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Original Article

Global prevalence and contributing factors of transplant renal artery stenosis in renal transplant recipients: A systematic review and meta-analysis

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Abstract

Transplant renal artery stenosis (TRAS) is a serious complication of renal transplantation, with its prevalence and associated factors remaining inconclusive. The aim of this study was to assess the global prevalence and risk factors associated with TRAS incidence in renal transplant recipients. We conducted a meta-analysis by collecting data on the prevalence and factors associated with TRAS from articles in Scopus, Embase, and PubMed. The prevalence of TRAS was determined using a single-arm meta-analysis. The factors associated with TRAS were determined using Mantel-Haenszel analysis or inverse variance analysis. Out of 28,599 articles from the searches, 31 of them were included in the analysis. The global prevalence of TRAS was 6% among renal transplant recipients. Diabetes mellitus, hypertension, longer duration of dialysis before transplant, deceased donor, acute rejection, delayed graft function, longer cold ischemic time, and prolonged peak systolic velocity were associated with an increased risk of TRAS. Age, sex, peripheral artery disease (PAD) comorbidity, causes of end-stage renal disease (ESRD), previous dialysis modality, and cytomegalovirus infection were not associated with TRAS incidence. In conclusion, the global prevalence of TRAS in renal transplant recipients is relatively high, and some of the contributing factors to the development of TRAS are preventable. These findings could serve as a guideline for informing the management of TRAS in the future.

Keywords: Renal transplant, transplant renal artery stenosis, prevalence, risk factor, meta-analysis

Introduction

End-stage renal disease (ESRD) remains a significant health problem, with a prevalence rate of 759 per million population [1]. In 2022, the United States had the highest number of patients, with 709,501 individuals or approximately 29% of the global ESRD patient population [1]. The

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mortality rate of ESRD is also quite high, with an annual mortality rate reaching 128 per 100,000 population [2,3]. The high prevalence and mortality rates of ESRD are of great concern because the management of ESRD remains an unresolved challenge to this day. Currently, the main therapeutic modality for ESRD is dialysis; however, this therapy is not a definitive solution. This has a significant impact on the economic burden and health insurance [4,5]. Currently, the definitive therapy for ESRD is kidney transplantation. However, kidney transplantation is not a completely safe procedure, as there are many potential complications, such as graft rejection, infection, incompatibility, and transplant renal artery stenosis (TRAS) [6]. Among these complications, TRAS is a particularly challenging phenomenon because it can accompany other complications. Cytomegalovirus (CMV) infection, acute rejection, and delayed graft function have been reported to be associated with the occurrence of TRAS [7]. Given this situation, it is important to conduct studies to evaluate the prevalence of TRAS.

TRAS is defined as the narrowing of the renal artery in a transplanted kidney, which can impede blood flow to the graft. TRAS is recognized as a vascular complication following kidney transplantation, affecting approximately 1% to 23% of transplant recipients [8]. The clinical manifestations of TRAS typically include worsening or new-onset hypertension, graft dysfunction, fluid retention, and potentially flash pulmonary edema [9]. For diagnosing TRAS, imaging studies, particularly angiography, are considered the gold standard as they provide detailed visualization of the renal arteries [10]. Additionally, non-invasive imaging modalities such as color Doppler ultrasonography and magnetic resonance angiography (MRA) can also be used to detect potential stenosis [9]. The complications of TRAS are very serious. If not properly managed, TRAS can lead to significant morbidity and mortality, ultimately resulting in allograft loss [6,11]. Due to the severity of these complications, it is crucial to conduct a more detailed identification of TRAS, including determining the risk factors of its incidence. To date, many studies have been conducted to evaluate the prevalence and factors associated with TRAS [7,12-41]. However, the results of these studies remain inconclusive. Therefore, the aim of this study was to identify the prevalence of TRAS and the risk factors that may contribute to its development in kidney transplant recipients using a systematic review and meta-analysis approach. The results of this systematic review are expected to serve as a guideline for evaluating TRAS management in the future.

Methods

Study design

A systematic review and meta-analysis were conducted to collect data on the prevalence and potential risk factors of TRAS incidence in renal transplant recipients. The purpose of this data analysis was to determine cumulative point estimates. The study was carried out between July and August 2024. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guideline [42] was used to guide the study to ensure transparency and methodological rigorousness. The study has been registered on PROSPERO under registration number CRD42024543720.

Eligibility criteria

All articles with observational study designs (cross-sectional, case-control, and prospective studies) that evaluated the prevalence and risk factors of TRAS incidence in renal transplant recipients were considered eligible. Articles were required to have complete data for calculating cumulative point estimates and to be written in English. Irrelevant studies based on their title and/or abstract, as well as reviews or commentaries, were excluded from the study.

Search strategy

Three databases (PubMed, Embase, and Scopus) were used to systematically search for eligible studies as of August 20, 2024. A combination of the keywords was used to identify potential studies: "TRAS" or "transplant renal artery stenosis" and "renal transplant" along with "prevalence" and "risk factor" or "predictor" or "determinant." These keywords were adapted from the Medical Subject Headings (MeSH). Additionally, potential articles were searched through the reference lists of related articles.

