

Controversies

A case of atheromatous renal artery stenosis with severe hypertension: is surgical revascularisation appropriate?

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Case History

A 62-year-old male was referred with a diagnosis of renovascular disease. His past history included cervical spondylosis, a transitional carcinoma of the bladder three years previously and resistant hypertension for the last year. He was intolerant of a number of anti-hypertensive agents. An angiotensin converting enzyme inhibitor (ACEI) was added to the treatment regime followed by a decline in renal function to a plasma creatinine of 400 $\mu\text{mol/l}$. The creatinine fell on withdrawal of the ACEI to 250 $\mu\text{mol/l}$. Ultrasound demonstrated a left kidney of 8.3 cm and right at 10.8 cm. A MRI scan showed an ostial stenotic lesion to the left kidney. He was referred for evaluation. On referral his blood pressure was 200/104 mm/Hg on three agents not including an ACEI or Angiotensin II (AII) blocker. At angiography the left renal artery was shown to be occluded. Two right renal arteries were demonstrated. There was a stenosis of the upper renal artery with the lower being normal. An attempt was made to angioplasty the upper lesion but the guide wire could not cross the stenosis. No flow could be demonstrated through the upper artery at the end of the procedure. A subsequent single kidney glomerular filtration rate (SKGFR) found 17.3 ml/min from the right kidney and 18.1 ml/min from the left kidney. The radiologist did not feel that it was possible to intervene in either of the two occluded arteries. The patient was referred to a vascular surgeon for assessment. His blood pressure was 170/96 on Indapamide, Labetolol and Methyl Dopa with a plasma creatinine of 249 $\mu\text{mol/l}$.

In summary, this is a 62-year-old man with inadequately controlled hypertension despite the usage of three anti-hypertensive agents, who has a small left kidney resulting from left renal artery occlusion, a reasonable sized right kidney although the upper pole artery is occluded resulting from failed angioplasty. The kidneys appear to have preserved renal function of 17 ml/min and 18 ml/min respectively and a serum creatinine of 249 $\mu\text{mol/l}$. The sizes of the renal arteries are not clarified. Is the lower or upper pole right renal artery the main arterial blood supply or are they of equal size? Also, we do not know the quality of the aorta, is it heavily diseased or not.

It is important to bear in mind that the current problem is the patient's difficult to control hypertension and not the level of renal function, which appears to be stable despite the occluded renal arteries. Clearly, blood supply to the kidneys from capsular and ureteric blood arteries is currently sufficient to provide an adequate combined GFR. What is not absolutely clear is whether the occlusion of the renal arteries will allow long-term adequacy of blood supply to the kidneys, now that the latter are in the main protected from cholesterol emboli from the aorta. Whether the kidneys continue to shrink down in size is not, therefore, certain. All kidneys that I have biopsied when operating on for renovascular disease, have exhibited considerable damage due to ischaemia and cholesterol embolisation. These renal changes may, and often do, progress despite surgical, radiological or medical management of hypertension.

It is important to recognise that both kidneys are a problem and any management needs to deal with both. The right kidney is, however, within normal size limits and preservation of that kidney is vital for long-term renal preservation of function. There are several options available to manage this patient:

Increase anti-hypertensive medication using additional calcium channel blocker, metolazone or minoxidil etc. This should resolve the hypertension although at the

Expert 1

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expense of taking more tablets with increased chances of side-effects. Using ACEI or angiotensin II inhibitor is likely to cause a reduction in renal blood flow and will result in an increase in serum creatinine once again. Of course the blood supply to the kidneys would remain indirect apart from that to the lower pole of the right kidney.

Surgical options are also available. Revascularisation of both kidneys is possible although we do not know whether the right upper pole renal artery supplies a sufficient amount of renal parenchyma to be worthwhile revascularising. Clearly, if the lower artery is the main supply to the right kidney, then the loss of the parenchyma supplied by upper pole artery can be ignored. The surgical options also depend also on the quality of the aortic wall—is it safe to clamp the aorta or is it too diseased to use?

