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β-Blockers in worsening heart failure: good or bad?

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This commentary refers to 'B-CONVINCED: Beta-blocker CONtinuation Vs. INterruption in patients with Congestive heart failure hospitalizED for a decompensation episode'[†], by G. Jondeau *et al.*, on page 2186

The use of a β-blocker for the treatment of heart failure was for a long time contraindicated. The reasons were mainly due to concerns that the failing circulatory system needed adrenergic support, and anti-adrenergic actions would cause harm, as clearly stated by Gaffney and Braunwald in 1963.[1] The first report of β-blocker therapy by Waagstein and colleagues in 1975[2] was followed by a report in 1979 from our group on improved survival.[3] We published more extensive observations in 1980.[4] However, it would take another 20 years before this treatment became widely accepted. In contrast, the use of a β-blocker in chronic heart failure (CHF) and left ventricular systolic dysfunction is now the best documented treatment and also the most effective in this condition. It has a class I recommendation and evidence level A in international guidelines.[5]

A remaining and unresolved concern is how to manage patients who deteriorate while on treatment with a β-blocker. This concern relates to the initial worry limiting the use of the agents. However, it is also well known that in CHF there are often periods of worsening symptoms and signs. In placebo-controlled trials where the benefits of β-blockers have been documented, there have been more cases of worsening heart failure in the placebo groups than in the actively treated groups.[6] In our early studies, we withdrew the β-blocker therapy in 15 patients with dilated cardiomyopathy and found that many of them deteriorated rapidly.[7]

It is common practice to withdraw a β-blocker when patients are admitted to hospital because of worsening CHF. This action, however, will cause problems with re-initiation of the treatment and produce a need for thorough up-titration. Furthermore, it is known that an important predictor of subsequent optimal treatment with a β-blocker is if and how a β-blocker is prescribed on discharge from hospital.[8] A practical recommendation by an expert panel was published to guide physicians in this difficult clinical situation.[9] When 'Worsening symptoms/signs (e.g. increasing dyspnoea, fatigue, oedema, weight gain) occur:

- If increasing congestion – increase dose of diuretic and/or halve dose of beta-blocker (if increasing diuretic doesn't work)
- If marked fatigue (and/or bradycardia—see below) – halve dose of beta-blocker (rarely necessary)'.

The ESC Guidelines state with a recommendation graded as Class IIa, Evidence level B:[10]

'In patients admitted to hospital due to worsening HF, a reduction in the β-blocker dose may be necessary. In severe situations, temporary discontinuation can be considered. Low-dose therapy should be re-instituted and up-titrated as soon as the patient's clinical condition permits, preferably prior to discharge.'

Jondeau and co-workers have reported on a randomized trial where the important clinical question of what to do with a β-blocker in patients who have worsening heart failure. In the B-CONVINCED study,[11] 169 patients were randomized and 147 patients evaluated. They found that keeping the β-blocker was as safe as withdrawing the therapy. After both 3 and 8 days, the clinical improvement reported by both the physician and the patient was similar whether the β-blocker therapy was pursued or discontinued.

Importantly, keeping treatment resulted in a significantly higher rate of β-blocker prescription 3 months after discharge. A limitation, and as stated by the authors, is that in >50% of the patients, the average dose of the β-blockers used was <50% of the recommended target dose level according to the ESC Guidelines. There are several further limitations in the study. It was open, and more patients were then withdrawn from active therapy in the 'Keep β-blocker' group than in the control group.

