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Renal Artery Stenosis in Patients Undergoing Major Surgery or otherwise Critically Ill: The Short-Circuit between Association and Causality

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Risk prediction is an intense field of research and there is an increasing need for an interest in being able to empirically estimate customized, patient-specific risks for virtually all surgical operations in a user friendly format. Surgical risk evaluation before major surgery should offer an opportunity to improve shared decision making and patient care [1]. Yet, there is ongoing debate on how to better identify patients at risk in several important clinical scenarios and when weighing a given risk factor for decision making or when trying to amend it [2,3].

Acute renal failure (ARF) occurs in approximately 1-5% of all hospitalized patients, yet there are no large studies addressing renal dysfunction after non-cardiac or non-vascular surgery [4]. Severe acute kidney injury (AKI) after a major surgical operation is associated with a high risk of morbidity and mortality [5]. Particular attention should be paid to postoperative patients that require renal replacement therapy (RRT), because this subgroup of patients, defined to be the most critical ones, need careful attention and have poor prognosis [6]. In addition, ARF without the need for RRT remains associated with increased mortality in critically ill patients and postoperative cardiac surgery patients. Similarly, there is a clinically important relation between ARF and increased postoperative mortality in non-cardiac surgery.

Several preoperative predictors, such as age, emergent surgery, liver disease, body mass index, high-risk surgery, peripheral vascular occlusive disease, and chronic obstructive pulmonary disease necessitating chronic bronchodilator therapy appear associated with ARF after cardiac surgery as well as after non-cardiac surgery [4,7-14]. There is also some evidence suggesting that renal artery stenosis could be associated with an increased risk for renal injury and ensuing clinical complications [15].

Renal artery stenosis is most commonly due to atherosclerosis and much more rarely fibromuscular dysplasia or inflammatory disease such as Takayasu arteritis [16,17]. Renal artery stenosis, which is present in 1 to 5% of people with hypertension, often occurs in combination with peripheral or coronary artery disease and its prevalence among persons older than 65 years of age may be as high as 7%. Thus, this condition is an important public health issue [18]. Renal artery narrowing is usually focal but can be more diffuse and is of great importance because of its consequent renal ischemia, which can in turn results in disturbance of renal function, blood pressure control, fluid and salt retention, and renal endocrine functions [19]. Philip et al. have recently reported that atherosclerotic renal artery stenosis (ARAS) is rather common, recognized in 29% of patients undergoing cardiac surgery at the renowned Cleveland Clinic, with an even higher prevalence in those with old age, low body mass index, peripheral artery disease and low level of high-density lipoprotein [20]. An additional important piece of the puzzle is that patients with atherosclerotic renal vascular disease have an high mortality, presumably partly conferred by their extensive vascular comorbidities [21,22].

When the functional evaluation bears out the severity of the stenosis it is necessary to make a clinical decision [23]. The role of and indications for intervention for renal artery stenosis have long been debated (Table 1) [30,31]. Recent evidence has shown that optimal medical treatment, including statins and risk reduction strategies tailoring important prognostic factors should be the preferred option for most patients with atherosclerotic renal artery disease [32]. Only a minority of patients with rapidly progressive hypertension or renal insufficiency and flash pulmonary

edema, or with specific lesions such as bilateral severe renal artery stenosis, or solitary kidney, are likely to a benefit from restoring kidney perfusion [32,33]. Ritchie et al. have indeed confirmed that flash pulmonary edema is a risk factor for adverse outcomes in patient with ARAS and have supported revascularization for this presentation [21]. Deterioration of renal function in the presence of ARAS may not reflect however true ischemia under normal conditions as blood flow to the kidney is far in excess of metabolic needs [22]. Moderate reductions in blood flow, as in ARAS, may not be the sole or even the major contributor to reduced renal function. Philip et al. have shown no association between the presence of ARAS and change in glomerular filtration rate (GFR) or lower GFR, need for RRT, length of intensive care unit (ICU) stay or mortality [20,34], in keeping with findings comparing percutaneous revascularization versus best medical therapy for renal artery stenosis [31].

Author	Year of publication	No. patients	Characteristics of the study population	Treatment and results
Plouin et al. [24]	1998	49	Hypertension and unilateral RAS	Balloon angioplasty (with or without stent placement): No significant change in SBP or DBP No significant change in SCr
Webster et al. [25]	1998	55	Resistant hypertension and bilateral or unilateral RAS	Balloon angioplasty: 1) Bilateral RAS: Significant improvement in SBP after angioplasty No significant change in DBP No significant change in SCr 2) Unilateral RAS: No significant change in SBP and DBP No significant change in SCr
Van Jaarsveld et al. [26]	2000	106	Resistant hypertension with normal or mild chronic renal insufficiency and RAS	Balloon angioplasty: No significant change in SBP or DBP No significant change in SCr
Bax et al. [27]	2009	140	Chronic renal insufficiency and ostial RAS	Renal artery stenting: No significant effect on progression of renal dysfunction No significant effect on BP
ASTRAL investigators [28]	2009	806	Resistant hypertension or unexplained chronic renal insufficiency and RAS	Renal artery stenting: No significant effect on renal function No significant effect on BP No significant effect on mortality
Scarpioni et al. [29]	2009*	52	Resistant hypertension with chronic renal insufficiency and RAS	Renal artery stenting: No significant effect on renal function No significant effect on BP No significant effect on mortality
Cooper et al. [18]	2014	947	Hypertension or chronic kidney disease and RAS,	Renal artery stenting: No significant benefit in the prevention of clinical events No significant difference in all causes mortality Modest reduction of BP

BP: blood pressure; DBP: diastolic blood pressure; RAS: renal artery stenosis; SBP: systolic blood pressure; SCr: serum creatinine. *Presented

Table 1. Randomized trials comparing to medical therapy for renal artery stenosis.

Most recent results stemming from the Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL) trial have confirmed these prior data, showing that, despite the fact that the treatment of renal-artery stenosis could improve blood pressure and renal function, renal artery stenting did not confer a significant benefit with respect to the prevention of clinical events when added to a comprehensive, multifactorial medical therapy in people with atherosclerotic renal artery stenosis and hypertension or chronic kidney disease [18,35]. Notwithstanding these lukewarm results for the primary and key secondary end-points in the CORAL study, it is also true that stenting yielded a moderate but statistically significant reduction in blood pressure (average of -2.3 mm Hg [95% confidence interval: -4.4 to -0.2], p=0.03).

In conclusion, until new treatments are found to be save and effective, patients who have moderately severe atherosclerotic renovascular disease and are critically ill or awaiting non-cardiac surgery should mainly receive medical therapy to control blood pressure and prevent the progression of atherosclerosis but should not be corralled into getting a renal-artery stent [18]. The best practice for those with critical or subocclusive renal artery stenosis should instead probably be individualized and decision-making shared with several specialists, to minimize the risk of complications but salvage a jeopardized kidney.

Conflicts of interest: None

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