

LETTERS TO THE EDITOR

To the Editor—Altered *in vivo* systolic function in the short QT syndrome anticipated *in silico*



A recent article by Frea et al¹ in *HeartRhythm* provides new evidence for altered systolic function in patients with the short QT syndrome (SQTS). They studied 15 patients with the SQTS (7 with the hERG mutation–linked SQT1 variant, 3 with KCNQ1 mutation–linked SQT2 variant, and 5 without known mutations) by using tissue Doppler imaging and speckle tracking electrocardiography to reveal reduced left ventricular contraction and increased mechanical dispersion in the SQTS group as compared with healthy controls.¹ A longer myocardial performance index was seen in patients with the SQTS, but without significant alterations in iso-volumetric contraction and relaxation times, implying that this results from reduced ejection time. Over half of the patients with the SQTS also displayed pathological values of global longitudinal shortening, which correlated positively with corrected QT interval shortening.¹ Mechanical dispersion affected the final stage of contraction in patients with the SQTS.¹

In 2013, we published a simulation study in which the functional effects of SQTS K⁺ channel mutations were incorporated into human ventricular electromechanical models.² The incorporation of the SQT1 N588K hERG mutation profoundly reduced the intracellular calcium transient, leading to greatly reduced active force. The SQT3 D172N Kir2.1 mutation, which predominantly influences late repolarization, produced a more modest effect.² Once stretch-activated channels (SACs) were incorporated into the base model, the effects of the SQT mutations on the Ca²⁺ transient and force generation were reduced and reduced further if SAC Ca²⁺ permeability was incorporated.² Under simulated action potential clamp, shorter action potentials led to a reduced sarcoplasmic reticulum Ca²⁺ content and Ca²⁺ transients in the control model, implicating abbreviated repolarization itself as a driver of altered contractility; the mitigating effects of SAC incorporation correlated with changes in Na⁺ homeostasis and sodium-calcium exchange (NCX) activity.² The extent to which mechanisms demonstrated in our “proof-of-concept” simulations, made in the absence of any compensatory remodeling, apply to the modest but significant systolic dysfunction in patients with the SQTS¹ remains to be established. However, given the important findings of Frea et al,¹ further investigation of altered mechanical function in the SQTS is now warranted.

Jules C. Hancox, PhD^{*†}
jules.hancox@bristol.ac.uk
Ismail Adeniran, PhD^{*}

Dominic G. Whittaker, MPhys^{*}
Henggui Zhang, PhD^{*}
henggui.zhang@manchester.ac.uk

^{*}Biological Physics Group, School of Physics and Astronomy, The University of Manchester Manchester, United Kingdom

[†]Cardiovascular Laboratories, School of Physiology and Pharmacology, University of Bristol Bristol, United Kingdom

References

1. Frea S, Giustetto C, Capriolo M, Scrocco C, Fornego C, Benedetto S, Bianchi F, Pidello S, Morello M, Gaita F. New echocardiographic insights in short QT syndrome: more than a channelopathy? *Heart Rhythm* 2015. pii: S1547-5271(15)00626-8. <http://dx.doi.org/10.1016/j.hrthm.2015.05.024>.
2. Adeniran I, Hancox JC, Zhang H. *In silico* investigation of the short QT syndrome, using human ventricle models incorporating electromechanical coupling. *Front Physiol* 2013;4:166.

Reply to the Editor—Altered *in vivo* systolic function in the short QT syndrome anticipated *in silico*



Our group recently demonstrated an *in vivo* association between short QT syndrome (SQTS) and a slight but significant systolic dysfunction.¹ Hancox and colleagues² partially anticipated this report showing an interesting correlation between SQTS channel mutations (mostly HERG mutation) and shortening of action potential with an *in vitro* reduction in Ca²⁺ transient and force generation.

These 2 studies seem to suggest that the association between SQTS and systolic impairment may be explained by 3 mechanisms: a greater mechanical dispersion, a shorter ejection time, and the presence of specific gene mutations.

In order to assess the relevance of each mechanism on the development of systolic impairment, we performed some further analysis of our data. First, we saw that a greater mechanical dispersion correlated with a lower global longitudinal strain ($r = 0.493$; $P < .001$) and a lower ejection fraction ($r = 0.393$; $P = .032$). Second, a shorter left ventricular ejection time, a mechanical consequence of a reduced action potential duration, correlated with a lower global longitudinal strain ($r = 0.474$; $P = .008$) and a lower ejection fraction ($r = 0.381$; $P = .038$). Notably both mechanical dispersion and ejection time correlated with QT interval ($r = 0.404$; $P < .05$ and $r = 0.397$; $P = .03$, respectively). In other words, a short QT interval, increasing mechanical dispersion and reducing ejection time, seems to be the leading cause of the systolic dysfunction identified. Third, by comparing patients with and without HERG

mutations, we failed to find any significant difference. However, the higher use of hydroquinidine in patients with HERG mutations (7 of 7 patients with HERG mutations vs 4 of 8 patients without HERG mutations; $P = .05$) could have leveled off the results, especially considering that the hydroquinidine effect is more relevant in patients with HERG mutations.³ Further investigation is needed to confirm this hypothesis.