Data extraction

Important information was extracted from each article, including the name of the principal investigator, year of publication, study location, study design, age of participants, TRAS diagnosis, outcomes, and sample size of cases and controls. Data extraction was carried out by investigators (FT, CG, RSW, ART, FNH, FRS, JAD, IEP, MAS, RP, MD, YF, and TMA). The investigators involved in data extraction independently collected the data within the specified timeframe, and the results of the data extraction were discussed. In cases of data discrepancies, resolution involved discussion with a senior researcher (JKF).

Quality assessment

The Newcastle-Ottawa Scale was used to assess the quality of the included studies. The components of this tool included sample selection, group comparability, and outcome or exposure, with the total scores ranging between 0 and 8. The interpretation of these scores was as follows: an article with a score between 0–3 was considered low quality, a score between 4–6 was considered moderate quality, and a score between 7–8 was considered high quality [43]. The assessment was conducted by FT, CG, RSW, ART, FNH, FRS, JAD, IEP, MAS, RP, MD, YF, and TMA. In conducting the article quality assessment, these investigators were divided into two teams. Team 1 consisted of FT, CG, RSW, ART, FNH, and FRS, while Team 2 included JAD, IEP, MAS, RP, MD, YF, and TMA. These teams evaluated the same number of articles, and the results were re-evaluated through a discussion. In case of discrepancy in the quality assessment, resolution was achieved through discussion with a senior researcher (JKF).

Study variables

The outcome of this study was the incidence of TRAS. Meanwhile, the risk factors included age, sex, comorbidities, cause of ESRD, duration of dialysis before transplantation, previous dialysis modality, type of donor, CMV infection, acute rejection, delayed graft function, cold ischemic time, and peak systolic velocity. These risk factors were determined after data collection, and it was ensured that each variable had complete data for analysis.

Statistical analysis

The stages of data analysis included assessing potential publication bias, potential heterogeneity, and the main findings, along with point estimates. First, for publication bias analysis, Egger's test and a funnel plot were used. A *p*-value from Egger's test (*p*-Egger) <0.05 and an asymmetric funnel plot indicated potential publication bias. If the data suggested potential publication bias, point estimates were adjusted using the trim-and-fill method [44]. Second, for heterogeneity analysis, the I-squared (I^2) and Q statistic were used. A *p*-value for heterogeneity (*p*-Het) <0.10 or I^2 ≥50% indicated potential heterogeneity. If heterogeneity was found, point estimates were calculated using a random-effects model; otherwise, a fixed-effects model was used [45]. Third, the single-arm meta-analysis was used to determine the global prevalence of TRAS among renal transplant recipients. Cumulative prevalence point estimates were presented as event rates along with 95% confidence intervals (95%CIs). To determine risk factors for TRAS incidence, the Mantel-Haenszel test for dichotomous variables and inverse variance for continuous variables were used. Risk factors point estimates were presented as odds ratios (ORs) for categorical variables and mean differences (MDs) for numerical variables, with 95%CIs [46]. Cumulative point estimates were presented in the form of a forest plot. The GraphPad Prism (GraphPad Software, Boston, MA) and Comprehensive Meta-analysis 2.0 software (CMA, New Jersey, USA) were used for data analysis.

Results

Article selection

The systematic search yielded 28,599 articles from the databases. From these, 172 articles were excluded due to duplication and 28,364 articles were excluded due to irrelevant topics and abstracts. Subsequently, 63 articles were included in the full-text analysis. Of these 63 articles, seven were excluded due to incomplete data and 25 were excluded because they were reviews. Therefore, 31 articles [7,12-41] were included in the final analysis. The study selection flowchart,

according to the PRISMA, is presented in **Figure 1**. The characteristics of the articles included in the study are presented in **Table 1**.

