Cardiovasc Intervent Radiol (2015) 38:1573–1588
DOI 10.1007/s00270-015-1134-z

CLINICAL INVESTIGATION NON-VASCULAR INTERVENTIONS

A Systematic Review of Outcomes Following Percutaneous Transluminal Angioplasty and Stenting in the Treatment of Transplant Renal Artery Stenosis

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Received: 16 December 2014 / Accepted: 10 May 2015 / Published online: 19 June 2015

Abstract

Purpose To evaluate outcomes following treatment of transplant renal artery stenosis by percutaneous transluminal angioplasty and stent insertion.

Materials and Methods A literature search was performed using Pubmed, MEDLINE, Embase, Wiley Interscience and the Cochrane Library databases. Outcome measures were glomerular filtration rate, creatinine, blood pressure and number of antihypertensive medications. Technical and clinical success, patency and complication rates were also analysed.

Results Thirty-two studies met the inclusion criteria, involving a total of 884 interventions including PTA, stenting, or combinations of both. Clinical success rates were in the range 65.5–94 %. The majority of studies reported technical success rates higher than 90 %. Patency rates were in the range of 42–100 %. However, the definition and diagnostic criteria for TRAS varied widely between studies. Also, marked heterogeneity was observed in the reporting of outcome measures with no consensus in outcome criteria or follow up schedule.

Conclusion Outcomes following PTA and stenting for the treatment of TRAS have been shown to be favourable. However, there is a distinct lack of well designed studies assessing outcomes following intervention. Outcome reporting may be improved by the introduction of standardised outcome measures with reporting of outcomes into a multi-centre registry.

Keywords Transplant renal artery stenosis · Percutaneous transluminal angiography · Angioplasty · Stent · Outcome

Abbreviations

PTA	Percutaneous transluminal angioplasty
TRAS	Transplant renal artery stenosis
DSA	Digital subtraction angiography
CTA	Computed tomography angiography
MRA	Magnestic resonance angiography
GFR	Glomerular filtration rate
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
MAP	Mean arterial pressure
CMV	Cytomegalovirus

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Introduction

Transplant renal artery stenosis (TRAS) is the most common vascular complication following renal transplantation with a reported incidence of 1–23 % [1]. The disease is often asymptomatic and unrecognised, and despite being a potentially reversible cause of refractory hypertension and graft dysfunction in kidney transplant recipients, it is associated with poor long term patient and allograft survival [2].

Reported cases of TRAS have progressively increased in parallel with the increasing use of non-invasive investigation procedures which may arouse suspicion of the disease even in non-symptomatic cases. The wide reported range of TRAS incidence may also reflect the lack of standardisation in the definition of haemodynamically significant disease [3].

A consensus regarding the management of TRAS remains elusive due to a lack of good quality published data, with some authors advocating intervention with percutaneous transluminal angioplasty (PTA) with or without endovascular stenting [4], whilst others recommend a more conservative approach [5].

PTA has been demonstrated to be efficacious in the treatment of TRAS in terms of short-term improvement in renal function. However, data on the long-term effects of PTA on graft survival are scarce and primarily from uncontrolled studies [3]. The recurrence rate of TRAS following PTA may be as high as 40 %, and the subsequent management in this setting remains controversial [6]. Therapeutic options include repeat PTA, surgery and intra-arterial stenting.

The aim of this systematic review is to evaluate the reporting of outcomes following treatment of TRAS with PTA and/or endovascular stenting.

Methodology

An electronic search was performed using Pubmed (January 2000 to May 2014), MEDLINE (January 2000 to May 2014), Embase (January 2000 to May 2014), Wiley Interscience (January 2000 to May 2014) and the Cochrane Library databases (2014). Search terms 'transplant renal artery', 'transplant renal artery stenosis', 'transplant renal artery stent', 'transplant renal artery PTA', 'transplant renal artery stenosis treatment', 'transplant renal artery stenosis management', 'kidney transplant artery stenosis', 'kidney transplant artery stent', 'kidney transplant artery PTA', 'transplant renal artery endovascular' and 'transplant renal artery intervention' were used in combination with the Boolean operator OR. Two authors performed the search independently in May 2014. The reference lists of articles obtained were also searched manually to identify further relevant citations.

Abstracts of the citations identified by the search were then scrutinised in order to determine eligibility for inclusion in this systematic review. Studies were included if they met each of the following criteria

- Describe the use of angioplasty and/or stenting to treat transplant renal artery stenosis.
- Published from 2000 onward.
- Published in English.
- Studied a minimum of ten patients.

Both case series and cohort studies were included in this review. In the case of serial publications by the same authors, this review considered only the most recent publication. Data from included studies was collated by Ngo, Lijister, and Markar. The outcome measures for the systematic review were glomerular filtration rate (GFR), creatinine, systolic blood pressure, diastolic blood pressure and number of anti-hypertensives pre- and post- intervention. Technical and clinical success, patency and complication rates were also studied.

Results

The literature search yielded 32 publications which comprised 26 (81 %) case series and 6 (19 %) cohort studies. Twenty-six studies (81 %) were performed retrospectively and 6 (19 %) prospectively. Twenty-eight were single centre studies. The majority of patients across the studies were male (67 %, M/F = 500/248, where recorded), with an age range of 10–79. The total number of patients included in the studies reviewed was 4048.

Intervention

A total of 884 interventions were performed for cases of transplant renal artery stenosis. These comprised 422 percutaneous transluminal angioplasties and 415 stent procedures. The remaining 47 procedures were performed in studies where PTA and stented patients were grouped into a single 'intervention' arm and could not be otherwise differentiated.

Seven studies included patients following PTA as the sole treatment for TRAS ($n = 137$) [7–13]. Eleven studies included patients following stenting alone ($n = 201$) [1, 2, 6, 14–21]. Twelve studies involved patients receiving either PTA alone or stenting with pre balloon dilatation ($n = 407$, of which PTA alone = 271, stent following PTA = 89, and PTA and/or stent following PTA not discriminated in a single intervention arm = 47) [3, 5, 22–31]. In all twelve studies, patients were followed up as a single intervention arm when considering outcomes, with

no differentiation made between those treated with PTA or stenting.

The final two studies followed patients having received PTA or stenting alone ($n = 139$, of which PTA only $n = 14$ and stent only $n = 125$), however, grouped all patients together when analyzing all outcomes other than patency rate [32, 33].

