# Multiple Renal Arteries in Kidney Transplantation

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# Multiple Renal Arteries in Kidney Transplantation: A Systematic Review and Meta-Analysis

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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**Background:** The use of grafts with multiple renal arteries (MRA) in renal transplantation has not been clearly established.

**Material/Methods:** A systematic literature review used predefined terms to search PubMed, EMBASE, and the Cochrane Library for all studies since 1985 that included more than 50 MRA grafts. A total of 23 studies, comprising a total of 18,289 patients, were eligible to be included in the meta-analysis.

**Results:** Patients who received an MRA graft compared to single renal artery (SRA) grafts showed significantly higher complication rates (13.8% *vs.* 11.0%, OR 1.393, $p<0.0001$), more delayed graft function (10.3% *vs.* 8.2%, OR 1.333, $p=0.022$), and had an associated significantly lower 1-year graft survival (93.2% *vs.* 94.5%, OR 0.819, $p=0.034$). Both the creatinine level and the warm ischemia time (WIT) were significantly higher in patients with MRA grafts but showed high heterogeneity ($I^2$ 98% for WIT and $I^2$ 70% for creatinine level). Although MRA grafts were associated with more complications compared to SRA grafts, long-term outcomes were similar for 5-year graft survival (81.4% *vs.* 81.6%) and 1- and 5-year patient survival (95.4% and 89.6% in MRA group *vs.* 95.4% and 87.0% in SRA group, respectively).

**Conclusions:** MRA grafts were associated with a higher risk of complication and delayed graft function but had comparable long-term outcomes for graft and patient survival.

**MeSH Keywords:** Kidney Transplantation • Meta-Analysis • Renal Artery • Review

**Full-text PDF:** http://www.annalsoftransplantation.com/abstract/index/idArt/898748





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## Background

Kidney transplantation remains the treatment of choice in patients with end-stage renal disease and leads to improved survival and quality of life [1]. Because of a continuing shortage of donors there is a growing pressure to find suitable donor organs. Different strategies have been used to try to resolve donor shortage issues by extending donor criteria and establishing living donor programs [2,3]. In addition, minimally invasive techniques, such as hand-assisted laparoscopic live donor nephrectomy, have made it more attractive to potential donors to donate a kidney, which has led to an increase in the donor pool and overall graft quality [4]. In The Netherlands, every year about 950 patients receive a kidney transplantation, and >50% are procured by laparoscopic living donor nephrectomy [5].

The use of grafts with multiple renal arteries (MRA) is a potential risk factor that could impair the outcome of kidney transplantations. Autopsy studies have reported an incidence of 17–35% MRA grafts, depending on the donor ethnic origin [6]. However, the influence of MRA on graft outcome is not well established. Contradictory results have been reported in the literature; however a higher incidence of vascular complications, delayed graft function (DGF), and increased WIT are frequently reported in grafts with MRA [7–10]. A systematic review using a pooled results analysis is needed.

The aim of this meta-analysis was to provide a comprehensive systematic review of the current literature on the outcomes of kidney transplantations from any type of donor with MRA grafts compared to SRA grafts in terms of graft function, graft survival, and graft complication rates.

## Material and Methods

### Literature search, quality assessment, and registration

All studies published since 1985 that reported more than 50 MRA grafts were assessed for eligibility; all donor types were included. Smaller studies were excluded because of the increased risk for heterogeneity, as it is generally acknowledged that large studies yield the most reliable estimates. Studies were excluded when no comparison between SRA and MRA was made or when only donor outcomes were reported. Other exclusion criteria were papers written in a non-English language, non-human trials, combined pancreas-kidney transplantations, studies where no full text was available or text was only published in a supplement, and studies reporting on patients younger than 18 years of age.

Data collection and analysis were performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and Meta-analysis of Observational Studies in Epidemiology (MOOSE) checklist [11,12]. A systematic literature search with predefined search terms was performed using PubMed, EMBASE, and the Cochrane Library for articles and abstracts published from 1985 to July 2014. A librarian assisted with and verified our electronic search using the following strategy:

