

# Multisystem Revascularization

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## ABSTRACT

Atherosclerosis affects all major vascular territories. Both surgical and endovascular revascularization techniques have evolved, with more and more patients presenting with disease in multiple vascular beds. This can lead to difficult decision-making and the potential for complications. In this article, we review the available literature to help the clinician decide on optimum sequence, timing, and mode of multisystem revascularization.

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## INTRODUCTION

The diagnosis and treatment of vascular disease in the aorta, carotid, coronary, renal, and peripheral arteries is associated with reductions in morbidity and mortality. Because atherosclerosis is a systemic process, patients often present with disease involving more than one vascular bed (Table).<sup>1</sup> In this situation, the clinician is often faced with a dilemma regarding the optimum sequence, timing, and mode of multisystem revascularization. The aim of this article is to review the available literature on this topic.

## CORONARY ARTERY AND CAROTID ARTERY REVASCLARIZATION Prevalence

Among patients with symptomatic coronary artery disease (CAD), 10% to 20% have >70% carotid artery stenosis (CAS).<sup>2,3</sup> Among patients awaiting coronary artery bypass grafting (CABG) procedures, 17% to 22% have  $\geq 50\%$  CAS and 6% to 12% have  $\geq 80\%$  CAS.<sup>4,5</sup> The prevalence of CAD in patients awaiting carotid endarterectomy (CEA) procedures is 35% to 45%.<sup>6,7</sup>

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## Timing of Concomitant Coronary and Carotid Revascularization

In a patient requiring both carotid and coronary revascularization, the sequence of procedures is generally dictated by the stability of the vascular beds, with the preference being to revascularize the more unstable vascular bed first. This approach is based on data showing poor outcomes when revascularization is deferred in these situations. In patients with CAS clinically manifesting as transient ischemic attack, stroke risk is markedly higher compared with that of an asymptomatic patient with CAS, with the highest risk immediately following the initial ischemic event. In one study, 11% of patients developed a stroke within 90 days after a transient ischemic attack, with 50% occurring within the first 48 hours.<sup>8</sup> In patients with symptoms of acute coronary ischemia, coronary revascularization via either a surgical or percutaneous route has been shown to be superior to medical therapy.<sup>9–12</sup>

## Planned Coronary Revascularization and Concomitant Carotid Artery Disease

When percutaneous coronary intervention (PCI) is chosen as the mode of coronary revascularization, the risk of periprocedural stroke is 0.3% to 0.4%.<sup>13,14</sup> There are no data suggesting increased stroke rates in patients with concomitant CAS undergoing PCI. Hence, screening for CAS prior to PCI is not recommended. If a patient presents for PCI with documented CAS, simultaneous or staged carotid intervention can safely be performed with the mode, sequence, and timing of the procedure determined by the anatomy and stability of the vascular beds.<sup>15–18</sup>

When CABG is planned, carotid duplex screening is recommended prior to elective surgery in asymptomatic patients with any of the following criteria: age >65 years, left main stenosis, peripheral arterial disease, history of smoking, and history of transient ischemic attack, stroke, or carotid bruit.<sup>19</sup> Carotid revascularization is recommended before or concomitant to elective CABG in patients with symptomatic carotid stenosis >50% or asymptomatic carotid stenosis >80%.<sup>20</sup> However, it should be noted that 50% of strokes occurring after CABG occur from other causes, such as atheroemboli.<sup>21</sup> Aortic cross-clamping, atrial fibrillation, and duration of bypass are

**Table. Prevalence of Multisystem Atherosclerosis**

Variable	Prevalence, %	Comment
CAS in CAD	10–20	Symptomatic CAD, CAS defined as $\geq 70\%$ stenosis
AA in CAD	10	Symptomatic CAD awaiting revascularization
RAS in CAD	11–18	RAS defined as $>50\%$ stenosis, CAD defined by $>50\%$ coronary stenosis
LE atherosclerosis in CAD	15–40	LE atherosclerosis defined by abnormal ankle brachial index
CAD in CAS	35–45	CAS defined as patients awaiting carotid endarterectomy
AA in CAS	9–20	CAS defined as $>50\%$ stenosis
RAS in CAS	7–27	CAS defined as $>50\%$ stenosis
CAD in AA	30–60	
CAS in AA	2–9	CAS defined as $>60\%$ stenosis
CAD in LE atherosclerosis	25–78	

