

ASTRAL—the story so far

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Abstract

Atherosclerotic renovascular disease (ARVD) is a relatively common and serious condition. Revascularisation is already widely used to open up the renal artery, despite the lack of evidence of any benefit on kidney function. To determine reliably whether or not there is any worthwhile benefit, large randomised trials are needed. Thus, the ASTRAL trial has been designed to compare revascularisation with medical management alone. Funded jointly by government, charity and industry, ASTRAL was fully launched in 2001 with the aim of randomising up to 1000 patients. ASTRAL is already by far the largest randomised trial in ARVD, with 225 patients by the end of 2002. To make participation easy, ASTRAL is a simple, pragmatic trial, with minimum paperwork and no extra clinic visits or tests. With widespread collaboration, ASTRAL will determine the role of revascularisation in the treatment of ARVD, enabling future patients to be offered the most appropriate therapy.

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Keywords

ARVD; revascularisation; angioplasty; stenting; randomised trial; ASTRAL.

Atherosclerotic renovascular disease (ARVD) is a relatively common condition that can lead to progressive renal impairment and eventually to end-stage renal failure with the need for dialysis or kidney transplant. Thus, the reliable identification of an intervention that can delay, or even prevent, the decline in renal function would be an important medical advance.

Revascularisation, usually by angioplasty with stent insertion, is being increasingly used in an attempt to delay the decline in renal function. While it has been shown that revascularisation improves arterial patency, there is as yet no good evidence that this translates into an effect on kidney function. A meta-analysis of the three small trials that have been reported of angioplasty versus no angioplasty (i.e. medical therapy only) does not provide clear evidence of an improvement in renal function^[1], though these trials were largely in hypertensive patients with well-preserved kidney function. The single trial of angioplasty with or without stenting did not demonstrate an advantage for stenting on renal function either.

From the meta-analysis we know that revascularisation does not have a very large effect, but the possibility remains that it has a moderate, and clinically worthwhile, benefit on renal function. Revascularisation is not, however, without risks, and the balance between the putative benefit on renal function and these risks remains unclear. This uncertainty leads to wide variation in clinical practice, with some clinicians routinely employing revascularisation for ARVD and others using it rarely or not at all. Thus, if revascularisation is beneficial, some patients are currently being denied an effective intervention. Alternatively, if revascularisation has no worthwhile effect on renal function, some patients are being subjected unnecessarily to a procedure that is not without risks and consumes valuable NHS resources.

This situation is clearly unsatisfactory, and much better evidence on the value of revascularisation for ARVD is still needed. Such evidence can only come from large

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randomised trials, since small numbers and potential biases related to patient selection make it impossible for any clinician to evaluate the role of revascularisation from their own, or other people's, case series. With this in mind, a group of clinicians (nephrologists, radiologists and surgeons) and trial methodologists got together to design such a study. The result, after several years of discussion and more than one design modification to reflect changing opinions, is the ASTRAL trial.

Initially, the ASTRAL start-up phase opened in 2000 with funding from Medtronic AVE, a stent manufacturer. A joint application to the Medical Research Council and the National Kidney Research Fund for the additional money needed to run the full-scale trial was successful and ASTRAL was fully launched in 2001. ASTRAL aims to randomise up to 1000 patients between revascularisation (with medical treatment) versus medical treatment only. With 700 to 800 patients, ASTRAL will provide good evidence on the overall effect of revascularisation, but if we can get to the upper target of 1000 patients, there will be the opportunity to investigate more reliably the effect in different types of patients (e.g. by degree of stenosis and by creatinine level). The broad eligibility criteria for entry into ASTRAL means that an appropriately heterogeneous population will be obtained (see Fig. 1) thereby permitting such analyses, albeit with cautious interpretation given the well known dangers of subgroup analyses.

After just 2 years of accrual, ASTRAL is already more than twice the size of the previous biggest randomised trial in ARVD, having accrued 225 patients from 44 centres in the UK at the end of 2002. Recruitment continues to increase as new centres come on board, and we expect the first international patients very shortly as New Zealand has recently obtained ethical approval to participate and there is strong interest being expressed in Australia.

We know that medical staff have a heavy workload, so ASTRAL has been designed as a simple, pragmatic trial, with minimum paperwork and no extra clinic visits or tests beyond those required as part of normal practice. Participation should not therefore be too onerous and with the widespread collaboration of a large number of clinicians in the UK, and further afield, ASTRAL will be able to demonstrate reliably whether or not

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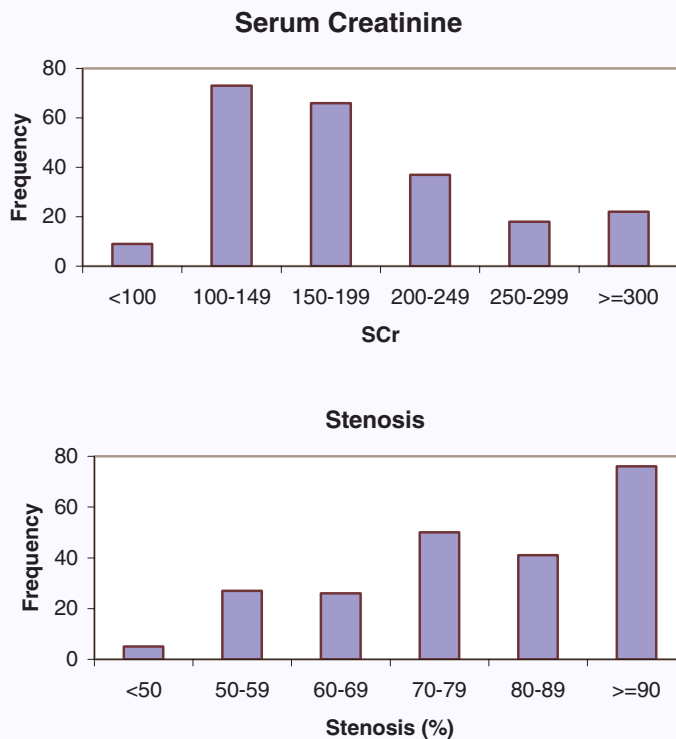


Fig. 1. Baseline features of the population at entry into ASTRAL showing the broad spectrum of patients: (a) creatinine; (b) stenosis.

revascularisation has a role in the treatment of ARVD, thereby enabling future patients to be offered the most appropriate therapy.

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