

The ADAMTS13-VWF axis is dysregulated in chronic thromboembolic pulmonary hypertension.

Newnham, Michael; South, Kieron; Bleda, Marta; Auger, William; Barberà, Joan ; Bogaard, Harm; Bunclark, Katherine ; Cannon, John; Delcroix, Marion ; Hadinnapola, Charaka; Howard, Luke; Jenkins, David; Mayer, Eckhard; Ng, Choo; Rhodes, Christopher; Screaton, Nicholas; Sheares, Karen; Simpson, Michael; Southwood, Mark; Su, Li

DOI:

[10.1183/13993003.01805-2018](https://doi.org/10.1183/13993003.01805-2018)

License:

None: All rights reserved

Document Version

Peer reviewed version

Citation for published version (Harvard):

Newnham, M, South, K, Bleda, M, Auger, W, Barberà, J, Bogaard, H, Bunclark, K, Cannon, J, Delcroix, M, Hadinnapola, C, Howard, L, Jenkins, D, Mayer, E, Ng, C, Rhodes, C, Screaton, N, Sheares, K, Simpson, M, Southwood, M, Su, L, Taboada, D, Traylor, M, Trembath, R, Villar, S, Wilkins, M, Wharton, J, Gráf, S, Pepe-Zaba, J, Laffan, M, Lane, D, Morrell, N & Toshner, M 2019, 'The ADAMTS13-VWF axis is dysregulated in chronic thromboembolic pulmonary hypertension.', *European Respiratory Journal*, vol. 53, no. 3, 1801805. <https://doi.org/10.1183/13993003.01805-2018>

[Link to publication on Research at Birmingham portal](#)

Publisher Rights Statement:

Checked for eligibility: 11/03/2019

This is an author-submitted, peer-reviewed version of a manuscript that has been accepted for publication in the *European Respiratory Journal*, prior to copy-editing, formatting and typesetting. This version of the manuscript may not be duplicated or reproduced without prior permission from the copyright owner, the European Respiratory Society. The publisher is not responsible or liable for any errors or omissions in this version of the manuscript or in any version derived from it by any other parties. The final, copy-edited, published article, which is the version of record, is available without a subscription 18 months after the date of issue publication. <https://erj.ersjournals.com/content/53/3/1801805>

General rights

Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

- Users may freely distribute the URL that is used to identify this publication.
- Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
- User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
- Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

Take down policy

While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact UBIRA@lists.bham.ac.uk providing details and we will remove access to the work immediately and investigate.