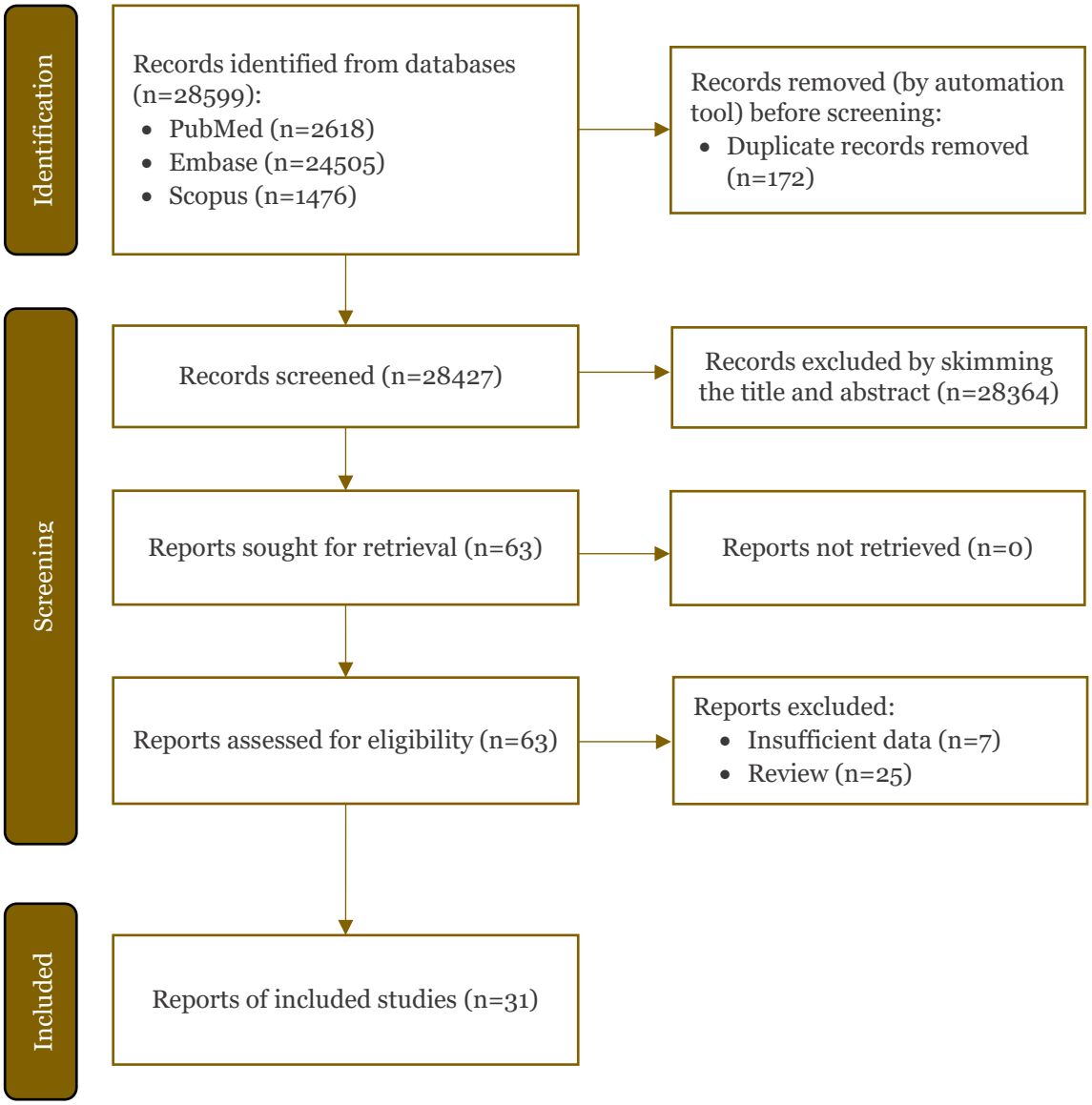

Figure 1. A flowchart of article selection in our study.

Prevalence of TRAS in renal transplant recipients

To determine the cumulative prevalence of TRAS among renal transplant recipients, we included 28 articles [7,13-20,22-34,36-41]. Our data showed that the global prevalence of TRAS among renal transplant recipients was 6% (95%CI: 4–9%; *p*-Egger: 0.0968; *p*-Het: <0.0001; overall *p*-value: <0.0001) (**Figure 2**).

Factors associated with TRAS incidence among renal transplant recipients

The risk factors analyzed in this meta-analysis included age, sex, comorbidities, cause of ESRD, duration of dialysis before transplantation, previous dialysis modality, type of donor, CMV infection, acute rejection, delayed graft function, cold ischemic time, and peak systolic velocity. Our study identified several factors associated with TRAS incidence: having diabetes mellitus (OR: 1.24; 95%CI: 1.09–1.42; *p*-Egger: 0.0227; *p*-Het: 0.1170; overall *p*-value: <0.0001) (**Figure 3A**), hypertension (OR: 1.27; 95%CI: 1.09–1.47; *p*-Egger: 0.4982; *p*-Het: 0.4450; overall *p*-value: 0.0020) (**Figure 3B**), longer dialysis duration before transplantation (MD: 3.98; 95%CI: 0.59–7.37; *p*-Egger: 0.3435; *p*-Het: 0.5950; overall *p*-value: 0.0210) (**Figure 3C**), and receiving a deceased donor (OR: 1.98; 95%CI: 1.10–3.57; *p*-Egger: 0.0849; *p*-Het: <0.0001; overall *p*-value: 0.0240) (**Figure 3D**).

In addition, acute rejection (OR: 1.83; 95%CI: 1.15–2.90; *p*-Egger: 0.6942; *p*-Het: 0.5720; overall *p*-value: 0.0110) (**Figure 3E**), delayed graft function (OR: 1.97; 95%CI: 1.24–3.12; *p*-Egger: 0.0710; *p*-Het: 0.0250; overall *p*-value: 0.0040) (**Figure 3F**), longer cold ischemic time (MD: 4.35; 95%CI: 3.74–4.96; *p*-Egger: 0.4826; *p*-Het: 0.7480; overall *p*-value: <0.0001) (**Figure 3G**), and higher peak systolic velocity (MD: 1.38; 95%CI: 0.73–2.02; *p*-Egger: 0.5573; *p*-Het: <0.0001; overall *p*-value: <0.0001) (**Figure 3H**) were also associated with TRAS incidence. Meanwhile, renal transplant recipients who received a living donor had a reduced risk of TRAS compared to those who received a deceased donor (OR: 0.51; 95%CI: 0.28–0.91; *p*-Egger: 0.0849; *p*-Het: <0.0001; overall *p*-value: 0.0240). Our meta-analysis indicated that age, sex, peripheral arterial disease (PAD) comorbidity, causes of ESRD such as hypertensive nephrosclerosis, glomerulonephritis, diabetic nephropathy, polycystic kidney disease, kidney malformation, previous dialysis modality (hemodialysis or peritoneal dialysis), or CMV infection did not increase the risk of TRAS.

