and recipients of a third, fourth or fifth graft will increase; thus, the ipsilateral re-transplantation approach, its technical feasibility, and appropriate outcomes will gain in importance.

INTRODUCTION

The number of kidney transplants (KTx) is increasing, with a new annual record of 25 498 KTx performed in the USA in 2022 [1]. In addition, the use of marginal organs from extended criteria donors is expanding, potentially compromising graft survival and exacerbating organ shortage [2, 3]. Consequently, the number of patients with chronic graft failure and the need for re-transplantation will increase. In 2022, 265 patients were listed for kidney re-transplantation in Germany, representing approximately 11% of all KTx registrations [4], with comparable rates in the USA [1]. In some countries, up to 25% of waiting list patients expect a re-transplant [5], making this issue highly relevant. There are conflicting reports in the literature on graft and patient survival after re-transplantation. On one hand, the outcome of re-transplanted grafts is reported to be equivalent to primary transplantation [6, 7]. On the other hand, most studies report an inferior graft and patient survival after re-transplantation [8–10]. From a surgical point of view, re-transplantation into the ipsilateral iliac fossa is associated with an increased risk for surgical complications such as venous thrombosis and perioperative blood loss [5, 11]. In addition, immunological risks are also increased after renal re-transplantation [6, 12, 13].

However, it is well known that morbidity and mortality after graft failure and resumption of dialysis are significantly increased compared with successfully re-transplanted patients [14–16] and transplant-naïve patients on dialysis [17].

In summary, healthcare professionals face an 'ethical dilemma' [18]: accepting inferior patient outcomes on dialysis upon primary graft failure or risking potentially increased morbidity and inferior graft survival after re-transplantation. The latter aspect is aggravated by the chronic organ shortage and the need for responsible allocation of scarce resources.

Most studies that analyse early surgical outcomes in renal re-transplantation generally focus on the incidence of perioperative complications. This study aims to clarify whether ipsilateral renal re-transplantation, also termed 'surgical re-transplantation' as opposed to a contralateral re-transplantation, is an independent risk factor for perioperative surgical complications and early graft loss.

MATERIALS AND METHODS

Study design

This retrospective, single-centre analysis included all kidney re-transplantations into a pre-transplanted iliac fossa performed at our institution between January 2007 and December 2017. Recipients were included regardless of the type of donation (deceased or living). Patients with simultaneous liver or pancreas transplantation were excluded from the analysis. Data from ipsilateral re-transplant patients were compared with those from primary transplantations and re-transplantations to the contralateral iliac fossa.

Recipients' baseline characteristics analysed were age, sex, body mass index (BMI), number of previous KTx, donor type, length of hospital stay, time on dialysis and graft survival. Operation and transplantation data included operation and cold ischemia time, number of arterial and venous anastomoses created, use of a left/right kidney and site of graft implantation. Surgical and graft outcomes were assessed by perioperative complications, the need for blood transfusions, the initial non-function rate, estimated glomerular filtration rate (eGFR) at discharge, and 1-, 3- and 5-year graft survival. The immunological risk was quantified using the recipient's highest and current panel reactive antibody (PRA) levels, number of HLA mismatches and ABO-incompatible transplantations.

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Definition of variables and complications

The eGFR was estimated using the Chronic Kidney Disease Epidemiology Collaboration formula [19]. Initial non-function was defined as the permanent need for dialysis after transplantation. Surgical revision was defined as any surgical procedure under general anaesthesia for transplant-related complications during the first 365 days after KTx. Arterial and venous vascular complications were categorized as early (<4 weeks) versus late depending on the day of the transplant.

Surgical procedure

Arterial and venous anastomoses were preferably created to the common or external iliac artery and the inferior vena cava or the common iliac vein, respectively. Ureteroneocystostomy, according to Lich–Gregoir [20, 21], was performed for ureteral reconstruction, with additional temporary ureteral stenting of the graft ureter in most cases. For renal re-transplantation, the preferred approach was heterotopic extraperitoneal graft implantation into the native iliac fossa via an arcuate incision in the lower abdomen. At our transplant centre, we consider transplant nephrectomy as the standard of care after allograft failure. Allograft nephrectomy has the advantages of a decreased risk of further sensitization and the possibility of weaning the immunosuppressive therapy. In our approach, a significant residual diuresis (>500 mL/day) is considered a relative contraindication to performing a graft nephrectomy.

Immunosuppressive regimen

The immunosuppressive regimen consisted of a standard triple therapy of mycophenolate acid, calcineurin inhibitor and prednisolone after immunosuppressive induction therapy with interleukin-2 receptor antagonists. In case of sensitization/immunization or biopsy-proven rejection, immunosuppressive therapy was extended by methylprednisolone pulse therapy, plasmapheresis, intravenous immunoglobulin therapy and anti-thymocyte globulin administration, depending on the individual case.

