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Brain natriuretic peptide: a marker of cardiac dysfunction with ventricular or dual-chamber pacing

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Background/Objectives The inability of trials to exhibit the superiority in survival of atrioventricular compared to ventricular pacing can be partially explained by the apical stimulation of the right ventricle, which adversely affects both short- and long-term ventricular performance. We evaluated the impact of pacing mode (DDDR vs VVIR) on the brain natriuretic peptide (BNP) level in patients with sick-sinus syndrome (SSS).

Methods Sixty-seven patients were treated with DDDR pacemaker implantation due to SSS. They were randomized during the first post-implant day either to DDDR or VVIR pacing mode and were reevaluated after 30 days. Group A comprised 35 patients on DDDR pacing mode and group B 32 patients on VVIR pacing mode. Peripheral blood samples were drawn for BNP measurement at the time of randomization and one month later.

Results BNP levels increased significantly in both groups at 30 days (group A: 85.6 ± 29.5 pg/ml to 107.2 ± 34.6 pg/ml, group B: 82.7 ± 27.6 pg/ml to 253.1 ± 60.2 pg/ml). On day 30, BNP levels in group B were significantly higher than in group A ($P < 0.0001$).

Conclusions Pacing from the apex of the right ventricle provokes an increase in the BNP levels regardless of the pacing mode. BNP is probably a very early marker predicting the structural and/or functional heart changes after long-term pacing from the apex of the right ventricle.

Keywords *Brain natriuretic peptide – pacemaker – cardiac dysfunction.*

INTRODUCTION

Large randomized controlled trials, such as the Canadian Trial of Physiologic Pacing, the Mode Selection Trial in Sinus Node Dysfunction and the United Kingdom Pacing and Cardiovascular Events Trial, have not shown any difference in mortality, incidence of stroke and atrial fibrillation between DDD and VVI pacing in bradycardic patients[1-3].

Some smaller trials showed that atrial pacing (AAI/R) reduces the incidence of heart failure, atrial fibrillation and death compared with VVI/R and DDD/R pacing mode, in patients with sick-sinus syndrome (SSS)[4,5]. Also dual-chamber minimal ventricular pacing, as compared with conventional dual-chamber pacing, prevents ventricular desynchronization and reduces the risk of persistent atrial fibrillation in patients with sinus-node disease[6].

The inability of these trials to demonstrate the superiority of normal atrioventricular pacing, compared with abnormal ventricular pacing, can be partially explained by the apical stimulation of the right ventricle, which affects short- and long-term ventricular performance[7]. In the MOST trial the hazard for heart failure and atrial fibrillation was related to pacing from the apex of the right ventricle, regardless of the pacing mode.

BNP is secreted by cardiomyocytes in response to ventricular volume expansion and pressure overload[8]. BNP plasma levels have been found to be a reliable marker of haemodynamic status and ventricular function (systolic and diastolic)[9]. Clinical practice has confirmed its value in evaluating patients with acute dyspnoea[10], in guiding heart failure treatment[11], and in the

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prognosis of patients with heart failure and acute coronary syndromes[12,13].

Previous studies have proven the deleterious effects of long-term right ventricular apical pacing on cardiac function[14-18]. We tried to investigate whether BNP plasma levels can detect these effects earlier in DDDR and VVIR pacing mode.

METHODS

Study population

Seventy-eight patients treated with DDDR pacemaker due to SSS, were initially enrolled. They were older than 18 years old, with a baseline sinus cardiac rhythm slower than 60 beats per min, normal ejection fraction of the right and left ventricles and NYHA class I functional status. Patients with atrial fibrillation were not included. Patients did not receive diuretics and any other medical treatment was steady throughout the study. As a result, BNP levels could not be influenced by any pharmacological agent. The exclusion criteria were: symptoms of overt heart failure, any form of acute coronary syndromes for the previous 3 months, documented atrial fibrillation at the time of study entry and ventricular pacing less than 80% for the 30-day period.

Study design

The study followed a prospective single-blind randomized design. Patients were enrolled consecutively and randomized during the first post-implantation day to either DDDR or VVIR pacing mode: (i) group A, 35 patients with DDDR pacing; and (ii) group B, 32 patients on VVIR pacing. Eleven patients (of the initially 78) were finally excluded because of less than 80% pacing of the right ventricle. A 12-lead surface ECG was obtained in each patient, just before enrolment. Patients with atrial fibrillation were excluded. In each mode, the percentage of ventricular paced beats was assessed by pacemaker telemetry. Peripheral blood samples were drawn under standardized conditions for BNP measurement at the time of randomization and one month later. At the same time, echocardiography was performed. The biplane ejection fraction of the left ventricle (according to the Simpson method), the fractional shortening of the left ventricle and the dimensions of right and left ventricle, were measured. On day 30 and before the second blood sample was drawn, each patient underwent a detailed interrogation and follow-up analysis of his pacemaker. The patients with more than 80% ventricular pacing during these 30 days, remained in the study. The 80% ventricular pacing was chosen arbitrarily. This percentage is representative and prevents misinterpreting of results. No measures were taken to reduce the amount of ventricular pacing. In both groups, pacemakers were programmed at a ventricular rate of 60-120 beats per minute. In group A, AV-delays were 150-180 msec and the mode switch was on, at a ventricular rate above 140 beats per minute.