Figures

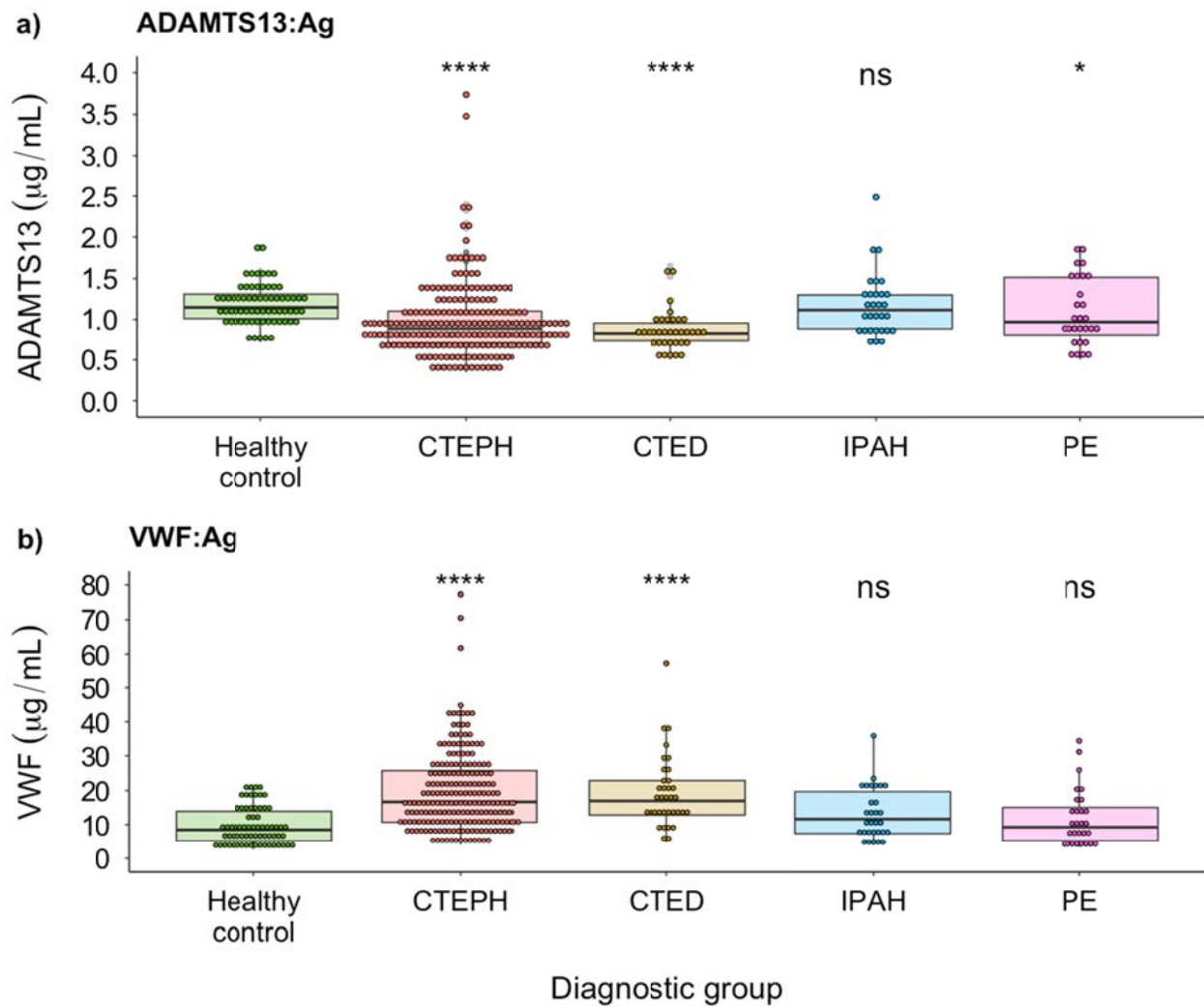


FIGURE 1

a) ADAMTS13 and b) VWF antigen (Ag) levels by diagnostic groups. Dunn's test with false discovery rate (FDR) adjustment was used to calculate p -values. ****: $p \leq 0.0001$, ***: $p \leq 0.001$, **: $p \leq 0.01$, *: $p \leq 0.05$, ns (not significant): $p > 0.05$. Healthy control (n=68), CTEPH (chronic thromboembolic pulmonary hypertension, n=208), CTED (chronic thromboembolic disease, n=35), IPAH (idiopathic pulmonary arterial hypertension, n=28), PE (pulmonary embolism, n=28).

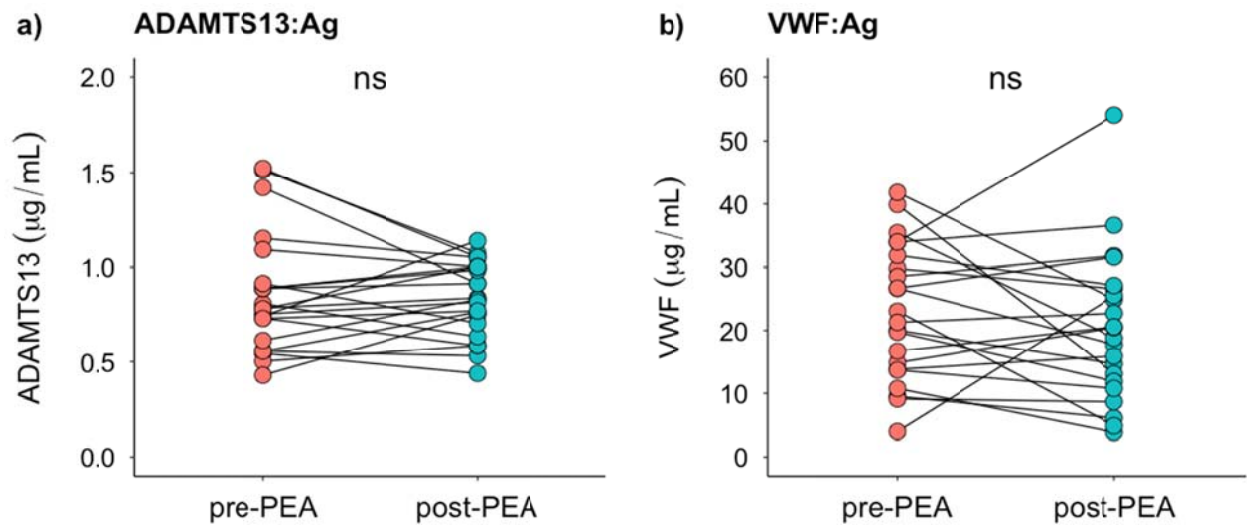


FIGURE 2

a) ADAMTS13 and b) VWF antigen levels pre- and post-pulmonary endarterectomy (n=22). Wilcoxon signed-rank test was used to calculate p -values.