The safest option is to perform an extra-anatomical bypass to the renal arteries. The right upper pole artery could be revascularised by a saphenous vein bypass from the hepatic artery and the left renal artery by using the splenic artery. Neither of these procedures involves clamping the aorta and hence avoids left heart strain. The spleen continues to be supplied by the short gastric arteries from the stomach. Alternatively, only one of these procedures may be necessary. If the right kidney upper polar vessel is large, then revascularising this kidney would be most valuable and a hepato-renal bypass may be best. The left kidney could be left alone since it is quite small. In this situation, the left kidney would still cause hypertension but this could be managed using an ACI.

Another extra-anatomical bypass could be performed from the common iliac arteries to the renal arteries. Again, aortic clamping would not be necessary. These bypasses would be longer in length and would depend on the quality of the inflow iliac arteries for blood supply.

If the patient is without significant cardiovascular risk then an aortic procedure can be contemplated. The first option would be to consider renal artery endarterectomy. This involves clamping the aorta above and below the renal arteries and removing the intimal atherosclerotic layer from the aortic ostia and the origins of the occluded renal arteries. This technique is practised in a few centres only. There is a danger of intimal dissection down the renal arteries and aorta if the endarterectomies are not performed properly and hence most surgeons avoid this method.

The next alternative is a bilateral aorto-renal saphenous vein bypass. This procedure involves using one saphenous vein and its major branch, thus only a single anastomosis onto the aorta is required. Provided the aorta is not heavily diseased, this option is attractive with only short bypasses being necessary.

It is imperative that further investigations to exclude significant cardiac disease is undertaken before surgery should be contemplated. Patients with renovascular

disease often have extensive other vascular disease, including the coronary, carotid and peripheral arteries. A MIBI scan/treadmill exercise test would be useful to exclude such high risk cases. One of the problems of surgical intervention remains post-operative myocardial infarction or stroke. Pre-operative risk assessment and full discussion with patient and physician is mandatory before embarking on surgery. The mortality of past series of surgical series reflects the degree of pre-operative co-morbid assessment of patients. If best risk cases are undertaken then a durable long-term result can ensue. However, there will remain a need for long-term anti-hypertensive medication since the already damaged kidneys will not return to normal. However, the number of drugs used to control hypertension would be reduced. In addition, ACEI could be tentatively prescribed following surgery.

Expert 2

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Thank you for asking me to comment on this case, which I think is difficult rather than controversial—clearly the options are to go for surgery or not and there are arguments in favour of either. Also, we need to remember the limitations of what we can learn from the outcome in a single case. If whichever path is finally chosen results in a ‘successful’ outcome, that is not the same as saying that the correct option was taken. Any option has a chance of success and a chance of failure, which we cannot now (or probably ever) calculate accurately. It is quite possible to miscalculate, opt for the low return option and get lucky.

A case such as this is particularly topical for two reasons. Firstly, it highlights the enormous limitations of evidence-based medicine. EBM has nothing to offer us here—don’t bother to consult the Cochrane collaboration or the latest issue of. Clinical evidence secondly, everyone is now very interested in surgical outcomes. The physicians can probably do what they want in this case without concern, but the surgeons have their mortality rates to consider. In a rational environment, it would be obvious that such infrequent operations (in the UK) as this cannot be meaningfully audited for their outcomes. It is not self-evident that consideration of surgical outcomes currently is always rational.

What we can do here is examine the case in great detail to see what we really know about this man. We also need to carefully formulate the questions that are making the decision about intervention difficult. The nature of such a case means there is always some data missing in the truncated summary. I’ll mention where this might have helped decision-making.

Analysis of the case

At first glance this looked like just another case of atheromatous renal artery stenosis (ARAS) but it turns out to have some quite interesting and unusual features. The failure of magnetic resonance angiography will be mentioned only to console those of us currently without access to this technique. (Another explanation is that the artery occluded between MRA and definitive angiography. If this was important, I'd expect to have seen a rise in serum creatinine, of which there is no mention in the case history). The split GFR results are fascinating—I would not have guessed that the small kidney with one occluded artery would have the same GFR as the big kidney with two arteries, one recently occluded but one unstenosed. I'm assuming that each of these arteries supplies about half the kidney. It is obvious therefore that all of the left kidney function and perhaps some of the right function depends on renal blood flow through collateral vessels. One thing we would like to know is whether or not restoring blood supply through the main arteries would improve renal function. There are some clues in the history as given, and probably more clues not given.