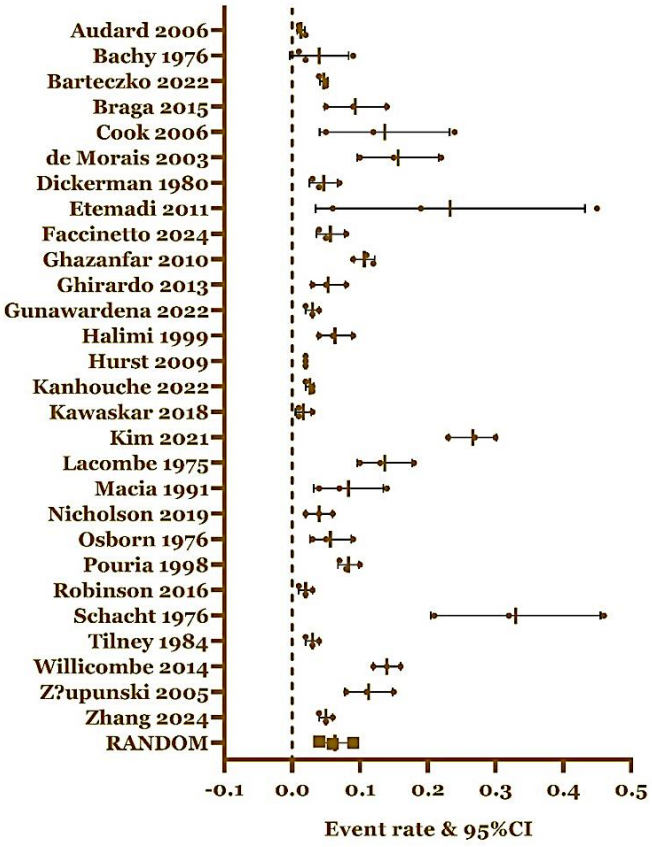

Figure 2. Global prevalence of transplant renal artery stenosis (TRAS) among renal transplant recipients was estimated at 6% (95%CI: 4–9%; *p*-value for Egger's test: 0.0968; *p*-value for heterogeneity: <0.0001; overall *p*-value: <0.0001).

Heterogeneity among studies and potential publication bias

We identified potential publication bias in the comorbidity variable of diabetes mellitus (*p*-Egger <0.05). Therefore, the point estimate was adjusted using the trim and fill method. The details of the funnel plots for this study are presented in **Underlying data**.

Additionally, potential heterogeneity was found in variables of age, the causes of ESRD, such as hypertensive nephrosclerosis, type of donor, CMV infection, delayed graft function, and peak systolic velocity. As a result, the point estimates for these variables were calculated using a random effects model. A summary of the analysis of potential publication bias and heterogeneity in this study is presented in **Table 2**.

Table 1. Baseline characteristics of articles included in the analysis to assess the global prevalence and factors associated with the incidence of transplant renal artery stenosis (TRAS)

