
We respond to recent correspondence relating to the Conduit Artery Function Evaluation study (CAFE),1 published in Circulation earlier this year.

We thank Drs Nieminen, Kahonen, and Kobie for their remarks and suggestions. We agree that increased stroke volume at lower heart rates should be considered as a contributor to the elevated pulse pressure (PP) seen with atenolol-based treatment in the CAFE study. We did not assess stroke volume, and further studies are required to define the impact of blood pressure (BP)-lowering therapies on stroke volume and its contribution to central aortic pressures. Nevertheless, our data do suggest an important role for increased wave reflections in determining higher central aortic pressures with atenolol-based when compared with amlodipine-based treatment. Indeed, the higher central but not brachial PP with atenolol-based therapy in the CAFE study supports the hypothesis that the main driver of differential central aortic pressures was drug effects on pressure wave reflections rather than changes in stroke volume.

We agree with Drs Safar and Fournier that the findings of the CAFE study are consistent with their report of differential drug reflections rather than changes in stroke volume.

We thank Drs Dart et al for their comments and interest in our study but would like to point out fundamental differences to their work related to the accuracy and validation of the transfer function rather than the derivation of central aortic pressures, which are prone to and dependent on the same level of inaccuracy as the measurement of brachial BP by cuff sphygmomanometry.

We thank Dr Dart et al for their comments and interest in our study but would like to point out fundamental differences between the design and objectives of the CAFE study and The Australian National Blood Pressure Study 2 (ANBP2). A substudy of central aortic pressures.4 The prespecified primary objective4 of the CAFE study was to examine the hypothesis that 2 different BP-lowering regimens would have different effects on derived central arterial pressures and hemodynamics despite similar effects on brachial pressures. This was convincingly demonstrated by the findings of the CAFE study. There is now understandably much interest in the relative importance of on-treatment central aortic BP and PP versus brachial BP and PP as determinants of clinical outcomes.

A secondary objective of the CAFE study was to explore the relationship between central aortic pressures and clinical outcomes, and we showed a significant relation between central aortic PP and the composite clinical outcome using Cox proportional hazards modeling. We recognized the limited statistical power of this secondary analysis, and, mindful of the fact that the end point comprised only 305 events, we attached appropriate cautions to our interpretation of this result.

In contrast, the ANBP2 substudy5 examined the relationship between baseline blood pressures and clinical outcomes in fewer than 500 people, all of whom were women, accumulating only 53 events. The ANBP2 substudy did not show a significant relation between baseline central aortic pressures and clinical outcomes. However, there are problems with the confidence of the authors in dismissing the importance of central aortic pressures: (1) The ANBP2 substudy was underpowered to test a clinical outcomes hypothesis and thus prone to a type 2 statistical error; and (2) baseline central aortic pressures are not the issue—importantly, the CAFE study showed that the kind of treatments used to lower BP can differentially influence central aortic pressures. This addressed the more important question regarding on treatment brachial versus central aortic pressures. This is the key question, and the ANBP2 substudy does not contribute to this debate.

Finally, we agree with the commentary of Oparil and Izzo6 that uncertainty remains regarding the utility of radial artery tonometry in routine clinical practice. We would go further and suggest that the findings of the CAFE study prompt the need for further studies to more effectively evaluate the effects of BP-lowering drugs and other agents with the potential to influence central aortic pressures and hemodynamics in clinical trials. In so doing, such suitably powered studies would define the relative importance of central aortic versus brachial pressures with regard to clinical outcomes.

Disclosures

Drs Williams, Cruickshank, Collier, Stanton, Thom, and Hughes have received research funding from Pfizer. Dr O’Rourke is the founder and medical director and a board member of Atcor Medical. Dr O’Rourke also holds shares in Atcor Medical. Drs Lacy and Thurston have no conflicts of interest to disclose.

Bryan Williams, MD, FRCP
Herbert Thurston, MD, FRCP
Simon Thom, MD, FRCP
Alun Hughes, MBBS, PhD
Kennedy Cruickshank, MD

Correspondence

(Circulation. 2006;114:e540-e541.)
© 2006 American Heart Association, Inc.
Circulation is available at http://www.circulationaha.org
DOI: 10.1161/CIRCULATIONAHA.106.640870


Response to Letters Regarding Article, "Differential Impact of Blood Pressure-Lowering Drugs on Central Aortic Pressure and Clinical Outcomes: Principal Results of the Conduit Artery Function Evaluation (CAFE) Study"

Bryan Williams, Peter S. Lacy, Herbert Thurston, Simon Thom, Alun Hughes, Kennedy Cruickshank, Alice Stanton, David Collier and Michael O'Rourke

_Circulation_. 2006;114:e540-e541
doi: 10.1161/CIRCULATIONAHA.106.640870

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2006 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/114/15/e540

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org/subscriptions/