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DISCUSSION FORUM

Common modulators of Brugada syndrome phenotype do not affect *SCN5A* prognostic value

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This commentary refers to the article 'Brugada syndrome genetics is associated with phenotype severity' by G. Ciconte *et al.*, doi:10.1093/eurheartj/ehaa942 and the discussion piece 'Different genotypes of Brugada syndrome may present different clinical phenotypes: electrophysiology from bench to bedside' by I El-Battrawy *et al.*, doi:10.1093/eurheartj/ehab070.

We thank the authors El-Battrawy *et al.*[1] for pointing out the studies on human cardiomyocytes from induced pluripotent stem cells, which demonstrate different phenotypes between cells with a mutation in the *SCN5A* gene vs. mutations in other genes, e.g., *SCN10A* or *SCN1B*, which could be in line to confirm our findings on a cellular level. While debated, variants in *SCN10A, SCN1B*, and other genes may, in fact, result in Brugada syndrome (BrS),[2] and their potential causative effects are the subject of current debate possibly only because of the lack of current data.[3] However, BrS has a complex pathology, and the effects of variants in these genes have yet to be verified in both additional clinical and functional studies. Results involving these genes were not included in our own present study only because of the low numbers in which they were discovered in the patients, which did not enable the obtainment of a reliable genotype–phenotype relationship, unlike for the *SCN5A* gene, for which more data were available, due to the higher prevalence of variants that were able to be identified.

Regarding the effects of quinidine or beta-blockers, as we do believe that these drugs could have an effect on the size of the arrhythmogenic substrate and affect the ablation procedure, patients using these drugs were excluded from this particular study. We wrote in our original study, 'None of the study subjects were taking any antiarrhythmic, antipsychotic, or other drugs known to have a significant effect on cardiac ion channels at the time of SAECG recording'.[4]

Regarding the effects of anaesthetics that are used during the ablation procedure, we have published a paper[5] demonstrating the safety of general anaesthesia using single-bolus propofol and volatile anaesthetics in high-risk patients with BrS, describing how it may exert a modulating effect by reducing the manifestation of the type 1 BrS pattern and arrhythmogenic substrate in the form of epicardial abnormal electrocardiograms. These anaesthetic drugs are used consistently across all patients, regardless of genotype, and thus, while they may affect the presentation of the phenotype as compared to when the patient is not sedated, their consistent use across all patients enabled us to still be able to ascertain differences in the phenotype between patients with or without a variant in the *SCN5A* gene.

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Conflict of interest: none declared.

References

1. El-Battrawy I, Lang S, Zhou X, Akin I. Different genotypes of Brugada syndrome may present different clinical phenotypes: electrophysiology from bench to bedside. *Eur Heart J* 2021;**42**:1270–1272.
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Corrigendum

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Corrigendum to: How to Diagnose Heart Failure with Preserved Ejection Fraction - The HFA-PEFF-SCORE An updated Consensus Statement of the Heart Failure Association (HFA) of the European Society of Cardiology (ESC)
Doi: 10.1093/eurheartj/ehz641

In the originally published version of this manuscript, several errors were noted and listed in this corrigendum.

Upon original publication, references made to "Supplementary material online" on pages 3, 5, 7, 9, 11 and 12. should read: "online supplementary *Appendix S1*".

Upon original publication, the legend for Figure 1. should read: "HFA-PEFF diagnostic algorithm. Overview of the diagnostic heart failure with preserved ejection fraction (HFpEF) steps 1–4 (P–F). CT, computed tomography; PET, positron emission tomography.".

Upon original publication, the text bubble for step E, in Figure 2., should read: "HFA–PEFF" instead of "HFA–PEFF Score".

Upon original publication, the first risk factor and finding listed in Table 1. should read: "Advanced age (age $\geq$ 70 in men or $\geq$ 75 in women)". In addition, the following abbreviations were omitted from the legend: "BNP, brain natriuretic peptide; NT-proBNP, N-terminal pro-brain natriuretic peptide".