Study, year	Country	Design	Age	Sample size	TRAS diagnosis	Outcomes	Quality assessment
Ali *et al.,* 2015 [12]	US	Retrospective cohort	53.9±11.8	75	Angiography	Graft function, survival	High
Audard *et al.,* 2006 [7]	France	Retrospective	40.1±10.0	2386	Angiography	Survival, graft loss, restenosis	High
Bachy *et al.,* 1976 [13]	Belgium	Retrospective	35.5±10.0	85	Angiography	Graft function, hypertension	Moderate
Barteczko *et al.,* 2022 [14]	Brazil	Retrospective	35.9±15.9	6829	Angiography	Mortality, allograft survival	High
Braga *et al.,* 2015 [15]	Brazil	Retrospective	50.1 (10–71)	183	Angiography, DUS	Restenosis	Moderate
Cook *et al.,* 2006 [16]	Canada	Retrospective	10.8 (1–18)	50	DUS	PSV	Moderate
de Morais *et al.,* 2003 [17]	Brazil	Retrospective cohort	41 (33–59)	142	CDUS	Incidence of TRAS	High
Dickerman *et al.,* 1980 [18]	US	Retrospective	NA	391	Angiography	Hypertension, graft function	Moderate
Etemadi *et al.,* 2011 [19]	Iran	Prospective	41.0±3.0	16	Angiography	Risk factors identification	Moderate
Faccinetto *et al.,* 2024 [20]	Brazil	Retrospective	15.0 (8–17)	367	Angiography	Mortality, allograft survival	Moderate
Fananapazir *et al.,* 2017 [21]	Canada	Retrospective	55.0±11.0		Angiography	Ultrasound stratification	Moderate
Ghazanfar *et al.,* 2010 [22]	UK	Retrospective	NA	1727	Angiography	Graft function	Moderate
Ghirardo *et al.,* 2013 [23]	Italy	Retrospective	11.0±6.3	216	DUS	Risk factors identification	Moderate
Gunawardena *et al.,* 2022 [24]	UK	Retrospective	59.0 (27–56)	1211	Angiography, DUS	Graft function	Moderate
Halimi *et al.,* 1999 [25]	France	Retrospective	44.0±2.0	402	Angiography	Restenosis, graft function	High
Hurst *et al.,* 2009 [26]	US	Retrospective	52.5±14.5	41867	Angiography	Mortality, allograft survival	Moderate
Kanhouche *et al.,* 2022 [27]	Brazil	Retrospective	46.3±12.0	6362	Angiography	Risk factors identification	Moderate
Kawaskar *et al.,* 2018 [28]	India	Retrospective	39.5 (25–56)	526	DUS	Graft function	Moderate
Kim *et al.,* 2021 [29]	Korea	Retrospective	49.2±9.3	711	Angiography	Graft function	Moderate
Lacombe 1975 [30]	France	Retrospective	NA	287	Angiography	Restenosis, graft function	Moderate
Macia *et al.,* 1991 [31]	Spain	Retrospective	42.2±11.2	110	Angiography	Degree of HLA compatibility	Moderate
Nicholson *et al.,* 2019 [32]	UK	Retrospective	44.7±13.6	506	Angiography	Risk factors identification	Moderate
Osborn *et al.,* 1976 [33]	UK	Retrospective	30 (17–38)	177	Angiography	Stenosis correction	Moderate
Pouria *et al.,* 1998 [34]	UK	Retrospective	43.6±15.0	917	Angiography	CMV infection	High
Qi 2020 *et al.,* [35]	China	Retrospective	42.3±14.6		Angiography	Stenosis correction	High
Robinson *et al.,* 2016 [36]	US	Retrospective cohort	18–83	857	DUS	Velocities of renal artery	Moderate
Schacht *et al.,* 1976 [37]	US	Retrospective	34.3±10.8	50	Angiography	Risk factors identification	Moderate
Tilney *et al.,* 1984 [38]	US	Retrospective	34.4±10.0	914	Angiography	Restenosis, graft function	Moderate
Willicombe *et al.,* 2014 [39]	UK	Retrospective cohort	52.5±11.9	999	Angiography, DUS	Graft function, antibody	Moderate
Z˘upunski *et al.,* 2005 [41]	Slovenia	Retrospective	43.0±13.0	1178	Angiography	Restenosis, acute rejection	High
Zhang *et al.,* 2024 [40]	China	Retrospective	42.0 (11–62)	300	Angiography	Mortality, allograft survival	High

CDUS: color Doppler ultrasonography; CMV: cytomegalovirus; DUS: duplex ultrasound; HLA: human leukocyte antigen; NA: not available; PSV: peak systolic velocity

Table 2. Summary of factors associated with transplant renal artery stenosis (TRAS) incidence among kidney transplant patients

Covariates	Case n (%) or mean±SD	Model	NS	MD*/ OR**	95%CI	*p*-Egger	*p*-Het	*p*-value
Age (years)	40.18±12.58	Random	14	1.53*	-0.64–3.70	0.1784	<0.0001	0.1670
Sex								
Male	1355 (64.49)	Fixed	11	1.01**	0.78–1.30	0.1811	0.4430	0.9540
Female	746 (35.51)	Fixed	11	0.99**	0.77–1.28	0.1811	0.4430	0.9540
Comorbidity								
Diabetes mellitus	10760 (24.82)	Fixed-TF	7	1.24**	1.09–1.42	0.0227	0.1170	<0.0001
Hypertension	29377 (69.27)	Fixed	6	1.27**	1.09–1.47	0.4982	0.4450	0.0020
Peripheral artery disease	2549 (6.06)	Fixed	3	1.07**	0.81–1.40	0.9309	0.2870	0.6450
Causes of ESRD								
Hypertensive nephrosclerosis	74 (22.63)	Random	3	0.72**	0.10–5.20	0.1194	0.0950	0.7440
Glomerulonephritis	150 (32.68)	Fixed	5	0.96**	0.59–1.56	0.1420	0.4900	0.8730
Diabetic nephropathy	59 (15.28)	Fixed	2	1.69**	0.91–3.13	NA	0.1760	0.0990
Polycystic kidney disease	16 (5.44)	Fixed	2	0.67**	0.24–1.84	NA	0.7750	0.4380
Kidney malformation	25 (46.30)	Fixed	2	0.83**	0.27–2.58	NA	0.7310	0.7490
Dialysis duration before transplant (month)	30.13±12.50	Fixed	5	3.98*	0.59–7.37	0.3435	0.5950	0.0210
Previous dialysis modality								
Hemodialysis	30 (57.69)	Fixed	2	0.53**	0.17–1.65	NA	0.3500	0.2740
Peritoneal dialysis	16 (30.77)	Fixed	2	2.08**	0.62–7.03	NA	0.6820	0.2370
Type of donor								
Living donor	12746 (29.50)	Random	7	0.51**	0.28–0.91	0.0849	<0.0001	0.0240
Deceased donor	30463 (70.50)	Random	7	1.98**	1.10–3.57	0.0849	<0.0001	0.0240
CMV infection	26176 (60.88)	Random	7	1.55**	0.87–2.77	0.5200	<0.0001	0.1360
Acute rejection	178 (21.34)	Fixed	7	1.83**	1.15–2.90	0.6942	0.5720	0.0110
Delayed graft function	8251 (19.42)	Random	7	1.97**	1.24–3.12	0.0710	0.0250	0.0040
Cold ischemic time (h)	25.94±8.69	Fixed	5	4.35*	3.74–4.96	0.4826	0.7480	<0.0001
Peak systolic velocity (m/s)	3.36±0.99	Random	8	1.38*	0.73–2.02	0.5573	<0.0001	<0.0001