Risk Factors

There was a wide variation in the reporting of patient co-morbidities and risk factors for TRAS. The most commonly assessed co-morbidity was diabetes mellitus, recorded in 12 studies and present in 26 % of patients ($n = 417$). Hypertension was recorded in eight papers and present in 69 % (range 11–100 %) of the study population ($n = 145$). Dyslipidaemia was documented in five studies and present in 57 % of patients ($n = 98$), and smoking was reported in 21 % of patients ($n = 53$). Five studies [3, 8, 12, 13, 27] recorded the CMV status in their study population, which was overall found to be 52 % ($n = 68$, range 10–100 %).

Assessment of TRAS

The diagnosis of TRAS was derived using a range of imaging modalities, either in isolation or in combination, including Doppler ultrasound, magnetic resonance angiography (MRA), computed tomography angiography (CTA) and digital subtraction angiography (DSA).

Doppler ultrasound was used as the sole modality in assessing for TRAS in seven studies [1, 3, 5, 16, 17, 19, 20], and in combination with DSA in ten studies [2, 7, 11, 23–28, 32]. A combination of Doppler ultrasound, MRA and DSA were used in six studies [10, 15, 18, 22, 30, 31]. One study utilised Doppler ultrasound followed by MRA and DSA, with CTA reserved for patients only in whom MRA could not be performed [33]. A combination of ultrasound, CTA, MRA and DSA were used in two studies [12, 13].

DSA was used as the sole method for diagnosing TRAS in four studies [6, 8, 14, 29]. The remaining two studies did not disclose the method of diagnosis of TRAS.

Diagnostic Criteria for TRAS

The diagnostic criteria for TRAS showed wide variability between studies. Where Doppler ultrasound was utilised (28 studies), the most commonly accepted flow measurement at which TRAS was deemed to be present was at a peak systolic velocity (PSV) of >2 m/s (13 studies). Several studies incorporated further parameters deemed to represent TRAS. Two separate papers defined TRAS as a PSV >2.2 and >2.5 m/s. One study measured the degree of narrowing, with a >50 % stenosis deemed diagnostic for TRAS [2] (Table 1).

Flow velocities were measured in five studies within the stenotic segment and compared with pre- and/or post-stenosis segments. In all five studies, TRAS was defined by an increase in PSV of 50 % within the stenotic segment. Where ratios in flow velocities were calculated between the stenotic:pre-/post- stenotic segment, a ratio of 2:1 was accepted to represent TRAS [22, 28]. Eleven studies did not disclose the ultrasound criteria for diagnosis of TRAS.

In the 22 studies whereby DSA was utilised, 4 defined TRAS as stenosis of >50 % at angiography. Three studies deemed a >10 % peak systolic blood pressure gradient across the stenosis to be significant for TRAS [23, 26, 31],

Table 1 Doppler diagnostic criteria

Doppler ultrasound TRAS criteria	Paper(s)
PSV > 2 m/s	15, 25, 32
PSV > 2 m/s or increase in PSV by >50 % within stenotic segment	3, 7, 17, 31
PSV > 2 m/s or increase in PSV by >50 % within stenotic segment or jet aliasing or RI > 0.8	21
PSV > 2 m/s or increase in flow velocity of ratio 2:1 in stenotic:pre-stenotic segment	22
PSV 2 m/s or increase in flow velocity ratio 2:1 within renal:external iliac artery	2
PSV 2 m/s or RI < 0.5 or velocity gradient across stenotic segment > 2:1 and marked distal turbulence	28
PSV > 2 m/s or RI < 55 % within segmental arteries	11
PSV > 2 m/s or reduced intraparenchymal PSV	12
PSV > 2.2 m/s or turbulent flow distal to stenosis of dampened flow within intrarenal arteries	20
PSV > 2.5 m/s	5
Criteria not stated	1, 10, 13, 16, 18, 19, 23, 24, 26, 27, 30, 33

PSV peak systolic velocity, *RI* resistive index

Table 2 DSA Diagnostic Criteria

DSA TRAS criteria	Paper(s)
>50 % luminal narrowing	8, 14, 22, 29
>50 % luminal narrowing or >10 % peak systolic BP gradient across stenosis	13, 23, 26
>50 % luminal narrowing or >15 mmHg pressure drop across stenotic segment	33
>60 % luminal narrowing	25
>70 % luminal narrowing	7, 31, 32
>75 % luminal narrowing	28
Criteria not stated	6, 10, 11, 12, 15, 18, 24, 27, 30

whilst one study considered a >15 mmHg pressure drop across the stenosed lesion to represent TRAS [33]. Three studies defined TRAS as 70 % luminal narrowing [7, 19, 20], with one study each defining TRAS at 60 and 75 % stenosis [25, 28]. The remaining nine studies failed to disclose their diagnostic criteria (Table 2).

In the seven studies where MRA was performed, TRAS was considered where there was >50 % stenosis in one study [22], and >70 % in another [31]. The remaining six studies did not state the diagnostic criteria [10, 12, 13, 15, 18, 30].

Interventional Technique

Nineteen studies (59 %) provided an account of the angiographic technique utilised in performing angioplasty and/or deployment of stents, where applicable. Of the 24 studies in which endovascular stents were deployed, only 9 (38 %) disclosed the type of stent used (Table 3) [2, 14, 18–21, 30, 32, 33].

Outcome Measures

Glomerular Filtration Rate

Eleven studies (34 %) recorded GFR as an outcome measure (n = 201) [1, 5, 6, 14, 15, 17, 18, 23, 25, 27, 32]. These included six studies where stent insertion was the primary intervention, with or without pre-angioplasty (n = 100) [1, 5, 14, 17, 18, 24]. These studies all reflect an improvement in GFR following intervention ranging from +18.3 ml/min/1.73 m^2 immediately post intervention [19] to +10 6 years later [15]. The largest improvement seen was +23 ml/min/1.73 m^2 at 2 years (n = 7) [1].

No studies observing patients receiving PTA alone recorded GFR as an outcome. The remaining five studies include cohorts who received PTA with or without stenting who were considered as a single 'intervention group' (n = 101). These all demonstrate an improvement in GFR, ranging from +9.6 ml/min/1.73 m^2 post intervention (n = 17) [32] to +19.4 ml/min/1.73 m^2 at 5 years (n = 44) [25].

In one study, not baseline measurements were disclosed and GFR change could therefore no be calculated. On a whole, following intervention, an improvement in GFR was demonstrated in all eleven studies averaging +8.6 at three months post-intervention (n = 71), +16.9 ml/min/1.73 m^2 at 1 year (n = 85) and +21.1 ml/min/1.73 m^2 at 2 years (n = 64) (Table 3).

