

Review Article

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Critical Appraisal of the Major Randomized Controlled Trails on the Management of Atherosclerotic Renovascular Disease (ARVD)

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Abstract

Background: In this article, the author discusses critical appraisals of the major randomized controlled trials on the management of Atherosclerotic Renovascular Disease (ARVD). The article will also discuss the limitations of the published trials, while highlighting the crucial aspect of appropriate patient selection, the serious flaws noted, and the quality of the main studies. Also included are the six major randomized controlled trials that compared the difference between revascularization, either surgical or PTRA (Percutaneous Renal Angioplasty), with or without stent versus conservative management (medication). The author also discusses the recommended research for the management of atherosclerotic renovascular disease.

Methodology and search strategies to identify studies: A comprehensive search of PUBMED including Medical Subject Headings (MeSH) data base from 1990 to may 2012 and The Cochrane library was completed. Searching was only for relevant English papers related to the management of Atherosclerotic renovascular disease.. CASP questionnaire, Jadad scaling and (Oxford Centre for Evidence-based Medicine) levelling of evidence are used for the purpose of the critical appraisal.

Criteria for considering studies for this article: To be considered, clinical studies had to be randomized trials comparing intervention; balloon angioplasty or stenting or both or surgical revascularization versus medical treatment, or surgical versus balloon angioplasty with or without stenting in hypertensive patients who had atherosclerotic renal artery stenosis with a minimum of three months of follow up after treatment Only those studies included with adult patients (age >18 years) who had uncontrolled hypertension (diastolic blood pressure ≥ 95mmHg, treated or untreated) and moderate-to-severe (≥50%) unilateral or bilateral atherosclerotic renal artery stenosis. Studies which were not randomized or those related to fibromuscular dysplasia, meta-analysis, and diagnostic studies were excluded.

Objectives: Explaining a critical appraisal of six major randomized clinical trials which compared Revascularization (intervention) to medication (conservative treatment) which includes Angioplasty and Stenting for Renal Artery Lesions Trial (ASTRAL), Stent Placement in Patients With Atherosclerotic Renal Artery Stenosis and Impaired Renal Function Trial (STAR), Dutch Renal Artery Stenosis Intervention Cooperative (DRASTIC), Essai Multicentrique Medicaments vs. Angioplastie trial (EMMA), Scottish and Newcastle Renal Artery Stenosis Collaborative Group trial (SNRASCG), and Prospective randomized trial of operative vs. interventional treatment for renal artery ostial occlusive disease (RAOOD) trials. We also highlighted some points about the ongoing CORAL (Cardiovascular Outcomes in Renal Atterosclerotic Lesions) trial.

Conclusions: Correction of Astherosclerotic Renal Artery Stenosis (ARAS), either by surgical revascularization or percutaneous methods, including stenting, has not been shown to be beneficial in treating Atherosclerotic RAS over conservative treatment, although some of the studies showed blood pressure control benefit in intervention groups like EMMA, SNRASCG and post hoc analysis of DRASTIC studies. Consequently, it seems reasonable to consider interventional procedures to correct Renal artery stenosis in patients who do not respond to medical therapy or with poorly-controlled or resistant hypertension; recurrent flash pulmonary edema; dialysis dependent renal failure resulting from atherosclerotic renal artery stenosis; chronic kidney disease and bilateral renal artery stenosis; or Renal artery stenosis to a solitary functioning kidney and waiting for the next available research with less flaws and biases.

Keywords: Renal artery obstruction; Stenosis; Atherosclerosis; Therapy; Management; Revascularization; Intervention; Randomized; Control; Trail; Evidence based

Introduction

Renal Artery narrowing and progressive renal impairment caused by atherosclerotic renovascular disease is a clinical problem that it's frequency increased in recent years [1-3]. There are many risk factors which may have roles in the development of atherosclerotic renovascular disease and they are the same as for other atheromatous vascular conditions like advanced age, smoking, hyperlipidemia, hypertension, renal failure, and diabetes [4]. There are various therapeutic options: a) Conservative or medical management with antihypertensive drugs including the general measures like smoking cessation, anti-lipid items, healthy diet and exercise b) Percutaneous angioplasty, usually with stent placement and c) Surgical revascularization [5,6].