\* CAS=carotid artery stenosis; CAD=coronary artery disease; AA=aortic aneurysm; RAS=renal artery stenosis; LE=lower extremity

other important risk factors for stroke occurring during CABG.<sup>22–24</sup>

Carotid revascularization in patients awaiting CABG can be surgical or percutaneous. The American College of Cardiology/American Heart Association (ACC/AHA) guidelines do not discuss mode but do suggest that carotid revascularization should precede coronary revascularization when significant carotid disease is present, except in the uncommon situation of the emergent CABG patient, in whom CEA should closely follow CABG.<sup>20</sup>

Carotid artery stenting has emerged as an attractive alternative to CEA. Potential issues with this procedure in patients with concomitant CAD are hemodynamic compromise leading to exacerbation of coronary ischemia and duration of antiplatelet therapy.<sup>25,26</sup> Because dual antiplatelet therapy after CAS is recommended for 4 weeks, CABG may be delayed during that time.<sup>27–29</sup> Anecdotal reports have shown surgery to be safe in patients receiving clopidogrel with carotid stenting done 1 to 5 days prior to surgery.<sup>30</sup> Current data do not show an advantage of staged CAS-CABG as compared with staged CEA-CABG.<sup>31–34</sup>

### Planned Carotid Revascularization and Concomitant Coronary Artery Disease

Stress testing to detect asymptomatic CAD is not indicated prior to elective carotid revascularization. The ACC/AHA 2007 preoperative guidelines consider elective CEA to be a low-risk surgery in which one can proceed without cardiac assessment provided there are no high-risk features such as decompensated congestive heart failure, unstable angina, recent myocardial infarction, uncontrolled arrhythmias, or severe valvular disease.<sup>35</sup>

During evaluation, if a patient scheduled for carotid revascularization is found to have symptoms suggestive of coronary ischemia, then the priority is to revascularize the more unstable bed first. In a patient with symptomatic carotid stenosis and concomitant symptomatic CAD, assessing the stroke risk can help guide timing of revascularization. Markers of increased stroke risk include male sex, irregular carotid plaque, increasing age, contralateral occlusion,  $>90\%$  CAS, hemispheric symptoms, cortical stroke, and more than 6 months of recurrent symptoms.<sup>36</sup>

### Simultaneous Coronary and Carotid Revascularization

For the unstable patient with both acute coronary ischemia and symptomatic carotid stenosis, simultaneous coronary and carotid revascularization may be performed, with best outcomes seen with percutaneous revascularization of both vascular beds.<sup>15–18,37,38</sup>

### Summary

Optimal treatment has yet to emerge despite various reports in 110 publications and with more than 9,000 patients treated during the past 30 years.<sup>20,39,40</sup> Revascularization needs to be individualized, and the most unstable vascular bed should be addressed first.

## CAROTID ARTERY REVASCULARIZATION AND AORTIC ANEURYSM REPAIR Prevalence

The prevalence of abdominal aortic aneurysm (AA) in patients with CAS  $>50\%$  ranges between 9% and 20%.<sup>41–43</sup> The prevalence of CAS that is  $>60\%$  in patients with AA is 2% to 9%.<sup>41,44–46</sup>

### **Timing of Concomitant Carotid Revascularization and Aortic Aneurysm Repair**

For patients with both CAS and AA, no guidelines exist to guide timing of revascularization. No large observational studies or trial data were identified during the literature search. If both symptomatic AA and CAS are present, as with an aortic dissection involving the carotid artery, concomitant treatment is necessary, with a few case reports showing the feasibility of this approach.<sup>47,48</sup>

### **Planned Carotid Artery Revascularization and Concomitant Aortic Aneurysm Repair**

Current guidelines do not discuss screening for AA in patients undergoing elective carotid revascularization.<sup>19</sup> If an AA is detected in a patient awaiting elective carotid revascularization, the sequence of procedures should be guided by symptoms. For symptomatic carotid stenosis, CEA can precede or be performed simultaneously with AA repair with good outcomes.<sup>43,49–51</sup> Data are lacking to support the use of carotid artery stenting in this situation. For patients with asymptomatic CAD awaiting CEA who have an incidental finding of AA meeting the criteria for repair, current data suggest that CEA can be safely deferred for AA repair, provided that CAS is <80%.<sup>49</sup> For asymptomatic stenosis >80%, the data are conflicting.<sup>49,51</sup>