Statistical analysis

Data sets were merged and analysed with Microsoft Excel (Microsoft® Excel® LTSC MSO 16.0 Version 2108, Microsoft Corporation). Statistical analyses were performed with SPSS statistical software (SPSS® Statistics 28.0.1.0, IBM® Corporation). Statistical significance was set at a two-sided *P*-value <.050. Continuous variables were tested for normal distribution using the Kolmogorov–Smirnov test. In the case of normal distribution, Student's *t*-tests were performed. Otherwise, Mann–Whitney U tests were applied. A statistical comparison of categorical variables between groups was performed using the Chi-square test. Univariate and multivariate binary logistic regression analyses were applied to identify independent risk factors of nominal study endpoints. In the multivariate regression model, stepwise forward selection was performed by purposeful selection of variables with a *P*-value <.200 in univariate regression analysis and with missing values of <10%. Graft survival was estimated using the Kaplan–Meier method, and statistical analysis was performed using a log-rank test.

Ethical approval

By the general policy of our institution, patients or their legal guardians provided informed consent that their data may be used for scientific purposes. The ethical committee at Hannover Medical School stated that no further approval for retrospective data collection is needed. Before analysis, patient data and records were anonymized and de-identified.

RESULTS

Recipients' characteristics

Of the 1489 kidney transplantations, 51 (3.4%) grafts were re-transplanted to the ipsilateral and 159 (10.7%) to the contralateral iliac fossa, respectively. The remaining 1279 (85.9%) cases were primary transplantations. Recipients' baseline characteristics, including age, BMI, sex, donor type and time on dialysis, were not different between the ipsilateral and contralateral re-transplant recipients. However, the current and highest PRA levels were higher in the ipsilateral re-transplant recipients compared with recipients of a primary ($P < .001$ for both variables) or a contralateral ($P = .02$ and $P = .04$) graft. The rates of ABO-incompatible transplantations and full-house matches were not different between the three groups. The median follow-up was 73.2 (0.03–168.6) months.

Out of the 51 ipsilateral re-transplantations, 9 recipients (17.6%) received their second (due to non-accessible contralateral iliac fossa), 34 their third (66.7%), and 8 their fourth transplant (15.7%), respectively. In third and fourth KTx recipients, a graft was implanted at least once in both iliac fossae. In the nine second graft recipients, the reasons for ipsilateral allograft placement were various: there were three cases of superior ipsilateral vascular status, one case with a history of sigmoid diverticulitis and two-step surgery on the contralateral left side, one case in need of ipsilateral native ureteropyelostomy, and three cases after simultaneous pancreas-kidney transplantation. In one case, the cause of the ipsilateral approach could not be determined retrospectively. Forty-six patients (90.2%) in our cohort of ipsilateral re-transplanted patients underwent allograft nephrectomy, almost three-quarters before ipsilateral re-transplantation (37; 72.5%). Simultaneous nephrectomy of a pre-existing graft and ipsilateral graft placement was performed in 11 patients (21.6%). Placement of the new graft next to the old graft without simultaneous graft nephrectomy was performed in seven cases (13.2%).

For complete data on all recipients' characteristics, see Table 1.

Operation and transplantation data

With a median of 137 (62–385) minutes, operation time was longer for the ipsilateral re-transplantations compared with contralateral re-transplantations [117 (52–320) min] and primary transplantations [109 (48–423) min] ($P = .002$ and $P < .001$). A transperitoneal approach ($n = 4$, 7.8%) was performed significantly more often in ipsilateral re-transplantations than in primary transplantations ($n = 16$, 1.3%; $P < .001$) and contralateral ($n = 3$, 1.9%; $P = .04$) re-transplantations. In contralateral re-transplantations, grafts were implanted in the left iliac fossa ($n = 90$, 57.3%) significantly more often than in ipsilateral re-transplantations ($n = 12$, 23.5%; $P < .001$).

One arterial anastomosis was created in most cases of ipsilateral renal re-transplantation ($n = 44$, 88.0%). Two or more

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Table 1: Baseline characteristics.