Methodology

CASP questionnaire [7], Jadad scaling [8] and (Oxford Centre for Evidence-based Medicine) [9] leveling of evidence are used for the purpose of the critical appraisal. Moreover, table 4 is for the CASP questionnaire details of the selected trials (Table 4).

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In this section, a critical appraisal of the major trials within studies which compared revascularization, either angioplasty with stent or without stent and surgical versus medical or conservative approaches will be discussed. The quality of the trials as well as their implications on current practice will be critically evaluated.

1-ASTRAL trail [10] (Angioplasty and Stenting for Renal Artery Lesions trial)

ASTRAL authors' conclusions: "We found substantial risks but no evidence of a worthwhile clinical benefit from revascularization in patients with atherosclerotic renovascular disease" [10].

Astral was a randomized controlled trial, patients were randomly assigned either to undergo revascularization with medical therapy versus receiving medical therapy alone, in a 1:1 ratio with the use of a computerized minimized-randomization procedure. The results were precise in the sense of showing Confidence intervals and showing the P values of the primary and secondary outcomes. However, patients included in the trial did not have the same severity of renal artery stenosis and renal function in which the majority of patients had severe renal-artery stenosis (59% had stenosis of more than 70%) or clinically significant renal impairment (60% had a serum creatinine level of 150 Mmol/l [1.7 mg/dl] or more or both. Jadad scoring [7] of the ASTRAL trail is 3/5 (Table 1) and good sample size thus the quality of the study was good and it's level Ib of evidence [9].

Major drawbacks of ASTRAL:

a) Normal renal function at baseline, 25% of patients in each group had normal renal function (eGFR > 50 ml/min/1.73 m2) at the entry of the trial.

b) No core laboratory were found in ASTRAL, some patients in the 50%–70% stenosis group (about 40% of patients entered) actually had a stenosis of less than 50%. Moreover, some patients in the group with stenosis greater than 70% had stenosis of less than 70% and 40% serum creatinine were less than 150 μ mol/dl.

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- c) Possible selection bias, the physicians were aware that which patients selected would benefit from either revascularization or medications.
- d) High complication rate: The major complication rate in the first 24 hours was 9%
- e) The measurement of GFR was calculated by the Cockcroft–Gault method not MDRD.
- f) Non-blinding: though it's difficult to blind treatments in such a trial, thus observer and selection bias is highly expected.
- g) "Rate of cross-over" was 6% from medication to intervention group.

2-DRASTIC [11] (Dutch Renal Artery Stenosis Intervention Cooperative) trial

DRASTIC author's conclusion: "In the treatment of patients with hypertension and renal-artery stenosis, angioplasty has little advantage over antihypertensive-drug therapy" [11]. The study was a prospective randomized controlled trail, serious issues that was identified in DRASTIC trail;

a) The sample size was not sufficient to detect a significant difference between treatment groups. In other words, the chance of a type two statistical error is high. Balloon angioplasty without stenting was used as the method of revascularization. Experts

Jadad Score Calculation		ASTRAL	STAR	DRASTIC	EMMA	SNRASCG	RAOOD
Item	Score						
Was the study described as randomized (this includes words such as randomly, random, and randomization)?	0/1	1	1	1	1	1	1
Was the method used to generate the sequence of randomization described and appropriate (table of random numbers, computer-generated, etc)?	0/1	1	1	1	0	0	0
Was the study described as double blind?	0/1	0	0	0	0	0	0
Was the method of double blinding described and appropriate (identical placebo, active placebo, dummy, etc)?	0/1	0	0	0	0	0	0
Was there a description of withdrawals and dropouts?	0/1	1	1	1	1	1	1
Deduct one point if the method used to generate the sequence of randomization was described and it was inappropriate (patients were allocated alternately, or according to date of birth, hospital number, etc).	0/-1	0	0	0	1	1	1
Deduct one point if the study was described as double blind but the method of blinding was inappropriate (e.g., comparison of tablet vs. injection with no double dummy).	0/-1	0	0	0	0	0	0
Total score		3	3	3	1	1	1

The scores that imply the negative point about the trial written in red

 Table 1: Jadad scoring of the selected trials.

now recognize that stenting is required for renal artery intervention to have a durable result [12,13].