There was a wide variation in the frequency at which GFR was measured pre and post-intervention, with no two studies recording results with a similar frequency or duration. In papers where a single follow up measurement was taken, studies compared GFR pre-intervention with recordings 1 month [14], 3 months [5], 6 months [23] post-intervention. Others recorded GFR with greater frequency, ranging from at baseline, 3 months, 1 and 2 years [1], to pre-intervention, immediately post-intervention, then at 3, 6, 9, 12, 18, 24 and 30 months post intervention [27]. The length of follow up ranged from measurements taken immediately post-procedure, to 6 years.

Creatinine

Twenty-eight studies (88 %) recorded creatinine as an outcome measure (n = 779). These include seven studies comprising patients receiving PTA only (n = 137) [7–13] and eight studies in patients receiving stents with or without pre-balloon dilatation (n = 141). The remaining 13 studies included both patients following PTA and stenting, who were followed up as a single mixed cohort where outcomes could not be differentiated (n = 501).

The seven studies comprising PTA only patients all demonstrated an improvement in creatinine levels following intervention. Reductions were seen of 80 μmol/L at 1 week (n = 17) [8], 25 μmol/L at 1 month (n = 26) [7], and 31 μmol/L at 6 months (n = 22) [10]. One study did not disclose baseline measurements and a calculation of change post-ntervention could therefore not be made, although yearly measurements between 1 and 3 years did demonstrate an improvement [11]. One study calculated creatinine clearance and demonstrated an improvement of 10.7 ml/min/1.73 m^2 at 30–60 days post intervention (n = 10) [12]. The final study [13] reported a 15 % reduction in creatinine in six patients at 6 months and eight patients at 1 year, although no crude measurements were given.

Similarly, the eight studies comprising stented patients only (n = 141) all demonstrated an improvement in creatinine following stenting. An average creatinine reduction of 22.8 μmol/L was seen at 1 month (n = 38) and 88.3 at

Table 3 Outcomes

Paper	*n*	PTA only	Stent	PTA/ Stent mixed	GFR change	Creatinine change (μmol/L)	Blood pressure change (expressed as MAP)	Change in number of anti-hypertensive medications
Abate et al. [2]	12		12		Not recorded	−0.8 post	−14 at 1 month −12 most recent	−0.5 at most recent follow up
Audard et al. [3]	29			29	Not recorded	−37 at 1 month −48 at 6 months	Not recorded	−1.2 at 1 month
Beecroft et al. [22]	21	13	8		Not recorded	−0.6 at 1 month	−24.3 at 1 month	Not recorded
Bruno et al. [14]	12		12		+6.1 at 1 month	−16 at 1 months	−11.4 at 1 month	Not recorded
Chew et al. [13]	27	27			Not recorded		No figures disclosed.	Decrease in 10 pts, unchanged in 14, increase in 2 (no timescale disclosed)
Chow et al. [23]	18			18	+0.6 at 6 months	−33.3 at 6 months	−7.8 at 6 months	No change
da Silva et al. [24]	30	3	27		Not recorded	−150 at 1 month	Not recorded	−0.7 at 1 month
Del Pozo et al. [1]	13		13		+16 at 3 months +18 at 1 year (n = 10) +23 at 2 years (n = 7)	−181 at 3 months −191 at 1 year (n = 10) -202 at 2 years (n = 7)	−15.3 at 3 months −16 at 1 year −40.7 at 2 years	Not recorded
Dimitroulis et al. [16]	16		16		Not recorded	Not recorded	Not recorded	Not recorded
Fluck et al. [6]	18		18		+3.6 at 3 months +3.8 at 6 months +5.7 at 1 year	Not recorded	−10 at 6 months −23.3 at 12 months	No change
Geddes et al. [5]	27	25	2		+6.6 at 3 months	Not recorded beyond baseline	−14.1 at 3 months	No change
Ghazanfar et al. [25]	44	35	9		+12.3 at 1 months +23.9 at 6 months +23 at 1 year +22 at 2 years +19.9 at 3 years +18.4 at 4 years +19.4 at 5 years	−34.7 at 1 month −97.8 at 6 months −112.1 at 1 year −115 at 2 years −116.9 at 3 years −119 at 4 years −120 at 5 years	−16.1 at 1 month −17.6 at 6 months −18.8 at 1 year −24.9 at 2 years −23.3 at 3 years −23.1 at 5 years	Not recorded
Ghirardo et al. [12]	10	10			Not recorded	Creatinine clearance +11 mL/min/1.73m2 Post (30–60 days)	Mean BP standard deviation scores Pre: 3.2 ± 1.4 Post: 1.04 ± 0.85 (30–60 days)	
Guzzardi et al. [21]	17		17		Not recorded	−73 post (mean 28.3 months)	−4.3 at mean 28.3 months	−2 at mean 28.3 months
Hagen et al. [26]	24	16	8		Not recorded	−3 at 1 month −10 at 6 months	Not recorded	−0.9 at 3 months

