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REVIEW ARTICLE

Graft survival and postoperative complications following orthotopic renal transplantation

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Abstract

The iliac fossa is the most commonly used site to place the graft in renal transplantation in adults. However, iliac fossa may not be used in various conditions. Thus, orthotopic renal transplantation becomes a viable alternative for these selected patients. Given the technically challenging surgery and limited number of patients, data on the long-term outcomes on this regard are scarce. This narrative review serves as an update on the clinical outcomes after orthotopic renal transplantation, focusing on overall recipient survival and renal graft survival, as well as postoperative complications. We found that studies to date showed a comparable survival rate in both recipients and renal grafts in the postoperative follow-up period after orthotopic renal transplantation with a lower complication rate compared to the published data on heterotopic renal transplantation. The results of our review may encourage transplant centers to reevaluate their policies to consider orthotopic renal transplantation as an alternative technique in cases where heterotopic kidney transplantation is not possible.

KEYWORDS
heterotopic, kidney, orthotopic, renal, transplantation

1 | INTRODUCTION

Renal transplantation, if possible, is the most appropriate treatment option in patients with end-stage renal disease (ESRD) as it has superior short and long-term benefits for survival and quality of life compared to dialysis.[1,2] Indications for renal transplantation have gradually expanded in recent decades based on the development of immunosuppressive therapy and the improvement of the surgical technique since the first surgery that was performed in 1954.[3] From the beginning to day, iliac fossa has been the most commonly used location to place the graft. On the other hand, complex situations may be encountered in which it is not suitable to perform conventional heterotopic renal transplantation (HRT). These complex conditions include vascular alterations (e.g., atheromatosis, iliac or vena cava thrombosis), unsuitable pelvic veins for renal drainage, retained bilateral iliac fossa due to previous renal transplant, pelvic malformations, obesity or abnormalities of the lower urinary tract (e.g., urinary diversion).[2] In recent years, it has been emphasized that orthotopic renal transplantation (ORT) is a viable alternative for these patients who are not suitable for HRT, although the surgery is technically challenging.[4]

Even though ORT was initially developed as a surgical treatment for renovascular hypertension due to left renal artery stenosis in the 1970s, it has been used as an alternative to HRT for selected cases in limited centers depending on the surgical experience gained over time.[4,5] Nevertheless, there is controversy for this technique as there is limited data on the long-term outcomes in the literature.[4] Therefore, in this narrative review, our primary outcome was to observe overall recipient survival and overall renal graft survival in this special patient group undergoing ORT, whereas our secondary outcome was to assess postoperative complications (e.g., vascular, urinary, and others).

2 | MATERIALS AND METHODS

For the present narrative review, PubMed, Web of Science, Scopus, and Google Scholar databases were searched to identify all reports published on ORT up to April 2023. The keywords used in our search strategy were followings: (orthotopic kidney transplant OR orthotopic renal transplant OR orthotopic kidney graft transplant OR orthotopic renal graft transplant) AND (survival OR overall survival OR complication OR adverse effect OR adverse event). Additionally, the clinical trial registries and relevant abstracts presented at annual conferences including the European Association of Urology and the American Urological Association were searched.

Observational studies with at least 1 month of postoperative clinical follow-up data for patients undergoing ORT were included in this narrative review. Single case reports, letters, editorials, replies from authors, systematic reviews and meeting abstracts were excluded from this analysis, while no language restrictions were applied. In addition, case series with a follow-up period of more than several years, although involving a small number of patients, were also included. The flowchart of included articles is shown in Figure 1.

Two independent investigators performed the initial screening based on the titles and abstracts of the papers to identify ineligible reports. The full-texts of potentially relevant reports were scanned based on pre-specified inclusion criteria. Disagreements on exclusions were resolved through consensus with the senior author. The following data were extracted from each article: study design, first author's name, publication year, number of patients, age, indications for ORT, type of donor, follow-up duration, surgical options for anastomosis, postoperative outcomes (overall recipient survival, overall renal graft survival, delayed graft function, complications), and other association measures.

