and the glucose metabolic disorder in the myocardium. However, further investigation is required to confirm that the glucose metabolism disorder in the myocardium may reflect the root cause or a secondary response in patients with tako-tsubo cardiomyopathy.

We agree with the hypothesis of sex hormones influencing the pathogenesis of tako-tsubo cardiomyopathy because all women in our current study were post-menopausal. However, we have no data concerning the function of sex hormones in patients with tako-tsubo cardiomyopathy. More recently, Ueyama et al. suggested that estrogen supplementation partially prevents emotional stress-induced cardiovascular responses, both by indirect action on the nervous system and by direct action on the heart. From this data, a reduction in estrogen levels following menopause may augment the reactivity to stress via the modulation of autonomic functions, resulting in the high incidence of tako-tsubo cardiomyopathy in post-menopausal women. This issue is considered to be very important and interesting. Estrogen supplementation therapy may possibly prevent the onset of tako-tsubo cardiomyopathy in post-menopausal women. We will try to investigate this issue and clarify the underlying true mechanism.

References


Tetsuro Yoshida
Department of Cardiovascular Medicine
Gifu Prefectural Government Tajimi Hospital
S-161 Maehata, Tajimi
Gifu 5078522 Japan
Tel: +81 572 22 5311
Fax: +81 572 25 1246
Email: tetsuro-moet@nifty.com

Takeshi Hibino
Department of Cardiovascular Medicine
Gifu Prefectural Government Tajimi Hospital
Tajimi
Japan

Nobuo Kako
Department of Radiology
Kizawa Memorial Hospital
Minokamo
Japan

Shunsuke Murai
Department of Cardiovascular Medicine
Gifu Prefectural Government Tajimi Hospital
Tajimi
Japan

Mitsutoshi Oguri
Department of Cardiovascular Medicine
Gifu Prefectural Government Tajimi Hospital
Tajimi
Japan

Kimihiko Kato
Department of Cardiovascular Medicine
Gifu Prefectural Government Tajimi Hospital
Tajimi
Japan

Kazuhiko Yajima
Department of Cardiovascular Medicine
Gifu Prefectural Government Tajimi Hospital
Tajimi
Japan

Nobuyuki Ohte
Department of Cardio-Renal Medicine and Hypertension
Nagoya City University Graduate School of Medical Sciences
Nagoya
Japan

Kiyoshi Yokoi
Department of Cardiovascular Medicine
Gifu Prefectural Government Tajimi Hospital
Tajimi
Japan

Genjiro Kimura
Department of Cardio-Renal Medicine and Hypertension
Kizawa Memorial Hospital
Tajimi
Japan

What is the level of evidence for combined cardiac resynchronization and defibrillation therapy in heart failure?

The recently published ESC Guidelines for cardiac pacing and cardiac resynchronization therapy (CRT-P) are comprehensive and very welcome. We would like to comment on the strength of evidence given for combined cardiac resynchronization and defibrillation therapy (CRT-D).

Section 3.2.1 of the guideline gives a class I, level of evidence B for the implantation of a CRT-D device in patients with NYHA classes III–IV heart failure who have an LVEF of <35% and a wide QRS complex (>120 ms). The efficacy of CRT-D relative to optimal medical therapy is supported by direct evidence of survival benefit from a randomized control trial (COMPANION) as well as a network meta-analysis specifically examining the evidence base for CRT-D. There is therefore sufficient current evidence to support a class I, level of evidence A recommendation for CRT-D when compared with optimal medical therapy.

Section 3.2.3 also gives a class I, level of evidence B recommendation for CRT-D for patients who fulfil the criteria for CRT-P and who also have a class I indication for an implantable cardioverter defibrillator (ICD) (first implant, upgrading, or device change). This recommendation is only based on randomized control trial evidence (MIRACLE-ICD; CONTAK-CD) that demonstrated functional (but not survival) incremental benefits of CRT-D when compared with ICD alone. We know that CRT-P alone improves function, as well as reducing sudden deaths and overall survival (CARE-HF). The important clinical question, therefore, is whether CRT-D offers any survival benefit over CRT-P in this group of patients (given the additional cost of the combined device and potential for inappropriate shocks). Evidence from individual trials comparing CRT-D with either device alone, and from a network meta-analysis incorporating the major CRT-P, CRT-D, and ICD trials, however has not demonstrated any survival benefit of CRT-D when compared with either device alone. There is therefore no current evidence to suggest that a combined device is better than CRT-P to improve mortality and morbidity among heart failure.

doi:10.1093/eurheartj/ehm646

Letters to the Editor
patients suitable for both CRT-P and ICD. We would therefore suggest that the current evidence base only supports a class IIa, level of evidence C recommendation for CRT-D when compared with CRT-P.