Characteristic	Re-Tx ipsi ($n = 51$)	Re-Tx contra ($n = 159$)	P-value*	Primary Tx ($n = 1.279$)	P-value**
Age (years), median (range)	47 (21–69)	48 (18–74)	.616	54 (18–77)	<.001
Sex, *n* (%)					
Male	34 (66.7)	98 (61.6)	.518	791 (61.8)	.487
Female	17 (33.3)	61 (38.4)		488 (38.2)	
BMI (kg/m^2), median (range)	23.2 (18.6–36.9)	23.9 (15.4–36.0)	.289	25.5 (15.9–43.7)	.010
Number of previous KTx, *n* (%)					
1	9 (17.6)	159 (100)	<.001		
2	34 (66.7)	0 (0)	<.001		
3	8 (15.7)	0 (0)	<.001		
Current PRA (%), mean (range)	46.4 (0–100)	33.2 (0–100)	.021	3.9 (0–100)	<.001
Highest PRA, (%) mean (range)	61.7 (0–100)	49.0 (0–100)	.042	7.5 (0–100)	<.001
HLA mismatches, mean (range)					
Locus A	0.65 (0–2)	0.79 (0–2)	.664	0.61 (0–2)	.137
Locus B	1.02 (0–2)	1.03 (0–2)	.500	0.94 (0–2)	.934
Locus DR	0.63 (0–2)	0.73 (0–2)	.924	0.62 (0–2)	.449
Full-house match, *n* (%)	8 (15.7)	24 (15.1)	.918	195 (15.2)	.934
ABO-incompatible Tx, *n* (%)	4 (7.8)	8 (5.0)	.452	79 (6.2)	.629
Donor type, *n* (%)					
Living	8 (15.7)	26 (16.4)	.911	371 (29.0)	.039
Deceased	43 (84.3)	133 (83.6)		908 (71.0)	
Time on dialysis (months), median (range)	46.4 (0.1–175.8)	62.5 (0.1–223.9)	.684	67.5 (0.2–225.4)	.208
Follow-up (months), median (range)	58.6 (0.03–156.3)	72.3 (0.03–162.9)	.90	74.2 (0.03–168.6)	.009
Previous abdominal surgery, *n* (%)	51 (100)	159 (100)		619 (48.9)	<.001
Residual diuresis (mL), median (range)	0 (0–2.000)	0 (0–3.500)	.092	200 (0–3.800)	<.001

*P-value = Re-Tx ipsilateral vs Re-Tx contralateral as control group.
**P-value = Re-Tx ipsilateral vs primary Tx as control group.
Re-Tx, re-transplantation; ipsi, ipsilateral; contra, contralateral.

arterial anastomoses were created in six cases (12%). Except for two cases with allogenic or alloplastic arterial reconstruction ($n = 2$, 4.1%), the arterial anastomosis was created to the common ($n = 31$, 63.3%) and external iliac artery ($n = 15$, 30.6%) or the aorta ($n = 1$, 2.0%), respectively. In all but one case (with two venous anastomoses; 2.0%), a single venous anastomosis was created (98.0%). Venous anastomoses were made to the inferior vena cava ($n = 14$, 28.6%) or the common ($n = 16$, 32.7%) and external iliac vein ($n = 19$, 38.8%), respectively. Ureteral reconstruction was mainly performed by Lich–Gregoir ureteroneocystostomy ($n = 47$, 92.2%), less frequently by ureteropyelostomy ($n = 3$, 5.9%) or by Boari-plasty ($n = 1$, 2.0%). The number of arterial ($P = .296$), venous ($P = .950$) and ureteral ($P = .160$) anastomoses did not differ between the ipsilateral and the contralateral re-transplant recipients. All operative data are shown in Table 2.

Surgical outcome

Major complications requiring surgical revision were more frequent in recipients of an ipsilateral re-transplant ($n = 13$, 25.5%; $P = .010$) than in primary transplant recipients ($n = 160$, 12.7%) but did not differ between ipsilateral and contralateral re-transplant recipients ($n = 28$, 17.6%; $P = .217$). The most common reason for re-exploration was postoperative haemorrhage in the ipsilateral ($n = 5$, 9.8%) and the contralateral re-transplant group ($n = 13$, 8.2%; $P = .727$). Intraoperative administration of packed red blood cells (PRBC) was necessary in 2 cases of ipsilateral re-transplantations (3.9%) and 4 (2.5%; $P = .600$) and 32 (2.5%; $P = .535$) cases of contralateral re-transplantations and primary transplantations, respectively.

Arterial vascular complications occurred in three ipsilateral re-transplantations (5.8%), each in the early postoperative course (<4 weeks). In one case undergoing renal transplantation with a total of four arterial anastomoses, intraoperative Doppler sonography showed an arterial flow signal, although with an unusually high resistance index. The graft was repositioned while leaving the anastomoses itself intact, and a vicryl mesh was implanted as a fascia substitute to ensure sufficient space for the graft. A few hours postoperatively, surgical revision was performed for intraoperative perfusion assessment. Macroscopically and by Doppler sonography, the hilar vessels were not impaired, and the graft was perfused sufficiently. Concerning decreasing diuresis in the further course, a graft biopsy showed an antibody-mediated rejection with microperfusion disorders. At discharge, the graft showed sufficient diuresis but no relevant creatinine clearance. In two cases, there was a dissection of the common iliac artery of the recipient, each with the need for vascular reconstruction using allogenic material. After a complicated postoperative course in one of these patients (including the occurrence of postoperative lymphocele formation requiring surgical revision and pneumonia), hemodialysis was necessary, and the graft function did not recover. In the other case, the graft had primary function in the postoperative course.

