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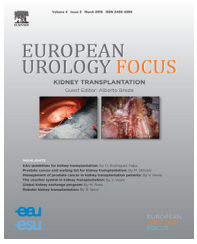

Renal Disease

Robot-assisted Kidney Transplantation with Regional Hypothermia Using Grafts with Multiple Vessels After Extracorporeal Vascular Reconstruction: Results from the European Association of Urology Robotic Urology Section Working Group

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Abstract

Background: Kidney transplantation using grafts with multiple vessels (GMVs) is technically demanding and may be associated with increased risk of complications or suboptimal graft function. To date, no studies have reported on robot-assisted kidney transplantation (RAKT) using GMVs.
Objective: To report our experience with RAKT using GMVs from living donors, focusing on technical feasibility and early postoperative outcomes.
Design, setting, and participants: We reviewed the multi-institutional, prospectively collected European Association of Urology (EAU) Robotic Urology Section (ERUS)-RAKT database to select consecutive patients undergoing RAKT from living donors using GMVs between July 2015 and January 2018. Patients undergoing RAKT using grafts with single vessels (GSVs) served as controls. In case of GMVs, ex vivo vascular reconstruction techniques were performed during bench surgery according to the case-specific anatomy.
Intervention: RAKT with regional hypothermia.
Outcome measurements and statistical analysis: Intraoperative outcomes and early (30 d) postoperative complications and functional results were the main study end-points. Multivariable logistic regression analysis evaluated potential predictors of suboptimal renal function at 1 mo.
Results and limitations: Overall, 148 RAKTs were performed during the study period. Of these, 21/148 (14.2%) used GMVs; in all cases, single arterial and venous anastomoses could be performed after vascular reconstruction. Median anastomoses and rewarming

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times did not differ significantly between the GMV and GSV groups. Total and cold ischemia times were significantly higher in the GMV cohort (112 vs 88 min, $p = 0.004$ and 50 vs 34 min, $p = 0.003$, respectively). Overall complication rate and early functional outcomes were similar among the two groups. No major intra- or postoperative complications were recorded in the GMV cohort. At multivariable analysis, use of GMVs was not significantly associated with suboptimal renal function at 1 mo. Small sample size and short follow-up represent the main study limitations.
Conclusions: RAKT using GMVs from living donors is technically feasible and achieved favorable perioperative and short-term functional outcomes. Larger studies with longer follow-up are needed to confirm our findings.
Patient summary: In this study, we evaluated for the first time in literature the results of RAKT from living donors using kidneys with multiple arteries and veins. We found that, in experienced centers, RAKT using kidneys with multiple vessels is feasible and achieves optimal results in terms of postoperative kidney function with a low number of postoperative complications.

1. Introduction

Anatomic variations in the renal vasculature are common, being reported in 25–40% of kidneys [1–3]. Supernumerary or accessory renal arteries and, to a lesser extent, renal veins, represent the most common variations [1,3].

Grafts with multiple vessels (GMVs) pose a technical challenge for kidney transplantation (KT). Several retrospective studies using different techniques for vascular reconstruction [4–8] have demonstrated feasibility and safety of KT using GMVs [2,9–16]. However, a recent review reported increased risks of complications, delayed graft function (DGF), and lower 1-yr graft survival using GMVs; however, long-term outcomes were comparable to those of KT using grafts with single vessels (GSVs) [9]. Moreover, previous studies have reported a potential increased rate of ureteral complications for grafts with accessory lower pole arteries [17,18]; however, this remains controversial [9].

In 2014, the European Association of Urology (EAU) Guidelines emphasized that grafts with multiple renal arteries or anatomical anomalies should not be considered *absolute* contraindications for living-donor KT due to the shortage of renal grafts and living donations [19].

In recent years, robot-assisted KT (RAKT) has been shown to mirror the principles of open KT while adding all the advantages of minimally invasive surgery [20,21].

The largest European multicenter study on RAKT has recently confirmed its feasibility, reproducibility, and safety when performed by skilled robotic surgeons [22]. Of note, overall evidence is still premature [23]; in a recent systematic review, no significant differences were observed between open and minimally-invasive KT in terms of patient and graft survival [24].

Given these promising results, RAKT has now been adopted at multiple institutions worldwide [2] and its performance will likely increase in the future.

To date, no studies have reported surgical technique and outcomes of RAKT using GMVs. Herein we report the EAU Robotic Urology Section (ERUS) Group experience with RAKT using GMVs from living donors, focusing on technical feasibility and perioperative and early functional outcomes.

2. Patients and methods

2.1. Patients and dataset

After obtaining the Ethical Committee approval and patients' informed consent, data were prospectively collected into the multi-institutional ERUS-RAKT group database.

For the current study, we retrospectively reviewed the database to select consecutive patients undergoing RAKT with regional hypothermia using GMVs from living donors between July 2015 and January 2018 at the eight European centers included in the ERUS-RAKT group.

We defined GMVs as those with greater than or equal to two renal arteries and/or greater than or equal to two renal veins. Patients undergoing RAKT using GSVs (one artery and one vein) were used as controls.