The findings are supported by a *post hoc* analysis of databases from clinical trials. The experience from COMET showed a higher subsequent mortality among those patients where the β-blocker was stopped during admission for worsening heart failure.[12] This analysis is obviously confounded by sicker patients

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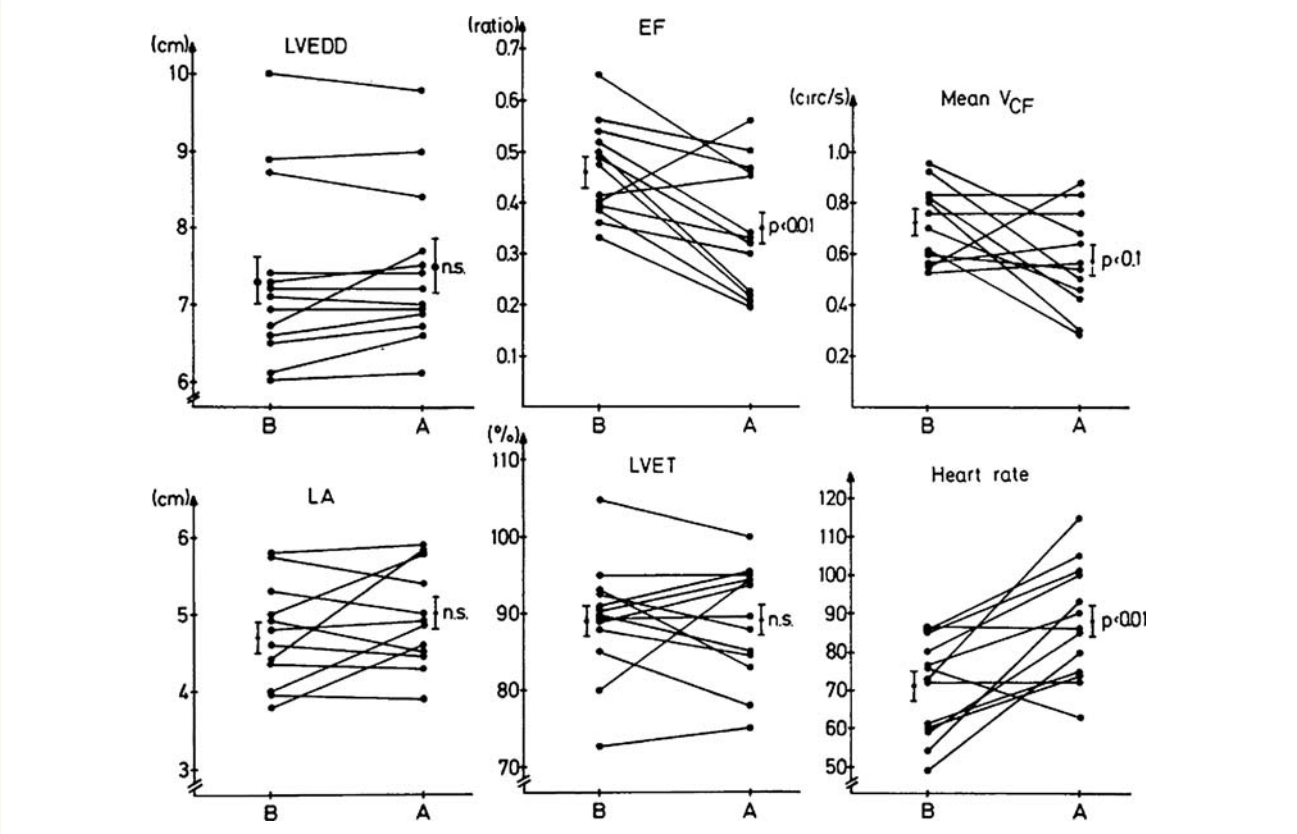

Figure 1 Non-invasive findings in patients with congestive cardiomyopathy on chronic β-blockade (B) and after withdrawal of treatment (A). EF, ejection fraction; LA, left atrium; LVEDD, left ventricular end-diastolic diameter; LVET, left ventricular ejection time; Mean VCF, mean velocity of circumferential fibre shortening. (Reproduced with permission from Swedberg K, Hjalmarson, Waagstein F, Wallentin I. Adverse effects of beta-blockade withdrawal in patients with congestive cardiomyopathy. *Br Heart J* 1980;**44**:134–142.)

