

Review – Renal Disease

Effectiveness and Harms of Using Kidneys with Small Renal Tumors from Deceased or Living Donors as a Source of Renal Transplantation: A Systematic Review

Vital Hevia^{a,*}, Rhana Hassan Zakri^b, Claire Fraser Taylor^c, Harman Maxim Bruins^d, Romain Boissier^{e,f}, Enrique Lledo^g, Heinz Regele^h, Klemens Buddeⁱ, Arnaldo Figueiredo^j, Alberto Breda^k, Cathy Yuhong Yuan^l, Jonathon Olsburgh^b

^a Urology Department, Hospital Universitario Ramón y Cajal, Alcalá University, Madrid, Spain; ^b Department of Urology and Transplant, Guy's & St Thomas' NHS Trust Hospitals, London, UK; ^c Department of Urology and Transplant, St Georges NHS Trust Hospitals, London, UK; ^d Department of Urology, Radboudumc, Nijmegen, The Netherlands; ^e Aix-Marseille University, Marseille, France; ^f Department of Urology & Renal Transplantation, La Conception University Hospital, Assistance-Publique Marseille, France; ^g Department of Urology, Hospital General Universitario Gregorio Marañón, Madrid, Spain; ^h Clinical Institute of Pathology, Medical University of Vienna, Vienna, Austria; ⁱ Department of Nephrology, Charité Medical University Berlin, Berlin, Germany; ^j Department of Urology and Renal Transplantation, Coimbra University Hospital, Coimbra, Portugal; ^k Department of Urology, Fundacion Puigvert, University Autònoma of Barcelona, Barcelona, Spain; ^l Department of Medicine, Health Science Centre, McMaster University, Hamilton, ON, Canada

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Abstract

Context: Kidney transplantation is the best treatment for patients with end-stage renal disease. Incidence of small renal masses (SRMs), which most frequently are renal cell carcinomas (RCCs), is highest in patients aged >60 yr. The increasing age of donors can lead to the diagnosis of a higher number of SRMs when assessing the patient for transplantation, and so can theoretically decrease the number of kidneys suitable for transplantation. Aiming to increase the pool of kidneys suitable for transplantation, a number of studies have reported their experience using kidneys with SRMs for transplantation.

Objective: To systematically review all available evidence on the effectiveness and harm of using kidneys with SRMs as a source of transplantation.

Evidence acquisition: A computerized bibliographic search of the Medline, Embase, and Cochrane databases was performed for all studies reporting outcomes of adult renal transplantation using kidneys with SRMs.

Evidence synthesis: Nineteen studies enrolling 109 patients were included and synthesized narratively. The mean recipient age was 44.2 yr, and kidneys used were retrieved from living donors in 86% (94/109) of cases. Tumor excision was performed *ex vivo* in all cases except for two. The vast majority of excised tumors were RCCs (88/109 patients), and clear-cell subtype was most common. The mean tumor size was 2 cm (range 0.5–6.0 cm) and tumor grade was G1–G2 in 93% (75/81) of patients. With a mean follow-up of 39.9 mo, overall survival rates at 1, 3, and 5 yr were 97.7%, 95.4%, and 92%, respectively, and the mean graft survival rates 99.2%, 95%, and 95.6%, respectively. Only one local relapse occurred 9 yr after transplantation, which was managed conservatively. Functional outcomes, although infrequently reported, appear to be similar to those of conventional transplants, with 1.6% of these patients needing reoperation.

Conclusions: The current literature, although with low-level evidence, suggests that kidneys with excised SRMs are an acceptable source of transplantation without

* Corresponding author. Urology Department, Hospital Universitario Ramón y Cajal, Ctra de Colmenar km 9,100, 28034 Madrid, Spain. Tel.: +34 913368760; Fax: +34 913368760. E-mail address: vital.hevia@salud.madrid.org (V. Hevia).

compromising oncological outcomes and with similar functional outcomes to other donor kidneys.

Patient summary: Renal transplantation using a kidney with a small renal mass does not appear to increase the risk of cancer recurrence and can be a good option for selected patients after appropriate counseling and allocation.

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1. Introduction

Kidney transplantation (KT) is the best treatment for patients with end-stage renal disease (ESRD). Unfortunately, it is not available to every patient with ESRD, mainly due to the increasing number of patients in the waiting list and the shortage of kidneys suitable for transplantation [1]. Dialysis has an important mortality risk, especially in elderly patients, which is approximately 6.3% per year for patients on the waiting list; moreover, patients who undergo a KT have better long-term survival compared with those receiving dialysis [2].