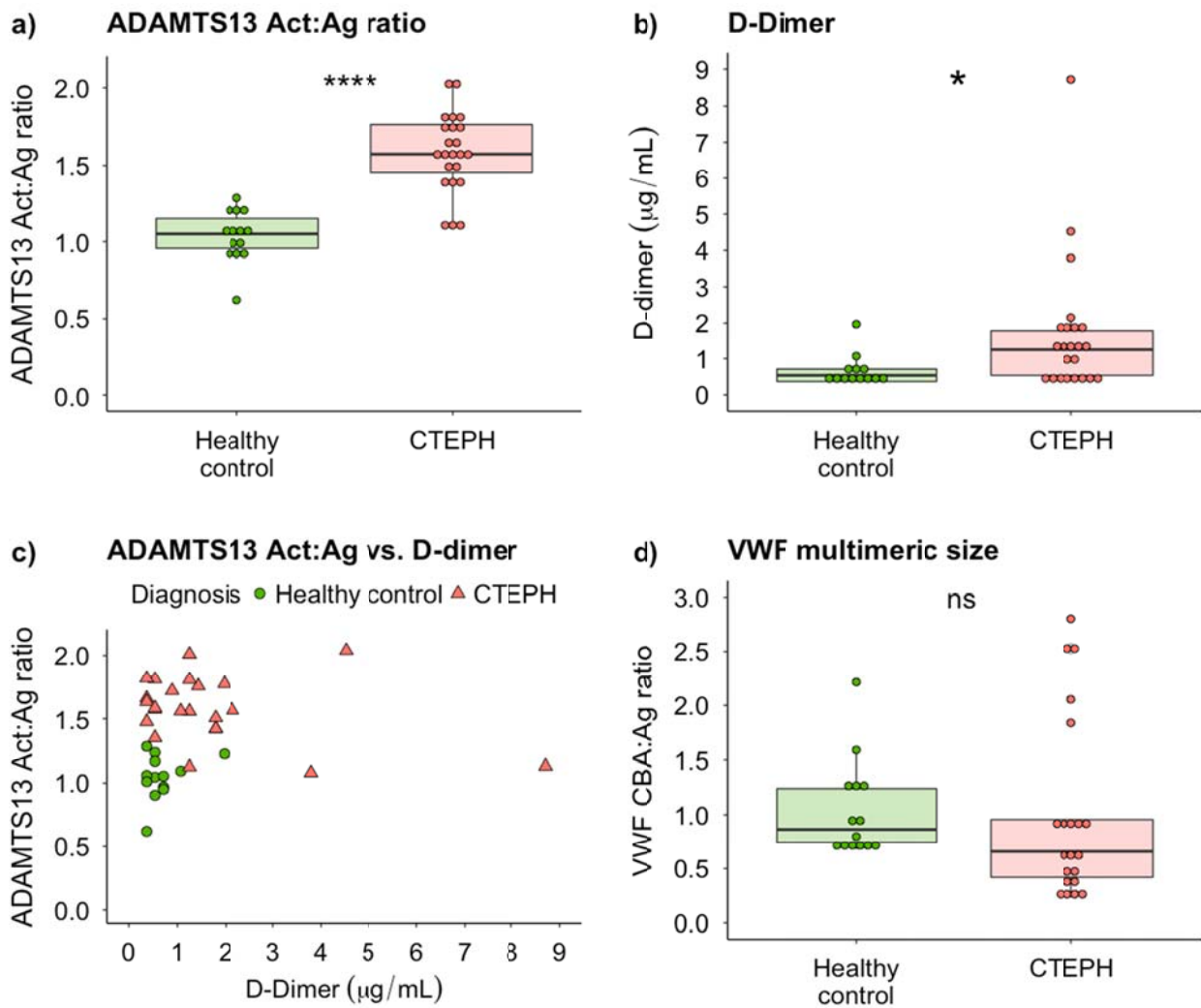


FIGURE 3

ADAMTS13 activity, D-dimer and VWF multimeric size in CTEPH and healthy controls. A subset of CTEPH patients (n=23) with the lowest ADAMTS13 antigen levels (below the first quartile of the CTEPH group) and healthy controls (n=14) were used for a-c). VWF multimeric size was measured in CTEPH (n=21) samples with the highest VWF antigen concentrations (above the third quartile of the CTEPH group) using the same healthy control subset and displayed in d). The Mann-Whitney *U* test was used to calculate group differences (a, b, d) and correlation was assessed with Spearman's rank correlation coefficients (c). A. Specific ADAMTS13 activity (Act:Ag ratio). b) D-dimer antigen levels. c) Specific ADAMTS13 activity and D-dimer antigen correlation. Healthy control correlation: $\rho=0.0938$, $p=0.761$;

CTEPH correlation: $\rho=-0.220$, $p=0.313$. d) VWF multimeric size (VWF Collagen binding assay:Antigen ratio).