Functional outcomes were evaluated with estimated glomerular filtration rate (eGFR) on postoperative day (POD) 1, 3, 7, and 30, calculated using the Modified Diet in Renal Disease equation [25]. DGF was defined as need for dialysis in the first postoperative week. A detailed overview of the study design is provided in Supplementary Information.

2.2. Preparation of the graft and RAKT technique

All transplant teams at the eight centers included in the ERUS-RAKT group were highly experienced in living donor nephrectomy, robotic urologic surgery, and open KT. Moreover, all surgeons involved in this study followed a standardized modular training program prior to starting their own RAKT experience [22].

All RAKTs performed by each surgeon at each center included in the study since the beginning of their experience were included in the final analytical cohort. As such, our study included the learning curve of all surgeons involved in the RAKT program at each center.

Living donor nephrectomy was performed with a laparoscopic or robotic approach according to hospital resources and surgeon's preference and skills.

After retrieval, the graft was defatted and perfused with cold storage solution as in conventional open KT.

In case of GMVs, specific ex vivo vascular reconstruction techniques, adapted from the open KT experience, have been employed before introduction of the graft into the recipient (Table 1; Fig. 1). In our series, the following reconstruction techniques have been employed according to the case-specific vascular anatomy: (1) conjoined (side-to-side) arterial anastomosis (in a *pantaloon* fashion), (2) reimplantation (end-to-side) of a polar artery into the main renal artery, or (3) a combination of these techniques in case of greater than or equal to three renal arteries

Table 1 – Overview of available surgical techniques for extracorporeal (ex vivo) or in situ vascular reconstruction for open and robot-assisted kidney transplantation from deceased and living donors using grafts with multiple vessels.[a]

Technique	Open kidney transplantation		Robot-assisted kidney transplantation	
	Deceased donor	Living donor	Deceased donor	Living donor
Grafts with multiple arteries				
1. Carrell aortic patch	✓ [5,9,23]	–	Technically feasible Not described in literature	–
2. Conjoined (side-to-side) arterial anastomosis (*pantaloon* fashion)	✓ [4,5,7,9]	✓ [5,7–11,13,16,17,23]	Technically feasible Not described in literature	§ 11/21 (52%)
3. Re-implantation (end-to-side) of polar artery into main renal artery	✓ [5,7]	✓ [5,7,8,10,13,16,23]	Technically feasible Not described in literature	§ 6/21 (28%)
4. Extracorporeal repair with autogenous branched vascular graft	✓ [5,7]	✓ [5,7,8]		–
5. Polar artery anastomosis to the inferior epigastric artery	✓ [5]	✓ [5,6,8,10,23]	Technically feasible Not described in literature	✓ [21]
6. Separate arterial anastomoses (end-to-side) to external/common iliac artery	✓ [5,7,9]	✓ [5,7,9–11,23]	Technically feasible Not described in literature	Technically feasible Not described in literature
7. Separate arterial anastomoses (end-to-end) to hypogastric artery and (end-to-side) external iliac artery.	✓ [5,7,9]	✓ [5,7,9,11,23]	–	–
8. Arterial anastomoses to branches of hypogastric artery.	✓ [5]	✓ [5]	–	–
9. Combined vascular reconstruction techniques	✓ [5]	✓ [5]	Technically feasible Not described in literature	§ 1/21 (5%) [technique no. 2 + no. 3]
10. None (ligation of small accessory artery, especially if supplying the upper renal pole)	✓	✓ [10,16,23]	Technically feasible Not described in literature	§ 1/21 (5%)
Grafts with multiple veins				
1. Conjoined (side-to-side) arterial anastomosis (*pantaloon* fashion)	✓	✓	Technically feasible Not described in literature	§ 1/21 (5%)
2. Combined vascular reconstruction techniques	✓	✓	Technically feasible Not described in literature	§ 1/21 (5%)

✓ = technique described in literature (selected key references are provided); § = technique used in our series.

[a] The following reconstruction techniques have been employed according to the case-specific vascular anatomy: (1) conjoined (side-to-side) arterial anastomosis (in a *pantaloon* fashion) in cases of multiple renal arteries of almost equal caliber; (2) re-implantation (end-to-side) of a polar artery into the main renal artery; or (3) a combination of these techniques in cases of greater than or equal to three renal arteries and/or complex vascular anatomy. Small accessory renal arteries supplying the upper pole and with a diameter of <2–3 mm were ligated during bench surgery. In one graft with two renal veins, a conjoined (side-to-side) venous anastomosis was performed in a pantaloon fashion to create a common venous ostium for subsequent single venous anastomosis to external iliac vein. The second graft with multiple renal veins ($n = 2$) in our series was found in a patient with a duplication of the inferior vena cava. In this case, the two renal veins were left intact on a caval patch and the patch anastomosed to the external iliac vein.

and/or complex vascular anatomy (Table 1). Grafts with one artery and one vein after ligation of small accessory arteries were not considered as GMVs.