In the general population, renal cell carcinoma (RCC) constitutes 3% of all malignancies, with the incidence being highest in patients aged >60 yr. The current increasing age of donors may lead to a higher number of incidental RCCs found in donor kidneys and can theoretically decrease the number of kidneys suitable for transplantation. Several high-quality studies suggest that optimal treatment for localized RCC includes partial nephrectomy (PN), with similar oncological outcomes to radical nephrectomy but with better preservation of renal function [3].

Experience in transplanting kidneys from both living and deceased donors after ex vivo small renal mass (SRM) excision and consequent renorrhaphy has encouraging results [4–6], although PN surgical complications such as bleeding or urinary leak need to be assessed. The main surgical approach to these kidneys is ex vivo tumor excision on the back-table with an oncological margin, frozen section biopsy, bench surgery renorrhaphy, and finally transplantation in the conventional fashion. Although feasible, oncological safety of this procedure is controversial, as immunosuppression use may increase the risk of local recurrence compared with the general urology PN population. To date, there is no clear consensus on the oncological outcomes, surgical safety, or functional results of KTs after the excision of an SRM.

The aim of this study was to perform a systematic review (SR) to appraise all available evidence on the potential effectiveness and harm of transplanting kidneys with an excised SRM.

2. Evidence acquisition

2.1. Data sources and searches

This SR was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the PRISMA statement [7]. The protocol for the review was

uploaded in the PROSPERO database (<http://www.crd.york.ac.uk/PROSPERO>). Databases searched were Embase, Medline, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, and Health Technology Assessment Database. Initial search was performed covering all papers published until October 2015 and was subsequently updated with an additional search covering papers up to June 2017. No language or year restrictions were applied. The full search strategy can be found in the Supplementary material. Database search was complemented by screening the reference list in the included studies.

2.2. Study selection

Studies eligible for inclusion were those reporting the oncological and/or functional outcomes of patients who underwent KT with a kidney containing an SRM excised before transplantation. There was no restriction on the size of the renal mass. All study designs were eligible for inclusion except for reviews and studies published as a conference abstract only. All identified abstracts were placed in a bibliography management software program (EndNote X7), and sorted according to inclusion and exclusion folders by drag and drop. Titles and abstracts of all identified studies were independently reviewed by three authors (V.H., R.H.Z., and C.F.T.) and discrepancies were resolved by a fourth reviewer (M.B.). The level of evidence of every included study was assessed following the recommendations and statements issued in the European Association of Urology (EAU) guidelines, using the modification from the Oxford Centre for Evidence-based Medicine.

2.3. Data extraction and risk of bias assessment

Data from eligible reports were extracted independently (V.H., R.H.Z., and C.F.T.), and discrepancies were resolved by a fourth reviewer (M.B.). A data-abstraction sheet was created a priori including the year of publication, study type and its level of evidence, number of patients, gender, age (donor and recipient), follow-up, donor type (living/deceased), recipient time on dialysis, tumor excision (technique and number of tumors), histology, tumor size, surgical margins, overall survival (OS), graft survival (GS), recurrence-free survival (RFS), graft-intervention-free survival (GIFS), functional outcomes (delayed graft function [DGF] and acute rejection), and complications (according to the Clavien grading system). Risk of bias (RoB) assessment was performed independently (V.H., R.H.Z., and C.F.T.) using

the Cochrane RoB tool. Since non-randomized studies were included, this tool was extended with a list of five important potential confounders established by a panel of experts in the field (European Association of Urology Renal Transplantation Guidelines Panel) [8–10]. The confounders included were the following: time on dialysis, donor type, clinical-pathological stage, recipient age, and recipient comorbidities. For each study, it was assessed whether each confounder was considered and whether, if necessary, the confounder was controlled for in the analysis. The RoB was considered to be high if the confounder had not been considered, had been imbalanced between patients, or had not been corrected for during analysis. The RoB summary and graphic were computed in Review Manager 5.2 (Informatics and Knowledge Management Department, Cochrane, London, UK).

2.4. Data synthesis

Methodological and clinical heterogeneity of the included studies meant that meta-analysis was inappropriate; therefore, a narrative synthesis of the data was performed. Primary outcomes were OS, GS, RFS, GIFS, and

perioperative complications (<30 d). Secondary outcomes were DGF, acute rejection, and biopsy role (diagnostic performance).