Simone Frea, MD
simone.frea@libero.it
Stefano Pidello, MD
Carla Giustetto, MD
Chiara Scrocco, MD
Fiorenzo Gaita, MD

*Division of Cardiology, Department of Medical Science
The University of Turin, Città della Salute e della
Scienza Hospital, Turin, Italy*

References

1. Frea S, Giustetto C, Capriolo M, Scrocco C, Fornengo C, Benedetto S, Bianchi F, Pidello S, Morello M, Gaita F. New echocardiographic insights in short QT syndrome: more than a channelopathy? *Heart Rhythm* 2015. pii: S1547-5271(15)00626-8. <http://dx.doi.org/10.1016/j.hrthm.2015.05.024>. [Epub ahead of print].
2. Adeniran I, Hancox JC, Zhang H. In silico investigation of the short QT syndrome, using human ventricle models incorporating electromechanical coupling. *Front Physiol* 2013;4:166.
3. Giustetto C, Schimpf R, Mazzanti A, Scrocco C, Maury P, Anttonen O, Probst V, Blanc J-J, Sbragia P, Dalmasso P, Borggrefe M, Gaita F. Long-term follow-up of patients with short QT syndrome. *J Am Coll Cardiol* 2011;58:587–595.

To the Editor— Higher incidence of esophageal lesions after atrial fibrillation ablation related to the use of esophageal temperature probes



The article illustrates an experiment aimed at checking whether it is safe and advisable to use esophageal probes equipped with thermal sensors during radiofrequency ablation procedures for pulmonary vein isolation. To this end, 2 cohorts of 40 patients each were treated with or without the probe (Sensitherm, FIAB SpA), and an endoscopic analysis was then performed to evaluate the incidence of esophageal lesions in the 2 groups. The experiment seems to have been carried out as rigorously as possible, but the conclusions are misleading. The result that 12 patients in the group with thermal control had esophageal “lesions” while only 1 patient with injury was detected in the other group is perhaps technically correct but substantially wrong, since 10 of the 12 lesions were simple erythemas. The 3 patients with ulcers found were split 2:1, which is not statistically significant. Erythemas are asymptomatic and self-healing irritations, usually not included in lesions. The mechanical action of a probe on an abnormally heated ($>40^{\circ}\text{C}$) esophageal mucosa may produce some irritation, but with no consequences for patients. The authors quote experiments

proving that metallic bodies in tissues may infer lesions when exposed to powerful RF fields. However, this is not our case. Such a circumstance has been confirmed, for example, in the recent article¹ by means of a mathematical model. Moreover, calculations performed at FIAB have shown that in normal cases the maximal power dissipated on a sensor ring of the probe is just of the order of 10^{-8} W (blood strongly attracts the electric field lines carrying away a large amount of the supplied energy).

The Sensitherm probe has been safely and successfully used in more than 200,000 ablation procedures, so there is no need to say more about it. Checking esophageal temperature is an absolute necessity, despite the implicitly negative advice of the article, as confirmed by the most important reports on ablation-related esophageal lesions. Therefore, it is important that clinicians receive a clear message: *Please, use any esophageal probe you like, but do it!* OK, your patient may get a mild irritation. Are you ready to exchange this with the risk that temperature goes out of control?

Prof. Antonio Fasano
a.fasano@fiab.it

FIAB SpA, Florence, Italy

Reference

1. Pérez JJ, D'Ávila A, Aryana A, Berjano E. Electrical and thermal effects of esophageal temperature probes on radiofrequency catheter ablation of atrial fibrillation: results from a computational modeling study. *J Cardiovasc Electrophysiol* 2015;26:556–564.

To the Editor— Are esophageal lesions caused by the use of esophageal probes or conductive heat after atrial fibrillation ablation?



We read with interest the study by Müller et al¹ on higher incidence of esophageal lesions after atrial fibrillation ablation and the use of Sensitherm esophageal probe (ETP). Contrary to their findings, the findings of our computer modeling study² suggest that temperature rises in the esophageal wall and the ETP were primarily produced by thermal conduction and not by electrical and/or thermal interactions between the ablation catheter and the ETP. A slight alteration in the electrical field was noted only when metallic surface probes (ETPs of Müller et al) were used.²

Esophageal thermal injury is thought to occur when temperature $>50^{\circ}\text{C}$ is reached in a sufficiently large volume of the esophageal wall to induce coagulative necrosis. The findings of Müller et al are compatible with this explanation because endoscopically detected esophageal lesions (EDELs) were found in patients with esophageal temperature higher (by 0.8°C) than that in those without EDELs. The proximity of the ablating electrode to the esophageal wall encountered in most patients supports the notion that thermal lesions created by radiofrequency energy