These points concerning the level of evidence given to a particular recommendation are of great importance to practising clinicians when considering the appropriate device or treatment generally for an individual patient.

**References**


**Simon K.H. Lam**

Chi Lin Medical Centre 5 Chi Lin Drive Hong Kong Tel: +852 6898 2200 Fax: +852 6898 2218 Email: simon.lam@medsci.oxon.org

**Andrew Owen**

Department of Cardiology Kent and Canterbury Hospital Ethelbert Road Canterbury Kent CT1 3NG UK

doi:10.1093/eurheartj/ehn002

**What is the level of evidence for combined cardiac resynchronization and defibrillation therapy in heart failure? reply**

In the letter, Doctors Lam and Owen offer some very relevant comments on the recommendations for cardiac resynchronization combined with defibrillation therapy (CRT-D) in the ESC guidelines.1 In regard to point 3.2.1, the authors provide further evidence from a network meta-analysis2 grouping randomized controlled trials on device therapy in heart failure (HF) and its effects on death from any cause. This meta-analysis observed a significant reduction in deaths of any cause (Odds ratio 0.57, 95% confidence interval 0.40–0.80) conferred by CRT-D compared with medical therapy. This recent contribution was not available at the time of publication of these guidelines and it strengthens further the indication for CRT-D.

In relation to the second point, the recommendation of section 3.2.3, is addressed to patients fulfilling the conventional indication for CRT and who present a concomitant Class I indication for the implantation of an ICD. This includes not only primary prevention, but also secondary prevention such as cardiac arrest survivors or patients with documented sustained ventricular tachycardia: it is clear that, in these cases, a CRT-P device is not adequate, and a CRT-D device is compulsory. Even considering primary prevention of SCD,3 the current recommendations indicate (class I) the use of an ICD. This includes not only primary prevention of SCD,4 the current recommendations indicate (class I) the use of an ICD in HF patients with LV impairment. This statement could not be neglected by the CRT guidelines. For these reasons, the consensus was that a class I recommendation should be given.

**References**


**Panos E. Vardas**

Department of Cardiology Heraklion University Hospital P.O. Box 1352 Stavrosia GR-711 10 Heraklion Greece Tel: +30 2810 392422 Fax: +30 2810 542055 Email: cardio@med.uoc.gr

**Angelo Auricchio**

Fondazione Cardiocentro Ticino - Division of Cardiology Via Tessere 48 CH-6900 Lugano Switzerland Tel: +41 91 805 3340 Fax: +41 91 805 3213 Email: angelo.auricchio@cardiocentro.org

**Jean-Jacques Blanc**

Département de Cardiologie Hôpital de la Cavale Blanche CHU de Brest Boulevard Tanguy Prigent FR-29609 Brest Cedex France Tel: +33 2 98 34 73 92 Fax: +33 2 98 34 78 03 Email: jean-jacques.blanc@univ-brest.fr

**Jean-Claude Daubert**


**Helmut Drexler**

Direktor Abt.Kardiologie u. Angiologie Zentrum Innere Medizin Med. Hochschule Hannover (MHH) Carl-Neubergstrasse 1 DE-30625 Hannover Germany Tel: +49 (511) 532 3840 Fax: +49 (511) 532 5412 Email: drexler.helmut@MHH-Hannover.de

**Hugo Ector**

Department of Cardiology University Hospital Gasthuisberg Herestraat 49 BE-3000 Leuven Belgium Tel: +32 (16) 34 42 35 Fax: +32 (16) 34 42 40 Email: hugo.ector@med.kuleuven.ac.be