- b) "High rate of cross over" Twenty-two of the 50 patients randomized to medical therapy crossed over to the angioplasty group because their blood pressure became difficult to control. In other words, 44% of the patients in the medical group underwent angioplasty, an astonishing percentage in an intention-to-treat analysis comparing one therapy with another.
- c) Renal artery stenosis was defined as greater than 50% stenosis (allowing hemodynamic stable patient to enter the trial). Jadad Scoring for DRASTIC trial is 3/5 (Table 1), thus according to Jadad it's of good quality. Moreover, it's of level Ib of evidence and grade A of recommendation [8,9]. Furthermore, high rate of selection and observer bias was expected because of none blinding.

3-STAR [14] (Stent Placement in Patients with Atherosclerotic Renal Artery Stenosis and Impaired Renal Function trial)

STAR author's conclusion: "Stent placement with medical treatment had no clear effect on progression of impaired renal function but led to a small number of significant procedure-related complications" [14].

The Serious draw-backs of the STAR trial:

- a) They included patients with mild renal artery stenosis; 33% of the patients in the trial had mild renal artery stenosis (50%-70%), and 12 (19%) of the 64 patients in the intervention group which supposed to recieve stenting actually they had renal artery stenosis of less than 50%. Hence, it's really difficult to expect from this trial the benefit of stenting in patients who had mild (hemodynamically insignificant) renal artery stenosis).
- b) This study was under-powered i.e. there was high chance of a type two statistical error. Moreover, four patients lost in follow up and 3% drop out (dilution of the power).
- c) Not all "stent" group or patients received stents. In the medical group, all of the patients received medication without any crossovers. However, only 46 (72%) of the 64 patients subjected to stenting infact received a stent, while 18 (28%) did not.
- d) More than half of the patients had unilateral disease. It seems logical that if one were to plan a study or a trial with change in renal function to be the primary end point, it is reasonable only patients with bilateral renal artery stenosis of more than 70% or with stenosis of more than 70% to a solitary functioning kidney should be included. It's not reasonable to expect that patients with stenosis of less than 70% or with unilateral disease would get any benefit from revascularization.
- e) Complication rates were high. The complications during procedures and death rates were much higher than in many other reports on renal artery stenting. Four deaths were due to procedure and CV events and 11% due to hematoma. Jadad Scoring of STAR trial is 3/5 (Table 1), so the quality of the study is good but it was underpowered and it's of level Ib of evidence and Grade A recommendation [8,9].

4-EMMA [15] (Essai Multicentrique Medicaments vs. Angioplastie trial)

EMMA author's conclusion: "We found that angioplasty made

BP control easier in the short term but was more frequently associated with complications than conservative management in patients with unilateral atherosclerotic RAS" [15].

Like other trials, EMMA had some serious flaws including the following:

- a) Only unilateral renal artery disease was enrolled.
- b) The groups were not well balanced, as there were 23 patients for angioplasty and 26 for control group at the entry point.
- c) There are some differences that might have explained confounding and bias in the results like five patients in the control group and three in the angioplasty group were receiving no antihypertensive treatment, whereas all others were taking one to three antihypertensive agents.
- d) "Cross-over" seven of the control-group got the interventiongroup participants and not all participants outcomes were analyzed by the groups to which they were originally allocated (no intention-to-treat analysis).
- e) High complication rate in angioplasty group which was about (6 of 23, or 26%). Another issue was one in three eligible patients declined inclusion, mostly because of the patient's (or referring physician's) preference for angioplasty.
- f) Power issue of the study: initially they needed to enroll 52 patients to allow 90% power, yet 49 patients randomized finally.
- g) No information about Patency rate: Moreover, the quality of study is poor as it's 1/50n Jadad scaling (Table 2) and level Ib of evidence and grade A recommendation [8,9].