("kidney transplantation"[Mesh] OR "nephrectomy"[Mesh] OR kidney transplant*[tw] OR renal transplant*[tw] OR renal graft*[tw] OR renal allograft*[tw] OR kidney graft*[tw] OR kidney allograft*[tw] OR nephrectom*[tw] OR ((living don*[tw] OR live don*[tw]) AND (kidney*[tw] OR renal*[tw]))) AND (multiple arter*[tw] OR multiple renal arter*[tw] OR multiple renal vessel*[tw] OR vascular varia*[tw] OR multiple vessel*[tw] OR double arter*[tw] OR triple arter*[tw] OR (multiple[TI] AND arter*[TI]) OR (multiple[tw] AND (variat*[tw] OR variant*[tw]) AND (arteries[tw] OR artery[tw] OR vessel*[tw] OR vascular[tw]))) AND eng[la]) NOT ("Animals"[Mesh] NOT "Humans"[Mesh]). The search and inclusion procedure was performed independently by two authors (MZ and RP) and in case of disagreement, consensus was reached by discussion. Additionally, the "related articles" algorithm was used along with a manual cross-reference search of all bibliographies for relevant articles that had not been identified in the initial search. Data collection was carried out by one author (MZ) and the essential variables were collected in an electronic database (Microsoft Excel©). After completion of the database, the variables were converted to Comprehensive Meta-analysis© to perform the analysis. The following variables were collected: patients' characteristics (donor age, body mass index (BMI), type of donor), sample size, type of donor procurement, body side of donation, delayed graft function, graft and patient survival, reported complications (both vascular and urological), WIT, and creatinine levels. The primary endpoint was graft survival after one year and five years. Secondary outcomes were patient survival, complication rates, creatinine levels, and WIT.

A quality assessment was performed using the Newcastle Ottawa Scale (NOS) on all studies that met the aforementioned criteria [13]. The assessment was performed by two investigators (MZ and RP) and disagreements were resolved by discussion. Studies were compared based on selection, comparability, and outcomes. According to the NOS, the following factors were assessed in terms of comparability: donor age, recipient BMI, recipient gender, donor side, type of donor procurement, and HLA mismatch.

Patient and graft survival at one year and five years were analyzed. Delayed graft function was defined as the need for dialysis in the first week after transplantation. WIT was defined as the time after cold storage to reperfusion in the recipient, also known as the 2nd WIT. Studies were excluded for analysis if these definitions could not be reliably determined.



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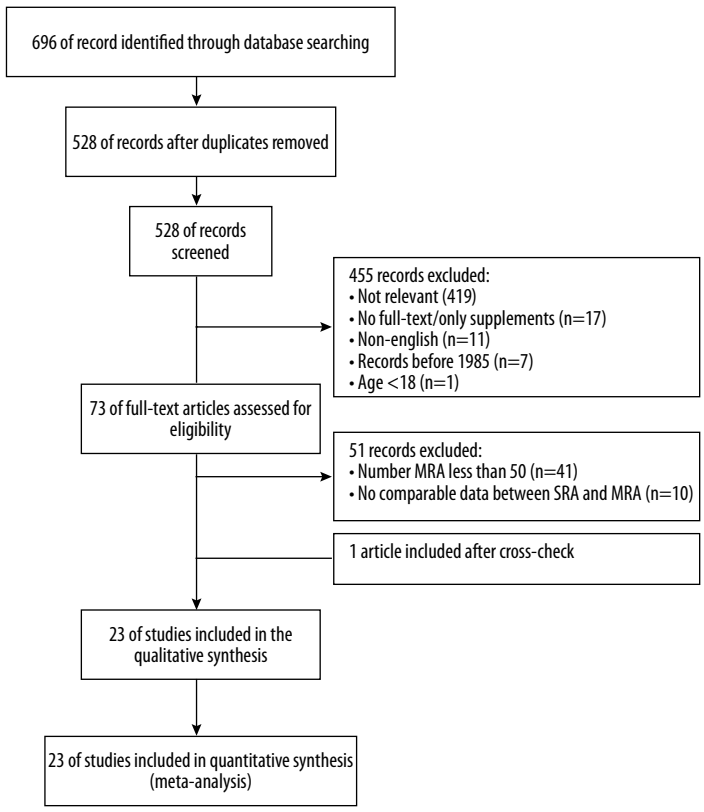


**Figure 1.** Study flow chart.

The overall complication rate was defined as any complication during or after transplantation excluding acute rejection, acute tubular necrosis, delayed graft function, new onset of hypertension, and postoperative hyperglycemia. Due to various late occurring complications (e.g., ureteral stenosis), follow-up time was noted for each study. When no follow-up period was described, the mean follow-up (SD and/or range) was used. A sub-analysis was performed for urological and vascular complications. Urological complications were defined as urinary or anastomotic leak, ureteral necrosis, fistulas, ureteral obstruction, ureteral stricture, and renal or bladder stones. Vascular complications were defined as arterial or venous thrombosis, transplant renal artery stenosis (TRAS), bleeding, hematoma, renal artery (pseudo) aneurysm, renal infarction, and lymphocele.

When studies described outcomes of multiple groups according to the number of arteries, the data were converted to SRA (1 artery, 1 anastomosis) and MRA (>1 artery, whether or not reconstructed to ≥1 anastomosis).

The study methods are described in a registered document, which is accessible at: *http://www.crd.york.ac.uk/PROSPERO/* (registration number: CRD42014013136).