CI: confidence interval; CMV: cytomegalovirus; ESRD: end-stage renal disease; MD: mean difference; NA: not available; NS: number of studies; OR: odd ratio; *p*-Egger: *p*-value for Egger's test; *p*-Het: *p*-value for heterogeneity; TF: trim and fille

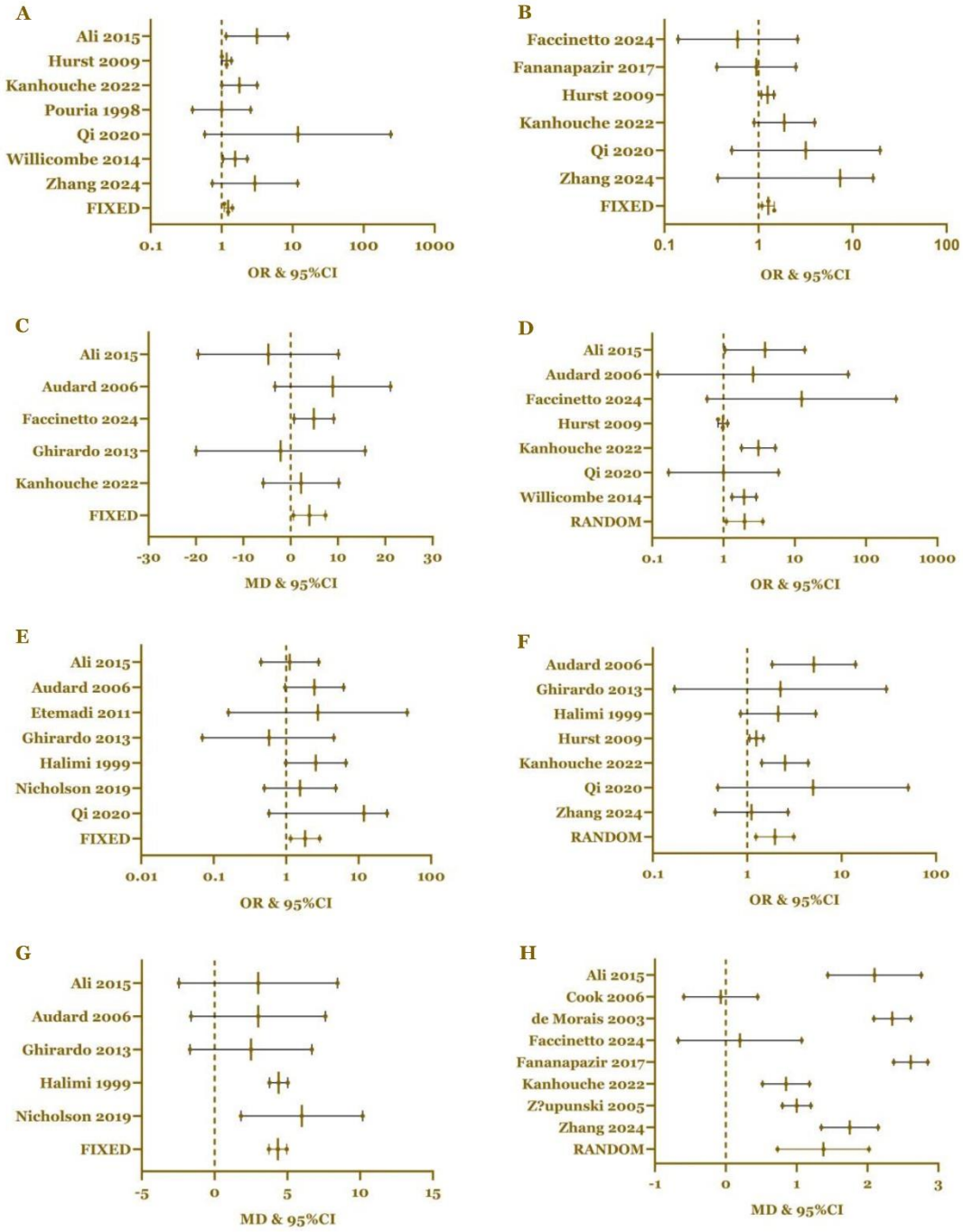

Figure 3. Risk factors for TRAS among renal transplant recipients included an increased risk in patients with diabetes mellitus (OR: 1.24; 95%CI: 1.09–1.42; *p*-value for Egger's test (*p*-Egger): 0.0227; *p*-value for heterogeneity (*p*-Het): 0.1170; overall $p<0.0001$) (A) and hypertension (OR: 1.27; 95%CI: 1.09–1.47; *p*-Egger: 0.4982; *p*-Het: 0.4450; overall $p=0.0020$) (B). The risk of TRAS was also found to be higher in patients who had undergone longer durations of dialysis (MD: 3.98; 95%CI: 0.59–7.37; *p*-Egger: 0.3435; *p*-Het: 0.5950; overall $p=0.0210$) (C), and in those who had received a kidney from a deceased donor (OR: 1.98; 95%CI: 1.10–3.57; *p*-Egger: 0.0849; *p*-Het<0.0001; overall $p=0.0240$) (D). Increased risk of TRAS was also observed in patients who had experienced acute rejection (OR: 1.83; 95%CI: 1.15–2.90; *p*-Egger: 0.6942; *p*-Het: 0.5720; overall $p=0.0110$) (E) and delayed graft function (OR: 1.97; 95%CI: 1.24–3.12; *p*-Egger: 0.0710; *p*-Het: 0.0250; overall $p=0.0040$) (F). The risk of TRAS was also higher in patients who had longer cold ischemic time (MD: 4.35; 95%CI: 3.74–4.96; *p*-Egger: 0.4826; *p*-Het: 0.7480; overall $p<0.0001$) (G) and prolonged peak systolic velocity (MD: 1.38; 95%CI: 0.73–2.02; *p*-Egger: 0.5573; *p*-Het: <0.0001; overall $p<0.0001$) (H).

Discussion

To the best of our knowledge, our study is the first meta-analysis conducted to identify the prevalence of TRAS in this population. Our results revealed that the prevalence of TRAS among renal transplant recipients is 6%. We were unable to compare our findings directly with those of previous studies. However, one review article summarized the prevalence of TRAS in renal transplant recipients, reporting a prevalence of 4.3% [47]. The article, however, used rough calculations, did not follow a systematic meta-analysis approach, and included only 14 studies. In contrast, our study employed a more systematic approach, adhering to meta-analysis principles, and included a larger dataset comprising 28 studies. As a result, our study provides more accurate and comprehensive information regarding the global prevalence of TRAS among renal transplant recipients. Our study is expected to have a significant contribution to a better understanding of TRAS prevalence and will aid in the management and treatment of TRAS in this population.

