

Detecting right ventricular dysfunction in patients diagnosed with low-risk pulmonary embolism: is routine computed tomographic pulmonary angiography sufficient?

David R. Vinson ^{1,2,3*}, Vignesh A. Arasu ^{1,4,5}, and Javier Trujillo-Santos ^{6,7}

¹The Permanente Medical Group, Oakland, CA, USA; ²Kaiser Permanente Division of Research, Oakland, CA, USA; ³Department of Emergency Medicine, Kaiser Permanente Sacramento Medical Center, Sacramento, CA, USA; ⁴Department of Radiology, Kaiser Permanente Vallejo Medical Center, Vallejo, CA, USA; ⁵University of California, San Francisco, CA, USA; ⁶Department of Internal Medicine, Hospital Universitario Santa Lucía, Cartagena, Murcia, Spain; and ⁷Universidad Católica San Antonio, Murcia, Spain

Online publish-ahead-of-print 23 September 2019

This commentary refers to ‘Early discharge and home treatment of patients with low-risk pulmonary embolism with the oral factor Xa inhibitor rivaroxaban: an international multicentre single-arm clinical trial’, by S. Barco et al., doi: 10.1093/eurheartj/ehz367.

We applaud Barco *et al.*¹ for their multicentre single-arm management trial of 525 adults with acute low-risk pulmonary embolism (PE) who were directed to outpatient care on rivaroxaban after no more than two nights hospitalization. The low incidence of 3-month adverse events in the HoT-PE trial demonstrates the safety and effectiveness of their patient selection criteria and adds to the growing evidence supporting an early transition to ambulatory care either directly from the emergency department or after a short hospital stay.²

To be eligible, patients were required to meet low-risk criteria including absence of right ventricular (RV) dysfunction on computed tomographic pulmonary angiography (CTPA) or echocardiography. Current European Society of Cardiology PE guidelines state that RV assessment is not necessary to site-of-care decision-making among low-risk patients. Yet more recent systematic reviews and meta-analyses suggest that RV enlargement on CTPA may identify a cohort of normotensive patients with acute PE at slightly higher risk for short-term adverse events, which may argue against immediate home discharge.^{3,4} But in one of our reviews (J.T.S.), we found that the relatively small likelihood ratios and minimal improvement in risk stratification with the addition of CT-defined RV functional data ‘suggest that basing therapeutic decision-making solely on CT results is not warranted’³

We have three questions that prepare the way for the translation of the HoT-PE study findings into routine patient care, should subsequent research undergird their findings. First, why did most CTPA cases also undergo echocardiography, when it was not required by study protocol? Does this imply a distrust of the CTPA

RV measurements? Second, most PE studies evaluating the prognostic role of RV dysfunction via CTPA have used only two-dimensional axial transverse images and did not undertake complex multiplanar reconstruction.³ What kind of CTPA images were used in the HoT-PE study? Third, in study centres apart from study protocol, do radiologists routinely report on RV dimensions in their CTPA interpretations? In our large 21-centre delivery system, we (D.R.V.) found only 287 of 1571 (18.3%) cases of positive CTPA reviewed for the eSPEED trial included a description of RV diameter.⁵

Conflict of interest: none declared.