### Statistical methods

A meta-analysis was performed for each endpoint if at least two studies could be combined. For dichotomous data (complications, DGF) odds ratio (OR) was used with 95% confidence intervals (CI). For continuous data (WIT and creatinine level), we calculated the mean difference (MD) with 95% CI. Heterogeneity among studies was tested by Higgins $I^2$ statistic and Cochran Q-test with a significant level of $p$=0.1. An $I^2$ <25% indicated a low heterogeneity, 25–50% indicated a moderate heterogeneity, and >50% a high chance of heterogeneity. In cases of statistical significant heterogeneity, a random effect model was used. All analyses were performed using Comprehensive Meta-Analysis version 2.2.064 (Biostat Inc., Englewood, NJ, USA).

## Results

### Methodological quality of included studies

Our systematic search of Pubmed, Embase, and Cochrane resulted in 696 hits and after removal of duplicates a total of 528 abstracts were screened for eligibility. After initial screening,



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**Table 1.** Study characteristics.

| Study | Sample size | Number of MRA (%) | Mean donor age (SD) | Mean BMI recipient (SD) | Type of donor procedure | % Right kidney donors | Deceased grafts included | Comparative groups |
|---|---|---|---|---|---|---|---|---|
| Hu 2014 [14] | 1195 | 308 (26) | 41 (11.1) | 25 (3.7) | LDN | 1.4 | No | None |
| Shedid 2013 [15] | 1134 | 210 (19) | 44 (35–51)* | 26.9 (23.7–31.7)* | HAL | 23.7 | No | SRA *vs.* MRA |
| Cooper 2013 [16] | 997 | 255 (26) | 40 (11) | ND | LDN/HAL | 3.1 | No | Gr I: SRA/Gr II: MRA 2 art/Gr III: MRA ≥ 3 |
| Kamali 2012 [17] | 718 | 60 (8.4) | 29 (6.8)/28 (8.4) | 23.9 (4.8)/24.8 (7) | ND | ND | No | SRA *vs.* MRA |
| Laouad 2012 [18] | 259 | 70 (27) | 38 (15.5)/42 (15.1)** | 24.1 (4.8) 23.7 (4.2) | Open | 46.7 | Yes (100%) | SRA *vs.* MRA |
| Cho 2012 [19] | 325 | 56 (17) | 39 (10.8)/38 (11.6) | ND | HAL | ND | No | SRA *vs.* MRA |
| Paragi 2011 [20] | 976 | 177 (18) | 41 (10.8)/41 (11.3) | ND | LDN | 2.8 | No | SRA *vs.* MRA |
| Tyson 2011 [21] | 510 | 117 (23) | 50 (ND)/48 (ND) | ND | LDN | ND | No | SRA *vs.* MRA |
| Soliman 2011 [22] | 2100 | 237 (11) | SRA <MRA*** | ND | Open | ND | No | SRA *vs.* MRA |
| Ghanzanfar 2010 [23] | 923 | 201 (22) | ND | ND | ND | ND | No | SRA *vs.* MRA |
| Hwang 2010 [24] | 1186 | 296 (25) | 33 (11.9)/39 (12.5)/ 37 (12.2)/35 (10.1) | ND | Open/LDN/ HAL | ND | Yes (16%)**** | Gr I: SRA/Gr II: MRA, 1 anastomosis/ Gr III: MRA, >1 anast. Gr IV: MRA, ligation polar art |
| Jafri 2009 [25] | 1250 | 120 (10) | 35 (8.5) | 22.7 (4.2)/22.3 (3.7) /24.5 (4.2) | ND | ND | No | SRA *vs.* MRA |
| Abbaszadeh 2009 [26] | 320 | 90 (28) | ND | ND | ND | ND | No | Gr I SRA/ Gr II MRA 2 art/ Gr III MRA >2 art |
| Paramesh 2009 [27] | 278 | 60 (22) | 38 (10.6)/38 (9.8) | ND | HAL | 2.2 | No | SRA *vs.* MRA |
| Kok 2008[28] | 288 | 60 (10) | 50 (14) | ND | LDN/Open | 54 | No | SRA *vs.* MRA |
| Mazzucchi 2005 [29] | 356 | 64 (18) | 41 (18–70)/ 39(18–70)# | ND | Open | ND | Yes (SRA 64% MRA 63%) | SRA *vs.* MRA |
| Başaran 2004 [30] | 1095 | 79 (7) | ND/31 (2.3) | ND | ND | ND | Yes (SRA 17% MRA 23%) | SRA *vs.* MRA |
| Ali-El-Dein 2003 [31] | 1200 | 113 (9) | 35 (9,9) | ND | ND | ND | No | SRA *vs.* MRA |
| Makiyama 2003 [32] | 393 | 96 (24) | 54 (11.4)/52 (11) | ND | ND | ND | No | SRA *vs.* MRA |
| Hsu 2003 [33] | 353 | 76 (22) | 41.4 (17–74)/ 40.8 (18-69)/ 30 (19–39)# | ND | LDN | 5.7 | No | Gr I SRA/Gr II MRA 2 art/Gr III MRA >2 |
| Emiroğlu 2000 [34] | 935 | 74 (8) | ND | ND | ND | ND | Yes (SRA 17% MRA 20%) | SRA *vs.* MRA |
| Han 1998 [35] | 500 | 65 (13) | ND | ND | ND | ND | Yes**** | SRA *vs.* MRA |
| Benedetti 1995 [36] | 998 | 163 (16) | ND | ND | ND | ND | Yes (SRA 47% MRA 71%) | Gr I: SRA/Gr II: MRA, 1 anastomosis/ Gr III: MRA, >1 anast. |