After vascular reconstruction, the graft kidney was wrapped in a gauze jacket filled with ice slush and subsequently introduced into the recipient through the umbilical incision.

At all centers participating in this study, RAKT was performed using a standardized operative protocol following the principles of the Vattikuti-Medanta technique [20,21], as previously described [22]. In particular, even in case of GMVs, end-to-side anastomoses of donor renal vessels to recipient external iliac vessels were always planned, as recommended (Fig. 2) [23].

Warm ischemia time (WIT) was defined as the time between renal circulatory arrest and beginning of cold storage; cold ischemia time (CIT) was defined as the duration of cold storage, with or without perfusion with a storage solution before introduction of the graft into the recipient; rewarming time (RT) was defined as the time between removal of the kidney from cold storage and start of reperfusion under regional hypothermia (achieved by using ice slush) [22].

2.3. Study endpoints

The main study endpoints included: (1) technical feasibility of RAKT using GMVs, defined as successful completion of RAKT without the need of open conversion, (2) intraoperative and early (30 d) postoperative complication rate, and (3) early (30 d) functional outcomes. Secondary endpoints included ischemia times and time to complete vascular anastomoses.

2.4. Statistical analysis

A detailed overview of statistical analysis for this study is provided in Supplementary Information.

First, descriptive statistics for the GMVs and GSVs groups were obtained reporting medians (and interquartile ranges, IQR) for continuous variables, and frequencies and proportions for categorical variables, as appropriate. The Pearson's chi-square and Mann-Whitney *U* tests were used to compare the distribution of key study variables among the GMVs and GSVs cohorts.

The same tests were used to compare the distribution of key variables (including presence of GMVs) among patients with *sub-optimal* and *good* renal function on POD 30 (defined as eGFR below and above the pre-specified cut-off of 45 ml/min/173 m^2).

Then, exploratory multivariable binary logistic regression analysis was used to test whether specific donor-, recipient-, and surgery-related factors (including GMVs) were associated with suboptimal renal function on POD 30.

Statistical analyses were performed using SPSS version 24 (IBM SPSS Statistics for Mac, Armonk, NY, IBM Corp). All tests were two-sided with a significance level set at $p < 0.05$.

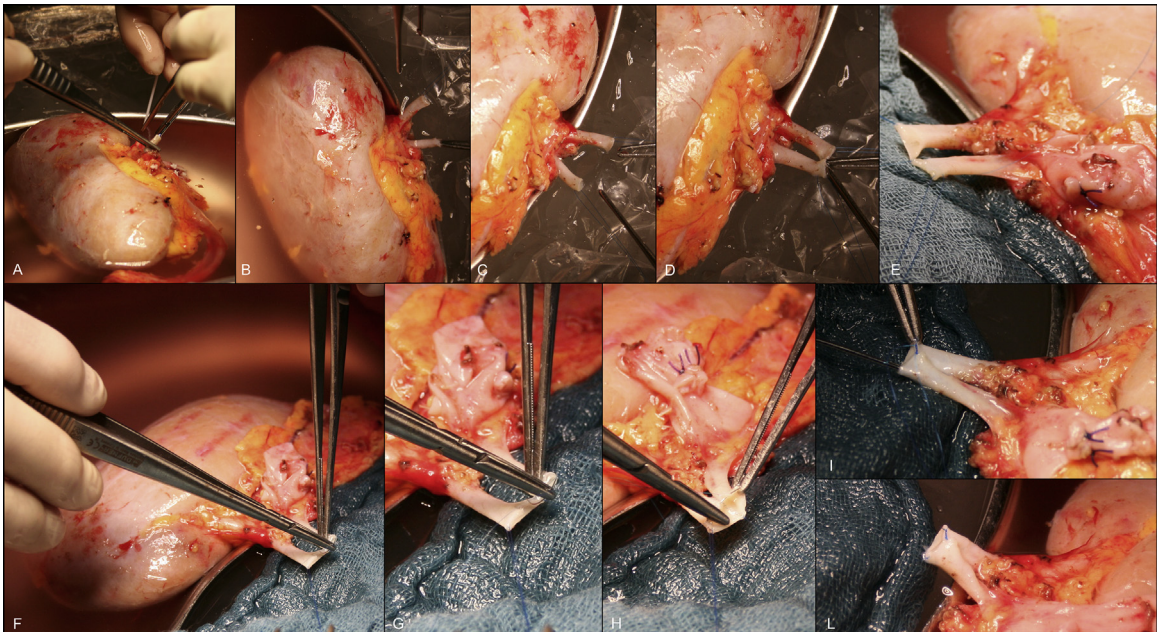


Fig. 1 – Intraoperative images showing consecutive phases of extracorporeal (ex vivo) bench vascular reconstruction prior to robot-assisted kidney transplantation in case of a graft with two separate renal arteries of approximately the same caliber from a living donor. (A–E) After careful preparation of the two renal arteries, vascular reconstruction was carried out using a conjoined (side-to-side) arterial anastomosis in *pantaloon* fashion to create (F–L) a common arterial ostium for subsequent single arterial anastomosis to the external iliac artery (see Fig. 2).