In contralateral re-transplantations, there were four early (100%) arterial vascular complications (2.5%; $P = .244$), three of which were arterial thromboses. One arterial anastomotic haemorrhage (common iliac artery) with the need for surgical revision was the fourth case.

After primary transplantation, 42 (3.3%; $P = .326$) arterial complications occurred ($n = 34$; 80.9% within <4 weeks after KTx). Of these, there were 17 arterial thromboses, 9 arterial stenoses, 7 cases of haemorrhage, 1 arteriovenous (AV) fistula,

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Table 2: Operative and transplantation data.

Parameter	Re-Tx ipsi ($n = 51$)	Re-Tx contra ($n = 159$)	P-value*	Primary Tx ($n = 1.279$)	P-value**
Operation time (min), median (range)	137 (62–385)	117 (52–320)	.002	109 (48–423)	<.001
Cold ischemia time (min), median (range)	846 (139–1625)	783 (96–1752)	.566	598 (77–2286)	<.001
Surgical approach, *n* (%)					
Extraperitoneal	47 (92.2)	155 (98.1)		1253 (98.7)	
Intraperitoneal	4 (7.8)	3 (1.9)	.040	16 (1.3)	<.001
Implantation side, *n* (%)					
Right	39 (76.5)	67 (42.7)		1016 (80.8)	
Left	12 (23.5)	90 (57.3)	<.001	242 (19.2)	.447
Donor kidney, *n* (%)					
Right	25 (49.0)	74 (48.1)		589 (48.5)	
Left	26 (51.0)	80 (51.9)	.905	626 (51.5)	.939
Arterial anastomoses (mean)					
Number	1.2	1.2	.296	1.2	.295
Number without patch	0.49	0.66	.051	0.74	.001
Venous anastomoses (mean)					
Number	1.02	1.02	.950	1.04	.674
Number without patch	0.92	0.93	.777	0.93	.809
Number of ureteral anastomoses (mean)	1.0	1.04	.160	1.04	.167

*P-value = Re-Tx ipsilateral vs Re-Tx contralateral as control group.
**P-value = Re-Tx ipsilateral vs primary Tx as control group.
Re-Tx, re-transplantation; ipsi, ipsilateral; contra, contralateral.

1 arterial kinking, 3 cases of inadequate arterial perfusion and 4 cases of other causes.

The incidence of arterial vascular complications did not differ between ipsilateral and contralateral re-transplant recipients ($P = .244$) or between ipsilateral and primary transplant recipients ($P = .326$).

One venous vascular complication was observed after 51 ipsilateral re-transplantations (1.9%). In this case, secondary haemorrhage of the venous anastomosis to the inferior vena cava occurred a few hours postoperatively and the graft had to be explanted for bleeding control.

Of the three venous vascular complications [1.9%; $P = .973$; each in the early postoperative course (100%)] in the contralateral re-transplantation group, there was one insufficient venous anastomosis with consecutive haemorrhage (common iliac vein), one venous thrombosis (external iliac vein) and one AV fistula.

In the primary transplant recipients, 13 (1.0%; $P = .523$) venous vascular complications were observed, each in the early postoperative course (100%). There were seven venous thromboses, four cases of haemorrhage due to insufficient venous anastomosis, one AV fistula and one venous stenosis.

Regarding perioperative venous vascular complications, there was no statistically significant difference between the ipsilateral re-transplant and both control groups ($P = .973$ and $P = .523$).

The rates of surgical revision for vascular complications did not differ between ipsilateral ($n = 3$, 5.8%) and contralateral re-transplantations ($n = 8$, 5.1%; $P = .827$) or between ipsilateral and primary transplantations ($n = 29$, 2.3%; $P = .102$).

We observed three lymphoceles requiring surgical revision for peritoneal fenestration (5.8%) in the ipsilateral re-transplant recipients and two (1.3%; $P = .062$) and 27 (2.1%; $P = .089$) in the contralateral re-transplant and primary transplant recipients.

In the ipsilateral re-transplant group, 1 surgical revision for urinary leakage ($n = 1$, 1.9%) was required compared with 1 (0.6%; $P = .424$) and 17 (1.3%; $P = .733$) in the re-transplant and primary transplant control groups. With 21 (8–75) days, the median length of hospital stay was longer after ipsilateral re-transplantation than after primary [15 (0–149); $P < .001$] and contralateral transplantations [18 (8–81); $P = .012$]. All complications and surgical outcomes are shown in Table 3.