SRA – single renal artery; MRA – multiple renal artery; LDN – laparoscopic donor nephrectomy; HAL – hand assisted laparoscopic nephrectomy. ND – no data available. # Mean (range). * Median (IQR). ** MRA donors were significant younger than SRA (p=0.03). *** Donor age was categorized into 4 groups, <30 years, 30–40, 41–50 and >50 years. Overall MRA donors were significant older than SRA (p=0,004). **** Deceased donor grafts were used but percentages of deceased grafts within the SRA and MRA cohorts could not be specified.



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**Table 2.** Newcastle Ottawa scale in cohort studies.

| Study | Selection* 0–2 | Comparability** 0–4 | Outcome*** 0–3 | Total 0–9 |
|---|---|---|---|---|
| Hu 2014 | 2 | 0 | 1 | 3 |
| Shedid 2013 | 2 | 3 | 2 | 7 |
| Cooper 2013 | 2 | 1 | 2 | 5 |
| Kamali 2012 | 1 | 3 | 2 | 6 |
| Laouad 2012 | 2 | 1 | 3 | 6 |
| Cho 2012 | 1 | 1 | 1 | 3 |
| Paragi 2011 | 2 | 2 | 3 | 7 |
| Tyson 2011 | 2 | 1 | 2 | 5 |
| Soliman 2011 | 2 | 1 | 2 | 5 |
| Ghanzanfar 2010 | 2 | 0 | 3 | 5 |
| Hwang 2010 | 2 | 2 | 2 | 6 |
| Jafri 2009 | 2 | 0 | 1 | 3 |
| Abbaszadeh 2009 | 2 | 1 | 2 | 5 |
| Paramesh 2009 | 2 | 1 | 2 | 5 |
| Kok 2008 | 2 | 2 | 2 | 6 |
| Mazzucchi 2005 | 2 | 0 | 1 | 3 |
| Başaran 2004 | 2 | 0 | 2 | 4 |
| Ali-El-Dein 2003 | 2 | 1 | 2 | 5 |
| Makiyama 2003 | 2 | 2 | 2 | 6 |
| Hsu 2003 | 2 | 0 | 1 | 3 |
| Emiroğlu 2000 | 2 | 0 | 2 | 4 |
| Han 1998 | 1 | 0 | 1 | 2 |
| Benedetti 1995 | 2 | 1 | 2 | 5 |

* A maximum of 2 points were given. One point was assigned when the exposed cohort is representative of the average patient with end stage renal failure and eligible for renal transplantation, one point when non-exposed cohort was drawn from the same community as exposed cohort ** 2 points were assigned for variables 1–3: Gender recipient, body mass index recipient, age donor. 2 points for 4–6: donor side, donor procurement (open or laparoscopic), HLA mismatch. In both cases, one point was given when one of the three variables was not reported, no points were assigned if the groups differed significantly *** 3 points were assigned, one for assessment of outcome, one for the length of follow-up (mean follow-up ≥1 year) and one of the adequacy of follow-up of cohorts (<20% lost to follow up).

111 articles were retrieved for full-text review. Of these manuscripts, a further 89 were excluded based on the aforementioned criteria (Figure 1). After cross-checking, which resulted in one additional article, a total of 23 articles were included in the analysis with a total of 18,289 patients. No studies were excluded based on the NOS analysis.

The incidence of MRA varied from 7–28% in this meta-analysis, which is in accordance with reports of 17–35% in autopsy studies [6]. All studies were retrospective cohort studies. The baseline study characteristics are shown in Table 1. Data on quality assessment are shown in Table 2.

**Graft survival**

The pooled 1-year graft survival was 93.2% in the MRA group and 94.5% in the SRA group (fixed OR 0.8, 95% CI 0.68–0.99, 17 studies, n=15,185, $p$=0.03) (Figure 2). There was no significant heterogeneity observed ($I^2$=16.9%, $p$=0.26), and the funnel plot showed no signs of publication bias (Figure 3). The 5-year graft survival was 81.4% in the MRA and 81.6% in the SRA group (random OR 0.8, 95% CI 0.70–1.04, 11 studies, n=10,217, $p$=0.11) (Figure 2). The heterogeneity was moderate but significant and therefore the random model was used. ($I^2$ 39.5%, $p$=0.09).