3. Results

Overall, 148 RAKTs from living donors were performed during the study period. Of these, 21 (14.2%) used GMVs. The graft had two renal arteries and one renal vein in 13/21 (62%) cases, three renal arteries and one renal vein in 6/21 (29%) cases, and one renal artery and two renal veins in 2/21 cases (9%).

Donor-, recipient-, and graft-related characteristics, as well as the key postoperative and functional outcomes for the overall cohort and stratified by number of graft vessels (single vs multiple) are shown in Table 2 and Figure 3.

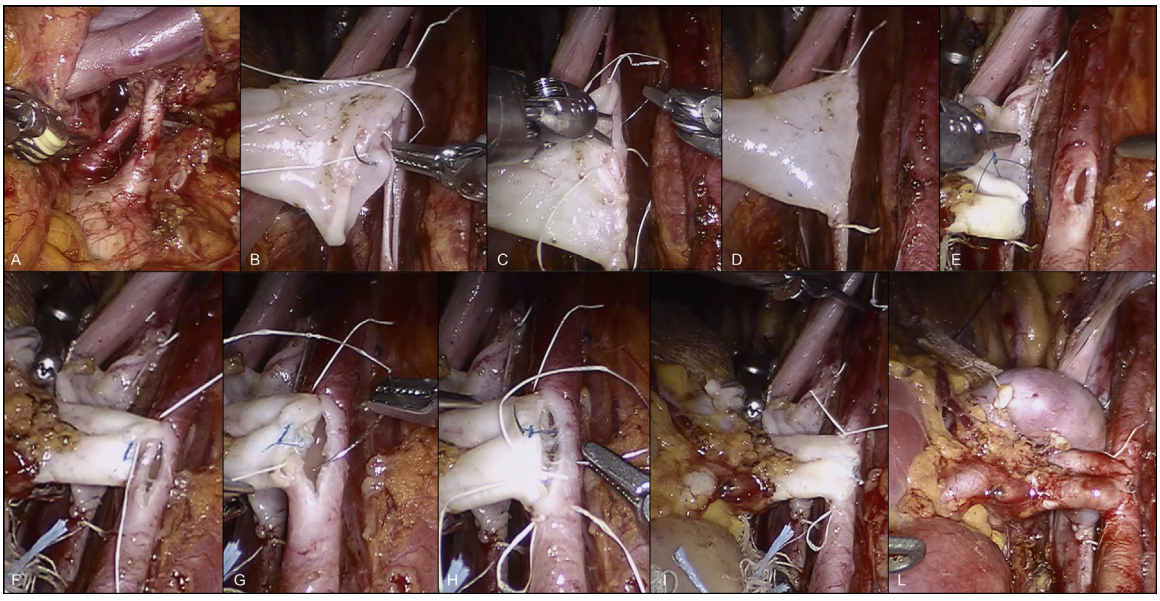


Fig. 2 – Intraoperative snapshots during robot-assisted living donor nephrectomy and robot-assisted kidney transplantation in case of grafts with multiple vessels. Surgical technique for bench vascular reconstruction in this case is shown in Fig. 1. (A) Intraoperative view of renal vascular anatomy during robot-assisted living donor nephrectomy. In this case, two separate arteries of approximately the same caliber were found. (B–D) Venous anastomosis between the single graft vein and external iliac vein during robotic kidney transplantation following the principles of the Vattikuti-Medanta technique [21]. (E) Creation of a circular arteriotomy by using an aortic punch. (F–I) Single arterial anastomosis between the reconstructed graft renal artery (side-to-side arterial anastomosis in a *pantaloon* fashion between the two renal arteries) and the external iliac artery following the principles of the Vattikuti-Medanta technique [21]. (L) Intraoperative snapshot showing the final surgical results after completion of venous and arterial anastomosis and graft reperfusion.

Table 2 – Descriptive graft-, donor- and recipient-related characteristics, as well as intraoperative, perioperative, and functional outcomes, for the overall cohort (*n* = 148) and stratified by number of graft vessels (single vessels and multiple vessels cohorts).[a]