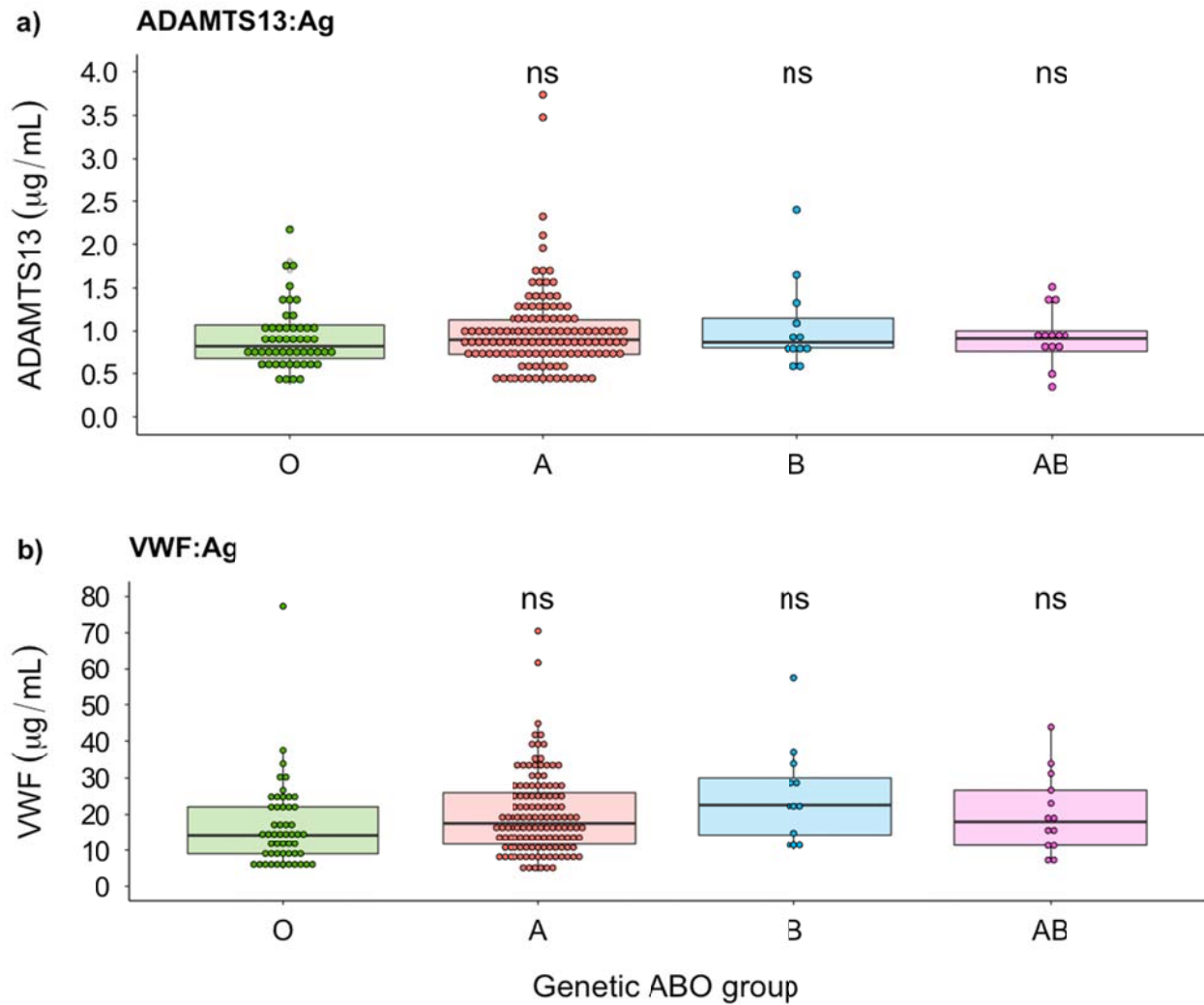


FIGURE 4

ADAMTS13 and VWF antigen levels by *ABO* genetic groups. CTEPH (n=182) and CTED (n=22) patients with genotypes and protein levels available (in n=3 a genetic *ABO* group could not be inferred) were included. Dunn's test with FDR adjustment was used to calculate p -values. Numbers in each group: O = 51, A = 128, B = 12, AB = 13.