5- SNRASCG [16] (Scottish and Newcastle Renal Artery Stenosis Collaborative Group trial)

SNRASCG author's conclusion: In hypertensive patients with atheromatous renal artery stenosis, percutaneous renal angioplasty results in a modest improvement in systolic BP compared with medical therapy alone. This benefit was confined to patients with bilateral disease. No patient was 'cured', renal function did not improve, and intervention was accompanied by a significant complication rate" [16].

The serious issues were the following:

- a) There were difference between intervention and medication group number at the entry point i.e. intervention group was 25 and medical therapy was 30 patients.
- b) Power calculation description was unclear, thus we cannot decide if there was sufficient number of patients to predict significant outcome that may change practice. In 135 patients only 55 randomized.
- c) The method of allocation and randomization were unclear.
- d) No intention to treat analysis.
- e) High complication rate: (9 out of 25 in intervention group) like stroke, bleeding from arterial site, severe pain, but no death reported. The quality of the study on Jadad Scale is 1/5 (Table 1) and it's of level II b of evidence and grade B of recommendation thus policy should not be changed as a result of this trial [8,9].

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Study ID					Participants Intervention	Intervention	
(author, year)	N	Design	Setting	Participants	(experimental group)	(control group) Study	Follow up
Weibull et al. (1993)	58	Randomized controlled clinical trial	Hospital, Sweden	58 patients without diabetes with severe hypertension and significant stenosis	Percutanesous Transluminal Renal Angioplasty (PTRA)	Operation	24 mo
Webster etal. SNRASCG-trial 1998	135	Randomized controlled clinical trial	Scottish Hospitals Endowments Research Trust.	135 eligible patients with hypertension and renovascular disease were identified	Percutanesous transluminal renal angioplasty (PTRA	Anti-hypertensive drug therapy	3–54 months
Plouin et al EMMA (1998)	49	Randomized controlled clinical trial	Hospital Broussais, and INSERM U-36 (PF.P.), Paris, France.	Patients were randomly assigned antihypertensive drug treatment (control group, n.(26) or angioplasty n. (23)	Percutanesous transluminal renal angioplasty (PTRA) with or without stent	Anti-hypertensive drug therapy	6 month
van deVen et al. (1999)	85	Randomized controlled clinical trial	Utrecht University hospital, Netherlands	85 patients with Ostial atherosclerotic renal artery stenosis	Percutaneous Transluminal Angioplasty (PTA)	Angioplasty with stent placement (PTAS)	6 mo
Jaarsveld et al. DRASTIC (2000)	106	Randomized controlled clinical trial	Multicentre, US	106 patients with hypertension who had atherosclerotic renal-artery stenosis	Percutaneous transluminal renal angioplasty	Anti-hypertensive drug therapy	12 mo
Uzzo et al(2002)	52	Randomized controlled clinical trail	Cleveland Clinic Foundation	52 patients with atherosclerotic renovascular disease and hypertension	surgical	medical	74 month
Wheatley et al ASTRAL trial (2007)	806	Randomized controlled clinical trial	57 hospitals (53 in the United Kingdom, 3 in Australia, and 1 in New Zealand).	806 patients with atherosclerotic renovascular disease either to undergo revascularization in addition to receiving medical therapy or to receive medical therapy alone	(angioplasty either alone or with stenting with or without medical management	Medical management (statins, antiplatelet agents, and optimal blood-pressure control)	34 months
Bax et al STAR trail (2009)	140	Randomized controlled clinical trial	10 European medical centers.	Stent placement and medical treatment (64 patients) or medical treatment only (76 patients).	stent placement and medical treatment	Medical treatment consisted of antihypertensive treatment, a statin, and aspirin	24 month
Balzer et al RAOOD (2009)	49	Randomised controlled clinical trial	University of Düsseldorf	49 patient with ARVD underwent either Open surgical reconstructive procedure or PTRA± stenting	surgery	Renal artery angioplasty± stenting	72 month

Table 2: Characteristics of included studies.