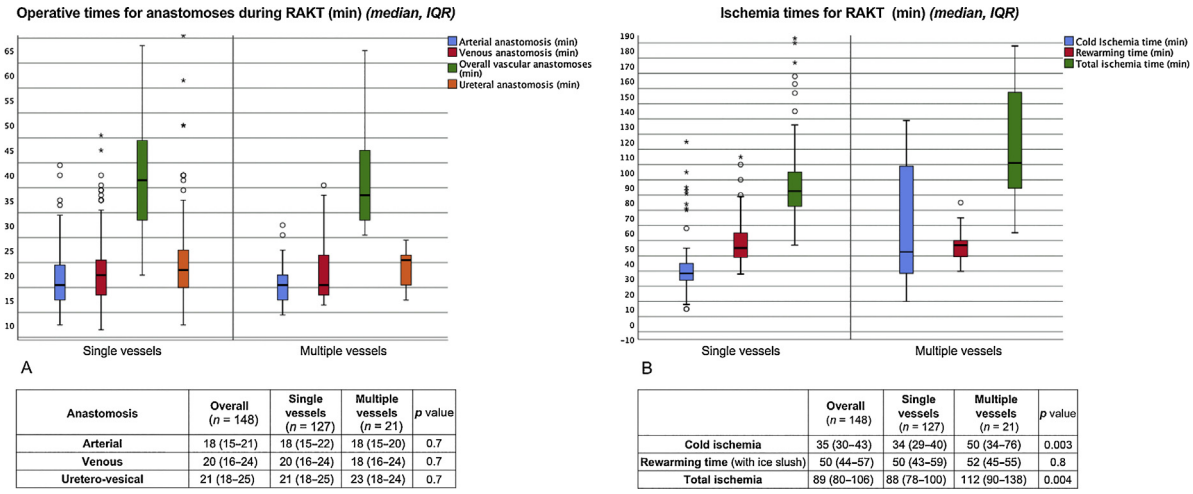
			Number of graft vessels			*p* value
			Single vessels (*n* = 127)	Multiple vessels (*n* = 21)	Overall (*n* = 148)	
Graft anatomy	Ureter, *n* (single: multiple)		126:1	21:0	147:1	–
	Vascular anatomy, *n* arteries: *n* veins (*n* [%])		1:1 (127 [100])	2:1 (13 [62]) 3:1 (6 [29]) 1:2 (2 [9])	1:1 (127 [86]) 2:1 (13 [9]) 3:1 (6 [4]) 1:2 (2 [1])	
Living donor	Age at surgery (yr)		50 (44–59)	53 (41–64)	50 (43–60)	0.8
	Male sex, *n* (%)		47 (37.0)	8 (42.1)	55 (37.7)	0.7
	BMI at surgery (kg/m^2)		25.3 (23.0–28.0)	23.9 (22.0–26.9)	25.1 (23.0–27.7)	0.09
	Preoperative eGFR (ml/min/1.73 m^2)		93 (84–103)	94 (88–101)	93 (85–103)	0.9
	Postoperative eGFR (ml/min/1.73 m^2)		61 (54–72)	67 (54–78)	62 (54–72)	0.4
	Left donor side, *n* (%)	Right	17 (13.4)	3 (14.3)	20 (13.5)	0.9
		Left	103 (81.1)	17 (81.0)	120 (81.1)	
		Missing	7 (5.5)	1 (4.7)	8 (5.4)	
Recipient	Age at surgery (yr)		45 (33–54)	43 (36–56)	44 (35–54)	0.8
	Male sex, *n* (%)		78 (61.4)	16 (76.2)	94 (63.5)	0.2
	BMI at surgery (kg/m^2)		25.0 (22.1–28.0)	25.7 (24.0–28.0)	25.1 (22.7–28.0)	0.5
	Pre-emptive, *n* (%)		58 (45.7)	12 (57.1)	70 (47.3)	0.3
	Dialysis duration (d)		300 (32–370)	365 (30–480)	300 (32–405)	0.9
	Charlson comorbidity index, *n* (%)	2	102 (80.3)	14 (66.7)	116 (78.4)	0.4
		3	16 (12.6)	5 (23.8)	21 (14.2)	
		4	9 (7.1)	2 (9.5)	11 (7.4)	
	Diabetes mellitus, *n* (%)		13 (10,2)	2 (9.5)	15 (10.1)	0.9
	Previous surgery, *n* (%)		34 (26.8)	4 (19.0)	38 (25.7)	0.4
	Preoperative Hb (mg/dl)		109 (95–124)	108 (96–111)	108 (95–122)	0.5
	Preoperative eGFR (ml/min/1.73 m^2)		10 (7.9–13)	10.3 (7.6–13.5)	10.0 (7.9–13.0)	0.8
Intraoperative outcomes	Operative time: incision to closure (min)		240 (215–300)	260 (225–300)	245 (220–300)	0.6
	Console time: console start to finish (min)		157 (130–190)	171 (135–190)	160 (130–190)	0.5
	Warm ischemia time (min)		2 (2–4)	3 (2–5)	2 (2–4)	0.09
	Estimated blood loss (cc)		135 (75–170)	150 (60–170)	140 (70–170)	0.8
	Intraoperative complications, *n* (%)	Major	0 (0)	0 (0)	0 (0)	0.3
		Bleeding (not requiring blood transfusions)	2 (1.7)	2 (9.5)	4 (2.7)	
	Conversion to open surgery, *n* (%)		2 (1.7) (reason: intraoperative bleeding [*n* = 1]; difficult graft allocation [*n* = 1])	1 (4.7) (reason: intraoperative bleeding)	3 (2.0)	0.2
Postoperative outcomes	Delta Hb values (mg/dl)	POD 1	–6 (–16; 10)	1 (–11; 14)	–6 (–16; 10)	0.6
		POD 3	–13 (–21; 1)	–10 (–16; 7)	–12 (–21, 1)	0.7
		POD 7	–10 (–21; 5)	–7 (–19; 1)	–10 (–20; 4)	0.4
		POD 30	7 (–11; 26)	8 (1; 23)	7 (–9; 26)	0.8
	Postoperative pain (VAS scale)	12 h	5 (3–6)	5 (2–6)	5 (3–6)	0.5
		24 h	4 (3–5)	3 (2–5)	4 (3–5)	0.5
		36 h	3 (1–3)	3 (3–5)	3 (1–4)	0.9
		48 h	2 (1–3)	2 (1–4)	2 (1–3)	0.5

