Atherosclerotic ischemic renal disease: Clinical challenges

Enfermedad renal isquémica arteriosclerótica: retos clínicos

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Ischaemic nephropathy is a loss of renal parenchyma caused by stenosis in a haemodynamically important renal artery. This is a frequent clinical entity that appears during atherosclerotic disease in elderly people that is probably underdiagnosed. Ischaemic nephropathy often coexists with peripheral vascular disease, coronary disease and aortic disease. The most important risk factors are age, arterial hypertension and diabetes mellitus.

This significantly occlusive disease can lead to a decline in renal function and reduced renal size. Ischaemic kidneys depend on angiotensin II to maintain the glomerular filtration rate. This hormone produces a vasoconstrictor effect in both efferent and afferent arterioles, although there is a preferential effect on the postglomerular arterioles. This selective vasoconstriction increases intraglomerular pressure and, thus, maintains the nphron flow rate. The administration of ACE inhibitors or ARA-II can cause haemodynamic alterations when reducing the tone of the efferent arteriole. This could be a sign for ischaemic renal disease diagnosis. Nonetheless, the disease has no specific clinical signs, even though diverse criteria have been proposed for suspicion, all of them with little sensitivity and even less specificity.

The diagnosis is confirmed when evidence of renal artery lesions is shown by imaging tests. Computed angiotomography (CT angiography) and MR angiography are the ideal tests for diagnosis, as they define the location of the lesion and are greatly reliable. Computed tomography (CT scan) contributes by providing information about vascular calcification, but the test requires nephrotoxic contrast material. The risk of developing contrast-induced nephropathy is low in the general population (incidence of 0.6-2.3%), but in the population at risk (particularly in patients with chronic kidney disease [CKD] and diabetes) it can increase significantly. However, in the CT scan studies performed with contrast in patients with CKD, none required dialysis and there were no significant reductions or severe consequences attributable to the contrast. In another observational study in patients with glomerular filtration (GF) rate <60 ml/min/1.73 m² there was no association found between contrast-induced nephropathy and a greater risk of hospitalisation or dialysis. Therefore, using adequate prevention measures, it is possible to even use this technique in patients with CKD.

MR angiography requires gadolinium contrast agents, which are contraindicated in CKD with a GF rate <30 ml/min because of nephrogenic systemic fibrosis risk. To prevent this problem, it is recommended to limit the gadolinium contrast agent dose to a maximum of 0.1 mmol/kg and to avoid using non-ionic compounds of this type. In patients who receive this dose, the global incidence is almost zero, regardless of renal function. On the other hand, the risk associated to each specific type of contrast agent seems to be different, and the European Medicines Agency considers gadobutrol, gadoteridol and gadoteric acid to have a low risk of producing nephrogenic systemic fibrosis. Therefore, they can be used at the lowest dose in patients with severe CKD when considered necessary.

The diagnosis test is a renal arteriography, which in addition could be therapeutic, but which also needs the use of greater amounts of contrast agents that can lead to renal failure by microembolisation. Even so, there were no differences found in the incidence of contrast toxicity in diabetic patients, who even received greater amounts of iodine. Therefore, neither is there an absolute counter-indication for the performance of arteriography in patients with CKD.

The major objectives of ischaemic nephropathy treatment are blood pressure control and preservation of renal function. Treatment options include medical treatment, percutaneous transluminal angioplasty and revascularisation surgery. Antihypertensive treatment is frequently necessary; nevertheless, the use of renin-angiotensin-aldosterone system (RAAS) inhibitors is controversial. On the one hand, they may block the increase of renin caused by systemic hypertension, but this is accompanied by renal function reduction mainly in the affected kidney. This completely contraindicates these inhibitors in cases with bilateral lesions, while they are also not recommended in cases where the affected kidney still has renal function. If they are not essential for the control of blood pressure and there is no refractory hypertension to other treatments, RAAS inhibitors should be avoided. Moreover, there is no published evidence confirming that their use

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improves the results of other antihypertensive treatments in this type of patient.

The use of statins is mandatory in these patients; in the first place, because of their high cardiovascular risk,21 and also because of statins’ specific effect in slowing down stenosis progression, with results similar to those of more intensive techniques.22 In the case of anticoagulants, their use is frequent, particularly with atherosclerotic disease,23 but there is no specific evidence of their use in renal artery stenosis. Nevertheless, the use of clopidogrel prior to intervention has demonstrated a reduction in the production of microemboli during angioplasty.24,25

On the other hand, endovascular revascularisation with stents has not shown long-term benefits in cardiovascular morbidity and mortality or in the progression of CKD.26,27 The last study published, Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL),28 has confirmed the results of previous studies.26,27 It had been considered that 40% stenosis, an inclusion criterion used in previous studies, was too broad and for that reason no clinical benefit had been found. However, the CORAL study included patients with stenosis equal or superior to 60% and did not show any improvement in the results; what they did show was a higher risk of haemorrhage.28 Moreover, one of the conclusions in the CORAL study is that, in the medical treatment branch, the number of events observed was 50% less than expected. This is not quite surprising if we consider that, in a 3-year period, the tendency to progression is inferior to 50% in the lesions <60%, and only 8% of those superior to 60% reach total occlusion.29

It is possible that a sub-group of patients could benefit from angioplasty. Before the publication of these studies, better results were expected for those patients that before intervention had required a greater number of antihypertensive drugs, in those who had a mean blood pressure superior to 110 mmHg, and in those with cases of bilateral stenosis.30 Recently, a comparison has been published of angioplasty results in patients who had ischaemic nephropathy with high cardiovascular risk (defined by the presence of acute pulmonary oedema, resistant hypertension or sudden loss of renal function) and those who presented no complications. Revascularisation reduced the risk of death but did not reduce the prevalence of cardiovascular events or terminal renal illness in patients with pulmonary oedema. Revascularisation did not offer any advantage to patients with rapidly progressive renal disease or with resistant hypertension.31 Therefore, perhaps the patients who present acute pulmonary oedema could benefit from angioplasty with the insertion of stents. Finally, there is the surgical option that would be reserved for those cases of combined aortic and renal disease that require it, after failure of the angioplasty, or when nephrectomy is needed.

The diagnosis of atherosclerotic ischaemic renal disease is difficult to determine in the absence of a simple or sensitive test. The techniques of choice for diagnosis are CT angiography and magnetic resonance angiography. The presence of CKD is not an absolute impediment when there are expected clinical benefits. Hypotensive agents, statins and anticoagulants should be used for treatment, although there is no clear evidence to recommend one type of hypertensive drug over another. Transluminal angioplasty does not improve the prognosis of these patients and should be reserved for very specific and select cases.

References

renal-artery stenosis. 