Graft and immunological outcome

Initial non-function was more common after ipsilateral ($n = 12$, 23.5%) and contralateral re-transplantations ($n = 26$, 17.2%) than after primary transplantation ($n = 161$, 13.0%; $P < .001$) but did not differ between the two re-transplantation groups ($P = .319$). The median serum creatinine and the corresponding eGFR at discharge were not different between the three groups. First-year graft loss was significantly less frequent in primary transplant recipients ($n = 81$, 6.4%; $P = .009$) but did not differ significantly between both re-transplantation groups (ipsilateral: $n = 8$, 15.7%; contralateral: $n = 14$, 8.8%; $P = .163$). 1-, 3- and 5-year graft survival was 84.3%, 76.3% and 71.8% in the ipsilateral re-transplant group versus 90.5%, 85.8% and 81.8% in the contralateral re-transplant group ($P = .056$) and 93.6%, 90.2% and 87.4% in the primary transplant group ($P < .001$). Figure 1 shows the graft survival of the three groups using a Kaplan–Meier curve. In the first year posttransplant, 23 (45.1%) ipsilateral re-transplanted patients suffered from biopsy-proven rejection compared with 54 (34.0%; $P = .151$) contralateral re-transplanted and 349 (27.3%; $P = .006$) primary transplanted patients. Outcome and immunological data are shown in Table 4.

Regression analyses for the identification of independent risk factors for severe morbidity and early graft-loss

Using the need for surgical revision under general anesthesia as the dependent variable in a multivariate logistic regression model as described above, recipient's age [odds ratio (OR) 1.022;

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Table 3: Surgical outcome.

Parameter	Re-Tx ipsi ($n = 51$)	Re-Tx contra ($n = 159$)	P-value*	Primary Tx ($n = 1.279$)	P-value**
Surgical revision, *n* (%)	13 (25.5)	28 (17.6)	.217	160 (12.7)	.010
Revision due to haemorrhage, *n* (%)	5 (9.8)	13 (8.2)	.727	35 (3.1)	.009
Intraoperative PRBC, *n* (%)	2 (3.9)	4 (2.5)	.600	32 (2.5)	.535
Vascular complications, *n* (%)					
Arterial complications	3 (5.8)	4 (2.5)	.244	42 (3.3)	.326
Venous complications	1 (1.9)	3 (1.9)	.973	13 (1.0)	.523
Revision for vascular complications	3 (5.8)	8 (5.1)	.827	29 (2.3)	.102
Lymphoceles requiring surgical revision, *n* (%)	3 (5.8)	2 (1.3)	.062	27 (2.1)	.089
Revision for urological complications, *n* (%)	1 (1.9)	1 (0.6)	.424	17 (1.3)	.733

*P-value = Re-Tx ipsilateral vs Re-Tx contralateral as control group.
**P-value = Re-Tx ipsilateral vs primary Tx as control group.
Re-Tx, re-transplantation; ipsi, ipsilateral; contra, contralateral.

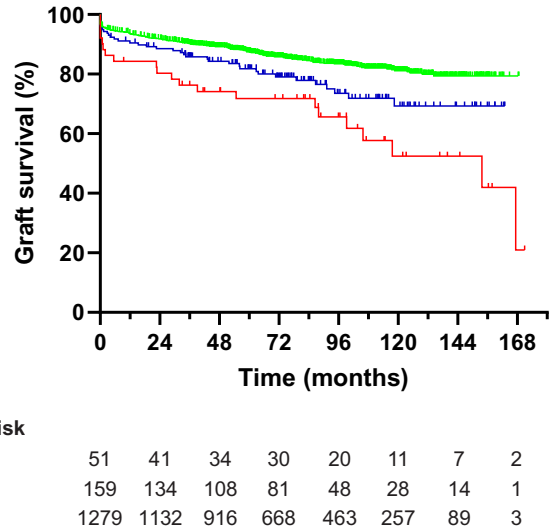


Figure 1: Graft survival. Kaplan–Meier survival curves after ipsilateral ($n = 51$; red line) and contralateral ($n = 159$; blue line) re-transplantation and after primary transplantation ($n = 1.279$; green line). Log-rank test (ipsilateral vs contralateral Tx, $P = .056$; and ipsilateral vs primary Tx, $P < .001$).

Table 4: Graft outcome.