Table 2 (*Continued*)

			Number of graft vessels			*p* value
			Single vessels (n = 127)	Multiple vessels (n = 21)	Overall (n = 148)	
	Postoperative complications (Clavien-Dindo classification), *n* (%)	I	5 (4.1)	1 (4.7)	6 (4.1)	0.4
		Bleeding (observation)	1 (0.8)	1 (4.7)	2 (1.4)	
		Wound infection	1 (0.8)	0 (0)	1 (0.7)	
		Postoperative ileus	3 (2.5)	0 (0)	3 (2.0)	
		II	4 (3.3)	1 (4.7)	5 (3.4)	
		Deep venous thrombosis	1 (0.8)	0 (0)	1 (0.7)	
		Bleeding requiring transfusions	3 (2.5)	1 (4.7)	4 (2.7)	
		IIIa	2 (1.7)	0 (0)	2 (1.4)	
		Nephrostomy tube placement	1 (0.8)	0 (0)	1 (0.7)	
		Percutaneous drainage of pelvic lymphocele	1 (0.8)	0 (0)	1 (0.7)	
		IIIb	7 (5.5)	0 (0)	7 (4.7)	
		Graft nephrectomy (reason: vascular thrombosis)	3 (2.4)	0 (0)	3 (2.0)	
		Surgical re-exploration (reason: bleeding [n = 2]; vascular complications [n = 1]; ureter complications [n = 1])	4 (3.1)	0 (0)	4 (2.7)	
		IV–V	0 (0)	0 (0)	0 (0)	
	JJ stent removal, POD (median, range)		28 (13–110)	29 (15–47)	28 (13–110)	0.9
	Length of hospital stay (d)		7 (4–8)	6 (4–8)	7 (4–8)	0.9
	90-d hospital re-admission, *n* (%) (fever [n = 5]; urinary tract infections [n = 2]; acute kidney injury due to dehydration [n = 1]; drug toxicity [n = 2]; acute rejection [n = 2])		12 (9.4)	3 (14.3)	15 (10.1)	0.6
Functional outcomes	eGFR (ml/min/1.73 m^2)	POD 1	20.7 (13.0–25.2)	20.0 (15.9–27.4)	20.2 (13.3–25.6)	0.9
		POD 3	44.7 (28.0–61.0)	42.5 (31.0–52.8)	44.0 (28.4–57.5)	0.6
		POD 7	55.0 (44.0–68.7)	45.5 (40.7–62.0)	53.0 (44.0–68.0)	0.2
		POD 30	60.0 (46.0–75.0) [n = 119]	49.6 (42.0–67.3) [n = 18]	58.0 (45.0–75.0) [n = 137]	0.2
	Delta eGFR, POD 3 − preoperative (ml/min)		31.0 (18.0–49.0)	30.8 (23.0–41.8)	31.0 (18.0–49.0)	0.8
	Delta eGFR, POD 7 − preoperative (ml/min)		42.8 (31.0–59.0)	35.4 (31.3–55.0)	42.5 (31.2–58.0)	0.4
	Delta eGFR, POD 30 − preoperative (ml/min)		47.5 (35.0–64.0) [n = 119]	41.0 (31.0–67.0) [n = 18]	44.0 (35.0–64.0) [n = 137]	0.3
	eGFR at 1 yr (ml/min)		58.0 (43.0–69.1) [n = 62] §	55.0 (48.0–56.0) [n = 10] §	57.1 (43.2–69.0) [n = 72] §	0.8
	Delayed graft function, *n* (%)		7 (5.5)	2 (9.5)	9 (6.1)	0.4
	Graft survival at 1 mo (%)		97.6	100	97.9	0.8

BMI = body mass index; eGFR = estimated glomerular filtration rate; Hb = hemoglobin; IQR = interquartile range; POD = postoperative day; VAS = visual analog scale; § = patients who were followed-up for >1 yr after robot-assisted kidney transplantation.

[a] Values are presented as median (IQR) unless otherwise indicated.



Anastomosis	Overall (*n* = 148)	Single vessels (*n* = 127)	Multiple vessels (*n* = 21)	*p* value
Arterial	18 (15–21)	18 (15–22)	18 (15–20)	0.7
Venous	20 (16–24)	20 (16–24)	18 (16–24)	0.7
Uretero-vesical	21 (18–25)	21 (18–25)	23 (18–24)	0.7

	Overall (*n* = 148)	Single vessels (*n* = 127)	Multiple vessels (*n* = 21)	*p* value
Cold ischemia	35 (30–43)	34 (29–40)	50 (34–76)	0.003
Rewarming time (with ice slush)	50 (44–57)	50 (43–59)	52 (45–55)	0.8
Total ischemia	89 (80–106)	88 (78–100)	112 (90–138)	0.004

Fig. 3 – Box-plots showing time for vascular and ureterovesical anastomoses and ischemia times during RAKT for the overall cohort (*n* = 148) and stratified by number of graft vessels.
IQR = interquartile range; RAKT = robot-assisted kidney transplantation.