6-RAOOD [17] (Prospective randomized trial of operative vs. interventional treatment for renal artery ostial occlusive disease)

RAOOD author's conclusion: "Both treatment modalities showed good early results concerning RVH, kidney function, and renal perfusion" [17].

The serious flaws of this study were the following:

- a) Single center and Allocation concealment was unclear
- b) The groups were not well balanced (PTRA+ stent group number = 22, Surgical group number = 27)
- c) Power calculation was not mentioned, so it's unclear whether the number of patients is sufficient or not to predict it's outcome and hard to predict how meaningful it was, thus we cannot say

the result is precise enough to make a decision.

- d) There were confounders which might have affected the results, like the difference in preoperative serum creatinine among the two groups which was higher in interventional group as compared to surgical group. 27% diabetics in the interventional group, 11% in the operative group. Moreover, PAOD was 54% in the interventional group, 40% in the operative group.
- e) Two patients crossed over to surgical treatment. The incidence of diabetes and Peripheral Arterial Occlusive Disease (PAOD) differed slightly; higher in interventional group. Serum creatinine as well as urea levels were slightly higher in the interventional group.
- f) Complication rate was high, 18% in interventional group and 19% in surgical group though the author claimed that it was low as

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compared to cohort studies. On Jadad Scoring its 1/5 (Table 1) and it's of level II b of evidence and grade B of recommendation thus the quality of the study is poor. Moreover, policy should not be changed as a result of this trial [8,9].

Discussion

Nine main Randomized Controlled Trials (RCTs) have completed enrollment and reported results on the management of aRVD, their characteristics are summarized in table 2. Four trials compared balloon angioplasty with medical management alone, one compared primary renal artery stenting with balloon angioplasty with stenting as needed, one compared stenting with medical therapy with medical therapy alone, two compared surgical revascularization with endovascular revascularization, and one compared surgical revascularization with medical management. In six of the nine trials, the primary end points were blood pressure control or renal artery patency. For this article we only criticized the major trials in which their methodological quality is summarized in Table 3 [18].

Not all of the five completed trials comparing angioplasty with medical management have demonstrated blood pressure, renal function, or survival results favouring renal artery angioplasty or stenting when the three of the study group was evaluated in an intention-to-treat analysis [10,11,14] and the other two were not [15,16]. The report by the Scottish Newcastle group demonstrated a significant benefit in blood pressure treatment for the subset of participants with bilateral ARVD [16]. Van Jaarsveld et al. [11] in DRASTIC trial, demonstrated significant reduction in blood pressure and medications in post hoc analyses of treatment received, without considering initial crossover s tatus and treatment assignment. Only ASTRAL had sufficient number of patients, all of the other trials were relatively small and significantly

underpowered to detect meaningful differences in solid outcomes such as survival rate, freedom from adverse cardiovascular events, and the development of dialysis-dependent renal failure. Furthermore, the studies excluded patients with severe baseline renal function impairment [11,16], suffered from obvious significant crossover between treatment groups [11,19], did not include renin-angiotensinbased antihypertensive medications into medical treatment [16], and used angioplasty without stenting for interventional approach or treatment [11,14,16,19]. Hence, it's impossible to generalize or apply the results from these trails to current endovascular treatment of Atherosclerotic Renal Artery disease because of the limitations we addressed. In a separate trial comparing primary renal artery stenting vs. angioplasty alone, Van de Ven et al. [20] evaluated disease recurrence at six months in patients with ostial renal artery stenosis randomized to angioplasty alone vs. Renal Artery Percutaneous Transluminal Angioplasty and Stent (RAPTAS). Superior technical success reported by the research group, they reported improved primary patency, and reduction in recurrent stenosis in the RA-PTAS group. These results contributed to widespread use of primary stent placement as a current standard endovascular management for ARVD. Three trials evaluating surgical renal artery revascularization have also been reported. In their comparison between angioplasty (without stenting) vs. surgical revascularization of ARVD, Weibull et al. [21] observed similar blood pressure responses between groups but low technical success and low primary patency rate with endovascular management. Balzer et al. [17] reported similar results in terms of patency, hypertension, and renal function responses. A single randomized comparison between surgical and medical management of ARVD has also been published. Uzzo et al. [19] randomized 52 patients to medical therapy vs. surgical intervention and evaluated a composite end point outcome that included blood pressure, renal function, cardiovascular morbidity, and