This study found that renal transplant recipients with diabetes mellitus and hypertension are at a higher risk of developing TRAS. Several theoretical mechanisms may explain these findings. First, vascular damage may serve as a critical link between diabetes mellitus, hypertension, and TRAS. Diabetes mellitus is known to cause vascular damage through multiple pathways. Elevated blood sugar levels lead to the formation of advanced glycation end-products (AGEs), which accumulate in the vascular walls and increase oxidative stress and inflammation. This process weakens the arterial walls, making them more prone to stenosis [48]. Second, chronic inflammation and atherosclerosis likely contribute to these outcomes. Both diabetes mellitus and hypertension are strongly associated with chronic inflammation, which plays a key role in the development of atherosclerosis. Atherosclerosis, characterized by the buildup of plaques in arterial walls, causes narrowing of the arteries and stenosis [49,50]. Third, endothelial dysfunction may also be a contributing factor. The endothelium, a critical regulator of vascular health, is often impaired in individuals with diabetes mellitus and hypertension. This dysfunction results in reduced vasodilation, increased vascular resistance, and heightened susceptibility to stenosis due to vasoconstriction and decreased blood flow [49]. Lastly, heightened immune and inflammatory responses may play a role in these findings. Post-transplant patients, particularly those with diabetes mellitus and hypertension, may experience amplified immune and inflammatory activity, which exacerbates vascular damage and promotes the development of TRAS [51].

Our study revealed that renal transplant recipients with a longer duration of dialysis before transplantation had a higher risk of developing TRAS. There are several theoretical foundations underlying these results. First, chronic vascular stress may serve as a link between a longer duration of dialysis and TRAS. It is well known that prolonged exposure to dialysis can lead to chronic vascular stress, which can weaken the arterial walls and increase susceptibility to stenosis [52]. Additionally, the repeated use of vascular access sites for dialysis can cause repeated trauma and inflammation. This circumstance potentially leads to vascular damage and fibrosis [53]. Second, chronic inflammation may also play a role in these findings. Dialysis is associated with chronic inflammation, which is a known risk factor for the development of atherosclerosis [54]. This inflammation can promote the buildup of plaque in the arterial walls, leading to narrowing of the arteries and subsequent stenosis [55]. Third, endothelial dysfunction may play a significant role. Long-term dialysis has been reported to impair endothelial function. Endothelial dysfunction can lead to reduced vasodilation and increased vascular resistance; as a result, this condition makes the arteries more prone to stenosis [56].