The adverse but reversible effect of ACE inhibition (ACEi) does not necessarily mean that surgical revascularisation will improve GFR. It could be that the GFR is angiotensin II dependent because of poor renal blood flow through collaterals and that revascularisation would improve this. It could also be that the roughly 30% of surviving nephrons are hyperfiltering, and the cessation of this following ACEi caused the rise in creatinine. Other explanations not pointing to reversible ischaemia include a coincident degree of volume depletion, or simply too much ACEi.

Whenever the contribution of ARAS to renal failure is considered, we also have to think of the other common problem in this setting which impairs GFR. This is an ill-defined but increasingly recognised nephropathy due to a combination of hypertension and severe atheroma—probably to be called athero-embolic nephropathy^[1]. This causes progressive renal failure and is not going to be helped by revascularisation. A kidney with ARAS is just as likely to have this as the cause of poor function^[2]. It is vitally important to distinguish between renal impairment due to low renal blood flow, which is therefore reversible by intervention, and renal impairment due to nephron loss because of other factors, which is not reversible. A recent study of split renal function in cases of unilateral stenosis due to atheroma or fibromuscular disease shows an average of 18 ml/min less GFR in the non-stenotic kidney when atheroma was the cause^[3].

So what do I think is going on here? If the renal impairment was solely due to athero-embolic nephropathy, the creatinine should have been rising steadily to the current level. The patient has an extensive medical history and probably has had lots of blood tests over the years—a reciprocal creatinine plot would be interesting. A steady rise in creatinine would favour this

diagnosis. Against the diagnosis is the asymmetry in kidney size.

If the renal impairment was solely due to ARAS, I'd expect the left kidney to have a lower GFR, and the right kidney GFR to be closer to 25% of normal total—about 25 to 30 ml/min. I'd also expect the creatinine to have risen after the unsuccessful angioplasty which occluded the upper right renal artery.

Perhaps the likeliest scenario is a bit of both! The left kidney had a longstanding ARAS, which encouraged collateral growth. When the artery occluded, the kidney remained viable due to the collaterals but many nephrons were lost causing low GFR and shrinkage. The reason that the better blood supply to the right kidney is not associated with better GFR may be that there was insufficient collateral growth and most of the upper pole died after occlusion. The kidney size was estimated before occlusion. A touch of athero-embolic disease might explain the less than perfect function in the lower half of the kidney.

This picture would suggest that revascularisation will not change right upper pole function, but might improve left kidney function. I don't think a left renal biopsy would help—there is bound to be a lot of nephrosclerosis but the kidney is clearly viable. Further clues to help decide about the right would include a renogram or Doppler ultrasound to look at regional blood flow in that kidney. A lower pole biopsy wouldn't help (that bit can't be improved). It is of course the case that the smaller the kidney or the worse its function, the less likely benefit will be seen with revascularisation^[4,5]. I am choosing to not be over influenced by this because I think there is a big difference between a small kidney beyond a stenosis of say 50 to 90%, and a small kidney beyond an occlusion with a documented GFR of 18 ml/min. In the former circumstance, significant loss of nephrons in the absence of a very tight stenosis is probably a sign of athero-embolic disease. This is the common scenario in many reports and it is not surprising that these kidneys don't stabilise after intervention. The current case is very different.

So, in short, there is a possibility that successful revascularisation might improve GFR from 35 ml/min to maybe 50 ml/min. So what?

Possible benefits of successful revascularisation

Revascularisation is not an end in itself. Would it help the patient? A modest increase in GFR in itself is unlikely to make a big difference to the patient or his prognosis. It might reduce the risk of renal anaemia, which of course could be treated with EPO, at some expense, BP permitting.

Would revascularisation reduce the risk of eventual end-stage renal disease? Quite possibly not in this case—the kidneys are surviving with collateral supply and I haven't seen any analysis of what happens to such kidneys in the medium to long term.

