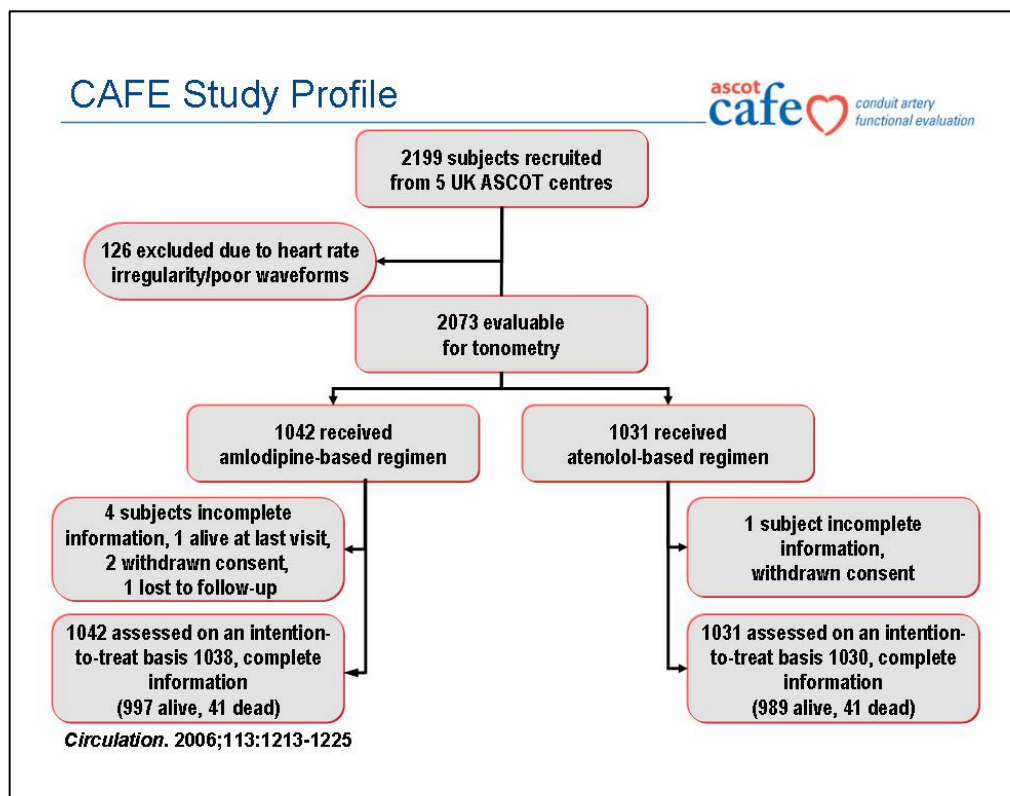


Backgrounder

Background to the CAFE (Conduit Artery Function Evaluation) sub-study of the ASCOT trial

What was the CAFE sub-study to the ASCOT trial?

The Conduit Artery Function Evaluation (CAFE) sub-study of the ASCOT trial involved more than 2,000 patients in the UK and was designed to evaluate the differential effects of amlodipine-based therapy compared with the atenolol-based regimen on brachial blood pressure and central aortic blood pressure measurements.¹ The sub-study also evaluated the impact that these differences have on cardiac outcomes as demonstrated in ASCOT. The CAFE study used radial artery applanation tonometry and pulse wave analysis to calculate derived central blood pressures and other parameters using a validated commercially available system (SphygmoCor).



What are the differences between brachial and central blood pressure measurement?

Standard peripheral or brachial blood pressure measured via an arm cuff is an imperfect surrogate measure of the aortic or central arterial blood pressure (CAP).

The relationship between brachial blood pressure and CAP is influenced by various factors such as arteriosclerosis, vascular stiffness and hypertension. CAP is an important determinant of cardiac workload and cardiac hypertrophy. Although brachial blood pressure measurement is a strong predictor of clinical outcomes in people with hypertension, CAP may provide a better indicator of cardiovascular risk and predictor of outcomes of therapy.

What were the key results of the study?

The sub-study provides a further insight into why certain drugs may be more effective than others in the treatment of hypertension. It demonstrates, for the first time in a large clinical outcomes trial, that the different classes of antihypertensive drugs have very different effects on the cardiovascular system, and that these effects cannot always be appreciated from the simple measurement of blood pressure.

Results from the study showed that amlodipine-based treatment is statistically more effective at reducing central aortic blood pressure than a standard beta-blocker regimen. Atenolol-based therapy was associated with higher central aortic systolic pressure and higher central aortic pulse pressure – despite similar brachial pressures – when compared with amlodipine-based therapy. The mean difference in central systolic arterial blood pressure between the two treatment regimens was approximately 3.5 mm/Hg greater than the mean difference in brachial blood pressure, in favour of the amlodipine-based regimen. The central BP was better correlated to the clinical outcome of ASCOT than the peripheral BP.

Brachial and Central Aortic Systolic
 Blood Pressure (\pm 95% CI)

Brachial SBP
 Diff Mean (AUC) = 0.7 (-0.4, 1.7) mm Hg



The study investigators suggested that measuring blood pressure in the arm underestimated the efficacy of drugs such as amlodipine and overestimated the efficacy of drugs such as atenolol in reducing central aortic pressures. These data have important implications for clinical practice, as they give a plausible explanation for the benefits of amlodipine-based high blood pressure treatment compared with the traditional atenolol-based treatment, as seen in the overall ASCOT study.

Blood pressure-lowering drugs can have substantially different effects on central aortic pressures and haemodynamics, despite a similar impact on brachial blood pressure. Moreover, central aortic pulse pressure may be a determinant of clinical outcomes, and differences in CAP may be a potential mechanism to explain the different clinical outcomes between the two blood pressure treatment arms in ASCOT.



Reference

1. Williams B, Lacey PS, Thom SM *et al.* Differential impact of blood pressure-lowering drugs on central aortic pressure and clinical outcomes: principal results of the Conduit Artery Function Evaluation (CAFE) study. *Circulation* 2006;**113**(9): 1213-25.

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