References

- Barco S, Schmidtman I, Ageno W, Bauersachs RM, Becattini C, Bernardi E, Beyer-Westendorf J, Bonacchini L, Brachmann J, Christ M, Czihal M, Duerschmied D, Empen K, Espinola-Klein C, Ficker JH, Fonseca C, Genth-Zotz S, Jimenez D, Harjola VP, Held M, Iogna Prat L, Lange TJ, Manolis A, Meyer A, Mustonen P, Rauch-Kroehnert U, Ruiz-Artacho P, Schellong S, Schwaiblmair M, Stahrenberg R, Westerweel PE, Wild PS, Konstantinides SV, Lankeit M. Early discharge and home treatment of patients with low-risk pulmonary embolism with the oral factor Xa inhibitor rivaroxaban: an international multicentre single-arm clinical trial. *Eur Heart J* 2019;doi: 10.1093/eurheartj/ehz367.
- Roy PM, Mounneh T, Penaloza A, Sanchez O. Outpatient management of pulmonary embolism. *Thromb Res* 2017;**155**:92–100.
- Trujillo-Santos J, den Exter PL, Gomez V, Del Castillo H, Moreno C, van der Hulle T, Huisman MV, Monreal M, Yusen RD, Jimenez D. Computed tomography-assessed right ventricular dysfunction and risk stratification of patients with acute non-massive pulmonary embolism: systematic review and meta-analysis. *J Thromb Haemost* 2013;**11**:1823–1832.
- Barco S, Mahmoudpour SH, Planquette B, Sanchez O, Konstantinides SV, Meyer G. Prognostic value of right ventricular dysfunction or elevated cardiac biomarkers in patients with low-risk pulmonary embolism: a systematic review and meta-analysis. *Eur Heart J* 2019;**40**:902–910.
- Vinson DR, Mark DG, Chettipally UK, Huang J, Rauchwerger AS, Reed ME, Lin JS, Kene MV, Wang DH, Sax DR, Pleshakov TS, McLachlan ID, Yamin CK, Elms AR, Iskin HR, Vemula R, Yealy DM, Ballard DW; eSpeed Investigators of the KP CREST Network. Increasing safe outpatient management of emergency department patients with pulmonary embolism: a controlled pragmatic trial. *Ann Intern Med* 2018;**169**:855–865.

* Corresponding author. Email: drvinson@ucdavis.edu

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author(s) 2019. For permissions, please email: journals.permissions@oup.com.

Response to ‘Detecting right ventricular dysfunction in patients diagnosed with low-risk pulmonary embolism: is routine computed tomographic pulmonary angiography sufficient?’

Stefano Barco ¹, Stavros V. Konstantinides^{1,2*}, and Mareike Lankeit^{1,3,4}

¹Center for Thrombosis and Hemostasis (CTH), University Medical Center of the Johannes Gutenberg University, Langenbeckstrasse 1, Building 403, 55131 Mainz, Germany; ²Department of Cardiology, Democritus University of Thrace, 68100 Alexandroupolis, Greece; ³Department of Internal Medicine and Cardiology, Campus Virchow Klinikum, Charité - University Medicine Berlin, Augustenburgerplatz 1, 13353 Berlin, Germany; and ⁴Clinic of Cardiology and Pneumology, Heart Center, University Medical Center Goettingen, Robert-Koch-Strasse 40, 37075 Goettingen, Germany

Online publish-ahead-of-print 20 September 2019

This commentary refers to ‘Detecting right ventricular dysfunction in patients diagnosed with low-risk pulmonary embolism: is routine compute tomographic pulmonary angiography sufficient?’, by D.R. Vinson et al., on page 3356.

Dr Vinson et al.¹ highlighted three important aspects concerning the assessment of right ventricular (RV) dysfunction in patients with acute pulmonary embolism (PE) who are haemodynamically stable at presentation. First, we fully agree with Dr Vinson et al.’s statement that therapeutic decision-making cannot be based on computerized tomography pulmonary angiography (CTPA) results alone. This is by no means the message of our trial.^{2,3} Below, we take the opportunity to clarify the points raised by Dr Vinson et al:

- (1) More than 85% of patients enrolled in the HoT-PE study underwent echocardiography.² In the study protocol, it was stipulated that (i) ‘RV function must be properly assessed by either CTPA or echocardiography’ and that (ii) ‘echocardiography is recommended, but not compulsory’.³ We added the latter, non-binding recommendation hoping to collect further data (for later analysis) on the concordance between these two imaging techniques, not because we did not trust the CTPA findings. In the study, echocardiography has performed a median of 19.0 (interquartile range 6.5–24.0; $n = 439$) hours after the initial presentation, which was after the enrolment in the study and initiation of anticoagulant therapy in the majority of the cases.
- (2) Right ventricular dysfunction, which was defined by the presence of a right/left short-axis diameter ratio of ≥ 1.0 , was assessed on CTPA on the 2D axial transverse plane and not by complex multiplanar reconstruction.³

- (3) We agree that the reporting on RV dimensions by radiologists is not (yet) routine outside the study protocol. However, this assessment is easy to perform and fast to report,⁴ and we hope that the results of our trial will motivate an increasing number of hospitals and their radiology departments to integrate reporting on the RV in clinical pathways of patients presenting with acute PE.

