Revascularization in patients with chronic kidney disease: the state of the ARTS

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Online publish-ahead-of-print 25 May 2005

This editorial refers to 'Five year clinical effect of coronary stenting and coronary artery bypass grafting in renal insufficient patients with multivessel coronary artery disease: insights from ARTS trial' by J. Aoki et al., on page 1488

Data from the Third National Health and Nutrition Examination Survey in the United States suggest that >8 million individuals have a glomerular filtration rate (GFR) <60 mL/min, whereas data from both the United States and Europe show an increasing number of patients with end-stage renal disease (ESRD) with a need for dialysis or renal transplantation. A major cause of death in patients with chronic kidney disease (CKD) is cardiovascular with a high incidence of death due to myocardial infarction.

Studies in the early 1990s found that patients with ESRD had a better long-term survival after undergoing coronary artery bypass graft surgery (CABG) than percutaneous coronary intervention (PCI). Since then the use of stent implantation has increased, resulting in lower incidence of restenosis compared with PCI alone, such that one might anticipate that a more contemporary comparison of PCI and CABG would favor PCI with stent implantation. However, a retrospective analysis of the Arterial Revascularization Therapies Study (ARTS) in which 142 patients with CKD (GFR < 60 mL/min) were randomized to PCI with stent implantation or CABG found that event-free survival at 5 years was 50.7% in the stent group compared with 68.5% in the CABG group (P = 0.04), mainly driven by a higher incidence of repeat interventions in the stent group. Although techniques for both stent implantation and CABG have continued to evolve since the time of randomization into the ARTS study (1997–1998), these results and the finding that cardiovascular events were higher in those patients with a GFR < 60 mL/min compared with those >60 mL/min, possibly due to the deleterious effects of contrast media on the kidney, are disappointing and point out our failure to effectively treat patients with CKD medically as well as by interventional techniques. The ARTS investigators are to be congratulated for bringing these issues to our attention and suggesting the need for further adequately powered prospective randomized trials comparing drug-eluting stents to CABG. However, I believe that the most important message from this study is that we need to intensify our efforts to prevent the development and progression of CKD.

While our understanding of the pathophysiology of CKD is increasing and new approaches are being developed and evaluated to slow its progression, more could be accomplished by applying current knowledge regarding early detection and more intensive blood pressure reduction and control of other cardiovascular risk factors. Recognition of the fact that even a slight decline in renal function increases cardiovascular risk independent of known cardiovascular risk factors should prompt the interventionalist to optimize risk factor control and baseline medical therapy before considering intervention and to assure that these efforts continue after revascularization. While renal dysfunction has been shown to an independent risk factor for an increased cardiovascular mortality, older patients with CKD than newer risk factors such as C-reactive protein suggesting the importance of their control. It should, however, be acknowledged that in the presence of CKD although risk factor control and current medical therapy including an angiotensin-converting enzyme inhibitor (ACE-I) and/or an angiotensin receptor blocking agent may be beneficial, it has not yet been proved to alleviate the increased cardiovascular risk associated with CKD. An increase in reactive oxygen species (ROS), in part due to angiotensin II activation of vascular NAD(P)H oxidase, is thought to be of importance in the progression of renal dysfunction and its increased cardiovascular risk. An increase in ROS has been suggested to result in the destruction of nitric oxide (NO), endothelial dysfunction, vascular inflammation, collagen formation, vascular remodelling, vascular stiffness, myocardial hypertrophy, progression of atherosclerosis, plaque instability, sympathetic nervous system activation, progressive renal damage, and further activation of the renin–angiotensin–aldosterone system, contributing to the long-term as well as the acute risks associated with PCI with stent implantation in these patients with CKD. Further efforts to determine the degree of oxidative stress, for example, by measuring isoprostanes and/or antioxidant reserve, and to alleviate any

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doi:10.1093/eurheartj/ehi288

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increase in oxidative stress after attempting risk factor control and optimizing baseline medical therapy before attempting revascularization would seem appropriate. The best means of achieving a reduction in oxidative stress in patients with CKD has not, however, been determined and is obviously an area in which we need to increase our basic and clinical research efforts. Thus, while we can anticipate further rapid evolution in the techniques for PCI and stent implantation the risks associated with revascularization in patients with CKD are more likely to be reduced by concentrating on the underlying pathophysiology associated with renal dysfunction and only secondarily by better stent and or myocardial reperfusion strategies.

References