Upon original publication, the following errors were noted in Table 2.:

Under the "Abnormalities of the myocardium" heading, the following toxic heavy metal should read: "copper (Wilson disease)62". In addition, the following immune and inflammatory abnormality of the myocardium, not related to infection, should read: "Raynaud's phenomenon[55]".

The following abbreviation in the legend should read: "HIV/AIDS, human immunodeficiency virus/acquired immune deficiency syndrome".

Upon original publication, the legend of Figure 3. Should read: "Echocardiographic and natriuretic peptide heart failure with preserved ejection fraction (HFpEF) workup and scoring system (diagnostic workup). AF, atrial fibrillation; BNP, brain natriuretic peptide; LAVI, left atrial volume index; LV, left ventricular; LVMI, left ventricular mass index; NT-proBNP, N-terminal pro-brain natriuretic peptide; PASP, pulmonary artery systolic pressure; RWT, relative wall thickness; SR, sinus rhythm; TR, tricuspid regurgitation.".

Upon original publication, the legend of Figure 4. should read: "Functional tests in cases of diagnostic uncertainty. (A) It shows the diastolic stress test workup with exercise echocardiography. If key haemodynamic abnormalities are identified, a definite heart failure with preserved ejection fraction (HFpEF) diagnosis can be made. (B) It shows the invasive haemodynamic measurements at rest (left) or during exercise (right) that may complement stress echocardiography and are recommended in cases with remaining diagnostic uncertainty. LVEDP, left ventricular end-diastolic pressure; PCWP, pulmonary capillary wedge pressure; TR, tricuspid regurgitation.".

Upon original publication, the following text bubble in panel B of Figure 5. should read: "Specific Cardiomyopathy?". In addition, the legend omitted the following abbreviation: "HFpEF, heart failure with preserved ejection fraction".

Upon original publication, the following errors were noted in the References:

References

For reference 19, the following text in should read: "Kraigher-Krainer E, Shah AM, Gupta DK, Santos A, Claggett B, Pieske B, Zile MR, Voors AA, Lefkowitz MP, Packer M, McMurray JJ, Solomon SD; PARAMOUNT Investigators".

For reference 35, the following text should read: "McKelvie RS, Komajda M, McMurray J, Zile M, Ptaszynska A, Donovan M, Carson P, Massie BM; I-Preserve Investigators.".

For reference 60, "e004692" was omitted.

For reference 111, the following text in should read: "Arcopinto M, Salzano A, Giallauria F, Bossone E, Isgaard J, Marra AM, Bobbio E, Vriz O, Aberg DN, Masarone D, De Paulis A, Saldamarco L, Vigorito C, Formisano P, Niola M, Perticone F, Bonaduce D, Sacca L, Colao A, Cittadini A; T.O.S.CA. (Trattamento Ormonale Scompenso CArdiaco) Investigators."

For reference 172, the following text should read: "*Clin Res Cardiol* 2019;**108**:203–211".

For reference 181, the full reference should read: "Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, Iung B, Lancellotti P, Lansac E, Rodriguez Munoz D, Rosenhek R, Sjogren J, Tornos Mas P, Vahanian A, Walther T, Wendler O, Windecker S, Zamorano JL, ESC Scientific Document Group. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J* 2017;**38**:2739–2791.".

For reference 231, the following text in should read: "*J Cardiovasc Med (Hagerstown)* 2018;**19**:304–309".

For reference 264, the full reference should read: "Charron P, Elliott PM, Gimeno JR, Caforio ALP, Kaski JP, Tavazzi L, Tendera M, Maupain C, Laroche C, Rubis P, Jurcut R, Calo L, Helio TM, Sinagra G, Zdravkovic M, Kavoliuniene A, Felix SB, Grzybowski J, Losi MA, Asselbergs FW, Garcia-Pinilla JM, Salazar-Mendiguchia J, Mizia-Stec K, Maggioni AP; EORP Cardiomyopathy Registry Investigators. The Cardiomyopathy Registry of the EURObservational Research Programme of the European Society of Cardiology: baseline data and contemporary management of adult patients with cardiomyopathies. *Eur Heart J* 2018;**39**:1784–1793.".

For reference 277, the following text should read: "*Eur Heart J* 2019;**40**:2155–2163.".

These errors have now been corrected online.