Do protection devices have a role in renal angioplasty and stent placement?

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In renal atherosclerotic vascular disease there is often no firm randomized trial data to guide clinical practice. Nephrologists often have to interpret trial data from other vascular territories. Vascular protection devices are now an issue in the carotid and cardiac territories. Should they have a role in renal atherosclerotic disease?

There is considerable literature on renal athero-embolic disease. The early paper of Thrulbeck and Castleman [1] showed that in post-mortem renal histology analysis after aortic aneurysm repair followed by death there was an incidence of renal atheroembolic
disease of >70%. It also showed that there was a >20% incidence of atheroembolic disease in individuals with no intervention but severe aortic atherosclerotic disease. Flory [2] showed that this condition is related to cholesterol crystal embolization to the renal vascular bed and suggested that the vessels occluded were between 55 and 900 μm in diameter. There is also some recent experimental evidence by Kimura et al. [3] using acrylic bead microspheres to mimic atheroembolic disease in rats. These microspheres were 20–30 μm in diameter and the histological features produced were similar to those with atheroembolic disease in humans. The spheres lodge in the small arterioles and glomeruli. They are probably a little smaller than the cholesterol clefts in vivo that may be 20 μm in diameter but have a greater length. Two important points emerged from this report. The first is that the outcomes in terms of proteinuria and renal dysfunction were dependent on the initial dose of microspheres. Only large doses induced proteinuria and only at the largest dose was there a decline in renal function. This is in keeping with the insidiously progressive form of atheroembolic disease rather than the acute catastrophic form. With low doses of microspheres there was no proteinuria or renal dysfunction. The second important point is that the maximum effect of embolization was only seen at 12 weeks. The important issue from these experimental scenarios is whether there is a dose–effect relationship in atheroembolic disease. Will reducing the dose of atheroembolic debris alter the outcome?

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cardiac saphenous vein graft intervention showed that particulate debris were found in 91% of cases. Particle size was $204 \times 83 \mu m$. All these studies show that in any intervention there is release of atheroembolic material of the size shown by Flory [2] to be important.

**Stent protection**

There is compelling evidence from cardiac stent placement that they are effective. A study by Baim et al. [13], with over 800 patients randomized to stent placement with or without a protective device, showed a significant difference in terms of the defined endpoints (Figure 2). The device used in this study was an occlusive balloon device. There was a significant reduction in the primary endpoint from 16.5 to 9.6% when a protection device was used. The endpoint was a composite of death, myocardial infarction, emergency bypass or target vessel revascularization. These represent very short-term events and there does not appear to be a similar scenario to the progressive dysfunction seen with renal atheroembolic disease. However, this is a major validation of the use of protective devices in the coronary circulation.

There is one preliminary report of protection device in patients with renal artery stenosis [14]. This was with a PercuSurge GuardWire device that is a balloon occlusive device. The patients had excellent renal function and were undergoing intervention for hypertension control. The authors noticed no change in renal function on follow-up but found debris with all the patients of a size that would fit the vessel size affected in the Flory article [2].

**Conclusion and perspective**

It is now clear from the new data that atheroemboli are the rule in any intervention in atherosclerotic disease [15]. The lack of frequency of this important clinical outcome is by luck rather than an understanding of the underlying pathophysiological processes or appropriate measures to avoid it. Angioplasty and stent placement will automatically release atheroemboli to the renal circulation. It is also clear that the effect of this cannot be overwhelming, as angioplasty/stent placement can be associated with an improvement in renal function. At the same time, the experimental evidence suggests that there is a dose effect of atheroemboli and that the result after angioplasty may depend on the dose of cholesterol crystals released to the renal circulation. It is unlikely that any device will preclude any cholesterol embolization as the experimental data show that even the guide wire placement will produce this. However, it is also possible that the heterogeneous response of the kidney to angioplasty in patients with atherosclerotic disease, compared with the beneficial response to angioplasty in fibromuscular dysplasia, may depend on the amount of cholesterol crystals released by the procedure. At present neither of the two randomized trials underway in Europe have addressed the issue of protection devices. However, it may be possible for smaller trials with single kidney function measurements to be performed to address this issue. If there were changes in outcome similar to the randomized trial in coronary artery disease then it would be difficult not to use protection devices in routine practice.

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**References**

An update on herpes virus infections in graft recipients

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Introduction

Acute rejection rates after renal transplantation are steadily decreasing due to more effective immunosuppressive therapies. However, more powerful prevention of immunological damage to the kidney by increasing immunosuppression is a two-edged sword, as infectious complications tend to rise in such a setting. Viral infections significantly contribute to morbidity and mortality after renal transplantation [1], and the spectrum of some viral diseases may have changed in recent years. Rapid diagnosis, appropriate antiviral treatment and management of concurrent medications are warranted to prevent patients from potentially severe disease manifestations. This brief review will focus on current considerations concerning infections with human herpes viruses (HHV) and their treatment in renal transplant recipients.

Cytomegalovirus (HHV-5)

Cytomegalovirus (CMV) infection is the most prevalent viral infection in renal transplant recipients [2]. Depending on the individual serostatus, patients may develop either primary infection, superinfection or reactivation of CMV infection. Seropositive transplant recipients with detectable CMV-IgG-antibodies develop a symptomatic CMV infection in ~10% of cases, whereas seronegative recipients transplanted from a seropositive donor (D+/R−) have a risk of up to 50% of developing CMV disease [1,2]. In order to minimize the occurrence of ‘tissue-invasive’ CMV disease (hepatitis, enteritis, pneumonitis), virus replication should be monitored weekly by immunostaining of the pp65 antigen in peripheral blood leucocytes or by quantitative real-time–PCR techniques during the first 3–4 months after transplantation. D+/R− recipients and patients with anti-lymphocyte induction or rejection therapy are recommended to receive antiviral prophylaxis. Most transplantation centres otherwise initiate preemptive antiviral treatment at the time when detection of virus replication becomes significant, but before symptoms of CMV disease occur. However, it is not clear whether this preemptive approach is indeed superior when compared with a deferred therapy, i.e. started at the time when overt CMV disease manifestations are present. There is also the unresolved question, at which threshold should preemptive therapy be initiated to prevent CMV disease? For example, are one to two pp65-positive cells per 50 000 leucocytes sufficient to justify antiviral treatment, or could reduction of immunosuppression alone be effective in suppressing CMV replication?

The recognition of CMV infection and disease seems to have changed in recent years. This may either be due to more sophisticated and more frequent testing, or to changing patterns of disease manifestations, possibly because of more effective immunosuppression. For example, CMV enteritis showing a variable clinical picture including diarrhoea, dysphagia, epigastric pain as well as upper and lower gastrointestinal bleeding is increasingly observed in transplant recipients, but