STATE-OF-THE-ART REVIEW

Hemodynamic Measurements for the Selection of Patients With Renal Artery Stenosis



A Systematic Review

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ABSTRACT

Interventions targeting renal artery stenoses have been shown to lower blood pressure and preserve renal function. In recent studies, the efficacy of catheter-based percutaneous transluminal renal angioplasty with stent placement has been called into question. In the identification of functional coronary lesions, hyperemic measurements have earned a place in daily practice for clinical decision making, allowing discrimination between solitary coronary lesions and diffuse microvascular disease. Next to differences in clinical characteristics, the selection of renal arteries suitable for intervention is currently on the basis of anatomic grading of the stenosis by angiography rather than functional assessment under hyperemia. It is conceivable that, like the coronary circulation, functional measurements may better predict therapeutic efficacy of percutaneous transluminal renal angioplasty with stent placement. In this systematic review, the authors evaluate the available clinical evidence on the optimal hyperemic agents to induce intrarenal hyperemia, their association with anatomic grading, and their predictive value for treatment effects. In addition, the potential value of combined pressure and flow measurements to discriminate macrovascular from microvascular disease is discussed. (J Am Coll Cardiol Intv 2017;10:973-85) © 2017 by the American College of Cardiology Foundation.

Renal artery stenosis is associated with increased risk for kidney failure and is an independent predictor of mortality (1,2). Balloon angioplasty with or without stent placement has been used as a treatment modality for renovascular hypertension and preservation of kidney function in patients with renal artery stenosis. However, recent large randomized studies such as the ASTRAL (Angioplasty and Stent for Renal Artery Lesions) and CORAL (Cardiovascular Outcomes in Renal Atherosclerotic Lesions) trials failed to show a beneficial effect of percutaneous transluminal renal angioplasty with stent placement (PTRAS) over medical therapy alone regarding blood pressure reduction, prevention of renal function deterioration, or cardiovascular outcome (3,4). This was confirmed in a recent meta-analysis of randomized clinical trials comparing revascularization and medical therapy for renal artery stenosis demonstrating that angioplasty with or without stenting was not superior to medical therapy across a wide range of clinical endpoints (5). Despite the lack of superiority of PTRAS in recent trials, a considerable range of smaller clinical studies have demonstrated that PTRAS was successful in improving blood pressure control and renal function (6-16). ASTRAL and CORAL enrolled large numbers of patients with moderate to severe chronic kidney disease.

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ABBREVIATIONS AND ACRONYMS

APV = average peak flow velocity

CFR = coronary flow reserve

CI = confidence interval

FFR_{myo} = myocardial fractional flow reserve

HSG = hyperemic systolic gradient

IA = intra-arterial

MHG = mean hyperemic gradient

PTRAS = percutaneous transluminal renal angioplasty with stent placement

rFFR = renal fractional flow reserve

RFR = renal flow reserve

These patients may have entered the trials too late for potential benefit of PTRAS. In addition, although ASTRAL and CORAL were performed in populations with large proportions of subjects with controlled hypertension, previous studies have shown benefits of PTRAS in patients with (recent histories of) uncontrolled hypertension, therapy resistant hypertension, recurrent flash pulmonary edema, or refractory heart failure (17-19). Next to differences in clinical characteristics, the selection of renal arteries suitable for intervention is currently on the basis of anatomic grading of the stenosis by angiography rather than functional assessment under hyperemia, whereas measurement of pressure gradients alone (without hyperemia) does not appear to have additional diagnostic value (20).

In the coronary circulation, anatomic abnormalities do not coincide with functional significance (21,22). Assessment of functional characteristics of the stenosis by sensor-equipped guidewires to measure pressure and/or flow under hyperemic conditions has significantly improved clinical outcomes (23-25), whereas coronary interventions based on anatomic criteria were not superior compared with optimal medical therapy alone (26). In addition, the combination of coronary pressure-derived myocardial fractional flow reserve (FFR_{mvo}) and coronary flow reserve (CFR) have been demonstrated to provide additional value for identifying clinically relevant flow impairment (27,28). Here, measurement of FFR_{myo} and CFR is synergistic, with FFR_{myo} providing information on the functional severity of a focal coronary artery stenosis, whereas CFR provides information on the functional properties of both focal and diffuse coronary artery disease and microvascular function. This information allows discrimination between solitary coronary lesions and diffuse or microvascular disease, thereby further improving the selection of patients who may benefit from mechanical revascularization (29). Translating these principles to renovascular disease might contribute to more optimal patient selection for renal intervention.

To assess the contribution of functional measurements in selecting patients with renal artery stenosis, we performed a systematic review on the feasibility, reproducibility, and clinical applicability of renovascular hemodynamic hyperemic measurements in patients with and without renal artery stenosis.

METHODS

We systematically retrieved reports on intrarenal hemodynamic measurements in patients with renal artery stenosis (Online Appendix). We selected studies that explored the diagnostic value of intrarenal hemodynamic responses with pressure and/or flow wires. We collected information on reproducibility, maximal hyperemic response, dose-effect responses for hyperemic agents, cutoff values, and associations of measurements with treatment outcomes. We included studies obtaining hyperemic physiological measures, including mean hyperemic gradient (MHG), hyperemic systolic gradient (HSG), renal flow reserve (RFR), and/or renal fractional flow reserve (rFFR) in patients with and without renal artery stenosis.

We defined MHG as the mean pressure gradient under hyperemic conditions (MHG = Pa - Pd during 1 cardiac cycle), HSG as the maximal systolic pressure gradient over a stenosis under hyperemic conditions (HSG = Pa - Pd during the systolic phase), RFR (sometimes referred to as renal flow velocity reserve because flow velocity rather than flow is measured) as the ratio of intrarenal flow velocity or average peak flow velocity (APV) at hyperemia to intrarenal APV during baseline conditions (RFR = APV_{hyperemia}/APV_{baseline}), and rFFR as the ratio of distal (i.e., renal) pressure to proximal (i.e., aortic) pressure during hyperemic conditions (rFFR = Pd/Pa), where Pd is the pressure distal to the lesion and Pa is the pressure proximal to the lesion. An example of intrarenal measurements under baseline and hyperemic conditions explaining MHG, HSG, RFR, and rFFR is shown in Figure 1.

DATA SOURCES AND SEARCHES. For this systematic review, we adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. MEDLINE, Embase, and PubMed were searched (until June 2015) for clinical studies performing intrarenal hyperemic measurements expressed as MHG, HSG, RFR, or rFFR. The electronic search strategy was verified by a clinical librarian who was trained in systematic review searches. Two reviewers (P.M.v.B. and T.P.H.) first evaluated the reports based on titles and abstracts. Case reports, guidelines, editorials, and reviews were excluded, as well as abstracts with combinations of title and abstract that indicated that there was no possibility that the abstract could fit the requirements of this review.

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