Coronary Revascularization in Patients with End-Stage Renal Disease: Risks, Benefits, and Optimal Strategies

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Patients with end-stage renal disease (ESRD) are at increased risk of death from cardiac causes. Traditionally, coronary artery disease (CAD) in this patient population has been treated conservatively. Despite the scope and complexity of the problem highlighted from large databases, there is a paucity of controlled, randomized data in patients with ESRD. In this paper we address the following two questions: 1) Should the patient with ESRD and CAD be treated with medical therapy or with mechanical revascularization? and 2) Which mechanical revascularization procedure is optimal—surgical or percutaneous? Although the mortality data in favor of coronary revascularization in patients with ESRD and clinically significant CAD is convincing, the data are based solely on retrospective analyses with relatively small numbers of patients. For now, the choice of the revascularization procedure itself must be individualized, taking into consideration such factors as comorbid conditions, coronary anatomy, and the likelihood of achieving complete revascularization. Data from large, prospective, randomized controlled trials are desperately needed to appropriately address the optimal application of coronary revascularization in patients with ESRD.
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Key words: Chronic kidney disease • End-stage renal disease • Coronary artery disease • Percutaneous revascularization • Surgical revascularization

Patients with end-stage renal disease (ESRD) are at increased risk of death from cardiac causes.[1] The prevalence of angiographically significant coronary artery disease (CAD) ranges from 25% in young, nondiabetic hemodialysis patients[2] to 85% in older ESRD patients with long-standing diabetes.[3] It has been estimated that the relative risk is highest among the young:

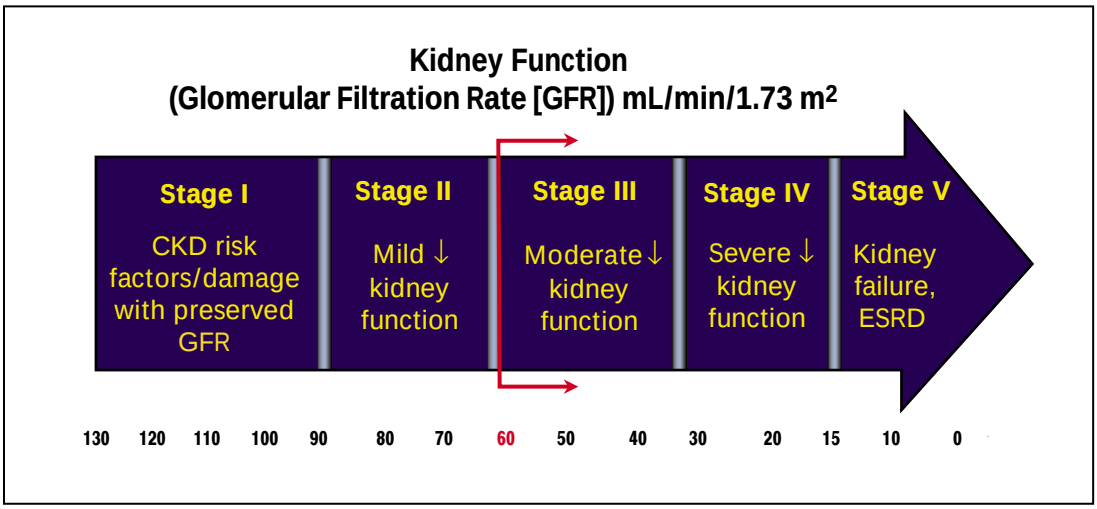

Figure 1. *Stages of chronic kidney disease (CKD) ranging to end-stage renal disease (ESRD), based on the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines. Adapted with permission from National Kidney Foundation (NKF) Disease Outcome Quality Initiative (K/DOQI) Advisory Board.*[6]

death from cardiac causes in dialysis patients younger than 45 years old is more than 100 times greater than in the general population.[4] Even more striking is that while only 0.1% of the population in the United States requires dialysis, more than 2.5% have some degree of renal insufficiency, and these individuals are also at increased risk of cardiovascular disease and its complications.[5] Renal insufficiency—better termed chronic kidney disease (CKD)—can be defined in five stages as shown in Figure 1.[6] The detectable risk for procedural complications typically occurs below an estimated glomerular filtration rate of 60 mL/min/1.73 m^2.

