
Response:

Schuchlenz1 makes important observations that help frame the conclusions we reached through analysis of the transesophageal echocardiography data from the Risk of Paradoxical Embolism (RoPE) database and appropriately highlights some of the limitations of this data set. Specifically, important anatomic features (presence or absence of a prominent eustachian valve) were not routinely reported across the component databases. Additionally, microbubbles were routinely injected via the antecubital vein, a site that Schuchlenz1 correctly identifies as correlating less well with anatomic size.

To create our RoPE database,2 component studies were combined and data were harmonized with the goals of improving on the methodological and statistical limitations of small individual studies. Yet harmonization across databases creates its own challenges and necessarily excludes details that might not be uniformly collected across component studies, including some transesophageal echocardiography variables. Our observation that proposed high-risk transesophageal echocardiography features do not correlate with the significance of an observed patent foramen ovale for patients with cryptogenic stroke3 should be viewed not as a failure of the imaging variables. Our observation that proposed high-risk features from the risk of paradoxical embolism database4 correctly identifies as correlating less well with anatomic size.

To create our RoPE database,2 component studies were combined and data were harmonized with the goals of improving on the methodological and statistical limitations of small individual studies. Yet harmonization across databases creates its own challenges and necessarily excludes details that might not be uniformly collected across component studies, including some transesophageal echocardiography variables. Our observation that proposed high-risk transesophageal echocardiography features do not correlate with the significance of an observed patent foramen ovale for patients with cryptogenic stroke3 should be viewed not as a failure of the imaging modality as ideally applied. Instead, we view it as a call for further refining the technique, improving standardization and conducting further research, and as a call too for development of complimentary techniques to better assess risk.

Sources of Funding
This study was partially funded by grants UL1 RR025752, R01 NS062153, and R21 NS079826 from the National Institutes of Health.

Disclosures
Drs Kent and Thaler have consulted for WL Gore Associates. Dr Thaler is a consultant to AGA Medical Corporation. The other authors report no conflicts.

Benjamin S. Wessler, MD
Division of Cardiology, Tufts Medical Center
Boston, MA

David E. Thaler, MD, PhD
Department of Neurology, Tufts Medical Center/Tufts University School of Medicine
Boston, MA

Robin Ruthazer, MPH
Predictive Analytics and Comparative Effectiveness Center
Institute for Clinical Research and Health Policy Studies, Tufts Medical Center/Tufts University School of Medicine
Boston, MA

Christian Weimar, MD
Department of Neurology, University of Duisburg-Essen
Essen, Germany

Marco R. Di Tullio, MD
Division of Cardiology, Columbia University
New York, NY

Mitchell S. V. Elkind, MD, MS
 Departments of Neurology and Epidemiology, Columbia University
 New York, NY

Shunichi Homma, MD
Division of Cardiology, Columbia University
New York, NY

Jennifer S. Lutz, MS
Predictive Analytics and Comparative Effectiveness Center
Institute for Clinical Research and Health Policy Studies, Tufts Medical Center/Tufts University School of Medicine
Boston, MA

Jean-Louis Mas, MD
Department of Neurology, Hôpital Sainte-Anne, Paris-Desescartes University
Paris, France

Heinrich P. Mattle, MD
Department of Neurology, Inselspital, University of Bern
Bern, Switzerland

Bernhard Meier, MD
Department of Cardiology, Swiss Cardiovascular Center, Inselspital, University of Bern
Bern, Switzerland

Krassen Nedeltchev, MD
Department of Neurology, Triemli Municipal Hospital
Zürich, Switzerland

Federica Papetti, MD
Department of Cardiology, University of Rome La Sapienza
Rome, Italy

Emanuele Di Angelantonio, MD, MSc, PhD
Department of Public Health and Primary Care, University of Cambridge
Cambridge, United Kingdom

Mark Reisman, MD
Cardiology Clinic, University of Washington
Seattle

Joaquin Serena, MD, PhD
Department of Neurology, Hospital Universitari Doctor Josep Trueta Institut d’Investigació Biomèdica de Girona
Girona, Spain

David M. Kent, MD, CM, MSc
Predictive Analytics and Comparative Effectiveness Center
Institute for Clinical Research and Health Policy Studies
Tufts Medical Center/Tufts University School of Medicine
Boston, MA

References
Response to Letter Regarding Article, "Transesophageal Echocardiography in Cryptogenic Stroke and Patent Foramen Ovale Analysis of Putative High-Risk Features From the Risk of Paradoxical Embolism Database"


_Circ Cardiovasc Imaging_. 2014;7:573
doi: 10.1161/CIRCIMAGING.114.001756

_Circulation: Cardiovascular Imaging_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2014 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-9651. Online ISSN: 1942-0080

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circimaging.ahajournals.org/content/7/3/573

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation: Cardiovascular Imaging_ 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: Cardiovascular Imaging_ is online at:
http://circimaging.ahajournals.org/subscriptions/