Parameter	Re-Tx ipsi ($n = 51$)	Re-Tx contra ($n = 159$)	P-value*	Primary Tx ($n = 1.279$)	P-value**
Initial non-function, *n* (%)	12 (23.5)	26 (17.2)	.319	161 (13.0)	<.001
Length of hospital stay (days), median (range)	21 (8–75)	18 (8–81)	.012	15 (0–149)	<.001
Serum creatinine at discharge (µmol/L), median (range)	166 (75–412)	153 (63–944)	.853	150 (32–1330)	.689
eGFR at discharge (mL/min/1.73 m²), median (range)	40 (12–119)	43 (5–96)	.828	41 (3–133)	.754
Rejection within first year after Tx, *n* (%)	23 (45.1)	54 (34.0)	.151	349 (27.3)	.006
Graft loss within first year after Tx, *n* (%)	8 (15.7)	14 (8.8)	.163	81 (6.4)	.009
1-year graft survival (%)	84.3	90.5	.056	93.6	<.001
3-year graft survival (%)	76.3	85.8		90.2	
5-year graft survival (%)	71.8	81.8		87.4	

*P-value = Re-Tx ipsilateral vs Re-Tx contralateral as control group.
**P-value = Re-Tx ipsilateral vs primary Tx as control group.
Re-Tx, re-transplantation; ipsi, ipsilateral; contra, contralateral.

95% confidence interval (CI) 1.010–1.034; $P < .001$], operation time (OR 1.006; 95% CI 1.003–1.010; $P < .001$), current PRA levels (OR 1.012; 95% CI 1.006–1.018; $P < .001$), the number of arterial anastomoses without patch (OR 1.385; 95% CI 1.070–1.794; $P = .014$) and ABO-incompatible Tx (OR 2.145; 95% CI 1.217–3.780; $P = .008$) were identified as independent risk factors. Notably, neither ipsilateral nor contralateral renal re-transplantation nor the number of previous KTx were found to have an independent significant impact on the incidence of complications requiring surgical revision (see Table 5).

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Table 5: Binary logistic regression analysis for identification of risk factors for the occurrence of major complications requiring surgical revision after kidney transplantation.

	Univariable analysis			Multivariable analysis		
Variables	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Donor data						
Age (in years)	1.017	(1.006–1.028)	.002			
Male sex (*n*)	0.880	(0.653–1.187)	.403			
BMI (in kg/m²)	1.023	(0.991–1.056)	.167			
Living donor (*n*)	1.043	(0.748–1.454)	.804			
Recipient data						
Age at transplant (in years)	1.017	(1.006–1.028)	.003	1.022	(1.010–1.034)	<.001
Male sex (*n*)	0.938	(0.727–1.342)	.938			
BMI (in kg/m²)	1.050	(1.014–1.087)	.006			
Ipsilateral KTx (*n*)	2.247	(1.175–4.297)	.014			
Contralateral KTx (*n*)	1.411	(0.910–2.187)	.124			
Primary transplantation (*n*)	0.597	(0.409–0.873)	.008			
Number of previous KTx (*n*)	1.492	(1.140–1.951)	.004			
Immunological data						
Current PRA (%)	1.011	(1.006–1.016)	<.001	1.012	(1.006–1.018)	<.001
Highest PRA (%)	1.008	(1.004–1.013)	<.001			
Full-house match (*n*)	0.651	(0.408–1.039)	.072			
ABO-incompatible Tx (*n*)	1.986	(1.224–3.223)	.005	2.145	(1.217–3.780)	.008
Operative details						
Operation time (min)	1.006	(1.003–1.010)	<.001	1.006	(1.003–1.010)	<.001
Cold ischemia time (min)	1.000	(1.000–1.000)	.625			
Surgical approach (*n*)						
Extraperitoneal	0.745	(0.251–2.214)	.597			
Transperitoneal	1.342	(0.452–3.985)	.597			
Implantation side (*n*)						
Right	0.938	(0.661–1.333)	.722			
Left	1.066	(0.750–1.513)	.722			
Transplanted kidney (*n*)						
Right	0.979	(0.720–1.332)	.894			
Left	1.021	(0.751–1.390)	.894			
Anastomoses (*n*)						
Number of arterial anastomoses	0.765	(0.528–1.109)	.158			
Number of arterial anastomoses without patch	1.329	(1.032–1.712)	.028	1.385	(1.070–1.794)	.014
Number of venous anastomoses	1.037	(0.507–2.118)	.921			
Number of venous anastomoses without patch	0.710	(0.433–1.164)	.175			
Number of ureteral anastomoses	1.384	(0.716–2.677)	.334			

For early graft loss in the first postoperative year, we were able to identify current PRA levels (OR 1.012; 95% CI 1.004–1.020; $P = .004$), occurrence of complications requiring surgical revision (OR 4.538; 95% CI 2.693–7.649; $P < .001$), arterial vascular complications (OR 3.546; 95% CI 1.520–8.268; $P = .003$), operation time (OR 1.007; 95% CI 1.002–1.012; $P < .001$) and initial non-function (OR 7.009; 95% CI 4.253–11.55; $P < .001$) as independent risk factors (see Table 6). Ipsilateral and contralateral kidney re-transplantation and the number of previous KTx were not identified as independent risk factors for early graft loss. Of note, living donor type was a protective factor for early graft loss (OR 0.387; 95% CI 0.167–0.896; $P = .027$).