This article will focus on Stage V CKD, which is mainly comprised of those with ESRD. Traditionally, CAD in the ESRD patient population has been treated conservatively. Medical therapy has become the standard of care "by default" in these patients as many physicians are reluctant to advocate invasive procedures because of poor outcomes compared to patients with normal renal function. Although it can be argued that this patient group has the most to lose, it may also have the most to gain from an aggressive treatment strategy, including mechanical coronary revascularization, for clinically significant CAD. Two main questions need to be addressed: 1) Should the patient with ESRD and CAD be treated with medical therapy or with mechanical revascularization? and 2) Which mechanical revascularization procedure is optimal—surgical or percutaneous?

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The Effectiveness of Mechanical Revascularization Compared to Medical Therapy

Despite the scope and complexity of the problem, there is a paucity of controlled, randomized data in patients with ESRD and CAD. In fact, ESRD and renal insufficiency are frequently two of the main exclusion criteria in large, prospective, randomized, controlled clinical trials concerning treatments of CAD. To date, only two published studies have compared outcomes in revascularized patients with ESRD to outcomes in medically treated patients. Opsahl and colleagues,[7] in 1988, performed a retrospective case-control analysis. The investigators found that those patients who underwent a revascularization procedure had a markedly improved 2-year survival compared to those treated medically. Manske and associates[2] reported, in 1993, the only prospective, controlled trial published in the literature. This study enrolled 26 diabetic patients with ESRD and asymptomatic CAD and randomized them to mechanical revascularization with either balloon angioplasty or coronary artery bypass graft (CABG) surgery, or to medical therapy consisting of calcium-channel blockade and aspirin. They found that the frequency of cardiac events during 2 years of follow-up was significantly lower in the revascularization group compared to the medically treated group—15% versus 76%, respectively; $P < .01$. Apart from these comparative studies, there are no trials to date that have been solely designed to answer the question of

which form of therapy is optimal for patients with ESRD and CAD—medical therapy or mechanical revascularization. Therefore, management strategies are primarily derived from observational, retrospective, nonrandomized trials and case series.

Much of the information used to guide therapy in patients with ESRD and CAD has been extrapolated from studies comprised of patients with normal renal function. Because ESRD patients are significantly different from their counterparts with normal renal function, it is not surprising that their outcomes are not only different, but also worse. Although it is true that several small studies have reported disappointing results for percutaneous and surgical revascularization—with lower acute success rates and higher in-hospital complication rates compared to populations with normal renal function[8–13]—these studies are inherently flawed because they compare two distinct and dissimilar patient populations.

Several potential contributing factors may play a role and, therefore, must be taken into account when considering a patient as a candidate for mechanical revascularization.[14] First, selection bias inevitably influences the physician's decision to refer these patients for invasive procedures. It is not uncommon for these patients to be referred for invasive procedures after they have "failed" maximal medical therapy. This, by definition, makes them a higher risk group. Second, many of these patients have comorbidities, such as peripheral vascular disease and poorly controlled hypertension and diabetes, that may influence the acute and long-term success rates of the mechanical revascularization procedure by predisposing the patient to suboptimal outcomes such as vascular complications, incomplete revascularization, stroke, and restenosis.[15–17] Third, physiologic, metabolic, and anatomic differences—for example, extensive coronary and aortic calcification,[18] poor distal targets, previously placed dialysis shunts, paucity of conduits, dysfunctional platelets, abnormal autonomic tone,[19] and chronic anemia[15,20]—add to the complexity of the revascularization procedure. These unique considerations usually necessitate a change from the universally accepted protocols that have been shown to be effective in patients with normal renal function undergoing revascularization procedures. For example, avoidance of antiplatelet therapy with glycoprotein IIb/IIIa inhibitors during percutaneous interventions and aortic cross-clamping during CABG, use of venous instead of arterial conduits, and increased transfusion requirements may result in suboptimal and less durable results. Nonetheless, it

Table 1
Risks Associated with Coronary Revascularization in Patients with End-Stage Renal Disease (ESRD)

Complication	Risk	References
Percutaneous revascularization:		
Short-term mortality	0.0%–14.0%	(9,10,22–29)
MI (with or without ST-segment elevation)	2.0%–23.0%	(9,10,24,26,27,30–32)
Stroke	0.6%–2.5%	(24,27,31)
Major bleeding	0.0%–43.1%	(24)
Acute renal failure	< 1.0%–37.0%	(27,33,34)
Vascular complications	1.6%–20.0%	(24,26,32)
Clinical restenosis	13.0%–81.0%	(27,29,35,36)
Recurrent angina	44.0%–71.0%	(9,10,23,26,30,37)
Need for emergent CABG	0.0%–5.0%	(10,24,27,32)
Surgical revascularization:		
Short-term mortality	0.0%–31.0%	(7,11,12,25,26,28, 30–32,38–43)
MI (with or without ST-segment elevation)	4.2%–18.0%	(26)
Stroke	0.0%–20.0%	(38,40)
Major bleeding	3.0%–11.0%	(7,11,12,41)
Worsened renal failure	1.1%–26.0%	(33,40,44)
Mediastinitis	3.6%–8.0%	(11,12,39,43)
Vascular complications	8.6%	(26)
Recurrent angina	6.0%	(26)

MI, myocardial infarction; CABG; coronary artery bypass grafting.