Both donor's and recipient's baseline characteristics did not significantly differ between the GMVs and GSVs study groups.

Median times to complete arterial, venous, and ureterovesical anastomoses, as well as the overall RT, did not significantly differ between RAKTs using GMVs or GSVs (Fig. 3). Likewise, overall operative time, console time, and WIT did not differ among the study groups (Table 2). On the contrary, total ischemia time was significantly higher for RAKTs using GMVs (112 vs 88 min, $p = 0.004$), driven by a significantly longer CIT (50 vs 34 min, $p = 0.003$; Fig. 3).

Median estimated blood loss was 135 cc and 150 cc for RAKTs using GSVs and GMVs, respectively ($p = 0.8$). There was no difference in delta-Hb values between RAKTs using GSV or GMV on all PODs (Table 2).

Conversion to open surgery due to intraoperative bleeding was required in two cases in the GSV cohort and in one case in the GMV cohort. In all other cases, no major intraoperative complications were reported in both study groups.

Patients undergoing RAKTs using GMVs did not experience early (30 d) major (Clavien-Dindo III–V) postoperative complications (Table 2). Overall postoperative complication rate, 90-d readmission rate, and length of hospital stay were similar among the study groups. Hospital readmissions were due to medical complications including fever, urinary tract infections, drug toxicity, acute kidney injury, and acute rejection and were managed conservatively without the need of any surgical intervention (Table 2).

The eGFR values on POD 1, 3, 7, and 30 showed no significant differences between the GSVs and GMVs cohorts (Table 2). Likewise, the rate of DGF did not differ significantly between the two groups.

Finally, among the 72/148 (48.6%) patients with follow-up of >1 yr after RAKT, eGFR did not significantly differ between RAKTs using GSVs or GMVs (58 vs 55 ml/min/1.73 m^2, respectively, $p = 0.8$).

Data on functional outcomes 1 mo after RAKT were available in 137/148 (92.6%) patients. Of 137, 30 (22.0%) patients had *suboptimal* renal function on POD 30 (eGFR <45 ml/min/1.73 m^2; Supplementary Table 1). At multivariable analysis, only donor age was a significant predictor of suboptimal renal function on POD 30 (odds ratio [OR] for each 5-yr increase: 1.46; 95% confidence interval [CI]: 1.06–2.01; Table 3). Recipient characteristics, use of GMVs, time to complete vascular anastomoses, and RAKT number were not associated with this outcome.

Table 3 – Binary multivariable logistic regression analysis evaluating donor-, recipient- and surgery-related factors associated with *suboptimal* renal function on postoperative day 30 (eGFR <45 ml/min/1.73 m^2).

	eGFR < 45 ml/min at POD 30	
	OR (95% CI)	*p* value
Donor age (5 yr-fold)	1.46 (1.06–2.01)	0.02
Donor BMI	0.79 (0.64–1.08)	0.3
Donor preoperative eGFR (5 ml/min-fold)	0.98 (0.84–1.15)	0.8
Recipient age (5 yr-fold)	1.01 (0.81–1.48)	0.5
Recipient BMI	1.05 (0.89–1.28)	0.5
Graft with multiple vessels (reference: grafts with single vessels)	3.21 (0.70–14.70)	0.1
Console time	1.01 (0.99–1.02)	0.5
Warm ischemia time	1.06 (0.67–1.67)	0.8
Cold ischemia time	1.03 (0.99–1.02)	0.7
Rewarming time	0.94 (0.86–1.03)	0.1
RAKT number		
>20 vs <10	0.17 (0.02–1.25)	0.08
>20 vs 10–20	0.67 (0.15–2.74)	0.5

BMI = body mass index; CI = confidence interval; eGFR = estimated glomerular filtration rate; OR = odds ratio; POD = postoperative day; RAKT = robot-assisted kidney transplantation.

4. Discussion

To the best of our knowledge, this is the largest experience on RAKT using GMVs from living donors. Our study showed that in this setting, RAKT was technically feasible and

achieved surgical and early postoperative outcomes comparable to those of RAKT using grafts with conventional vascular anatomy.

RAKT has demonstrated to reproduce the principles of open KT adding all the advantages of minimally invasive surgery from both patient's and surgeon's perspectives [21,22]. On one hand, KT recipients are ideal candidates for minimally invasive surgery [2,26]; on the other hand, the EndoWrist technology, the high-magnification and the three-dimensional vision provided by the robotic platform, facilitates performance of precise reconstructive procedures, such as KT, improving surgeon's ergonomics and quality of operative field, and reducing technical difficulty compared with standard laparoscopic techniques [24].