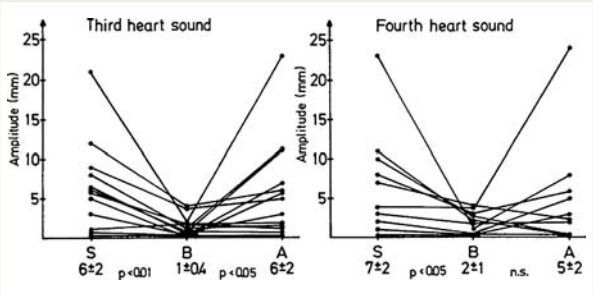

Figure 2 Amplitude of third and fourth heart sounds in 15 patients with congestive cardiomyopathy before (S) and during (B) β-blocker treatment, and after (A) withdrawal of the drug. (Reproduced with permission from Swedberg K, Hjalmarson, Waagstein F, Wallentin I. Adverse effects of beta-blockade withdrawal in patients with congestive cardiomyopathy. *Br Heart J* 1980;**44**:134–142.)

having a higher rate of withdrawal but, even after correction for this problem, the findings remained similar.

What are the clinical implications of these findings? The present recommendations in the ESC Guidelines can now be implemented with the addition of keeping the dose of any ongoing β-blocker therapy as the major first-line recommendation. The text as cited above is still very valid. Routine withdrawal of β-blocker therapy in patients admitted to hospital for worsening heart failure caused by left ventricular dysfunction should be avoided. This advice based on B-CONVINCED by the French group will most probably prolong the life of many patients.

Conflict of interest: none declared.

References

1. Gaffney TE, Braunwald E. Importance of the adrenergic nervous system in the support of circulatory function in patients with congestive heart failure. *Am J Med* 1963;**34**:340–345.
2. Waagstein F, Hjalmarson Å, Varnauskas E, Wallentin I. Effect of chronic beta-adrenergic receptor blockade in congestive cardiomyopathy. *Br Heart J* 1975;**37**:1022–1036.
3. Swedberg K, Hjalmarson, Waagstein F, Wallentin I. Prolongation of survival in congestive cardiomyopathy during treatment with beta-receptor blockade. *Lancet* 1979;**1**:1374–1376.
4. Swedberg K, Hjalmarson, Waagstein F, Wallentin I. Beneficial effects of long-term beta-blockade in congestive cardiomyopathy. *Br Heart J* 1980;**44**:117–133.
5. McMurray J, Swedberg K. Treatment of chronic heart failure: a comparison between the major guidelines. *Eur Heart J* 2006;**27**:1773–1777.
6. Brophy JM, Joseph L, Rouleau JL. Beta-blockers in congestive heart failure. A Bayesian meta-analysis. *Ann Intern Med* 2001;**134**:550–560.

7. Swedberg K, Hjalmarson, Waagstein F, Wallentin I. Adverse effects of beta-blockade withdrawal in patients with congestive cardiomyopathy. *Br Heart J* 1980;**44**:134–142.
8. Fonarow GC, Abraham WT, Albert NM, Stough WG, Gheorghiade M, Greenberg BH, O'Connor CM, Sun JL, Yancy CW, Young JB. Influence of beta-blocker continuation or withdrawal on outcomes in patients hospitalized with heart failure: findings from the OPTIMIZE-HF program. *J Am Coll Cardiol* 2008; **52**:190–199.
9. McMurray J, Cohen-Solal A, Dietz R, Eichhorn E, Erhardt L, Hobbs FD, Krum H, Maggioni A, McKelvie RS, Piña IL, Soler-Soler J, Swedberg K. Practical recommendations for the use of ACE inhibitors, beta-blockers, aldosterone antagonists and angiotensin receptor blockers in heart failure: putting guidelines into practice. *Eur J Heart Fail* 2005;**7**:710–721.
10. Dickstein K, Cohen-Solal A, Filippatos G, McMurray JJ, Ponikowski P, Poole-Wilson PA, Stromberg A, van Veldhuisen DJ, Atar D, Hoes AW, Keren A, Mebazaa A, Nieminen M, Priori SG, Swedberg K. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the diagnosis and treatment of acute and chronic heart failure 2008 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM). *Eur J Heart Fail* 2008;**10**: 933–989.
11. Jondeau G, Neuder Y, Eicher J-C, Jourdain P, Fauveau E, Galinier M, Jegou A, Bauer F, Trochu JN, Bouzamondo A, Tanguy M-L, Lechat P, for the B-CONVINCED Investigators. B-CONVINCED: Beta-blocker CONtinuation Vs. INterruption in patients with Congestive heart failure hospitalizED for a decompensation episode. *Eur Heart J* 2009;**30**:2186–2192. doi:10.1093/eurheartj/ehp323.
12. Metra M, Torp-Pedersen C, Cleland JG, Di Lenarda A, Komajda M, Remme WJ, Dei Cas L, Spark P, Swedberg K, Poole-Wilson PA. Should beta-blocker therapy be reduced or withdrawn after an episode of decompensated heart failure? Results from COMET. *Eur J Heart Fail* 2007;**9**:901–909.