To date, only two published studies have compared outcomes in revascularized patients with ESRD to outcomes in medically treated patients.

is widely accepted that patients with ESRD undergoing mechanical coronary revascularization procedures are at increased risk for adverse events, including death, compared to their counterparts with normal renal function (Table 1).[7,9–12,21–44]

The most important comparison, however, is between ESRD patients treated medically and those treated with mechanical revascularization. Over the past decade, significant advances in medical therapy—including the use of β-blockers, platelet glycoprotein IIb/IIIa and angiotensin-converting enzyme inhibitors, strict glycemic control, and aggressive lipid-lowering—have led to improved short-term and long-term outcomes in patients with CAD and normal renal function. In addition, mechanical revascularization procedures have been refined; these include the use of minimally invasive surgical techniques, improved cardioplegia, increased use of arterial conduits, smaller sheath sizes, stents, debulking devices, brachytherapy, and distal protection devices. These mechanical devices and techniques have been associated with improved outcomes in patients with CAD and normal renal function.

It is not uncommon for these patients to be referred for invasive procedures after they have "failed" maximal medical therapy.

In light of these advances, we recently re-addressed the question of which therapy for CAD is optimal for patients with ESRD—medical therapy or mechanical revascularization? Our hypothesis was that recent advances in medical therapy and mechanical revascularization procedures would be associated with improved survival in this group of patients. Therefore, we analyzed data from 4620 patients with varying degrees of renal insufficiency and an acute ischemic syndrome, who were admitted to an urban, tertiary care center, coronary care unit (Henry Ford Hospital, Detroit, MI).[21] We showed that coronary revascularization, achieved either percutaneously or surgically, was associated with overall improved survival compared to medical therapy alone, even in those patients with more advanced renal insufficiency. Although we believe that this, in addition to other published reports, supports the contention that mechanical coronary revascularization is associated with better outcomes compared to medical therapy alone in patients with ESRD, data from large, prospective, randomized, controlled trials is needed to definitively address this very important clinical question.

Percutaneous Versus Surgical Revascularization

The second question is whether surgical revascularization has a better outcome than percutaneous revascularization in patients with ESRD. In a study of 279 dialysis-dependent patients undergoing CABG, renal failure was associated with a 4.4 times greater risk of in-hospital death, a 3.1 times greater risk of mediastinitis, and a 2.6 times greater risk of stroke compared to those patients undergoing CABG who were not on dialysis.[11] Even mild renal insufficiency is associated with a 2 times greater risk of death after CABG.[45] Although newer surgical techniques have been successful in high-risk patients with renal failure, the long-term results, compared to traditional surgical and percutaneous techniques, are not yet known. In general, despite this significant "up-front" risk of surgery, the literature suggests that CABG is superior to percutaneous intervention in patients with ESRD.[25,26,29] These studies are small and retrospective, inherently limited by the physician's treatment allocation bias. In addition, they do not reflect the current standard of care for percutaneous revascularization, including the use of stents, debulking devices, and adjunct pharmacologic agents such as platelet glycoprotein IIb/IIIa inhibitors.

The data for conventional balloon angioplasty comes from several small, single-centered retrospective studies.[9,10,23,30,35,37] These studies, each comprised of fewer than 40 patients, reported success rates as low as 57% and restenosis rates as high as 80%. Over the past decade, however, stents have improved the outcome of patients with CAD undergoing percutaneous interventions, including those with ESRD. Although restenosis rates lower than 35% in ESRD patients have been reported, these studies are similarly comprised of small numbers of patients (< 70 patients).[31,32]

We showed that coronary revascularization, achieved either percutaneously or surgically, was associated with overall improved survival compared to medical therapy alone, even in those patients with more advanced renal insufficiency.