3. Evidence synthesis

3.1. Search results

The search retrieved 504 articles; the abstracts of these articles were screened and 474 of these were excluded. A total of 30 full-text articles went on for eligibility assessment. Of these, 16 were excluded. After the update search and hand search of the reference lists of the included full-text papers, another five studies were included. Thus, a total of 19 studies were included in this SR (Figs. 1 and 2).

3.2. Characteristics of studies, population, and interventions

The 19 studies included a total of 109 patients (Table 1). One of the included studies was a nonrandomized controlled study [11], while the remaining 18 studies were retrospective comparative studies or case series/reports. The mean recipient age was 44.2 yr, and kidneys used were

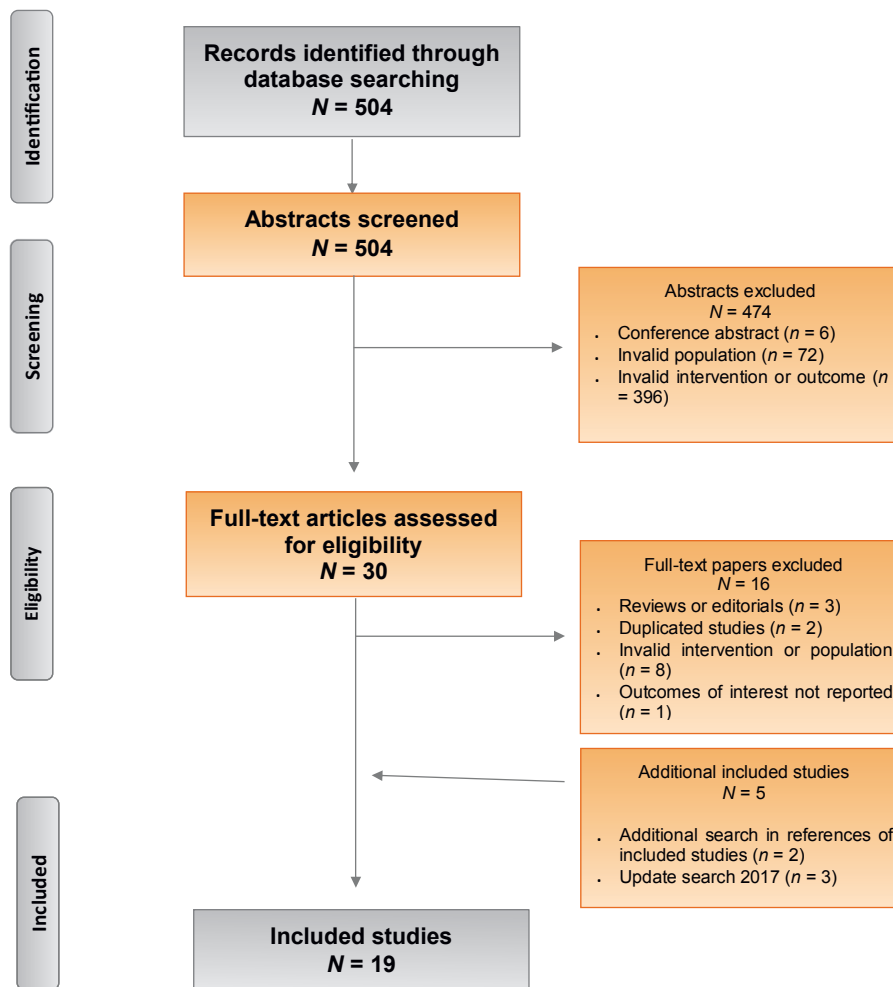


Fig. 1 – PRISMA flow chart.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias	A priori protocol	A priori analysis plan	Confounder: time on dialysis	Confounder: donor type (living vs deceased)	Confounder: clinical and pathological stage	Confounder: age of recipient	Confounder: recipient comorbidities or PS
Brook 2010	●	●	●	●	+	+	?	?	?	+	●	●	●	●
Ogawa 2015	●	●	●	●	+	+	?	?	?	+	●	●	+	●

Risk of bias summary: review authors' judgment about each risk of bias item for each included study (nonrandomized comparative studies).

Fig. 2 – Risk of bias summary for non-randomized comparative studies.

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retrieved from living donors in 86% (94/109) of cases. Tumor excision was performed ex vivo in all cases except for two. The vast majority of excised tumors were RCCs (88/109 patients), with the clear-cell subtype being most common, and tumor grade was G1–G2 in 93% (75/81) of patients. The most common benign tumor was angiomyolipoma. The mean tumor size was 2 cm (range 0.5–6.0 cm). Immunosuppression scheme was not properly reported in 72 patients (66%) and not needed in two, due to HLA-identical matching (monozygotic twins). Of the total 35 patients with immunosuppression reported, 14 (40%) received sirolimus-based therapies.