### **Planned Aortic Aneurysm Repair and Concomitant Carotid Artery Disease**

Current guidelines support screening for atherosclerotic carotid stenosis prior to AA repair only in patients with history of transient ischemic attack, prior ischemic strokes, or retinal ischemic events.<sup>41</sup>

If CAS is detected in a patient awaiting elective AA repair, the sequence of procedures should be guided by symptoms. In a patient with symptomatic atherosclerotic carotid stenosis, carotid revascularization takes precedence.<sup>51</sup> In a patient with an incidental finding of asymptomatic CAS, carotid revascularization can be deferred for AA repair, provided carotid stenosis is <80%.<sup>41,52</sup>

We did not find any published literature on carotid artery stenting for atherosclerotic carotid disease in patients awaiting elective AA repair.

### **Simultaneous Carotid Revascularization and Aortic Aneurysm Repair**

Published data reveal no difference in outcomes when CEA precedes or is performed simultaneously with surgical AA repair.<sup>43,50,53</sup> Simultaneous carotid stenting and AA repair (open or endovascular) have been described in case reports of patients presenting with aneurysms of the aortic arch needing carotid

stenting for anatomical reasons. In this case, the sequence depends on the urgency of aneurysm repair and symptoms of cerebral malperfusion.<sup>54–59</sup>

### **Summary**

Screening and treatment of atherosclerotic carotid artery disease is indicated prior to elective AA repair only in patients with symptoms of carotid artery disease.

Simultaneous repair of symptomatic carotid stenosis is feasible. Treatment of asymptomatic carotid stenosis <80% in patients needing AA repair can be deferred. For asymptomatic carotid stenosis >80%, CEA, either preceding AA repair or simultaneous AA repair, appears to be safe. In patients with both symptomatic AA and carotid stenosis, the sequence of revascularization is guided by severity of symptoms.

### **CAROTID ARTERY AND RENAL ARTERY REVASCULARIZATION Prevalence**

In an autopsy study of 346 patients with stroke, 36 (10%) of the patients had renal artery stenosis (RAS)  $\geq 75\%$  and 101 (29%) had CAS >50%. Patients with CAS were 4 times more likely to have RAS.<sup>60</sup> Other studies have shown the prevalence of RAS in patients with significant carotid artery disease to range from 7% to 27%.<sup>60–62</sup>

### **Planned Carotid Revascularization and Concomitant Renal Artery Disease**

Renal insufficiency is a known marker of increased morbidity and mortality in patients undergoing carotid revascularization. Perioperative death and stroke rates in patients with renal insufficiency (serum creatinine  $\geq 1.5$  mg/dL) undergoing CEA are 2% to 7%, and 2-year survival is 41%.<sup>62–67</sup> Because of poor short-term and long-term outcomes, carotid revascularization in patients with impaired renal function, especially if asymptomatic, is debated.<sup>65</sup> The theoretical benefits of identifying and treating RAS in patients awaiting carotid revascularization are improvement of renal function and better blood pressure control with renal revascularization.

There are no randomized trials or natural history studies to guide management for these patients, and current guidelines do not recommend screening or treatment of RAS prior to elective carotid revascularization.<sup>68</sup>

### **Planned Renal Revascularization and Concomitant Carotid Artery Disease**

In a patient with significant RAS, screening for carotid disease prior to revascularization is not recommended.<sup>68,69</sup>

## Simultaneous Carotid and Renal Revascularization

There is a paucity of data regarding simultaneous revascularization of both vascular beds. Small case series have shown the safety and feasibility of this approach.<sup>70</sup>

### Summary

Although more than a quarter of patients awaiting carotid revascularization may have significant RAS, clinical data are lacking regarding the management of these patients. Published studies are needed to determine if the theoretical benefit of detection and treatment of RAS prior to elective carotid revascularization is beneficial. Simultaneous revascularization in patients presenting with symptoms of both vascular beds appears feasible.