Although data are still premature, RAKT achieved similar patient and graft survival as open KT [24]. Moreover, surgeons who have extensive experience in robotic surgery appeared to have only minimal or even no learning curve at all for RAKT [2,27]. These findings suggest that robotic technology may allow in the future a broader adoption of minimally invasive KT, especially in high-volume centers. As such, while RAKT has been adopted at multiple institutions worldwide [2], its use will likely increase in the near future. In this scenario, given the high rate of anatomic variations in renal vasculature [1–3], the shortage of living donations and renal grafts [19], the current conflicting results of open KT literature on safety of GMVs [9–18], assessing the outcomes of RAKT using GMVs is a key clinical and research priority.

Our study provides evidence on this topic for the first time in literature.

A key finding of our study is that RAKT using GMVs from living donors is technically feasible. Using appropriate vascular reconstruction techniques (Table 1) and a standardized operative protocol for RAKT [21,22], it was possible to perform *single* arterial and venous anastomoses in all cases, thereby reducing RT and total ischemia time. Accordingly, time to complete vascular anastomoses, as well as overall console time and RT, did not significantly differ between RAKTs using GMVs or GSVs (Table 2; Fig. 3). Notably, the robotic platform facilitates the performance of vascular anastomoses, thanks to the articulated instruments, three-dimensional view, and optimal surgeon ergonomics.

A second finding of our study is that RAKT using GMVs from living donors appears to be safe, achieving optimal early (30 d) postoperative outcomes, with no reported major intra- or postoperative complications. Also, estimated blood loss, length of hospital stay, recipient's Hb values, and overall complication rates were comparable to RAKTs using GSV (Table 2).

A third key finding of our study is that despite longer CIT and total ischemia time (Fig. 3), probably reflecting a longer time required for extracorporeal bench vascular reconstruction, RAKT using GMVs from living donor provided optimal early functional results that were comparable to those of RAKT using GSVs (Table 2). However, larger studies with longer follow-up are needed to confirm these findings.

Despite the larger proportion of GMVs among patients with suboptimal renal function on POD 30 (defined as eGFR $<$45 ml/min/1.73 m^2; Supplementary Table 1), at multivariable analysis, the only factor that was significantly associated with reduced renal function on POD 30 in our series was donor age. Neither donor- or recipient-related characteristics nor surgery-related variables, including case number (a *proxy* of learning curve), use of GMVs, and time for vascular anastomoses, were significantly associated with suboptimal renal function 1 mo after RAKT (Table 3). Due to the exploratory nature of our analysis, these findings need to be confirmed by larger studies in different clinical and healthcare scenarios.

Despite its novelty, our study is not devoid of limitations.

First, although data were prospectively collected, our study is retrospective with a limited sample size. Second, we could evaluate only *short-term* perioperative and functional outcomes after RAKT. Third, as this series included all consecutive RAKTs since the beginning of each center's experience, an inclusion bias may be present, with more favorable cases included in the dataset. Since RAKT was performed at referral high-volume centers by highly trained transplant teams, our findings might not be generalizable to all clinical scenarios.

Finally, results of multivariable analysis in our series should be interpreted as *hypothesis-generating* rather than definitive due to the relatively small sample size and the lack of information on all potential confounders.

These limitations acknowledged, our study represents a significant first step toward the standardization of surgical techniques of RAKT in case of GMVs and provides foundation for further research perspectives. In this regard, high-quality studies using appropriate designs [28] are needed to (1) confirm the outcomes of RAKT using GMVs in larger series with longer follow-up and in broader clinical scenarios, comparing its outcomes with those of *open* KT; (2) define the most appropriate ex vivo reconstruction techniques in case of GMVs to reduce CIT and RT during RAKT; (3) outline potential contraindications for RAKT in case of GMVs, selecting those patients most likely to experience complications and adverse functional outcomes; (4) evaluate technical feasibility and outcomes of RAKT using GMVs from *deceased* donors; (5) evaluate novel intra-abdominal cooling system devices to reduce ischemia-reperfusion injury [29] and specific biomarkers to monitor graft function after RAKT [30]; and (6) evaluate the mid-long-term functional outcomes of RAKT, focusing on predictors of DGF and suboptimal graft function.

5. Conclusions

This is the largest European multicenter study on RAKT from living donors using GMVs. In experienced hands, this procedure was technically feasible and achieved optimal perioperative and early functional outcomes that were comparable to those of RAKT using grafts with conventional vascular anatomy.

Larger studies with longer follow-up are needed to standardize the surgical technique and confirm the long-term safety of RAKT using GMVs.

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Study concept and design: Siena, Campi, Decaestecker, Breda, Serni.
Acquisition of data: Campi, Decaestecker, Sahin, Musquera, Territo, Randon, Janssen, Mohammed, Guirado, Facundo, Doumerc.
Analysis and interpretation of data: Campi, Siena, Decaestecker.
Drafting of the manuscript: Campi, Siena.
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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.euf.2018.07.022.

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