3.3. Oncological outcomes: recurrence and survival

Seventeen studies enrolling 107 patients were considered for oncological outcome assessment, and the results are summarized in Table 2. The mean follow-up period was 39.9 mo (range 12–96 mo). The mean OS rates at 1, 3, and 5 yr were 97.7%, 95.4%, and 92.0%, respectively. The mean GS rates at 1, 3, and 5 yr were 99.2%, 95%, and 95.6%, respectively. The RFS rate was 100% after 5 yr of follow-up; however, one local relapse occurred 9 yr after transplantation, which was treated with surveillance. GIFS at

1 yr was 97.9%. No differences in oncological outcomes were found related to different immunosuppression drugs used.

3.4. Non-oncological outcomes

Table 3 summarizes non-oncological outcomes. These outcomes were not reported in three studies and were not consistently reported in the remaining 16 studies. Of the patients for whom data are available, 1.8% had DGF, 26.5% suffered acute rejection, 1.6% needed reoperation, and 6.4% developed urinary leak. Mean creatinine levels at 1 mo and 1 yr were 1.59 and 1.56 mg/dl, respectively.

3.5. RoB and confounder assessment

RoB and confounder assessment was performed for all the included studies. The results were reported separately for comparative (Fig. 1) and noncomparative (Fig. 3) studies. None of the included studies were randomized; hence, all were at a high risk of selection bias, performance bias, and attrition bias. Regarding confounder assessment, the majority of the studies did not recognize or adjust for important confounding variables.

Table 1 – Descriptive data of population with a small renal mass prepared for donation and transplant.

Study	Study type	LOE	Recruitment period	N	Recipient mean age, yr (range or SD)	Country	Donor type		Tumor excision		Histology		Tumor size, cm (range)				
							Living	Deceased	Ex vivo	In vivo	Malignant	Benign		RCC subtype	Fuhrman grade		
Ogawa (2015) [11]	Nonrandomized trial	2b	2009–2012	10	65.3 (SD 10.2)	Japan	10	0	10	0	10	0	9 1	ccRCC Granular	9 1	G1–G2 G3–G4	3.2 (1.5–3.9)
Brook (2010) [12]	Retrospective case series	3	1996–2007	41	60.9	Australia	38	3	41	0	31	10	25 5 1	ccRCC pRCC crRCC	28 4	G1–G2 G3–G4	2.2 (1.0–2.9)
Lugo-Baruqui (2015) [16]	Retrospective case series	3	2009–2013	4	57.1 (20–79)	USA	4	0	4	0	4	0	2 1 1	ccRCC pRCC Multiloc	4 0	G1–G2 G3–G4	1.4 (0.9–2.5)
Musquera (2013) [6]	Retrospective case series	3	2007–2012	11	53.3 (38–73)	Spain	4	7	11	0	10	1	8 2	ccRCC crRCC	7 0	G1–G2 G3–G4	1.5 (0.3–4.3)
Sener (2009) [5]	Retrospective case series	3	1996–2008	5	54 (47–61)	USA	5	0	5	0	3	2	2 1	ccRCC pRCC	2 1	G1–G2 G3–G4	1.7 (1.0–2.3)
Mannami (2008) [17]	Retrospective case series	3	1991–2006	10	50.9 (28–69)	Japan	10	0	10	0	8	2	NR NR	NR NR	8 0	G1–G2 G3–G4	2.5 (1.2–3.5)
Buell (2005) [18]	Retrospective case series	3	NR	14	40.8 (SD 9.2)	USA	11	3	14	0	14	0	14	RCC	14	G1–G2 G3–G4	2.0 (0.5–4.0)
Lim (2016) [19]	Case report	3	NR	2	43 (34–52)	Korea	2	0	2	0	2	0	1 1	ccRCC pRCC	1 0	G1–G2 G3–G4	0.8 (0.7–0.9)
McGregor (2016) [20]	Case report	3	NR	1	NR	Canada	1	0	1	0	0	1	NA NA	NA NA	NA NA	NA NA	2.2
Nyame (2016) [21]	Case report	3	NR	1	NR	USA	1	0	1	0	0	1	NA NA	NA NA	NA NA	NA NA	2.6
Khurana (2013) [13]	Case report	3	NR	1	58	USA	0	1	0	1	1	0	1	ccRCC	1	G1–G2 G3–G4	1.5
Meyyapan (2012) [22]	Case report	3	NR	1	36	India	0	1	1	0	0	1	NA NA	NA NA	NA NA	NA NA	2.0
Abboudi (2012) [23]	Case report	3	NR	1	54	UK	1	0	1	0	0	1	NA NA	NA NA	NA NA	NA NA	6.0
Ali (2012) [24]	Case report	3	NR	2	64	UK	2	0	2	0	2	0	2	ccRCC	NR	NR	1.0 (0.5–1.4)
Johannes (2008) [14]	Case report	3	2006	1	55	USA	1	0	0	1	0	1	NA NA	NA NA	NA NA	NA NA	1.5
Dainys (2007) [25]	Case report	3	2001	1	38	Lithuania	1	0	1	0	1	0	1	ccRCC	1	G1–G2 G3–G4	2.0
Ghafari (2007) [15]	Case report	3	NR	1	12	Iran	1	0	1	0	1	0	NR NR	NR NR	NR NR	NR NR	0.5
Hetet (2004) [26]	Case report	3	2001	1	29	France	1	0	1	0	0	1	NA NA	NA NA	NA NA	NA NA	0.8
Stubenbord (1982) [27]	Case report	3	NR	1	43	USA	1	0	1	0	1	0	1	RCC (ossified)	NR	NR	3.0