Table 3 continued

Paper	*n*	PTA only	Stent	PTA/ Stent mixed	GFR change	Creatinine change (μmol/L)	Blood pressure change (expressed as MAP)	Change in number of anti-hypertensive medications
Halimi et al. [7]	26	26			Not recorded	−25 at 1 month	−9.6 at 1 month	−0.3 at 1 month
Henning et al. [27]	13	2	11		+11.4 Post	−265 post	−4.5 post (*n* = 10)	−0.4 post (*n* = 13)
					+12.1 at 3 months	−97 at 3 months	−3.2 at 3 months (*n* = 12)	+0.1 at 3 months (*n* = 13)
					+9.6 at 6 months	−203 at 6 months	−1.5 at 6 months (*n* = 12)	No change at 6 months (*n* = 13)
					+10.5 at 9 months	−212 at 9 months	+2.8 at 9 months (*n* = 12)	−0.1 at 9 months (*n* = 12)
					+10.6 at 12 months	−203 at 12 months (*n* = 11)	−3.8 at 12 months (*n* = 11)	No change at 12 months (*n* = 11)
					+12.6 at 18 months		−2.2 at 18 months (*n* = 9)	No change at 18 months (*n* = 9)
					+17 at 24 months	−239 at 18 months (*n* = 9)	−1.5 at 24 months (*n* = 7)	−1.3 at 24 months (*n* = 7)
					+14 at 30 months	−248 at 24 months *n* = 8)	−4.9 at 30 months (*n* = 7)	−1.3 at 30 months (*n* = 7)
						−212 at 30 months		
Marini et al. [28]	90	79	11		Not recorded	−62 at 1 months	−11 at 6 months	−0.7 post
						−62 at 6 months	−10.4 at 12 months	
						−71.2 at 12mo		
Marques et al. [29]	29	26	3		Not recorded	Paed: −9 post	Paed: −12 post	No change in paed group
						Adult: −11 post	Adult:−8 post	−0.5 post in adult group
Patel et al. [8]	17	17			Not recorded	−80 at 1 week	Figures not stated	Not recorded
Peregrin et al. [30]	58	53	5		Not recorded	−34 at 1 week	−12 at 1 week	−0.5 at 1 week
						−81 at 6 months	−14 at 6 months	−0.5 at 6 months
						−45 at 1 year	−15 at 1 year	−0.5 at 1 yr
						−28 at 2 years	−16 at 2 years	−0.7 at 2 years
						16 at 3 years	−16 at 3 years	−0.4 at 3 years
Polytimi et al. [17]	26		26		No baseline measurements disclosed	Not recorded	No baseline measurements disclosed	−2 at end of observation
Ridgway et al. [18]	13		13		+18.3 post	−33 post	−7 post	−0.4 post
Salvadori et al. [19]	26		26		Not recorded	−26 at 1 months	−17 at 1 months	−0.5 at 3 years
						−37 at 1 year	−14.3 at 1 yearr	
						−45 at 3 years	−14.5 at 3 years	
Stribrna et al. [9]	20	20			Not recorded	(Creatinine clearance) Pre: 56.6	−23 at 1 month	−1 post
						1 months: +14.1	−22 at 3 months	
						3 months: +14.1	−23 at 6 months	
						9 months: +14.1	−22 at 9 months	
						12 months: +12.4	−25 at 12 months	
Su et al. [15]	18		18		+10 at 6 years[a]	−52 post	−16.8 24-48 h post	−2.05 at 6 years
Tang et al. [10]	22	22			Not recorded	−31 at 6mo	Not recorded	−0.75 at 6 months

Table 3 continued

Paper	*n*	PTA only	Stent	PTA/Stent mixed	GFR change	Creatinine change (μmol/L)	Blood pressure change (expressed as MAP)	Change in number of anti-hypertensive medications
Touma et al. [32]	17	5	12		+9.6 post	−25 post −10 at latest follow up	+0.6 post	No change
Valpreda et al. [20]	30		30		Not recorded	−132 post	−3 post	−0.6 post
Voiculescu et al. [31]	24	19	5		Not recorded	−44 post −35 at end of observation	−7.4 post −12.7 at end of observation	−0.4 post treatment, no change at end of observation
Willicombe et al. [33]	122	9	113		Not recorded	−29.2 at 2 months	−6 at 1 months −6 at 6 months −10 at 1 year	No change at 2 months
Zupunski et al. [11]	15	15			Not recorded	No baseline measurements disclosed	No baseline measurements disclosed	No baseline measurement

[a] Graphical data

1 year (n = 39). The largest reduction of 202 μmol/L was seen at 2 years in one study (n = 13) [2]. Four further studies demonstrated an improvement "post-procedure" of 0.8, 33, 52 and 132 μmol/L [3, 19, 24, 31, respectively] but did not disclose the time period following intervention that the measurements were taken.

All 28 studies demonstrated an improvement in creatinine following intervention with PTA or stenting for TRAS. Allowing for heterogeneity of the study populations, pooled analysis demonstrates a reduction of 42.5 μmol/L at 1 month (n = 302), 72.6 μmol/L at 6 months (n = 274), 79.7 μmol/L at 1 year (n = 239) and 42.1 at 3 years post-intervention (n = 128).

Four studies took measurements pre and 1 month post-intervention [7, 14, 22, 24]. Two studies recorded creatinine at baseline, then at 1 and 6 months post-intervention [3, 26]. The remainder of papers varied widely in their approach to recording creatinine. The shortest period of follow up was 1 week [8], whilst another study studied creatinine levels for up to 6 years [15]. In terms of the most frequently assessed subjects, one took 9 measurements over a 30 month period [27]. Five papers referred to measurements taken pre- and post-procedure but failed to state the length of time either before or after [12, 18, 20, 21, 29] (Table 3).

Blood Pressure

Blood pressure (BP) was measured as an outcome in 26 studies (81 %). Twenty papers (63 %) recorded systolic and diastolic blood pressure (SBP and DBP), whilst 6 papers (19 %) calculated the mean arterial blood pressure (MABP). For the purposes of pooled analysis, all blood pressure recordings have been converted to MAP using the equation [(2 × DBP) + SBP]/3].

Of the 26 studies, 5 were in patients who received PTA only as treatment for TRAS (n = 88) whilst 10 were in patients who had received stenting with or without pre-dilatation (n = 185). The remaining 11 studies included both patients following PTA and stenting, who were followed up as a single mixed cohort where outcomes could not be differentiated (n = 445).

The five studies in PTA only patients all demonstrated an improvement in blood pressure readings following angioplasty. This ranged between a reduction in MAP of 9.6 mmHg at 1 month (n = 26) [7] to a reduction of 25 mmHg at 12 months (n = 20) [9]. One study calculated the 'mean BP standard deviation score' and saw a reduction from 3.2 pre-intervention to 1.04 post, although no time frame was disclosed. One study failed to disclose baseline measurements, although serial measurements at 1, 2 and 3 years demonstrated a reduction from 112.7 mmHg to 109.7 mmHg to 103.3 mmHg (n = 15) [11]. The final study

[8] did not disclose figures but stated all but one patient had a substantial improvement in mean DBP (n = 17).

Nine of the ten studies in stented patients demonstrated an improvement in blood pressure following intervention. In studies reporting outcomes at 1 month, the average reduction in MAP was 14.9 mmHg (n = 50). At 1 year the average seen was 17.5 mmHg (n = 57). The largest reported improvement was 23.3 mmHg (MAP) at 1 year in a cohort of 18 patients receiving stent only as treatment for TRAS [6]. The one study which failed to demonstrate an improvement did not disclose baseline measurements but recorded BP at 1 year of 129(± 4)/79(± 3) and 131(± 3)/79(± 2) at 3 years in a cohort of 26 patients all receiving stenting with pre-dilatation.