DISCUSSION

Ipsilateral renal re-transplantation is associated with an increased risk of surgical complications compared with primary transplantation into a surgically naïve iliac fossa [5, 11]. In this single-centre analysis, we demonstrated that patients after renal re-transplantation have an increased risk for major complications requiring surgical revision—irrespective of an ipsilateral or contralateral re-transplantation approach. Therefore, confounding factors rather than the surgical procedure itself seem to be the cause of increased perioperative morbidity.

The most common cause of surgical revision in both ipsilateral and contralateral re-transplantation was severe postoperative haemorrhage. Consistent with these findings, previous reports showed that the estimated intraoperative blood loss was significantly higher during re-transplantation [5, 22]. However, PRBC administration was required in only 2 of 51 ipsilateral re-transplantations with a resulting transfusion rate of 3.9%, which is not increased compared with that after primary or contralateral transplantation in our cohort and is significantly lower when compared with other reports with rates of up to 52% [23].

Compared with primary and contralateral transplantations, we did not observe an increased risk of venous vascular complications after ipsilateral re-transplantation; in particular, there was not a single case of venous thrombosis in our cohort, which was reported to be the most common vascular complication with 33% and 100% in selected reports [5, 24]. The risk of perioperative arterial complications was also not increased in the ipsilateral re-transplant recipients. Notably, three of nine (33%)

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Table 6: Binary logistic regression analysis for identification of risk factors for graft loss within the first year after kidney transplantation.

	Univariable analysis			Multivariable analysis		
Variables	OR	95% CI	P-value	OR	95% CI	P-value
Donor data						
Age (in years)	1.062	(1.044–1.080)	<.001			
Male sex (*n*)	1.559	(1.040–2.336)	.031			
BMI (in kg/m²)	1.056	(1.016–1.097)	.006			
Living donor (*n*)	0.210	(0.101–0.437)	<.001	0.387	(0.167–0.896)	.027
Recipient data						
Age at transplant (in years)	1.034	(1.017–1.051)	<.001			
Male sex (*n*)	0.775	(0.517–1.161)	.217			
BMI (in kg/m²)	1.082	(1.033–1.133)	<.001			
Ipsilateral KTx (*n*)	2.622	(1.199–5.737)	.016			
Contralateral KTx (*n*)	1.342	(0.744–2.419)	.328			
Primary transplantation (*n*)	0.580	(0.353–0.952)	.031			
Number of previous KTx (*n*)	1.526	(1.088–2.141)	.014			
Immunological data						
Rejection within first year after Tx (*n*)	1.386	(0.908–2.115)	.130			
ABO-incompatible Tx (*n*)	0.915	(0.399–2.095)	.833			
Current PRA (%)	1.013	(1.006–1.020)	<.001	1.012	(1.004–1.020)	.004
Highest PRA (%)	1.009	(1.003–1.015)	.004			
Full-house match (*n*)	0.577	(0.296–1.125)	.106			
Initial non-function (*n*)	11.43	(7.343–17.79)	<.001	7.009	(4.253–11.55)	<.001
Operative details						
Operation time (min)	1.012	(1.008–1.016)	<.001	1.007	(1.002–1.012)	<.001
Cold ischemia time (min)	1.001	(1.001–1.002)	<.001			
Surgical approach (*n*)						
Extraperitoneal	1.646	(0.220–12.33)	.628			
Transperitoneal	0.608	(0.081–4.553)	.628			
Transplanted kidney (*n*)						
Right	1.043	(0.693–1.569)	.840			
Left	0.959	(0.637–1.443)	.840			
Implantation side (*n*)						
Right	0.688	(0.440–1.076)	.102			
Left	1.453	(0.929–2.271)	.102			
Complications (*n*)						
Surgical revision	8.289	(5.417–12.68)	<.001	4.538	(2.693–7.649)	<.001
Arterial vascular	10.32	(5.575–19.12)	<.001	3.546	(1.520–8.268)	.003
Venous vascular	11.29	(4.115–30.99)	<.001			
Haemorrhage postoperative	4.65	(2.288–9.471)	<.001			
Urological	0.964	(0.410–2.264)	.933			
Anastomoses (*n*)						
Number of arterial anastomoses	0.979	(0.618–1.549)	.927			
Number of arterial anastomoses without patch	0.885	(0.625–1.253)	.490			
Number of venous anastomoses	0.921	(0.323–2.628)	.878			
Number of venous anastomoses without patch	1.003	(0.483–2.081)	.995			
Number of ureteral anastomoses	0.805	(0.260–2.493)	.707			