ccRCC = clear-cell renal cell carcinoma; crRCC = chromophobe renal cell carcinoma; LOE = level of evidence; N = number of patients; NR = not reported; NA = not applicable; pRCC = papillary renal cell carcinoma; RCC = renal cell carcinoma; SD = standard deviation.

Table 2 – Oncological outcomes of included patients with a kidney transplant after small renal mass excision.

Study	N	IS scheme (I/M)	Mean follow-up, mo (range or SD)	Patient OS (%)			GS (%)			RFS (%)			GIFS (%)		
				1 yr	3 yr	5 yr	1 yr	3 yr	5 yr	1 yr	3 yr	5 yr	1 yr	3 yr	5 yr
Ogawa (2015) [11]	10	I: NR M: Tac-MMF-Pred	46.1 (32–58)	100	100	NR	100	100	NR	100	100	NR	100	100	NR
Brook (2010) [12]	41	NR	32	92	88	88	90	85	85	100	100	100 ^a	100	100	NR
Lugo-Baruqui (2015) [16]	4	I: thymoglobulin + basiliximab M: Tac-MMF-Pred	36	100	100	NR	100	75	NR	100	100	NR	100	100	NR
Musquera (2013) [6]	11	I: thymoglobulin M: Sir-MMF-Pred	32.3 (1–57)	100	NR	NR	100	NR	NR	100	NR	NR	75	NR	NR
Sener (2009) [5]	5	I: NR M: Tac-MMF-Pred	15 (1–41)	80	NR	NR	100	NR	NR	100	NR	NR	100	NR	NR
Mannami (2008) [17]	10	NR	54.1 (3–135)	90	71	71	NR	NR	NR	100	100	NR	100	100	NR
Buell (2005) [18]	14	NR	69 (14–200)	100	100	93	100	100	93	100	100	100	NR	NR	NR
Lim (2016) [19]	2	I: NR M: Sir	36	100	NR	NR	100	NR	NR	100	NR	NR	100	NR	NR
McGregor (2016) [20]	1	NR	12	100	NR	NR	100	NR	NR	100	NR	NR	100	NR	NR
Nyame (2016) [21]	1	NR	24	100	NR	NR	100	NR	NR	100	NR	NR	100	NR	NR
Abboudi (2012) [23]	1	I: basiliximab M: Tac-MMF-Pred	36	100	100	NR	100	100	NR	100	100	NR	100	100	NR
Ali (2012) [24]	2	NR	60 (48–72)	100	100	100	100	100	100	100	100	100	NR	NR	NR
Johannes (2008) [14]	1	NR	18	100	NR	NR	100	NR	NR	100	NR	NR	100	NR	NR
Dainys (2007) [25]	1	I: NR M: Sir	72	100	100	100	100	100	100	100	100	100	100	100	100
Ghafari (2007) [15]	1	I: NR M: Cyclo-MMF-Pred	15	100	NR	NR	100	NR	NR	100	NR	NR	100	NR	NR
Hetet (2004) [26]	1	NR	24	100	NR	NR	100	NR	NR	100	NR	NR	100	NR	NR
Stubenbord (1982) [27]	1	NR	96	100	100	100	100	100	100	100	100	100	100	100	100

Cyclo = cyclosporine; GIFS = graft-intervention-free survival; GS = graft survival; I = induction; IS = immunosuppression; M = maintenance; MMF = mycophenolate; N = number of patients; NR = not reported; OS = overall survival; Pred = prednisone/prednisolone; RFS = recurrence-free-survival; Sir = sirolimus; Tac = tacrolimus.