3 | RESULTS

3.1 | Study selection and characteristics

After collecting a total of 820 publications, 109 articles remained after the elimination of the duplicates. Further, a total of 90 articles were excluded as per the study policy, and only 10 studies met the inclusion criteria (Figure 1). Full-text reviews were performed on ten articles comprising 269 patients for this narrative review.[1,2,5–12]

Six of the articles were from Spain, one from the United States, one from Germany, one from Canada, and one from Japan. These studies were published between 2001 and 2022. While gender was not specified in 123 patients, male predominance was found in the remaining population (111 male, 35 female). The mean age of the 269 patients included in this narrative review was 42.17 (range from 4.2 to 73.6) years. The demographic characteristics, etiologies of ESRD, indication of ORT, type of donor, and anastomosis techniques during ORT in these patients are shown in Table 1. In these studies, severe iliac atherosclerosis (56 of all 269 cases) appeared to be the main indication for ORT. However, Musquera et al.[2] performed ORT as an elective indication in a significant part (130/207) of their cases. The graft was obtained from deceased donors (54.6%) in most cases (147/269).

3.2 | Overall patient and graft survival

After analysis of these ten articles,[1,2,5–12] the average follow-up period of all 269 patients included in this narrative review was 196.7 months (16.3 years), while the patients provided by the study from Spain constituted the majority. Therefore, it was not possible to access overall survival rates beyond 1 year for all publications due to missing data. However, the survival outcomes regarding overall recipient survival and overall renal graft survival after ORT as well as the rates of delayed graft function and transplantectomy are described in Table 2.

3.3 | Surgical complications

Postoperative complication rates for 269 patients included in this narrative review are described in Table 2. The total rate of vascular