Sensitivity analysis that included exclusion of studies with deceased donor grafts showed similar results for 1- and 5-year graft survival. (fixed OR 0.7, 95% CI 0.59–0.93, $p$=0.01;



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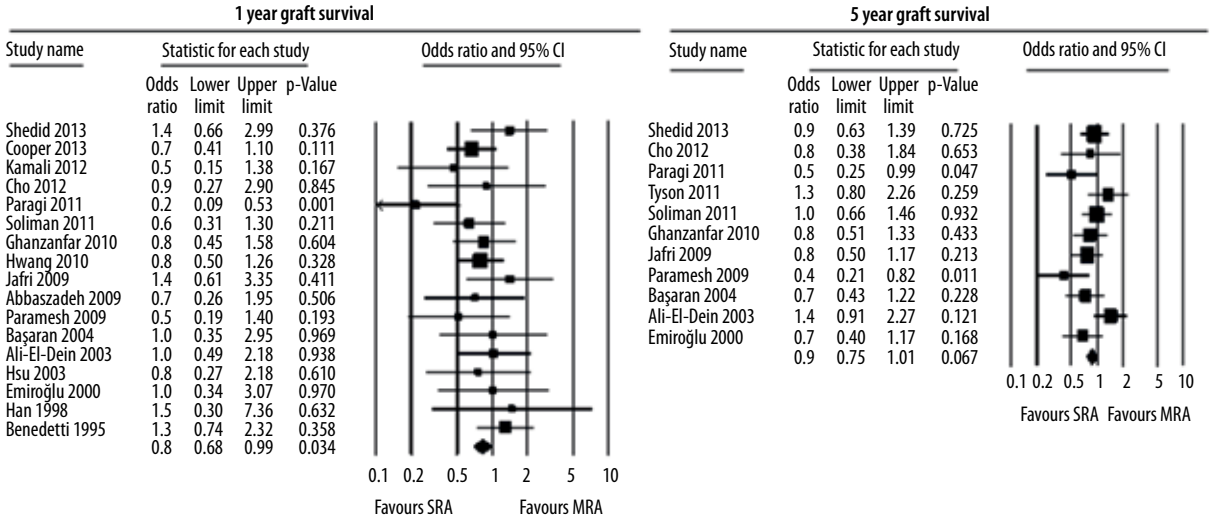


**Figure 2.** Forrest plots of 1- and 5-year graft survival. Comparison of the 1- and 5-year graft survival between grafts with single renal artery (SRA) and multiple renal arteries (MRA). Grafts with MRA showed a worse 1-year graft survival compared to SRA (OR 0.8, $p$=0.03), but the 5-year survival difference was insignificant (OR 0.9. $p$=0.07). Heterogeneity analysis of 1-year graft survival: Q=19.3, $p$=0.26. Heterogeneity analysis of 5-year graft survival: Q=16.5, $p$=0.09. The fixed model could be used because of low heterogeneity. Sizes of boxes represents study weights.

heterogeneity $I^2$=27.1%, $p$=0.18; 5-year: random OR 0.9, 95% CI 0.70–1.11, $p$=0.28; heterogeneity $I^2$=47.1%, $p$=0.06).

**Patient survival**

The 1- and 5-year patient survival rates were comparable between MRA and SRA grafts, (95.4% and 89.6% in the MRA group and 95.4% and 87.0% in the SRA group, respectively). The nine-study pooled OR for 1-year patient survival rate was 1.0 (95% CI 0.73–1.25, n=9,873, $p$=0.74) and the ten-study pooled 5-year patient survival rate was 1.2 (95% CI 0.99–1.43, n=10,465, $p$=0.07). No signs of heterogeneity were seen in 1- and 5-year patient survival rates ($I^2$=0%, $p$=0.49 and $I^2$=4.6%, $p$=0.40, respectively) (Figure 4).

Sensitivity analysis that excluded studies with deceased donor grafts showed similar results concerning the 1-year patient survival rate (fixed OR 1.0, 95% CI 0.72–1.51, $p$=0.84; heterogeneity: $I^2$=20.5%, $p$=0.28). The 5-year patient survival rate was significantly higher in the MRA group (fixed OR 1.3, 95% CI 1.04–1.63, $p$=0.02; heterogeneity: $I^2$=0%, $p$ = 0.72.) However, only 6 of 23 studies could be included in the sub-analysis regarding 5-year patient survival.

**Complication rate**

There was a significant difference in overall complication rates, with 13.8% in the MRA group compared to 11.0% in the SRA group (fixed OR 1.4, 95% CI 1.23–1.58 for 21 studies, n=16,720,

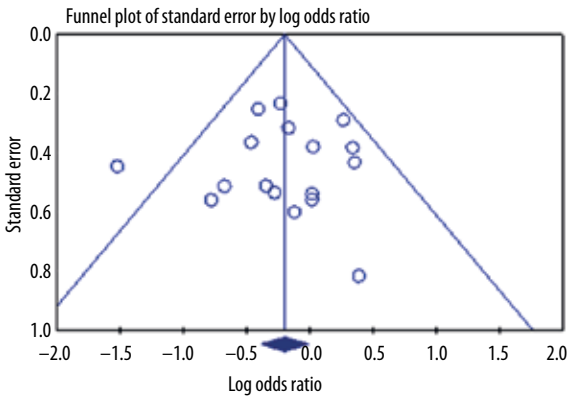


**Figure 3.** Funnel plot of 1-year graft survival. A funnel plot of 1-year graft survival rates was used to evaluate publication bias. Each dot represents a study which was included in the analysis of 1-year graft survival. A symmetrical distribution of studies shows no significant publication bias.