Twenty four of 26 studies demonstrated a reduction in blood pressure following intervention with either PTA or stenting for TRAS. Pooled analysis of all studies demonstrates an average reduction in MAP of 12 mmHg at 1 month (n = 283), 13.4 mmHg at 1 year (n = 402) and 17.5 mmHg over 1 year (n = 171).

Where SBP and DBP were recorded, there was a wide variation in the frequency and length of follow up. Three studies reported measurements taken pre-intervention and 1 month afterwards [7, 14, 22]. In two studies, measurements were taken pre-intervention, then 1 and 12 months post-intervention [6, 28]. Of the remaining studies, no two studies shared a common follow up schedule, ranging from pre-intervention and 1 week post-intervention [8], to 24–48 h pre- and post-intervention, then monthly for up to 6 years [15]. Four studies stated measurements were taken pre- and post-intervention but failed to disclose time periods [13, 20, 21, 29] (Table 3).

In the six studies reporting MABP, no two shared a common schedule, with follow up ranging from 2 months [33] to 3 years [19, 30]. One study recorded MABP pre- and post-intervention at varying time points between their subjects [18].

Anti-Hypertensive Medications

Twenty-six studies (81 %) recorded the number of anti-hypertensive medications taken by subjects prior to and after intervention as an outcome measure (n = 743). Of these, six studies were in patients receiving PTA only as treatment for TRAS (n = 120), whilst eight studies included patients receiving stenting with or without pre-dilatation (n = 160). The remaining 12 studies included both patients following PTA and/or stenting who were followed up as a single mixed cohort (n = 463).

Of the six studies in patients receiving PTA only as treatment, one study demonstrated a reduction in anti-hypertensive therapy of one medication following intervention in a cohort of 20 patients, although no timescale post intervention was disclosed [9]. Smaller reductions were seen in two further studies which demonstrated a reduction of 0.3 at 1 month (n = 26) [7] and by 0.75 at 6 months (n = 15) [10]. One study failed to disclose baseline measurements, therefore a calculation of change following intervention could not be made [11]. One study calculated an 'Anti-hypertensive score' pre-intervention but failed to disclose scores post-intervention for comparison [12]. One study reported a decrease in number of anti-hypertensives in 10 patients whilst observing an increase in two, however, no timescale was disclosed [13].

Seven of the eight studies in patients receiving stents as primary treatment for TRAS demonstrated some decrease in the number of anti-hypertensive medications following intervention. These included reductions of 0.5 "at the most recent follow up" (n = 12) [2], 0.4 "following stenting" (no time disclosed) (n = 13) [18], 0.6 post-intervention (no time disclosed) (n = 30) [20], 2 at the "end of observation" (no time disclosed) (n = 26) [17] and 2 at mean 28.3 months (n = 17) [21]. The largest decrease of 2.05 at 6 years post-intervention was seen in a cohort of 18 patients [15]. The only study not to record an improvement declared "no significant change" in the number of medications following treatment (n = 18) [6].

Follow up ranged from the number of anti-hypertensives taken recorded pre- and 1 month post-intervention in four papers [3, 7, 14, 24], to pre-intervention, then at 3, 6, 9, 12, 18, 24 and 30 months post intervention [27]. The longest follow up was up to 6 years in one study [15] (Table 3).

Periprocedural Outcomes and Re-Intervention

Technical Success

Technical success rates were reported in 23 studies (72 %), however, a definition for technical success was provided in only 11 cases. There was a wide variation in what was considered to constitute a technical success. Table 4 lists the definitions of technical success where provided.

Allowing for variability in its definition, pooled analysis demonstrates an overall average technical success rate of 93.7 % across the 23 studies disclosing a technical success rate following intervention by means of PTA and/or stenting for treatment of TRAS (n = 555). In the five studies in patients treated with PTA only, the average technical success rate of 93.1 % (80–96.3 %) (n = 102). In the 11 studies in patients receiving stents as primary treatment (n = 201) the average technical success rate was 97.3 % (83.3–100 %), with eight such studies recording a technical success rate of 100 % (Table 7).

Table 4 Definitions for Technical Success

Paper	Definition of technical success
2	Immediate procedural success = restoration of renal perfusion with 0 % residual stenosis
8, 13	Residual stenosis <30 % after angioplasty and no flow limiting intimal flap
10	>50 % reduction in stenosis and in pressure gradient across stenosis
12	>50 % reduction in stenosis at angiography
14	No residual stenosis documented after revascularization
15	Residual stenosis <20 % without dissection or extravasation
22	Residual stenosis <30 %, no flow limiting dissection, and residual peak systolic pressure gradient less than 10 % systolic blood pressure across the lesion
25	<50 % residual stenosis
26	Systolic pressure gradient 10 mmHg or less. Where measurement could not be performed, angiographic residual stenosis diameter <50 % accepted as success
32	No restenosis requiring redo intervention

Clinical Success

Clinical success was less widely defined, being reported in only six studies (19 %). Table 5 lists the definitions for clinical success where provided. Clinical success rates were in the range from 65.5 to 94 %. Of the six studies reporting clinical success following intervention, five recorded a success rate of 75 % or higher (Table 5).

Allowing for variability in the definition of clinical success, the two studies in patients treated with PTA only (n = 44) demonstrated an average clinical success rate of 78.9 %. No studies involving patients treated by stenting as a primary intervention recorded clinical success.

Table 6 Definitions for patency

Paper	Definition of patency
14	No residual stenosis documented after revascularization
15	<20 % residual stenosis
21	residual stenosis <60 %, PSV < 160 cm/s RI 0.56–0.7
22	Restenosis suggested by rising creatinine and blood pressure. On Doppler suspected if (i) PSV > 2 m/s (ii) velocity gradient between stenotic:prestenotic segments >2:1 and (iii) marked distal turbulence with spectral broadening. On MRA if stenosis >50 % luminal diameter
25	<50 % residual stenosis

The overall clinical success rate was 76.7 %, including studies in which PTA and stented patients were grouped as a single cohort (n = 191).

Patency Rate

Long term patency rates following either PTA or stenting were recorded in 24 (75 %) studies, however, only five studies attempted to define what was considered to be a patent graft or stent, with the remaining 18 studies failing to define what constituted restenosis. Table 6 lists the definitions for patency where provided. Post-procedural follow up of renal artery/stent patency varied widely, with two studies documenting patency only immediately after intervention [18, 26], whilst one study followed patients up for up to 146 months [29].