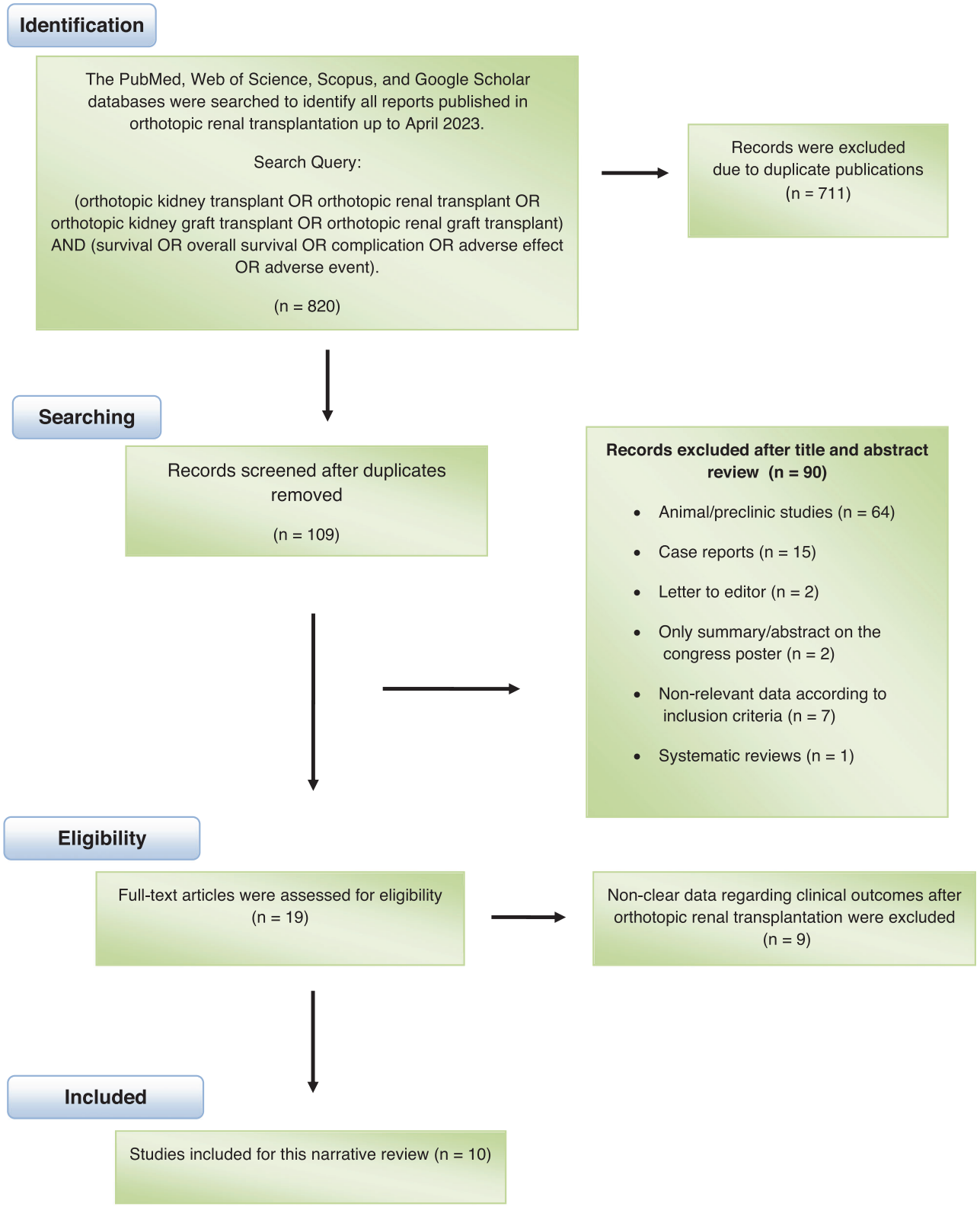

FIGURE 1 Flowchart of included articles.

TABLE 1 The demographic and clinical characteristics of patients in included studies.

Study	*n*	Age	Gender	Etiology of end-stage renal disease	Indication for orthotopic renal transplantation	Donor type
Musquera, 2020[1]	2	55 y (47–63)	2 M	- Unknown (2/2)	- Severe aortoiliac atheromatosis and bilateral iliac arterial stenosis (1/2) - Bilateral diffuse iliac atherosclerosis (1/2)	- Living donor (2/2)
Musquera, 2010[2]	207	40.34 y (4.2–73.6) - No data for remaining 123 patients	68 M/16 F	- Diabetic nephropathy (55/207) - No data for remaining 152 patients	- Elective surgery (130/207) - Severe iliac atherosclerosis (40/207) - Bilaterally retained iliac fossae from a previous kidney transplant (24/207)	- Living donor (84/207) - Deceased donor (123/207)
Hevia, 2015[5]	9	48.5 y (23.6–63.4)	7 M/2 F	- Interstitial nephropathy (4/9) - Glomerular pathology (2/9) - Unknown (3/9)	- Unsuitable iliac region (6/9) - Abnormalities in the low urinary tract or urinary diversions (3/9)	- Deceased donor (9/9)
Paduch, 2001[6]	5	56 y (47–69)	4 M/1 F	- Systemic lupus erythematosus (1/5) - Focal segmental glomerulosclerosis (1/5) - IgA nephropathy (2/5) - Diabetes mellitus (1/5)	- Bilateral severe iliac atherosclerosis (2/5) - Bilaterally retained iliac fossae from a previous kidney transplant (2/5) - Aortoiliac occlusion (1/5)	- Living donor (2/5) - Deceased donor (3/5)
Medina, 2022[7]	21	52.66 ± 13.99 y	16 M/5 F	- Diabetic nephropathy (4/21) - Interstitial nephritis (4/21) - Glomerulopathies (5/21) - Nephroangiosclerosis (1/21) - Cyclosporine nephropathy (1/21) - Renal dysplasia (1/21) - Secondary to obstructive uropathy or reflux nephropathy (2/21) - Unknown origin (3/21)	- Unsuitable iliac region due to vascular abnormality (12/21) - Unsuitable iliac region due to prior transplantations (4/21) - Unsuitable iliac region due to prior urinary diversions (5/21)	- Living donor (21/21)
Gutiérrez-Zurimendi, 2021[8]	3	49.6 y (42–55)	2 M/1 F	- Vascular nephropathy (3/3)	- Severe aortoiliac atheromatosis (3/3)	- Living donor (3/3)
Felgendreff, 2021[9]	7	54.14 ± 3.98 y	3 M/4 F	- Autosomal dominant polycystic kidney disease (7/7)	- Simultaneous liver and kidney transplantation (7/7)	- Living donor (7/7)
Chan, 2019[10]	3	55.6 y (44–69)	2 M/1 F	- Drug nephrotoxicity (1/3) - Obstructive uropathy (2/3)	- Inferior vena cava thrombosis (2/3) - Inferior vena cava stenosis/stent (1/3)	- Deceased donor (3/3)
Shishido, 2016[11]	6	9.3 y (5–15)	3 M/3 F	- Hypoplastic/dysplastic kidney (2/6) - Congenital nephrotic syndrome (1/6) - Autosomal recessive polycystic kidney (1/6) - Missing data (2/6)	- Unsuitable iliac region (6/6)	- Living donor (3/6) - Deceased donor (3/6)
De Gracia, 2007[12]	6	50.1 y (41–62)	4 M/2 F	- IgA nephropathy (1/6) - Diabetic nephropathy (2/6) - Tubulointerstitial nephropathy (2/6) - Nephroangiosclerosis (1/6)	- Severe iliac atherosclerosis (5/6) - Bilaterally retained iliac fossa from a previous kidney transplant (1/6)	- Deceased donor (6/6)