$p$<0.001) (Figure 5). No significant heterogeneity was observed ($I^2$=18.5%, $p$=0.22).

Recipients of an MRA graft showed a significantly higher incidence of vascular complications compared to those who received an SRA graft, 10.8% *vs.* 8.1%, respectively (fixed OR 1.6, 95% CI 1.37–1.94 for 14 studies, n=12,194, $p$<0.001). Again, no heterogeneity was observed ($I^2$=3.8%, $p$=0.401).



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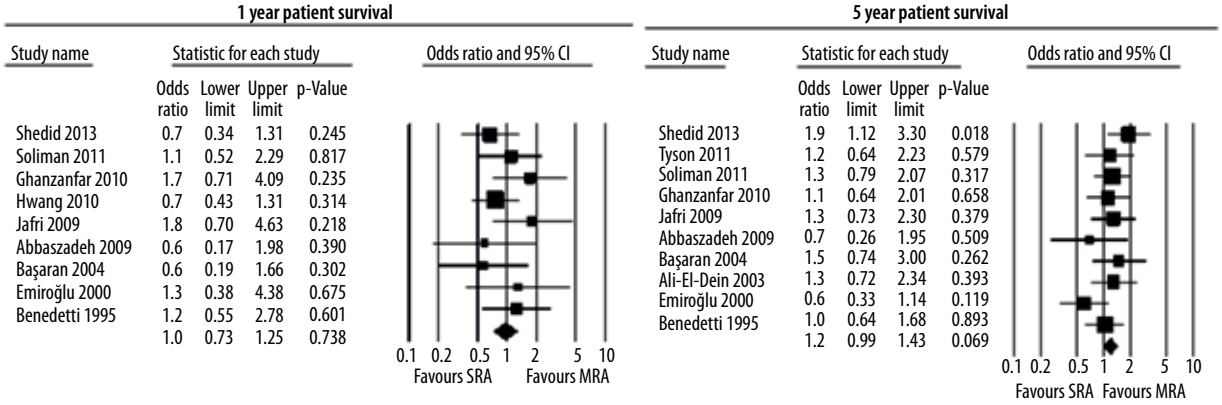


**Figure 4.** Forrest plots of 1- and 5-year patient survival. Comparison of the 1- and 5-year patient survival rates between grafts with single renal artery (SRA) and multiple renal arteries (MRA). There was no significant difference between SRA and MRA ($p$=0.74 and $p$=0.07). Heterogeneity of 1-year patient survival: Q=7.5, $p$=0.49. Heterogeneity of 5-year graft survival: Q=9.4, $p$=0.40. The fixed model could be used because of low heterogeneity. Sizes of boxes represents study weights.