Funding

HoT-PE is an independent, investigator-initiated trial with an academic sponsor (Centre for Thrombosis and Haemostasis, University Medical Centre Mainz, Germany). The work of S.B. and S.V.K. was supported by the German Federal Ministry of Education and Research (BMBF 01EO1003 and 01EO1503). In addition, the sponsor has obtained the study drug (rivaroxaban) and a grant from the market authorization holder of rivaroxaban, Bayer AG.

Conflict of interest: S.B. reports personal fees from Biocompatibles Group UK, LeoPharma, and Bayer HealthCare, non-financial support from Bayer HealthCare and Daiichi Sankyo, outside the submitted work. S.V.K. reports grants and nonfinancial support from Bayer AG, during the conduct of the study; grants and personal fees from Boehringer Ingelheim, personal fees from Bayer AG, grants and personal fees from Actelion, grants and personal fees from Daiichi-Sankyo, grants and personal fees from Biocompatibles Group UK, personal fees from Pfizer-Bristol-Myers Squibb, grants and personal fees from MSD, outside the submitted work. M.L. reports personal fees and non-financial support from Actelion, personal fees and non-financial support from Bayer, personal fees and non-financial support from Daiichi-Sankyo, personal fees from MSD, personal fees from Pfizer—Bristol-Myers Squibb, grants from BRAHMS—Thermo Fisher scientific, outside the submitted work.

* Corresponding author. Tel: +49 6131 17 8382, Fax: +49 6131 17 3456, Email: stavros.konstantinides@unimedizin-mainz.de

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author(s) 2019. For permissions, please email: journals.permissions@oup.com.

References

1. Vinson DR, Arasu VA, Trujillo-Santos J. Detecting right ventricular dysfunction in patients diagnosed with low-risk pulmonary embolism: is routine compute tomographic pulmonary angiography sufficient? *Eur Heart J* 2019;**40**:3356.
2. Barco S, Schmidtman I, Ageno W, Bauersachs RM, Becattini C, Bernardi E, Beyer-Westendorf J, Bonacchini L, Brachmann J, Christ M, Czihal M, Duerschmied D, Empen K, Espinola-Klein C, Ficker JH, Fonseca C, Genth-Zotz S, Jimenez D, Harjola VP, Held M, Iogna Prat L, Lange TJ, Manolis A, Meyer A, Mustonen P, Rauch-Kroehnert U, Ruiz-Artacho P, Schellong S, Schwaiblmair M, Stahrenberg R, Westerweel PE, Wild PS, Konstantinides SV, Lankeit M, HoT-PE Investigators. Early discharge and home treatment of patients with low-risk pulmonary embolism with the oral factor Xa inhibitor rivaroxaban: an international multicentre single-arm clinical trial. *Eur Heart J* 2019;doi:10.1093/eurheartj/ehz367.
3. Barco S, Lankeit M, Binder H, Schellong S, Christ M, Beyer-Westendorf J, Duerschmied D, Bauersachs R, Empen K, Held M, Schwaiblmair M, Fonseca C, Jimenez D, Becattini C, Quitzau K, Konstantinides S. Home treatment of patients with low-risk pulmonary embolism with the oral factor Xa inhibitor rivaroxaban. Rationale and design of the HoT-PE Trial. *Thromb Haemost* 2016; **116**:191–197.
4. Ende-Verhaar YM, Kroft LJM, Mos ICM, Huisman MV, Klok FA. Accuracy and reproducibility of CT right-to-left ventricular diameter measurement in patients with acute pulmonary embolism. *PLoS One* 2017;**12**:e0188862.