Of the 25 studies which recorded patency rates following intervention, 5 involved patients receiving PTA only as treatment for TRAS (n = 102) [7, 8, 10, 12, 13], with a further two with mixed PTA/stenting treatment arms which

Table 5 Definitions for clinical success

Paper	Definition of clinical success	Clinical success rate
8	(a) >15 % reduction in serum creatinine level, (b) >15 % reduction in mean DBP with the same number of antihypertensive medications as before PTA, or (c) >10 % reduction in mean DBP with a reduction in number of antihypertensive medications	82 %
13	normalisation of BP or reduction in DBP by >15 mmHg and/or reduction in number or dosage of anti-hypertensive medications. If treated for impaired renal function, defined as serum creatinine reduction of 15 % or a less than 15 % change from baseline serum creatinine	76.9 % at 1 year
22	At 1 month: (i)more than a 15 % reduction in serum creatinine (ii) more than a 15 % reduction in mean diastolic BP with the number of antihypertensive medications equal to that before angioplasty, (iii) >10 % reduction in mean diastolic BP with a reduction in number of antihypertensive medications	94 %
25	>25 % improvement in serum creatinine and eGFR levels after 12 weeks post treatment	82 %
26	Reduction in no of antihypertensive meds and/or reduction in creatinine of >27 μmol/L	75 % at 3 months
30	Improvement and stabilization of graft function	65.5 %

disclosed separate patency rates for the PTA (n = 28) and stenting groups (n = 118) [31, 33). Patency rates were in the range from 42 % at 45 months [31] to 100 % at a median 4.1 years [12]. Allowing for variability in definition of patency rate and follow up time, the overall average patency rate across PTA patients was 73 % (n = 130).

Nine studies recording patency rates involved patients receiving stenting as the primary intervention for TRAS (n = 176) [1, 2, 6, 15–17, 19–21], with a further two with mixed PTA/stenting treatment arms which disclosed separate patency rates for the stenting (n = 118) and PTA groups [31, 33]. Patency rates were in the range from 77.8 % (n = 18, no time of follow-up disclosed) [6] to 100 % in four studies, two of which were at 3 years post intervention [1, 2, 17, 19]. Allowing for variation in definition of patency rate and follow up time, the overall average patency rate across stented patients was 90.4 % (n = 294).

Across all studies which recorded patency rate following intervention for TRAS, allowing for variation in definition of patency, the rate at 1 year was 83.6 % (n = 525) (Table 7).

Secondary patency was recorded in one study of 17 patients receiving PTA only as treatment for TRAS who found a re-intervention rate of 13 % with a secondary patency rate of 50 % (one of two patients represented with recurrent stenosis) [8].

Re-Intervention Rates

Twenty-two studies recorded re-intervention rates following intervention for TRAS. As seen with the measurement of patency rate above, there was a wide variation in follow up time following treatment. The longest period of follow up seen was 5 years in two studies [5, 21].

Allowing for this variation, the overall re-intervention rate across all studies was 14.7 % (n = 623). Of the eight studies evaluating patients following PTA only [7, 8, 10, 12, 13, 28, 31, 33], the average re-intervention rate was 18.9 % (n = 209). Of the 11 studies documenting re-intervention rates following treatment by means of stenting [1, 2, 6, 20, 23, 25, 27–29, 32, 33], the average re-intervention rate was 9.1 % (n = 289). Of these, 5 studies recorded a re-intervention rate of zero (n = 87) [1, 17, 19, 21, 31] (Table 7).

Complications

Twenty-six studies disclosed peri-procedural complications. However, only three papers provided definitions or criteria for their reported complications [14, 15, 31]. Two papers defined complications according to severity, assessing events as major or minor [22, 23].

Seventy-five complications were recorded in total across the 26 studies (n = 760), giving a global complication rate of 9.9 %. Of the 75 total complications recorded, the most frequently observed was vessel dissection, reported in 19 cases, thus constituting 25 % of the overall complications. Fifteen puncture site haematomas and 14 vessel thromboses were reported, constituting 20 and 18.7 % of the complications reported, respectively. Other complications reported included 10 malpositioned/migrated stents (13.3 %), 8 pseudoaneurysms (10.7 %), one iliac artery rupture and one stent occlusion. Two PTA procedures were listed as unsuccessful or failed, constituting 2.7 % of the complications. Of these, one was a patient in whom a double stenosis was found whereby only one vessel was amenable to angioplasty where thrombosis of the non-angioplasted kidney was proven on subsequent arteriography [29]. In the final case the authors did not to elaborate beyond reporting that one patient required vascular reconstruction due to unsuccessful PTA [10]. One study reported three cases of nephrotoxicity, constituting 4 % of the complications, one leading to graft loss [30]. The final two complications included one patient requiring vascular oversewing at the site of arterial puncture site and one listed as allograft loss [20] (Table 8).

Of the four studies concerning patients following PTA only (n = 85), there were five reported complications, giving an overall complication rate of 5.9 %. The complications listed were renal artery thrombosis (2), dissection (2) and one unsuccessful PTA resulting in vascular reconstruction.

Of the nine studies concerning patients following stenting only (n = 173), there were nine reported complications, giving an overall complication rate of 5.2 %. The complications listed were puncture site haematoma (5), stent migration (2) and pseudoaneurysm (2) (Table 8).

Discussion

This systematic review demonstrates percutaneous intervention with transluminal angioplasty (PTA) or endoluminal stenting to be effective in the treatment of TRAS. The current body of evidence supports the use of angioplasty and/or stenting, with favourable outcome in terms of technical success, clinical success and long term patency, with few reported serious complications. However, there is a distinct lack of robust well-designed studies, with no randomised controlled trials and preponderance towards retrospective single-arm cohort studies, although we accept that this may, in part, be due to the low overall incidence of TRAS which may limit the feasibility of large randomised trials. The positive findings are in contrast to those found in the treatment of native renal artery stenosis, where the