Abbreviations: y, year; M, male; F, female.

TABLE 2 Overall survival outcomes and postoperative complication rates following orthotopic kidney transplantation.

Postoperative outcomes	Musquera (2020)[1]	Musquera (2010)[2]	Hevia (2015)[5]	Paduch (2001)[6]	Medina (2022)[7]	Gutiérrez-Zurimendi (2021)[8]	Felgendreff (2021)[9]	Chan (2019)[10]	Shishido (2016)[11]	De Gracia (2007)[12]
Patient numbers	**2**	**207**	**9**	**5**	**21**	**3**	**7**	**3**	**6**	**6**
Survival outcomes										
Overall recipient survival	100% at 5 y	92.23% at 1 y 78.3% at 10 y 62.5% at 20 y	100 % at 1 y 66.6% at 5 y	100% at 6 mos.	84.9% at 1 y 66.6% at 5 y	100% at 5 y	100% at 3 mos.	100% at 3 y 66.6% at 5 y	100 % at 1 y	80% at 1 y
Overall renal graft survival	100% at 5 y	87.7% at 1 y 59.3% at 10 y 34.5% at 20 y	88.9% at 1 y 66.6% at 5 y	100% at 6 mos.	84.9% at 1 y 66.6% at 5 y	100% at 5 y	100% at 3 mos.	100% at 3 y 66.6% at 5 y	100 % at 1 y	80% at 1 y
Delayed graft function (*n*, %)	1 (50%)	0 (0%)	2 (22.2%)	1 (20%)	8 (38.1%)	0 (0%)	1 (14.2%)	1 (33.3%)	0 (0%)	0 (0%)
Transplantectomy (*n*, %)	0 (0%)	11 (5.3%)	0 (0%)	0 (0%)	3 (14.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Vascular complications										
Arterial stenosis	0	7 (3.3%)	0	0	0	0	0	0	0	2 (33.3%)
Arterial thrombosis	0	4 (1.9%)	1 (11.1%)	0	2 (9.5%)	0	0	0	0	0
Venous thrombosis	0	1 (4.8%)	0	0	0	0	0	0	0	0
Severe vascular rejection	0	5 (2.4%)	0	0	0	0	0	0	0	0
Others	0	2 (.9%) (unspecified)	1 (11.1%) (bleeding)	0	1 (4.7%) (hypoperfusion)	0	0	0	0	0
Urinary complications										
Urinary fistula	0	16 (7.7%)	0	0	1 (4.7%)	0	0	0	0	0
Ureteral stricture	0	2 (.9%)	1 (11.1%)	0	0	0	0	0	0	0
Acute urinary retention	0	0	0	0	2 (9.5%)	0	0	0	0	0
Vesicoureteral reflux	0	0	1 (11.1%)	0	0	0	0	0	0	0
Other complications										
Peri graft fluid collection	0	0	0	0	1 (4.7%)	0	0	0	0	0
Surgical site infection	0	0	0	0	1 (4.7%)	0	0	0	0	2 (33.3%)
Obstructive lymphocele	0	0	0	0	1 (4.7%)	0	0	0	0	0
Pancreatic fistula	0	0	1 (11.1%)	0	1 (4.7%)	0	0	0	0	0
Graft lithiasis	0	3 (1.4%)	0	0	0	0	0	0	0	0