second graft recipients were transplanted with an ipsilateral approach due to a superior ipsilateral vascular status. Hence, vascular status was a main determinant regarding the site of graft implantation in our cohort of ipsilateral second kidney recipients. In this context, the degree of atherosclerotic disease would be a valuable variable to analyse for both the site of graft implantation and the occurrence of perioperative arterial complications. Unfortunately, a reliable and statistically sound analysis is not possible in our cohort since a significant number of patients underwent (ipsilateral/contralateral) KTx without a computed tomography scan immediately before transplant. Taken together, except for one graft that was explanted for bleeding control, we did not observe any graft loss due to vascular complications. These findings are remarkable since the dissection of the retroperitoneal vascular axis is significantly more difficult due to adhesions and scar tissue resulting from the previous operations [25]. In this context, the observed significantly longer operation times in comparison with primary or contralateral transplantations are to be expected and were also reported by other authors [5, 23, 26].

Regression analyses statistically confirmed these observations and led to one key finding of our study: Neither ipsilateral nor contralateral re-transplantation nor the number of previous KTx could be identified as independent risk factors for the occurrence of severe complications requiring surgical revision. Our results are supported by 108 cases of third, fourth or fifth kidney transplantation in which surgical complications were not different between recipients of a second or a third, fourth or fifth graft

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[26]. Moreover, Ahmed *et al*. could not demonstrate a significant influence of the number of previous KTx on the outcome of the subsequent graft [27].

Regression analyses revealed three especially relevant risk factors for severe surgical complications. First, the number of arterial anastomoses without a patch, which seems reasonable as every single anastomosis bears additional risks for complications. Second and third, ABO-incompatible transplantation and current PRA levels were identified as independent risk factors, which is probably due to the adverse effects of increased immunosuppressive therapy, leading to a higher rate of plasmapheresis or immunoadsorption, which is known to increase perioperative bleeding risk [28, 29].

We could also exclude ipsilateral re-transplantation as an independent risk factor for early graft loss within the first year after transplantation, consistent with previous reports [30, 31]. Compared with primary transplantations, the observed inferior 1-, 3- and 5-year graft survival rates in these patients are more likely caused by a more complex medical history, a longer time on dialysis, previous abdominal surgeries, and higher immunization and more deceased donor transplantations. Patients following contralateral re-transplantation also share some of these characteristics and tend to have an inferior graft outcome compared with primary transplantation. However, 1-, 3- and 5-year graft survival after ipsilateral and contralateral re-transplantation was not yet significantly different in our cohort—despite the ipsilateral re-transplanted patients (with a substantial proportion of third or fourth kidney graft recipients) accumulating higher immunological risks as indicated by significantly higher current and highest PRA levels. Benkö *et al*. demonstrated higher immunological risks in recipients of a third or more grafts than first graft recipients [26].

Consequently, these immunological risks likely contribute to the observed numerically higher rejection rates in the ipsilateral re-transplant recipients in the first year after transplantation in this study and in other patient collectives [10, 32]. Early rejections are a common problem in pre-sensitized patients and have been the primary cause of early graft loss in previous reports [30, 31], especially with a significant proportion of antibody-mediated rejections [30]. In this regard, patients who suffered from rejection after their primary transplant or lost their previous graft due to acute rejection are at high risk of repeated rejection episodes after re-transplantation [6, 12]. In conclusion, the reasons for surgical complications and inferior outcomes after renal re-transplantation are due to the higher immunization of re-transplanted patients and the resulting need for increased immunosuppressive therapy (with the associated adverse effects) rather than to the surgical procedure or the site of graft implantation itself.

The important limitation of this study is its retrospective design.

CONCLUSION

The results of our study demonstrate that ipsilateral renal re-transplantation *per se* is not a risk factor for major surgical complications. Higher immunization and deceased donor transplantations sufficiently explain an inferior early graft outcome.

Thus, repeated renal transplantation to the ipsilateral iliac fossa is a valid therapeutic option. The chronic organ shortage should mainly be counteracted by increasing the number of organ donors via preconditioning of marginal organs and more living donations rather than by reducing the number of re-transplantations.

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O.B. and F.O. designed the study. P.T. and A.M. acquired the data. P.T. analysed and interpreted the data. P.T. and O.B. wrote the main manuscript. C.A.W., A.M., B.A.W., W.G., G.E., J.K., F.W.R.V., N.R., F.O. and O.B. critically revised the manuscript. All the authors approved the final manuscript for publication.

DATA AVAILABILITY STATEMENT

The data underlying this article will be shared on reasonable request to the corresponding author.

CONFLICT OF INTEREST STATEMENT

None declared.

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