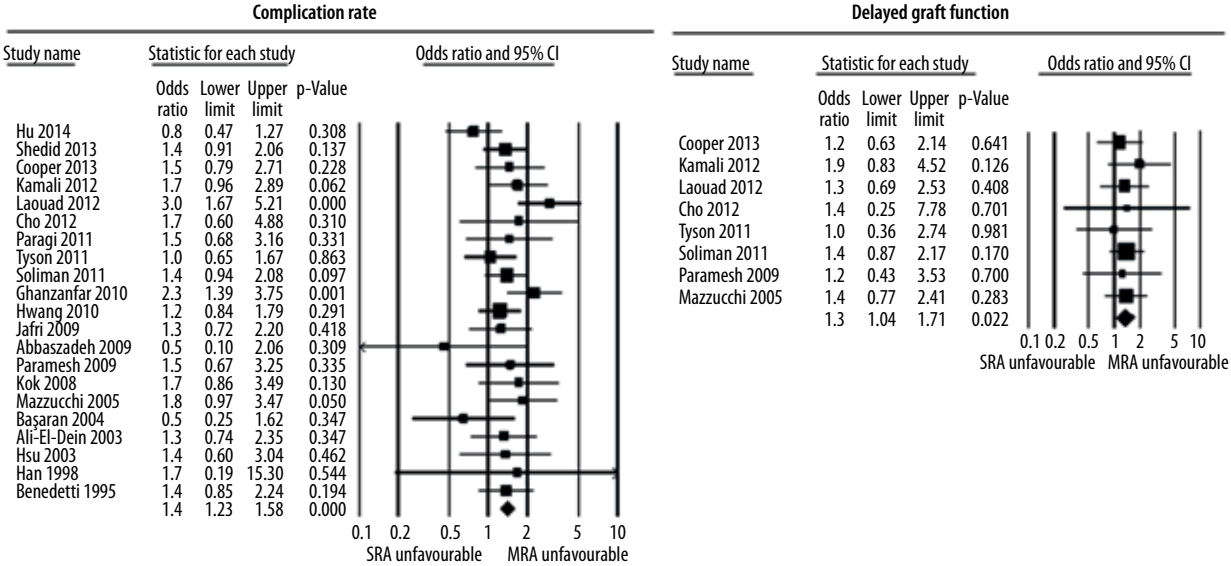


**Figure 5.** Forrest plots of complication rate and delayed graft function (DGF). Comparison of the complication rate (left) and DGF (right) between grafts with single renal artery (SRA) and multiple renal arteries (MRA). The complication rate was significantly higher in the MRA group compared to SRA (OR 1.4, $p$<0.001). The DGF was also significantly higher in the MRA group (OR 1.3, $p$=0.02). Heterogeneity of complication rate: Q=24.5, $p$=0.22. Heterogeneity of DGF: Q=1.3, $p$=0.99. The fixed model could be used because of low heterogeneity. Sizes of boxes represents study weights.

The incidence of urological complications was also higher in patients who received an MRA graft, 5.5% *vs.* 5% in SRA grafts (fixed OR 1.3, 95% CI 1.02–1.56 for 17 studies, n=13,855, $p$=0.03). No significant heterogeneity was observed ($I^2$=0.0%, $p$=0.87)

No sufficient data could be obtained concerning the time between transplantation and the occurrence of complications. Therefore, no further distinction could be made between early and late complications.

The overall complication rate remained the same after exclusion of studies with deceased donor grafts (fixed OR 1.4, 95% CI 1.17–1.57, $p$<0.001; heterogeneity: $I^2$=0%, $p$=0.47)



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### Delayed graft function

Delayed graft function (DGF) was described in eight studies. There was a small but significant difference in DGF in favor of the SRA group, 10.3% and 8.2%, respectively (fixed OR 1.3, 95% CI 1.04–1.71 for 8 studies, n=5,543, $p$=0.02). There was no significant heterogeneity ($I^2$=0%, $p$=0.99) (Figure 5). When excluding studies with deceased donor grafts there was no longer a significant difference between the MRA and the SRA groups (fixed OR 1.3, 95% CI 0.98–1.79, $p$=0.07; heterogeneity: $I^2$=0%, $p$=0.93).

### Creatinine level

The mean creatinine level after 1 year and 5 years was, respectively, 1.44 and 1.72 mg/dL in the MRA group, compared to 1.38 and 1.55 mg/dL in the SRA group. The overall mean difference was 0.059 mg/dL after 1 year (95% CI 0.01–0.11 for 13 studies, n=12,027, $p$=0.03) and 0.18 mg/dL after 5 years (95% CI 0.01–0.35 for 5 studies, n=5,393, $p$=0.04). The random effect model was used in both analyses because of the high rate of heterogeneity ($I^2$=70%, $p$<0.001 and $I^2$=73%, $p$=0.005).

### Warm ischemia time (WIT)

The mean WIT was 40 minutes in the MRA group and 32 minutes in the SRA group. The overall mean difference was 5.6 minutes (95% CI 1.92–9.23 for 8 studies, n=4,621, $p$<0.001). A random effect model was used because of extreme high heterogeneity ($I^2$=98%, $p$<0.001).

### Arterial reconstruction

Various techniques for arterial reconstruction in cases of MRA grafts were reported. In six studies, the type of arterial reconstruction was not clearly described [14,17,19,20,22,33]. In the remaining studies, different types of reconstruction were reported, but the outcomes were not stratified by type of arterial reconstruction, and this made pooled analysis not feasible. In 13 studies, ligation of accessory polar arteries was occasionally performed when arteries supplied less than <5–10% of the renal parenchyma. The reported incidence of ligation of accessory arteries in the MRA grafts was 1.6–20.5% [15,21–24,29,32,34] Two studies described ligation of lower polar arteries [21,24]. Six studies reported on whether a ureteral stent was placed during transplantation [15,17,18,20,27,29]. The time of removal of the stent varied from 3 days to 6 weeks. Most studies provided a sub-analysis based on the number of renal arteries and found similar results. However, data on grafts with >2 arteries were limited. Unfortunately, the available data did not allow for comparison of donor type (deceased versus living) in relation to the type of arterial reconstruction.