^a A recurrence is reported 9 yr after kidney transplant managed with surveillance.

Table 3 – Non-oncological outcomes of included patients with a kidney transplant after small renal mass excision.

Study	N	DGF (%)	Acute rejection (%)	Reoperation (%)	Urinary leak (%)	Creatinine (mg/dl)		eGFR (ml/min)		Biopsy method
						1 mo	Last	1 mo	Last	
Ogawa (2015) [11]	10	NR	80	0	0	NR	1.8	NR	NR	Frozen section + deferred
Brook (2010) [12]	41	NR	18.6	7	2.3	1.6	NR	NR	NR	Deferred
Lugo-Baruqui (2015) [16]	4	0	0	0	0	NR	1.4	NR	NR	Frozen section + deferred
Musquera (2013) [6]	11	NR	NR	18	0	1.4	1.2	NR	NR	Frozen section + deferred
Sener (2009) [5]	5	20	20	0	0	NR	NR	80.4	46.0	Frozen section + deferred
Mannami (2008) [17]	10	NR	NR	NR	NR	NR	NR	NR	NR	Frozen section + deferred
Buell (2005) [18]	14	NR	NR	NR	NR	NR	NR	NR	NR	NR
Lim (2016) [19]	2	0	0	0	0	NR	0.9	NR	NR	Frozen section + deferred
McGregor (2016) [20]	1	NR	NR	0	0	NR	1.2	NR	NR	Frozen section + deferred
Nyame (2016) [21]	1	0	0	0	0	NR	1.5	NR	NR	Frozen section + deferred
Khurana (2013) [13]	1	0	NR	0	0	2.5	NR	NR	NR	Frozen section + deferred
Meyyapan (2012) [22]	1	0	NR	0	0	NR	0.9	NR	NR	Deferred
Abboudi (2012) [23]	1	0	0	0	0	NR	1.8	NR	40	Frozen section + deferred
Ali (2012) [24]	2	NR	NR	NR	NR	NR	NR	NR	NR	Frozen section + deferred
Johannes (2008) [14]	1	0	100	0	0	1.5	NR	NR	NR	Frozen section + deferred
Dainys (2007) [25]	1	0	0	0	0	1.5	1.4	NR	NR	Frozen section + deferred
Ghafari (2007) [15]	1	NR	100	0	0	0.7	0.9	90	85	Frozen section + deferred
Hetet (2004) [26]	1	0	0	0	0	1.9	1.5	NR	NR	Frozen section + deferred
Stubenbord (1982) [27]	1	0	0	0	100	NR	1.9	NR	68	Frozen section + deferred

DGF = delayed graft function; eGFR = estimated glomerular filtrate rate; N = number of patients; NR = not reported.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias	A priori protocol	A priori analysis plan	Confounder: time on dialysis	Confounder: donor type (living vs deceased)	Confounder: Clinical and Pathological stage	Confounder: age of recipient	Confounder: recipient comorbidities or PS
Abboudi (2012)	⊖	⊖	⊖	⊖	⊖	⊖	⊖	⊖	⊖	?	⊖	⊖	⊖	⊖
Ali (2012)	⊖	⊖	⊖	⊖	⊖	⊖	?	⊖	⊖	?	⊖	⊖	?	⊖
Buell (2005)	⊖	⊖	⊖	⊖	⊖	⊖	?	⊖	⊖	?	⊖	⊖	⊖	⊖
Dainys (2007)	⊖	⊖	⊖	⊖	+	?	?	⊖	⊖	+	⊖	⊖	⊖	⊖
Ghafari (2007)	⊖	⊖	⊖	⊖	⊖	⊖	?	⊖	⊖	⊖	⊖	⊖	⊖	⊖
Hetet (2004)	⊖	⊖	⊖	⊖	⊖	⊖	⊖	⊖	⊖	?	⊖	⊖	⊖	⊖
Johannes (2008)	⊖	⊖	⊖	⊖	⊖	?	?	⊖	⊖	+	⊖	?	⊖	+
Khurana (2013)	⊖	⊖	⊖	⊖	⊖	+	⊖	⊖	⊖	?	?	⊖	⊖	⊖
Lim (2016)	⊖	⊖	⊖	⊖	⊖	⊖	?	⊖	⊖	?	⊖	⊖	⊖	?
Lugo (2015)	⊖	⊖	⊖	⊖	⊖	⊖	?	⊖	⊖	?	⊖	⊖	+	⊖
Mannami (2008)	⊖	⊖	⊖	⊖	?	?	⊖	⊖	⊖	?	⊖	⊖	⊖	⊖
McGregor (2016)	⊖	⊖	⊖	⊖	⊖	⊖	?	⊖	⊖	?	⊖	⊖	?	?
Meyyapan (2012)	⊖	⊖	⊖	⊖	⊖	+	⊖	⊖	⊖	?	?	⊖	⊖	⊖
Musquera (2013)	⊖	⊖	⊖	⊖	+	+	⊖	⊖	⊖	+	⊖	⊖	⊖	⊖
Nyame (2016)	⊖	⊖	⊖	⊖	⊖	⊖	?	⊖	⊖	?	⊖	⊖	?	⊖
Senner (2009)	⊖	⊖	⊖	⊖	?	+	?	⊖	⊖	?	⊖	⊖	⊖	⊖
Stubenbord (1982)	⊖	⊖	⊖	⊖	⊖	⊖	?	⊖	⊖	?	⊖	⊖	⊖	⊖