## CORONARY ARTERY REVASCULARIZATION AND AORTIC ANEURYSM REPAIR

### Prevalence

The prevalence of CAD in patients with AA is 30% to 60%.<sup>71,72</sup> The prevalence of AA in patients awaiting coronary revascularization is 10%.<sup>73</sup>

### Planned Coronary Artery Revascularization With Concomitant Aortic Aneurysm

Screening for AA is not recommended prior to PCI. Current guidelines do not recommend screening for AA prior to planned CABG,<sup>20</sup> despite the fact that concomitant AA adds to operative morbidity and mortality.<sup>74,75</sup> The role of endovascular aneurysm repair (EVAR) in patients awaiting CABG is unclear at present.<sup>76</sup>

In a patient undergoing CABG with a known AA, both staged and simultaneous surgical repair of the AA has been reported.<sup>77</sup> A combined procedure is recommended for patients with a high risk of rupture, such as in symptomatic AA, size >8 cm, or recent leaks.<sup>78–80</sup>

### Planned Aortic Aneurysm Repair and Concomitant Coronary Artery Disease

One challenge during AA repair is that aortic cross-clamping increases systemic vascular resistance and decreases the cardiac index.<sup>81</sup> Elective surgical AA repair is considered a high-risk surgery.<sup>68</sup> Current ACC/AHA perioperative guidelines state that clinicians treating patients with poor (<4 metabolic equivalents [METs]) or unknown functional capacity and 3 or more clinical risk factors (ischemic heart disease, history of heart failure, diabetes mellitus, renal insufficiency, and cerebrovascular disease) consider stress testing to detect coronary ischemia prior to surgical AA repair if it will change manage-

ment. If these patients have poor (<4 METs) or unknown functional capacity and only 1 or 2 clinical risk factors, clinicians can proceed with planned surgery with heart rate control.<sup>35</sup>

There is no known benefit to elective coronary revascularization of asymptomatic lesions prior to AA repair.<sup>82</sup> If symptomatic CAD and AA are detected, then coronary revascularization generally precedes AA repair. Coronary revascularization can be performed via PCI or CABG. If CABG is needed, a staged approach with CABG preceding AA repair is preferable, provided there are no signs of impending rupture of AA.<sup>83,84</sup> When the staged approach is chosen, AA repair is typically performed within 2 weeks of CABG because of a perceived increased risk of postoperative AA rupture.<sup>84</sup>

Little information has been published about risks associated with EVAR. However, the current guidelines consider EVAR to be an intermediate-risk procedure as it does not involve aortic cross-clamping and there are fewer hemodynamic changes as compared with surgical repair.<sup>35,68</sup> EVAR is associated with lower periprocedural mortality rates than open repair, and long-term outcomes are similar.<sup>85,86</sup> Although ACC/AHA perioperative guidelines do not specifically address EVAR, they do state that CAD assessment prior to intermediate-risk procedures with stress testing is unnecessary unless a patient has poor (<4 METs) or unknown functional capacity, in which case it is optional.<sup>35</sup>

### Summary

Concomitant CAD and AA is common. Revascularization should be guided by symptoms. Surgical bypass, when needed, should precede AA repair, except in symptomatic or large (>8 cm) aneurysms, when simultaneous surgeries may be performed. Data are needed on prevalence and management options of CAD in patients undergoing EVAR.

## CORONARY ARTERY AND RENAL ARTERY REVASCULARIZATION

### Prevalence

Significant atherosclerotic RAS (>50%) is seen in 11% to 18% of patients with CAD.<sup>87,88</sup>

### Planned Coronary Artery Revascularization and Concomitant Renal Artery Disease

Screening for the presence of RAS should be considered in the setting of refractory angina, unexplained congestive heart failure and multiple-vessel CAD, refractory hypertension, and unexplained renal insufficiency.<sup>68,89</sup> Guidelines do not discuss the sequence of revascularization in patients with concomitant coronary and renal artery disease.<sup>20,90</sup> We

found no trial data or large observational series addressing this issue. Case reports and series have shown feasibility of simultaneous or staged endovascular and surgical revascularization of coronary and renal artery stenosis.<sup>91-97</sup> The available data are too limited to recommend one strategy over another.