Study (Reference)	Allocation Concealment	Method of Randomization	Blinding of Main Outcome	Intention-to- Treat Analysis	Number of Patients Withdrawn or Lost to Follow-up	Quality Assessment Score* (Jadad Scoring)
ASTRAL 2008	Adequate	Computerized Minimized- randomization procedure	No	Yes	38	3
STAR 2009	Adequate	Computer generated	No	Yes	4	3
DRASTIC 2000	Adequate	Computer generated	No	Yes	2	3
EMMA 1998	Unclear	Sealed envelopes	No,But objective measurement (24-hour ambulatory blood pressure)	No	1	1
SNRASCG 1998	Unclear	Not mentioned	Yes	No	6	1
RAOOD 2008	Unclear	Unmarked envelope	No	Yes	11	1

Adapted from Nordmann AJ, Woo K, Parkes R, Logan AG. Balloon Angioplasty or Medical Therapy for Hypertensive Patients with Atherosclerotic Renal Artery Stenosis? A Meta-Analysis of Randomized Controlled Trials

Randomized Controlled Trials

*Range of 0 (low) to 5 (high).

ASTRAL_Angioplasty and Stenting for Renal Artery Lesions trail

STAR_Stent Placement in Patients with Atherosclerotic Renal Artery Stenosis and Impaired Renal Function

DRASTIC _ Dutch Renal Artery Stenosis Intervention Cooperative trial;

EMMA _ Essai Multicentrique Medicaments vs. Angioplastie trial; SNRASCG _ Scottish and Newcastle Renal Artery Stenosis Collaborative Group trial

RAOOD trail. Renal Artery Ostial Occlusive Disease

Table 3: Methodological Quality of Included Trials that compared Angioplasty to medical management.

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Did the study ask a clearly featiend question?	Vac	Vaa	Vaa	Vaa	Vaa	Vee
Did the study ask a cleany-locused question?	Tes	Tes	Tes	Tes	Tes	Tes
Qustiones of CASP	ASTRAL	STAR	DRASTIC	EMMA	SNRASCG	RAOOD
1. Did the study ask a clearly-focused question?	Yes	Yes	Yes	Yes	Yes	Yes
2. Was this a randomised controlled trial (RCT) and was it appropriately so?	Yes	Yes	Yes	Yes	Yes	Yes
3-Were participants appropriately allocated to intervention and control groups?	Yes	Yes	Yes	Can't tell	Can't tell	Can't tell
4-Were participants, staff and study personnel 'blind' to participants' study group?	No	No	Can't tell	No	No	No
5-Were all of the participants who entered trial accounted for at its conclusion?	Yes	Yes	Yes	Yes	Yes	Yes
6-Were the participants in all groups followed up and data collected in the same way?	Yes	Yes	Yes	Yes	Yes	Yes
7-Did the study have enough participants to minimize the play of chance?	Yes	No	No	No	No	No
8-How precise are these results	precise	No	No	No	No	No
9-Were all important outcomes considered so the results can be applied?	No	No	No	No	No	No
Level of evidence	lb	lb	lb	llb	llb	llb
Total questions answered	7	5	5	4	4	4

Table 4: CASP Questionnaire for the selected randomized controlled trails.

death. The authors did not find any significant difference in event-free survival between treatment groups at a median follow-up of 74 months, but they noted a trend towards reduced mortality in those patients with renal impairment managed surgically.