Table 7 Technical success, patency and re-intervention rates

Paper	*n*	PTA	Stent	PTA/Stent mixed	Technical success rate (%)	Patency rate (%)	Re-intervention rates (%)
Abate et al. [2]	12		12		100	100 % (mean follow up 16 ± 10 months)	17 %
Audard et al. [3]	29			29	93.10	72.5 % (mean follow up 26 months [3–126])	Not reported
Beecroft et al. [22]	21	13	8		100	94 % at 3 months 72 % at 6 months 72 % at 12 months	14 %
Bruno et al. [14]	12		12		100	Not recorded	Not reported
Chew et al. [13]	27	27			96.30	73.1 % (at mean 14.3 months)	26 %
Chow et al. [23]	18			18	Not reported	83 ± 8 % at 2 years	28 %
da Silva et al. [24]	30	3	27		Not reported	Not recorded	Not reported
Del Pozo et al. [1]	13		13		100	100 % at 2 years	Nil
Dimitroulis et al. [16]	16		16		90	87.5 % at 1 yr	Not reported
Fluck et al. [6]	18		18		83.30	77.80 %	33 %
Geddes et al. [5]	27	25	2		Not reported	66.6 % at 5 years	33 % in 5 years
Ghazanfar et al. [25]	44	35	9		Not reported	Not recorded	Not reported
Ghirardo et al. [12]	10	10			80	100 % at median 4.1 years	Nil at med 4.1 year
Guzzardi et al. [21]	17		17		100	82.4 % at average 28.3 months	Nil 5 years
Hagen et al. [26]	24	16	8		91.70	75 % at 3 months	Not reported
Halimi et al. [7]	26	26			92.30	77.90 %	23 %
Henning et al. [27]	13	2	11		92.30	Not recorded	Nil
Marini et al. [28]	90	79	11		90.3	95 % at 1 month 87.9 % at 3 months 85 % at 12 months	8 % PTA 36 % PTA + stent (mean 1.5mo)
Marques et al. [29]	29	26	3		Not reported	75.9 % at 144 months	24 %
Patel et al. [8]	17	17			94.10	88 % at mean 26.9 months follow up	13 %. Secondary patency 50 %.
Peregrin et al. [30]	58	53	5		88.4	93.7 % (3 year follow up)	Not reported
Polytimi et al. [17]	26		26		96.70	100 % (3 year follow up)	Nil
Ridgway et al. [18]	13		13		100	Not recorded	Not reported
Salvadori et al. [19]	26		26		100	100 % (3 year follow up)	Nil at 3 yrs
Stribrna et al. [9]	20	20			Not reported	Not recorded	Not reported
Su et al. [15]	18		18		100	94.4 % at 12 months	6 %
Tang et al. [10]	22	22			95.50	73 % (median 4.8 months)	22 %
Touma et al. [32]	17	5	12		88.2	77 %[a] (median follow up 19.6 months)	12 %
Valpreda et al. [20]	30		30		100	84.4 % (at mean 36 months)	3 %
Voiculescu et al. [31]	24	19	5		Not reported	Angioplasty group: 42 % Stent group: 80 % (45.2 ± 35 months)	PTA group: 53 %, Stent group: nil
Willicombe et al. [33]	122	9	113		Not reported	PTA group 66 %, Stent group 89 %	PTA group: 33 %, Stent group 11 %
Zupunski et al. [11]	15	15			Not reported	Not recorded	Not reported

[a] Graphical data

Table 8 Complication Rates

Paper	*n*	PTA only	Stent	PTA/stent mixed	Complication(s)	Complication rate (%)
Abate et al. [2]	12		12		1 Loss of undeployed stent with distal dislodgement in deep profunda. No reported adverse consequences	8.3
Audard et al. [3]	29			29	2 Thrombosis main renal artery 1 Dissection renal artery branch	10.3
Beecroft et al. [22]	21	13	8		1 Puncture site pseudoaneurysm 1 Puncture site haematoma	9.5
Bruno et al. [14]	12		12		Not recorded	–
Chew et al. [13]	27	27			1 Dissection	3.7
Chow et al. [23]	18			18	2 Groin haematoma	11.1
da Silva et al. [24]	30	3	27		1 Femoral puncture haematoma 1 Pseudoaneurysm 1 Occluded polar renal artery post PTA	10
Del Pozo et al. [1]	13		13		1 Puncture site haematoma	7.7
Dimitroulis et al. [16]	16		16		not recorded	–
Fluck et al. [6]	18		18		1 Stent migration to profunda femoris (Attempted placement of second stent led to arterial thrombosis and graft loss)	5.6
Geddes et al. [5]	27	25	2		2 Renal artery thrombosis. Immediate transplant graft loss as direct result of endovascular intervention 1 stent migration requiring restenting	11.1
Ghazanfar et al. [25]	44	35	9		Not recorded	–
Ghirardo et al. [12]	10	10			Nil	0
Guzzardi et al. [21]	17		17		1 Pseudoaneurysm	5.9
Hagen et al. [26]	24	16	8		1 Iliac artery rupture requiring surgery 1 Intimal dissection 1 Femoral access haematoma 1 Pseudoaneurysm	16.7
Halimi et al. [7]	26	26			2 Main RA thrombosis 1 RA branch dissection	11.5
Henning et al. [27]	13	2	11		Nil	0
Marini et al. [28]	90	79	11		1 segmental occlusion 2 RA thromboses 1 RA dissection 1 late arterial graft pseudoaneurysm	5.6
Marques et al. [29]	29	26	3		1 Unsuccessful angioplasty resulting in graft loss [(graft thrombosis)]	3.4
Patel et al. [8]	17	17			Not recorded	–
Peregrin et al. [30]	58	53	5		3 Nephtotoxity leading to 1 loss of graft 4 haematoma/pseudoaneurysm 5 Dissection requiring stent 1 Peripheral branch occlusion	25.4
Polytimi et al. [17]	26		26		Nil	0
Ridgway et al. [18]	13		13		3 Groin haematoma	23.1
Salvadori et al. [19]	26		26		Nil	0
Stribrna et al. [9]	20	20			Not recorded	–
Su et al. [15]	18		18		1 Puncture site haematoma	5.6
Tang et al. [10]	22	22			1 Unsuccessful PTA requiring vascular reconstruction	4.5
Touma et al. [32]	17	5	12		1 Dissection 1 Stent misplacement	5.9

Table 8 continued

Paper	*n*	PTA only	Stent	PTA/stent mixed	Complication(s)	Complication rate (%)
Valpreda et al. [20]	30		30		1 Puncture site pseudoaneurysm surgically corrected	3.3
Voiculescu et al. [31]	24	19	5		1 Dissection requiring stenting	4.2
					1 Dislocation stent to femoral artery	
					3 Thrombotic occlusion immediately post PTA	
Willicombe et al. [33]	122	9	113		3 Local haematoma	15.1
					5 Dissection - Minor, non flow-limiting	
					2 Dissection - Major, requiring intervention	
					5 Stent malposition	
					1 Stent occlusion	
					1 Vascular repair	
					1 Allograft loss	
Zupunski et al. [11]	15	15			Not recorded	–

Table 9 Complication Frequency

Complication	Frequency	% of Total complications (*n* = 75)	% of study population[a] (*n* = 760)
Puncture site haematoma	15	20	2.0
Stent migration	4	5.3	0.5
Stent malposition	6	8	0.8
Vessel thrombosis/occlusion	14	18.7	1.8
Dissection	19	25.3	2.5
Pseudoaneurysm	8	10.7	1.1
Iliac artery rupture	1	1.3	0.1
Failed procedure resulting in graft loss	2	2.7	0.3
Nephrotoxicity	3	4	0.4
Stent occlusion	1	1.3	0.1
Vascular repair	1	1.3	0.1
Allograft loss	1	1.3	0.1

[a] Of which complication rates were recorded

clinical benefit from revascularization [34] or stenting [35] in patients with atherosclerotic renovascular disease has been widely debated [36] (Table 9).