Abbreviations: y, year; mos, months.

complication was 9.9% as follows: arterial stenosis (9/269), arterial thrombosis (7/269), severe vascular rejection (5/269), venous thrombosis (1/269), hypoperfusion (1/269), bleeding requiring transfusion (1/269), and others (2/269). On the other hand, the total rate of urinary complication was 8.5%. These included urinary fistula (17/269), ureteral stricture (3/269), acute urinary retention (2/269), and vesicoureteral reflux (1/269). Additionally, various other complications were reported at a much fewer rate (3.7%) such as surgical site infection (3/269), graft lithiasis (3/269), pancreatic fistula (2/269), obstructive lymphocele (1/269), and perigraft fluid collection (1/269).

4 | DISCUSSION

Despite the longer graft survival duration when compared to previous decades, there is a growing need for recurrent renal transplantation as both the pool and the need for renal transplantation increase.[13,14] Thus, a rise in both surgically and immunologically complex renal transplantations. Regarding secondary or tertiary renal transplantation, in challenging cases that are not feasible for HRT, ORT may be a useful approach to consider with promising graft outcomes in the lack of another surgical option despite a relatively high complication rate.[7] According to the proponents of this technique, ORT may simplify a subsequent third transplantation attempt when needed.[5] Additionally, it preserves the upper urinary tract with its normal physiology since the graft is placed in the relatively normal anatomical position.[2,5]

In the largest known ORT series to date, involving 207 patients between 1978 and 2009, no differences in overall patient survival at 20 years were reported between orthotopic and heterotopic renal transplants (62.5% vs. 65.9%; $p = .456$). Similarly, no significant difference was found in overall graft survival rates at 20 years between orthotopic and heterotopic renal transplants (34.5% vs. 29.2%; $p = .092$).[2] In this cohort, the study term was also divided into two periods: the first period from April 1978 to January 1987, and the second period from February 1987 to September 2009. However, a higher mortality rate was seen in cases included in the latter study period possibly due to the increasing selection of an older, unfit patient population as transplant candidates (40.7% vs. 33.3% at 20-year follow-up, $p = .031$, respectively). Nevertheless, this significant decrease in overall patient survival which was observed in the last period, was not observed in overall graft survival (35.9% vs. 30.3% at 20-year follow-up, $p = .22$, respectively).[2] In the more recent report of the same group, which also included the cases who underwent ORT until 2021, overall graft survival rates were 86%, 71%, and 68% at 1, 10, and 20 years, respectively, whereas overall patient survival rates were 92%, 66%, and 60% at 1, 10, and 20 years, respectively.[15]

Delayed graft function is one of the most important factors affecting overall graft survival. This rate was found to be 20%-21% in a few publications involving ORT cases.[4,16] In the present narrative review, an average rate of 23% ranging from 0% to 50% was observed for delayed graft function. However, risk factors for delayed graft function are multifactorial, including donor, recipient, and perioperative parameters.[17] Therefore, it is not possible to provide strong evidence because there is a lack of data in several studies on primary graft dysfunction.[17] Besides, it should be remembered that the definition of early graft dysfunction differs between institutions.