The clinical outcomes of more than 350 patients with varying degrees of renal failure undergoing

percutaneous coronary intervention was reported by Rubenstein and colleagues.[24] Not only was this analysis performed in a large group of patients, it also reflected recent advances in interventional cardiology, including debulking devices and stents. The investigators showed that patients with varying degrees of renal failure could be treated and demonstrated a high procedural success rate in the new device era. The use of stents and debulking devices was associated with improved immediate-term and long-term outcomes in this patient population. Lastly, in a population of more than 5000 patients who were treated with percutaneous coronary revascularization, renal insufficiency, even when mild, was independently associated with increased morbidity and mortality (Figure 2).[27]

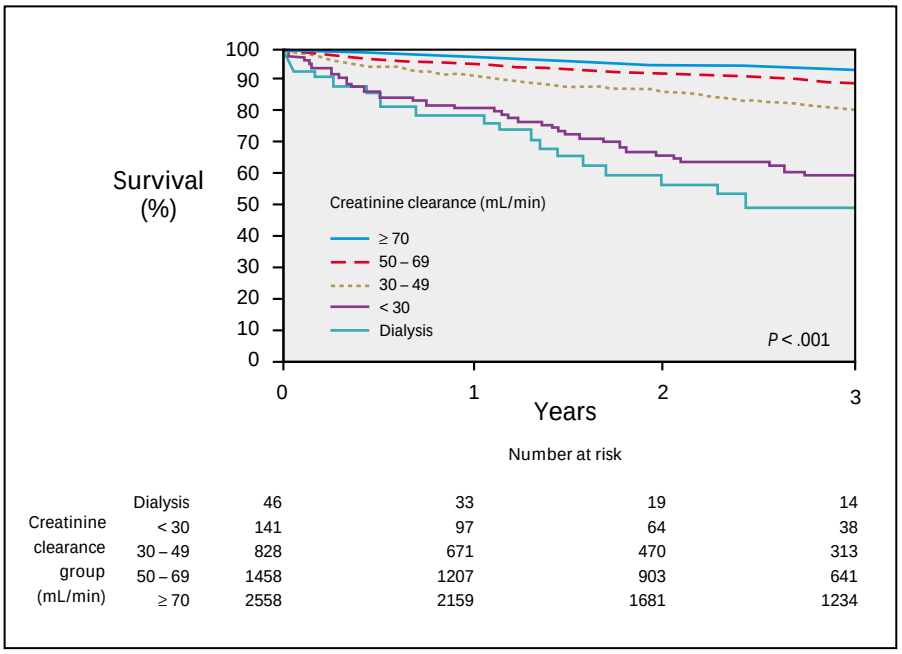

Figure 2. *All-cause mortality after successful percutaneous coronary intervention, based on the patients' estimated creatinine clearance or whether the patients were on dialysis. Reproduced with permission from Best et al.*[27]

Summary

In summary, clinical data suggest that mechanical coronary revascularization, performed either percutaneously or surgically, is associated with improved outcomes compared to medical therapy alone in patients with ESRD. Advances in interventional cardiology equipment, surgical techniques, and adjunctive pharmacologic therapies have enabled interventional cardiologists and cardiothoracic surgeons to be more successful in treating the complex coronary disease seen in patients with ESRD. Despite higher procedural success rates, patients with ESRD still have significant short-term and long-term morbidity and mortality compared to those with normal renal function. Although the mortality data in favor of coronary revascularization in patients with ESRD and clinically significant CAD is convincing, it must be remembered that the data are based solely on retrospective analyses with relatively small numbers of patients. For now, the choice of the revascularization procedure itself must be individualized and take into consideration such factors as comorbid conditions, coronary anatomy, and the likelihood of achieving complete revascularization. Large, prospective, randomized, controlled trials are desperately needed to appropriately address the issue of coronary revascularization in patients with ESRD. ■

Main Points

- It is widely accepted that patients with ESRD undergoing mechanical coronary revascularization procedures are at increased risk for adverse events, including death, compared to patients with normal renal function.
- Coronary artery disease in ESRD patients has traditionally been treated conservatively with medical therapy.
- Clinical data from small, retrospective analyses suggest that mechanical coronary revascularization, performed either percutaneously or surgically, is associated with improved outcomes, compared to medical therapy alone in patients with ESRD.
- Large, prospective, randomized, controlled trials are desperately needed to address the issue of coronary revascularization in patients with ESRD. Until then, the choice of revascularization procedure must be individualized, taking into consideration factors such as comorbid conditions, coronary anatomy, and the likelihood of achieving complete revascularization.

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