Our results showed that individuals who received a kidney transplant from a deceased donor had a higher risk of developing TRAS compared to those who received a transplant from a living donor. The use of aortic patches may be a contributing factor. It is known that in the context of deceased donor transplants, aortic patches are more frequently used to connect the donor artery to the recipient's artery. The use of these patches could potentially increase the risk of stenosis due to the foreign material and the surgical techniques involved [57]. In addition, deceased donor transplants often involve more complex surgical procedures and longer ischemia times. As a result, these factors can increase the risk of vascular complications, including TRAS. Additionally, the perfusion techniques used during surgery might also contribute to vascular damage [58].

Kidneys from deceased donors may experience longer periods of ischemia before transplantation, leading to endothelial dysfunction and increased susceptibility to stenosis [59].

We found that individuals with acute rejection after transplantation have an increased risk of developing TRAS. It is known that acute rejection involves an intense immune response against the transplanted kidney, which leads to an inflammatory reaction that can further cause endothelial damage and vascular injury. As a result, this condition makes the arterial walls more susceptible to stenosis [60]. The inflammatory process associated with acute rejection could impair endothelial function, and this impairment could lead to reduced vasodilation and increased vascular resistance. Consequently, this contributes to the development of stenosis [61]. In addition, acute rejection could disrupt graft function, which can further lead to ischemia and vascular damage. This ischemic environment can worsen endothelial dysfunction and increase the risk of developing TRAS [62].

Our results showed that an increased risk of TRAS was found in individuals with delayed graft function. We formulated several theoretical explanations that might clarify these findings. Increased immune activity may be one of the underlying factors. Delayed graft function is often associated with an intense immune response against the transplanted kidney. This heightened immune activity can lead to inflammation and endothelial damage, ultimately making the arterial walls more susceptible to stenosis [63]. This finding may also involve ischemia and reperfusion injury. Delayed graft function is often a result of ischemia and reperfusion injury during the transplantation process. This injury can cause direct damage to vascular structures, including the renal arteries. Consequently, this can trigger fibrosis and the formation of scar tissue, which narrows the arteries and increases the risk of stenosis [64]. In addition, compromised graft function may also be a contributing factor. Delayed graft function can impair the performance of the transplanted kidney, leading to ischemia and further vascular damage. This ischemic environment can exacerbate endothelial dysfunction and increase the risk of TRAS [63].

This study also found that longer cold ischemic time increased the risk of TRAS incidence. There are some explanations for this. Prolonged cold ischemic time leads to more extensive cellular damage due to ischemia. When the organ undergoes reperfusion, this triggers a strong inflammatory response and oxidative stress; this condition can affect vascular structures, including the renal arteries [65]. The immune system activation may also play a role. Ischemia-reperfusion injury exposes antigens and releases pro-inflammatory cytokines, which further activates the immune system. This immune activation may increase the risk of vascular complications, including TRAS, as the immune response can target the graft's vascular structures [66]. Another factor that may contribute is renal hypoperfusion. TRAS often causes renal hypoperfusion, which can activate the renin-angiotensin-aldosterone system (RAAS) and this can lead to sodium retention, volume expansion, and sustained hypertension. Consequently, this condition further contributes to vascular injury and stenosis [67].

There are some advantages to this study. This study is the first meta-analysis to evaluate the global prevalence and factors contributing to the development of TRAS in renal transplant recipients. The results of this study could provide new insights into TRAS and may serve as preliminary data for further research. Furthermore, because this is a meta-analysis, the data might reflect the true global burden of TRAS. Our study could aid in stratifying the risk of developing TRAS based on specific factors. This could help in facilitating early detection and intervention. This step is crucial for improving patient outcomes. The findings from our meta-analysis could support the development of clinical guidelines for the management of renal transplant patients [68]. This would help healthcare providers become more aware of potential risks and take appropriate measures to prevent or manage TRAS. With a good understanding of the contributing factors and prevalence of TRAS, healthcare providers could tailor their care strategies for managing high-risk patients, including regular monitoring with Doppler ultrasound and early intervention with angioplasty.

This meta-analysis study, however, has some limitations. Our study did not include factors that might also have contributed to TRAS incidence, such as treatment history, surgical techniques, and types of immunosuppressants used. This was due to our inability to obtain such data in our search. The sample sizes in the individual articles were not uniform, which could have introduced a potential risk of bias that could not be statistically accounted for. Third, the study

locations in the articles were not evenly distributed across the world, which required special attention when generalizing the results of this study. The age of patients in the studies varied, and this needed special consideration since age might also have contributed to the final findings of this study. The methods of diagnosing TRAS among the studies differed, and these differences might have posed a serious risk of bias. Therefore, this required careful attention when interpreting the results of this study.

Conclusion

The global prevalence of TRAS is relatively high, at 6% with 95%CI: 4–9%. Diabetes mellitus, hypertension, longer duration of dialysis, deceased donor, acute rejection, delayed graft function, prolonged cold ischemic time, and prolonged peak systolic velocity are associated with an increased risk of TRAS. This study may provide new insights and highlight the actual impact of TRAS. Nevertheless, future studies should be conducted while considering the limitations of our study.

Ethics approval

Not required.

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Competing interests

All the authors declare that there are no conflicts of interest.

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Underlying data

The raw collected data, funnel plots of the meta-analysis, and the quality assessment of each study using the Newcastle–Ottawa scale are available from: https://doi.org/10.6084/m9.figshare.27786429.v1.

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