Fig. 3 – Risk of bias summary for non-comparative studies.

4. Discussion

4.1. Principal findings

This analysis has demonstrated 100% RFS at 1, 3, and 5 yr and excellent patient OS, suggesting that oncological outcomes are favorable.

Despite the theoretical higher risk of relapse related to immunosuppression, risk of renal tumor recurrence when transplanting a kidney with an excised SRM seems to be very low. Tumors included in this SR were low stage (T1a), with a mean size of 2 cm, and, in the vast majority of cases, were retrieved from living donors. The predominant size of all the lesions in the entire data set was <4 cm (except for one study showing a 6-cm lesion that turned out to have benign pathology). Despite a not very long follow-up period (39 mo), oncological outcomes seem to be quite safe, given that the vast majority were T1a, of low risk, and with 2 cm median size, as well as all of them had negative surgical margins. Immunosuppression regimes reported were very heterogeneous or even absent in some of the included studies. This SR demonstrates 100% RFS at 1, 3, and 5 yr and excellent patient OS, with only one local relapse (9 yr after transplantation) in a total of 109 patients. Although the role of immunosuppressive therapy could not be systematically addressed, immunosuppression appeared not to significantly increase the risk of local or distant tumor recurrence.

Functional outcomes including reported surgical complications, acute rejection, DGF, and renal function were more heterogeneous, and it was difficult to draw strong conclusions. The relevance of these outcomes is important; however, unless a significant portion of nephrons is excised, long-term graft function should be comparable. There appeared to be a relatively higher urinary leak rate compared with standard transplantation.

If electing to transplant a kidney from a deceased donor with a known and then subsequently excised SRM, it appears acceptable to transplant the unaffected kidney with ensuring follow-up, but the data in the report series specifically addressing this are very limited.

4.2. Findings in the context of existing evidence

Although KT is the best treatment for patients with ESRD, many patients remain on dialysis due to an important shortage in the donor pool. The incidental finding of an SRM is not uncommon in general population >60 yr old. If kidneys with incidentally discovered SRMs were to be routinely discarded, organ shortage would worsen further. Consequently, the question of whether a live donor with an identified SRM or a deceased donor with an incidental SRM can donate is of obvious importance. In this SR, data from OS, GS, and GFS are excellent with 100% RFS at 1, 3, and 5 yr and only one local relapse 9 yr after the transplantation, which was managed with surveillance for a further 18-mo follow-up at the time of publication. From an oncological point of view, and despite the study limitations, results are very reassuring [12].

4.2.1. Oncological outcomes

This SR has addressed neither the issue of the optimal diagnostic and management pathway for a potential living donor who is unexpectedly found to have an incidental SRM, nor any long-term risk to the living donor. There is increasing use of percutaneous diagnostic biopsy of SRMs with improved diagnostic yields providing better pathological diagnosis. Many SRMs can be confirmed as benign allowing the donor to safely donate. Equally, malignant SRMs can be assessed by grade in addition to stage. Whereas studies suggest that, in the general population, PN has long-term cardiovascular benefit compared with radical nephrectomy in T1a RCCs, potential living donors with an appropriate glomerular filtrate rate (GFR) are known to have similar life expectancy and cardiovascular risk after donation to age-matched people. Therefore, in appropriate potential living donors with an incidental low-grade (G1–G2) and T1a RCC, it appears safe to perform donor (radical) nephrectomy, excise *ex vivo*, and transplant without unnecessary harm to either the donor or the recipient.