## Discussion

This study showed that kidney grafts from any type of donor with MRA were associated with a lower 1-year graft survival, a higher complication rate, and an increased frequency of DGF compared to SRA grafts. Both vascular as well as urological complications are more frequent in MRA grafts. However, no significant differences were observed in the 5-year graft survival and 1- and 5-year patient survival rates. Furthermore, there was a trend towards a longer WIT and higher 1- and 5-year creatinine levels in MRA grafts. Due to the high heterogeneity the statistical evidence of these variables was limited. With respect to WIT, this could be explained by the different definitions used in the literature and the inclusion of both open and laparoscopic donor procurement. To minimize this bias we only included studies that used the 2nd WIT, defined as the time after cold storage to reperfusion in the recipient [20–22,24,35]. It seems obvious that performing vascular anastomoses with a reconstructed renal artery entails an additional difficulty which is likely to prolong the 2nd WIT. In most studies, the actual arterial reconstruction was performed with the graft still on ice, therefore not adding to the WIT. Furthermore, accessory arteries which perfuse <5–10% of renal parenchyma were frequently ligated or anastomosed on a main artery *ex vivo*. Also, information on bench time and the actual size and number of MRAs could have influenced this analysis, but these data were unfortunately not available in most of the studies. These uncertainties probably caused a significant heterogeneity in the analysis of WIT.

In most cases of MRA grafts, the anastomoses were performed end-to-side or end-to-end onto the iliac vessels. In deceased donor grafts with MRA, an aortic patch was frequently used to avoid an individual reconstruction, a technique which is not possible after living donor procurement. Accessory arteries that vascularize less than 5–10% of the kidney are frequently ligated. In general, it is believed that ligation of lower pole accessory arteries could lead to ureteral ischemia or necrosis and should therefore be avoided. In two studies, lower pole artery ligation was described in which, remarkably, no increased complication rate was found [21,24]. However, contradictory results have also been reported in which ligation of these accessory lower pole arteries was associated with a significantly higher rate of urological complications [28].

Our analysis showed a trend of prolonged WIT in MRA grafts, as well as a significantly higher rate of DGF and impaired lower 1-year graft survival.

The high heterogeneity of creatinine levels was not surprising because the levels are influenced by many variables like rejection, complications, and especially immunosuppressive regimens, of which only 11 studies described the type of



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immunosuppressive therapy used [17,18,20,21,25,27,30–34] It therefore seems unlikely that differences in creatinine levels were caused by the number of renal arteries.

Next to ligating lower pole accessory arteries, another factor that could have influenced the rate of urological complications was the use of a ureteral stent. Previous meta-analyses showed that routine ureteric stenting decreased the rate of major urological complications [37,38]. The effect of the type of stent and the ideal time of removal are still unclear, and data from the included studies were too variable to come to a clear conclusion.

The most common vascular complications in MRA recipients were thrombosis and bleeding, which was most likely due to the complexity of an anastomosis with a reconstructed artery combined with the small diameters of accessory arteries, especially in cases where there was severe atherosclerosis in the recipient. Decent vascular screening of both donor and recipient is therefore unquestionable and will help to minimize the risk of both vascular and urological complications in renal transplantation. When considering potential living donors, kidneys with MRA should not be rejected based on the number of arteries because the long-term outcomes may be excellent.

This study has a few limitations that need to be addressed. Unfortunately, no randomized controlled trial comparing MRA and SRA grafts was available for inclusion and probably will never be established. Also, we included only studies with more than 50 patients with MRA grafts. We believe this was a justified choice, as it is generally acknowledged that larger studies yield the most reliable results and a lower level of heterogeneity. Despite the fact that we excluded non-English manuscripts, we believe the language bias that has occurred is minimal, because the included studies were performed in a variety of countries worldwide and represent a global experience. Also, we did not have access to the raw data, making a formal pooled analysis not possible. Unfortunately, no sub-analysis could be made between grafts which were procured by a laparoscopic or open technique or by the type of donor because of the lack of such data in the selected studies. However, a previous randomized controlled trial [39] showed similar outcomes between open and laparoscopic procurement, suggesting that the effect of this on our study was probably limited.

Whereas long-term outcomes are similar for grafts from donors who died from cardiac or brain causes, the long-term outcomes for grafts from living donors are known to be superior compared to grafts from deceased donors. This important difference could have induced bias [40]. However, in an attempt to correct for this we conducted a sensitivity analysis in which we excluded all studies with deceased donors. This resulted in a higher complication rate and lower 1-year graft survival in grafts with MRA. The DGF rate was lower for SRA grafts but proved not significant in the final analysis ($p$=0.07). The 5-year patient survival rate was significantly better in the MRA group. However, only 25% of the studies could be included in this analysis, making the outcome very unreliable. Finally, a pooled analysis on a large patient population results in small but statistically significant differences. We are fully aware that some of the outcomes are therefore less relevant to daily practice.

## Conclusions

This meta-analysis demonstrated that grafts with MRA were associated with a higher risk of complication and DGF, but had comparable long-term outcomes in terms of graft and patient survival rates. For this reason, the presence of MRA in a living kidney donation should be a contributing factor in the decision regarding which kidney is best suited for donation.

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