Approaches to the diagnostic assessment of TRAS varied widely, with a number of combinations of Doppler ultrasound, MR angiography (MRA) and digital subtraction angiography (DSA) techniques employed. The use of Doppler ultrasonography in assessing TRAS is well established with a reported sensitivity of 90–100 % and a specificity of 87–100 % [37]. Catheter angiography, however, remains accepted as the 'gold standard' investigation in determining TRAS, whilst the use of ultrasound, CTA and/or MRA has been advocated in the setting of screening for disease.

The heterogeneity of patients was compounded by the large degree of heterogeneity in the definition of TRAS. Where disclosed, studies using MRA or DSA were consistent in defining TRAS as >50 % stenosis. However, in the 25 studies using Doppler ultrasound, three different PSV levels (>2, >2.2 and >2.5 m/s) were used to define TRAS. This may have introduced bias to patient selection, as those with less severe, albeit relevant, TRAS, which may have demonstrated significant stenosis on angiography, may have been overlooked on the basis of Doppler criteria set to detect only severe stenoses.

The majority of interventions performed were angioplasty alone, seen in around half of cases, with stents deployed in 37 % of patients, either in combination with angioplasty, or alone. Nearly half of studies failed to disclose the technique in performing angioplasty. Where the technique was documented, a Seldinger DSA was standard. In studies including subjects receiving angioplasty and/or

stenting, justification of stent deployment was poorly documented. Where reasoning was given, the most common indication for stenting was failed PTA, namely due to residual stenosis or the presence of a flow limiting dissection flap. This patient subgroup may represent disease intrinsically more resistant to treatment, thus introducing possible bias to a significant proportion of stented patients.

The lack of disclosure on the stent types used may reflect that the cohort(s) analysed were offered treatment at a time when the use of stents in the management of TRAS was in its infancy meaning several differing products may have been trialled.

Overall, outcomes in terms of GFR, creatinine, blood pressure the number of anti-hypertensive medications have been shown to improve following both treatments. In assessing outcomes, a number of trials including both 'angioplasty only' and stented patients considered subjects together as a common 'intervention group' in reporting outcomes, as the main objective was not to compare the therapies, but to establish the efficacy of the intervention as a whole. The remaining dataset is too small to allow for any formal pooled analysis to be carried out in order to determine the efficacy of angioplasty against stenting.

Although we have been unable to use meta-analysis due to this inherent study heterogeneity preventing formal pooled analysis, some interesting observations can be made from the available grouped data. When compared to treatment with PTA alone, treatment by means of stenting alone or with pre-balloon dilatation demonstrates superiority in various outcomes including patency rate (73 vs. 90.4 %), re-intervention rate (18.9 vs. 9.1 %) and technical success (93.1 vs. 97.1 %). However, complication rates appear to be comparable between the two groups (5.9 vs. 5.2 %).

In addition to variability in diagnostic techniques, there was an obvious lack of consensus in the recording of outcome measures in the reported literature. While all studies assessed some combination of GFR, creatinine, BP and the number of antihypertensive medications, there was a total lack of concordance in the frequency and length of follow up. Furthermore, technical success was widely reported but definitions varied widely, with five different criteria used in eight studies. Clinical success was similarly also poorly defined. Patency rate was widely reported but very few studies disclosed any criteria for assessing graft patency, with a wide variation in the time of assessment.

A number of peri-procedural complications were recorded with the vast majority undefined. Only two studies referenced the criteria established by the Standards of Practice Committee of the Society of Interventional Radiology. Of the commonly reported complications, puncture site haematoma and puncture site pseudoaneurysm were reported in 8 (25 %) and 6 (19 %) papers, respectively, yet defined in none.

This raises the question of whether a standardised method of recording outcome measures may be of benefit in future studies. The development of "core outcome sets" has been pioneered in rheumatology with the OMERACT (Outcome Measures in Rheumatology) initiative, and more recently been suggested as a method to improve outcome reporting in surgical oncology [38]. A core outcome set is a minimum set of endpoints measured and reported in all studies in a given disease entity. This allows cross-study comparisons for at least the core outcomes to take place. Investigators may add outcomes of particular interest, but always measure and report as a minimum the 'core set'. In the context of transplant renal artery stenosis, a core outcome set might include short-term clinical outcomes such as creatinine, GFR, BP and antihypertensive therapies, immediate technical success and patency, as well as longer term outcomes such as patency rate at 1 year, and 5 year graft survival rates/mortality.

This review has a number of limitations. The search was limited to studies published after 2000. In addition to potentially excluding important trials, it is possible that standard outcome definitions may have been published prior to this, with the more recently published articles omitting definitions on the assumption of common general knowledge. In the case of serial publications by the same authors, this review considered only the most recent publication. Differing datasets, definitions of TRAS assessment, graft patency and outcome measures previously published may have been omitted from the most recent article. Limiting the inclusion of studies to those published in English may have introduced further selection bias. Lastly, the omission of smaller studies may further compound an already limited dataset.

Conclusion

Whilst current research supports the use of interventional therapy in the treatment of transplant renal artery stenosis, this study demonstrates a lack of standard methodology and inconsistency in the reporting of outcome measures following intervention for TRAS. The introduction of 'core outcome sets' may improve this and is recommended to improve data collection in all studies assessing intervention in treatment of TRAS.

The current body of literature demonstrates preponderance towards retrospective cohort studies and this systematic review highlights the requirement for more robust trials and outcome reporting into a multi-centre registry in order to shape future best practice.

Conflict of interest The authors wish to declare no disclosures or conflicts of interest.

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