Although different alternatives of surgical techniques have been reported for vascular and urinary anastomoses, artery and vein anastomoses were performed mainly to the splenic artery and renal vein in most of the ORT cases of the last two decades, whereas urinary tract anastomosis was mainly pyelo-pyelic and pyelo-ureteral anastomosis.[2,15]

In several series of HRT, the rate of overall vascular complications was around 3%–15%.[16–18] Among these, the most frequently reported complications were as follows: arterial stenosis (2.8%), arterial thrombosis (2.1%), perirenal hematoma (1.5%), venous thrombosis (1.4%), hemorrhage (.8%).[19] In the studies related to ORT, arterial stenosis (3.6%–10%), arterial thrombosis (4.8%–6%), venous thrombosis (1.1%–6%), and severe vascular rejection (1.1%) were particularly reported as vascular complications, whereas the main postoperative urinary complications included urinary fistula (11%–15%).[2,4,15]

One of the latest systematic reviews in this topic revealed the overall patient survival as 92% (ranged from 88% to 95%), and the overall graft survival as 88% (ranged from 83% to 91%).[4] These survival rates are quite high, especially considering that patients undergoing ORT are at increased risk of mortality due to various comorbidities. It could be considered that the significant increase in these rates may be due to the developments in surgical techniques and medical treatments in the last decades regardless of the publication date of the studies. However, this review should be criticized for not specifying how many years the overall patient and graft survival rates have been. Further, this systematic review included only four papers published before 2014 whereas five more recent articles published in 2016 and later were added to our narrative review,[1,7–9] and similar survival rates at the postoperative 1st year were observed when compared to the previous studies.[2,11]

In the same systematic review comparing two transplantation techniques head-to-head, the rate of overall vascular complications following ORT was found to be slightly higher than those in HRT series (19% vs. 15%).[4] On the other hand, both ORT and HRT series had a similar rate of urinary complications, including ureteral obstruction/stenosis (11.9%–15%) and urinary fistulas (2%–15%).[15,20–22] According to our narrative review, total vascular and urinary complication rates in patients undergoing ORT (9.9% and 8.5%, respectively) were even lower than previously reported rates.

Other complications besides the vascular and urinary systems were even uncommon.[1,4,5] Graft lithiasis was present in 1.3% of ORT cases. Previous reports indicated successful treatment with ESWL or open pyelolithotomy.[2] Unlike HRT cases, a pancreatic leakage is a specific complication related to ORT. This condition may be caused by dissection of the splenic artery, which is close to the tail of the pancreas anatomically. In a case series of nine patients, one patient developed a pancreatic leakage and was initially treated with percutaneous drainage and finally underwent surgical pancreatic necrosectomy.[5] Compatible with previous reports, we found other complications at a much fewer rate (3.7%); these mainly included surgical site infection (1.1%), graft lithiasis (1.1%), and pancreatic fistula (.7%).

Clinical studies evaluating the surgical safety and efficacy of ORT are not common in the literature. Majority of the papers include case series with a small number (less than 5) and a short follow-up period (less than a few months).[2,4] The lack of data from clinical trials with long follow-up periods is main limitation of this review. Additionally, the high heterogeneity related to the surgical technique in publications on ORT may also affect clinical outcomes. This is another limitation that prevents us from reaching a robust interpretation. Besides, it should be remembered that there were no control groups and indication for carrying out an ORT was largely based on the preferences of the surgeons as an elective indication in the largest patient population included in the review (130 of 207 cases).[2]

In conclusion, results of this narrative review showed a comparable survival rate in both recipients and renal grafts following ORT with a lower complication rate compared to the data on HRT in the literature. Therefore, based on our findings, we conclude that all transplant candidates for whom HRT is impossible should have their vascular anatomy evaluated by CT angiography scanning before being removed from the transplant list, since ORT is a feasible, safe, and reproducible alternative for patients who are contraindicated for HRT.

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The authors declare that they have no relevant financial interests.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest and has nothing to disclose.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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