The methodological quality of all published randomized controlled trials comparing either PTA [11,15,16,19], with medical therapy, analyzed according to the method of Jadad [7] was low to moderate [18]. The risk of bias, defined according to the Cochrane Collaboration handbook [22] ranged from moderate to severe [23,24]. Major points of criticism are the non blinded analysis of the study results, the high rate of cross-over to angioplasty - in particular in the largest of the three PTA trials (DRASTIC: 44%) - and the long enrolment periods - especially in the DRASTIC trial (seven years for 106 patients), but also in the ASTRAL trial (eight years). Moreover, the most severe bias of all of the studies, including the ongoing CORAL trial, is the criteria for defining the severity of renal artery stenosis. They enrolled 1080 patients and the power of the study is 90% Lesion severity started with a narrowing of the luminal diameter by \geq 60% with 20 mmHg gradient or \geq 80%, respectively, and even patients with systolic gradient of 20 mmHg with systolic gradient in ≥ 1 renal arteries of ≥ 3.5 in diameter and supplying at least 50% of the ipsilateral kidney will be eligible for randomization [25]. 30% of the patients included in the trials had RAS with a diameter stenosis of less than 70%; some even less than 50% [26]. None of the studies asked for proof of the hemodynamic relevance of the RAS before enrolment. Experimental studies have shown that a drop of post-stenotic flow lumen does not occur until the diameter reduction exceeding 70% [27,28]. Although the results of CORAL trial is not published yet officially, if we compare CORAL trial to ASTRAL, the power of study in CORAL is 90% and number of patients enrolled is 1080 compared to ASTRAL which is 80% and 806 patients. In the Coral trial they are using genesis stent. In Astral trial 25% of patients had normal and 15% near normal renal function. 41% has renal artery stenosis of less than 70%, so this had definitely made biases in the study. Furthermore, we could not find population data of the CORAL trial as the study has not published yet. Moreover, it seems reasonable to consider interventional procedures to correct Astherosclerotic Renal artery stenosis in patients who do not respond to medical therapy or with poorly-controlled or resistant hypertension; recurrent flash pulmonary edema; dialysis dependent renal failure resulting from atherosclerotic renal artery stenosis of more than 70%; chronic kidney disease and bilateral renal artery stenosis of more than 70%; or Renal artery stenosis to a solitary functioning kidney more than 70% or even less, though there is no solid evidence for supporting the above recommendation, but until the next available clinical trial will be available-CORAL probably answers some of the questions, it seems reasonable if revascularization tried for the above group.

Recommended research or RCT in management of Atherosclerotic renal artery disease

A long-term, multi-central (1:1) randomized controlled trial will be of great value in changing practice, focusing on comparison of the effect of medical treatment versus Percutaneous Transluminal Renal Angioplasty (PTRA) with stenting on controlling blood pressure, kidney disease progression, and cardiovascular morbidity and mortality. Such trial should aim to clarify and the research questions of who is the ideal candidate for interventional therapy, it should include patients with renal artery stenosis more than 70% narrowing, either bilateral or unilateral in equal numbers and both control group and intervention group should have the same number of patients at entry point. Hypertensive population should include African American, Hispanics, and Native Americans as well as Caucasians. The study should use MDRD formula, and minimizing selection, observer bias, clear method of allocation and blinding if possible.

Conclusions

Intervention in atherosclerotic renovascular disease including

Balloon angioplasty, stenting or even surgical revascularization did not show any significant benefit over medication on improvement of renal function except with some of the trials showed slight improvement on blood pressure control in intervention group compared to control groups. Moreover some them are level Ib evidence and some are IIb and on Jadad Scoring their quality did not cross more than 3/5, high selection and observer bias in all of them, high complication and cross over in most of them. they did not include all races, they did not use MDRD in their calculation of eGFR and even some trials only used serum creatinine in the follow up, thus another trial will probably answer the questions, which should be of an excellent quality and level Ia evidence, using MDRD formula for renal function measurement and because of the fact that blinding is impossible thus getting level Ia evidence with excellent quality of 4-5/5 on Jadad scoring will be challenging. Moreover, we cannot conclude on current evidence that any kind of intervention is better than conservative treatment.

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