BP control might be helped, although it should be pointed out that the tablet burden in this case could be considerably eased by simply changing to once-a-day drugs.

Will the patient live longer? Possibly. I get the impression that high levels of angiotensin II are a bad thing. Successful revascularisation addresses this problem both directly, by switching off the stimulus, and indirectly, by allowing use of ACEi or AIIr blockers. (In the interests of fairness, it needs to be pointed out that the use of these might precipitate anaemia of a degree sufficient to require EPO treatment.)

On balance, therefore, there is a sufficient possibility that revascularisation would help for us to consider the downside of surgery.

Possible risks of surgery

The information in the case summary doesn't help us decide. There are two factors to consider—the patient, and the surgical team.

The concern with the patient relates to anaesthesia and possible sudden fluctuations in BP in either direction in someone who could have critical stenoses of carotid, coronary or mesenteric arteries. I would imagine that carotid dopplers and coronary angiography or some form of testing for reversible ischaemia would be sensible. The mesenteric vessels may have been visualised on renal angiography. As the main renal arteries are already occluded, the risks of precipitating renal failure may be less than when trying to improve on a tight stenosis, and principally related to episodes of hypotension.

The surgical team will need to provide not only surgical expertise for this type of operation, but aggressive pre-, peri- and post-operative management of BP and fluid state. This operation is rarely carried out in the UK. There are very few surgeons who could tell prospective patients meaningful results in similar previous cases.

Decision time

Ultimately, my job here would be to tell the patient what he needs to know to allow him to decide. If testing suggested he was reasonably fit for surgery, and if a good surgical team was available, I would summarise our hopes for intervention as possibly improving his kidney function (which may or may not make him feel any different), but more importantly allowing us to use the best drugs in this setting to control BP and prevent future related problems, i.e. ACEi or AIIr. Unfortunately, the surgery would carry a small but not insignificant risk of major complication including death, stroke, heart attack, renal failure and peripheral or mesenteric ischaemia. Other than the risks, the strongest reason not to proceed would simply be that surgery might well make no difference to how he felt or his future health. Clearly, in such a complex case, there will be a large variation between patients in how they interpret what the various

possibilities mean to them. A significant proportion will ask me to do whatever I think is for the best. Such a decision would be based on many factors which can never be addressed in this sort of exercise. If pre-operative assessment was favourable (and I suspect it might well not be), if the patient was keen on intervention, and if a suitably skilled surgical team were available, then this is case where surgery might have something to offer. In this particular case, because the benefits of surgery are not clearly defined in advance, it would not take much in the way of extra anaesthetic/operative risk to dissuade me from recommending that approach.

Whether or not surgery is performed, this patient has a high risk of coronary artery disease and should take aspirin and almost certainly an HMG CoA reductase inhibitor.

I await the surgeon's opinion with interest.

Conclusion

The left kidney has an occluded renal artery and a GFR of 18 ml/min—presumably filtering blood from a collateral supply. I don't know of any studies that tell us if revascularisation in this setting improves GFR, prevents eventual end-stage renal failure, and/or allows ACE inhibitor use without an acute decline in GFR. Given that these are at least reasonable theoretical possibilities, intervention should be considered if the surgical expertise is available and significant vascular disease in other vital organs is absent.

The function in the right kidney is similarly low despite adequate perfusion of the lower half. It seems less likely that there is much to salvage in the upper half—a repeat ultrasound scan and possibly renogram six weeks after the occlusion might confirm that.

References

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Case Management

The patient was reviewed by a vascular surgeon. The major issue addressed was the fate of the

function in the occluded kidney as his kidney had significant function. The patient had had a left aorto renal bypass graft. The SKGFR are shown below:

Date	SKGFR R	SKGFR L
October 1999	17.3	18.1
March 2000 Revascularization		
May 2000	10.9	15.1
April 2001	13.7	17.4

There appears to be preservation of function in the left with a decrement in the right. This may have been the result of the attempted angioplasty to the right upper vessel. Post-operatively the patient suffered an episode of pancreatitis after discharge but is at present well. Although now on two agents, the blood pressure is well controlled. The clinicians involved felt sufficiently confident for one of these agents to be an ACEI.