CARDIOVASCULAR FLASHLIGHT

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Magnetic resonance diagnosis of cardiac fat-containing tumours in tuberous sclerosis

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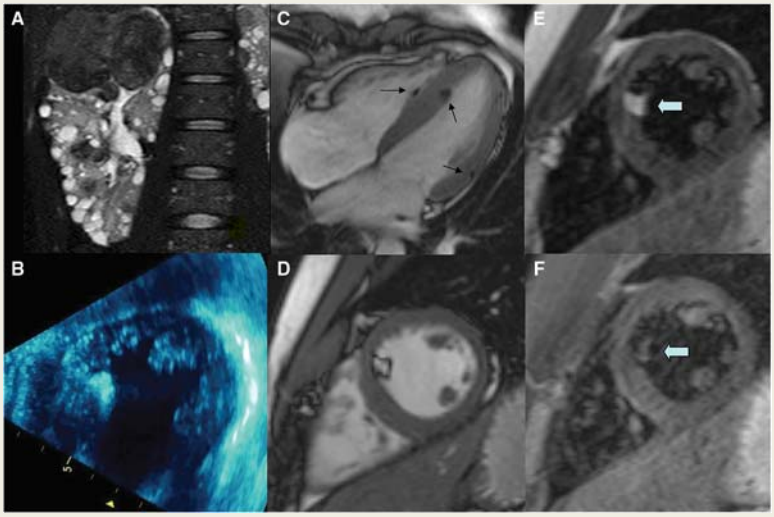

The patient, 23-year-old man, was known to have tuberous sclerosis (TS). He had been previously diagnosed with renal angiomyolipomas (*Panel A*), and intracranial lesions. He had neither cardiac, nor pulmonary symptoms. Since TS can involve various organs, a chest and abdominal multi detector computed tomography was performed. It incidentally revealed a cardiac mass.

This homogeneous non-enhancing tumour displayed a negative Hounsfield unit number, but no calcification. The transthoracic echocardiography found a hyperechoic mass (*Panel B*), appended to the septum, with no visible vascularization. A cardiac MR examination (Symphony, Syngo 1.5 T, Siemens, Erlangen, Germany) confirmed the 1 cm diameter septal neoplasm and identified two other comparable lesions (*Panel C*). The myocardial contractility was normal. Two masses were attached to the endocardial border, one arose from the epicardium. These tumours showed high signal surrounded by a dark rim related to chemical shift artefact (*Panel D*). On T2-weighted images, the mass displayed fatty signal intensity (*Panel E*), which was decreased by fat saturation (*Panel F*). The diagnosis of angiomyolipoma was suggested.

Tuberous sclerosis is characterized by the development of benign tumours in multiple organs. Angiomyolipomas are basically renal tumours, but cardiac localization, as a possible metastasis, has previously been described in patients with renal angiomyolipomas. Angiomyolipoma is a well-limited mass comprising vessels, fat, and muscle tissue, but no calcification. The differential diagnosis is lipoma. Only histology can make the difference but, in this case, there was no justification to perform a biopsy since those lesions are rarely responsible for symptoms.