### **Planned Renal Artery Revascularization and Concomitant Coronary Artery Disease**

When RAS is found in a patient with acute coronary syndrome, renal revascularization can be deferred unless significant RAS is thought to be responsible for the patient's presentation. If a clinician is unable to ascertain which vascular bed is the culprit, small case reports show that simultaneous renal artery stenting and PCI is feasible.<sup>70,95,98</sup>

In a patient awaiting renal revascularization requiring bypass surgery, current guidelines identify renal artery disease as a risk factor for poor outcomes but do not address management options.<sup>20</sup> We did not find any published trial or good-quality natural history studies that address this issue.<sup>91-93</sup> The outcome of cardiac surgery with or without renal revascularization in patients with concomitant renal disease and CAD is unclear.

### **Summary**

Data are limited regarding evaluation and management of concomitant coronary and renal artery stenosis. In a patient awaiting renal revascularization, simultaneous percutaneous revascularization of both vascular beds can be achieved when both are symptomatic.

## **CORONARY ARTERY AND LOWER EXTREMITY REVASCLARIZATION**

### **Prevalence**

The prevalence of lower extremity (LE) peripheral arterial disease (defined by an ankle-brachial index <0.9) in patients with CAD is 15% to 40%.<sup>99,100</sup> The reported prevalence of CAD in patients with LE peripheral vascular disease is 25% to 78%.<sup>72,101</sup>

### **Timing of Concomitant Coronary Artery and Lower Extremity Revascularization**

Coexisting LE arterial disease in a patient awaiting coronary revascularization is common and becomes part of decision making only if symptomatic or when it is an anatomical factor affecting coronary revascularization. For example, severe LE arterial disease affecting femoral access for PCI or intra-aortic balloon pump may necessitate treatment. In a patient awaiting surgical LE revascularization, evaluation and treatment of concomitant CAD is necessary, as it is considered a high-risk surgery.

Endovascular management of LE arterial disease, however, does not necessitate workup for concomitant CAD.<sup>35</sup>

### **Planned Coronary Artery Revascularization and Concomitant Lower Extremity Arterial Disease**

Patients with both LE arterial and CAD have poor long-term prognosis compared with patients with isolated CAD. However, prior to planned coronary revascularization, evaluation and treatment of LE arterial disease is not indicated.<sup>12,20,90,102</sup>

In planned PCI with LE arterial disease amenable to endovascular repair, both vascular beds can be addressed during the same intervention or multiple procedures can be planned.<sup>70,98</sup> We did not find data showing the superiority of one strategy over the other. Treatment needs to be individualized on a case-by-case basis.

Knowledge of LE arterial disease can modify the surgical plan for CABG. For example, in patients with aortoiliac occlusion with collateral vessels to the leg via the internal thoracic artery, CABG using that conduit can result in LE ischemia.<sup>103</sup> Current guidelines, however, do not discuss screening for LE arterial disease prior to elective CABG.<sup>20</sup>

### **Planned Lower Extremity Arterial Revascularization and Concomitant Coronary Artery Disease**

Prior to surgical LE arterial repair, current ACC/AHA perioperative guidelines state that clinicians who treat patients with poor (<4 METs) or unknown functional capacity and 3 or more clinical risk factors (ischemic heart disease, history of heart failure, diabetes mellitus, renal insufficiency, and cerebrovascular disease) can consider stress testing to detect coronary ischemia if it will change management. If these patients have poor (<4 METs) or unknown functional capacity and only 1 or 2 clinical risk factors, they can proceed with planned surgery with heart rate control.<sup>35</sup>

Endovascular management of LE arterial disease does not require a workup for coronary ischemia. Current preoperative guidelines do not discuss periprocedural risk of endovascular treatment for LE arterial disease. Published data show excellent outcomes without any major periprocedural adverse events.<sup>104,105</sup>

Case reports of successful simultaneous endovascular management of coronary and LE arterial disease have been published.<sup>70,98</sup> Studies on management of patients with symptomatic coronary ischemia and critical limb ischemia are limited.<sup>70,91,98,103,106,107</sup>

## Summary

Concomitant CAD and LE arterial disease is common. Revascularization should be guided by symptoms, with coronary revascularization generally taking precedence.

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