Two SRMs were removed *in vivo*. One was from a living donor with a known lesion, which was performed as an open PN and then converted to donation once the pathology was made available [13]. The other was an angiomyolipoma removed after implantation [14]. The remaining and vast majority of lesions were dealt with *ex vivo* and on the back-table. From the available literature, performing *in vivo* surgery appears to have no advantage.

4.2.2. Non-oncological outcomes

The non-oncological outcomes were heterogeneously reported. In particular, renal function, either creatinine or estimated GFR, was often not presented. When excising SRMs, as well as good oncological outcomes sparing nephrons is beneficial. Various scoring systems have been established to help classify SRMs. The complication profile of a small exophytic lesion is very different from that of a deep endophytic hilar SRM. There was a reasonable reoperation rate in Brook et al's [12] series, and two urine leaks were likely to have been formed as a direct link to the excision surgery.

4.3. Implications for practice

The currently considered gold standard for an SRM includes PN. However, if an incidental lesion is found during living-donor assessment and renal function is adequate to donate the entire kidney anyway, total nephrectomy and *ex vivo* excision for transplantation may be suitable. Nevertheless, a small percentage of pT1a RCC SRMs may recur in the ipsilateral renal bed, and papillary cell subtype is known to be multifocal. Therefore, preoperative percutaneous biopsy to exclude grade 4 RCC and involvement of bench frozen section to ensure complete excision may be key diagnostic steps.

The optimal age for recipients of kidneys with excised SRMs needs consideration. In most of the larger studies, the mean recipient age was >60 yr [12]; however, in one paper by Ghafari [15], the recipient age ($n = 1$) was 12 yr. Inclusion

criteria for receiving a kidney with an excised SRM may include older patients, dialysis access issues, and high HLA (panel reactivity) antibody levels leading to reduced life expectancy. It is paramount to have well-consented, appropriately matched recipients for these specific kidneys.

When an incidental SRM is found at retrieval for deceased donors, these data would support the use of these kidneys depending on multiple factors, including specific donor features at the time of retrieval, the lesion itself, and recipient factors. Counseling of and consent from patients, while on the deceased donor waiting list, regarding these possibilities is good clinical practice. There were a large percentage of benign lesions in published series emphasizing the importance of urgent pathology reports to prevent loss of potentially useable kidneys for transplantation.

4.4. Implications for research

The length of follow-up for these studies is mostly of medium term. Brook et al [12] reported one recurrence at 9 yr, making transplanting in younger recipients theoretically riskier. When assessing whether it is safe to donate these kidneys to the recipient, matching and consenting are crucial. The limited data support the safe use of these kidneys when available, factoring in recipient informed consent at all times. Ideally, a European register of all KTs after excision of SRMs supported and led by the EAU appears to be an excellent route to clarify questions not answered in this SR.

4.5. Limitations of the study

This SR is the first assessing and appraising all the existing evidence in literature regarding KT using kidneys after the excision of an SRM. Despite the best available evidence to date, there were important limitations. The most important one is that the level of evidence of the individual studies ranged from level 2b to 3, and many were case reports. As a result, the RoB was considered high in many studies. In addition, functional outcome data were often lacking, insufficient, or not systematically reported.

5. Conclusions

Renal transplantation using kidneys with excised low-grade small renal tumors appears to be safe in terms of OS, GS, and oncological outcomes in appropriate transplant recipients. Despite the limitations of this study, data support the safe use of these kidneys when available, always factoring in informed consent of the potential recipient.

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Study concept and design: Hevia, Zakri, Taylor, Bruins, Boissier, Budde, Figueiredo, Lledo, Olsburgh, Regele, Breda.

Acquisition of data: Hevia, Zakri, Taylor, Boissier, Bruins, Yuan.

Analysis and interpretation of data: Hevia, Zakri, Taylor, Boissier, Bruins.

Drafting of the manuscript: Hevia.

Critical revision of the manuscript for important intellectual content: Hevia, Zakri, Taylor, Bruins, Boissier, Buddde, Figueiredo, Lledo, Olsburgh, Regele, Breda.

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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.2018.01.018>.

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