A questionnaire was completed, aiming to detect any symptom that could be related to the pacemaker syndrome, such as syncope, palpitation, dyspnoea, blood pressure fall >20 mmHg and malaise. The lowering of the blood pressure was documented by a relative who could measure blood pressure during the symptoms.

Written informed consent was obtained from each patient. The protocol was approved by the local ethics committee.

BNP measurement

Blood samples were drawn from a peripheral vein, with the patient in the supine position for at least 15 min. The venipunctures were performed at the randomization day and 30 days later with the patient always on the same pacing mode since randomization. BNP was measured by a two-step chemiluminescent immunoassay on an automated immunoassay analyzer (Architect 16200, Abbott laboratories, Illinois, USA). This BNP assay is a sandwich immunoassay that uses two anti-BNP mouse monoclonal antibodies to capture human BNP that is present in human plasma. Samples were collected in plastic tubes containing EDTA (BD Vacutainer K2-EDTA, Becton Dickinson, New Jersey, USA) because the BNP molecule has been shown to be unstable in glass containers. Whole blood samples were collected and centrifuged within 2 hours from collection and stored in plastic tubes at 2-8°C until tested. Processed samples were tested within 24 hours from collection.

Statistical analysis

BNP levels of group A and B were compared, with a paired sample *t*-test, at randomization and day 30. A *P* value <0.05 was considered as statistically significant.

RESULTS

Patients' characteristics as displayed in table 1, showed no significant differences between the two groups. At the end of the study the ejection fraction among group A tended to be higher compared with group B, but the difference was not statistically significant. The dimensions of right and left ventricle, left atrium and fractional shortening of the left ventricle did not differ between the two groups, neither before nor after pacing (table 2).

Table 1

Baseline characteristics of patients			P
	Group A	Group B	
Age	67 ± 6	66 ± 9	ns
Men	21	20	ns
Women	14	12	ns
Hypertension	18	19	ns
Coronary artery disease	12	14	ns
Valvular heart disease	5	4	ns
EF%	53 ± 7	51 ± 9	ns

BNP measurements

There was a statistically significant increase of the BNP levels for both groups A and B. In group A the initial value was 85.6 ± 29.5 pg/ml and 30 days later 107.2 ± 34.6 pg/ml ($P < 0.001$) while the values in group B were 82.7 ± 27.6 pg/ml and 253.1 ± 60.2 pg/ml ($P < 0.001$), respectively (figure 1).

The baseline values of BNP before pacemaker implantation (figure 1) between the two groups were not statistically different (85.6 ± 29.5 pg/ml versus 82.7 ± 27.6 pg/ml). However, on day 30 the BNP values of group B were significantly higher than those of group A (253.1 ± 60.2 pg/ml versus 107.2 ± 34.6 pg/ml, $P < 0.0001$) (figure 2). BNP levels did not correlate with the percentage of ventricular pacing in the patients who had ventricular pacing above 80%.

Pacing data

The telemetry assessed percentage of ventricular paced beats was 94 ± 8% in the DDDR/VDD mode and 93 ± 9% in the VVIR mode (ns). In group A AS-VP pacing was 36% and AP-VP 64%.

Clinical indexes

According to the completed questionnaires no patient in group A had symptoms compatible with pacemaker syndrome. On the other hand, 5 patients in group B had symptoms. Three of them mentioned mild symptoms and two moderate symptoms (blood pressure lowering, malaise, dizziness).

DISCUSSION

An ideal pacemaker should not only restore the heart rhythm but also conserve the atrioventricular synchrony and adapt heart rate whenever possible. Therefore, in SSS and atrioventricular block, atrioventricular pacing is preferable to single-lead ventricular pacing[19]. Large randomized trials failed to demonstrate superiority of dual-chamber pacing versus single-lead ventricular pacing, regarding end points such as overall mortality, prevalence of cerebral ischaemic attacks and atrial fibrillation[1-3]. Furthermore, atrioventricular, as well as single-ventricular pacing, impairs normal ventricular function and provokes ventricular asynchrony. This rarely appears in patients with DDDR mode and a small percentage of ventricular pacing[7]. Recent heart pacing strategies have

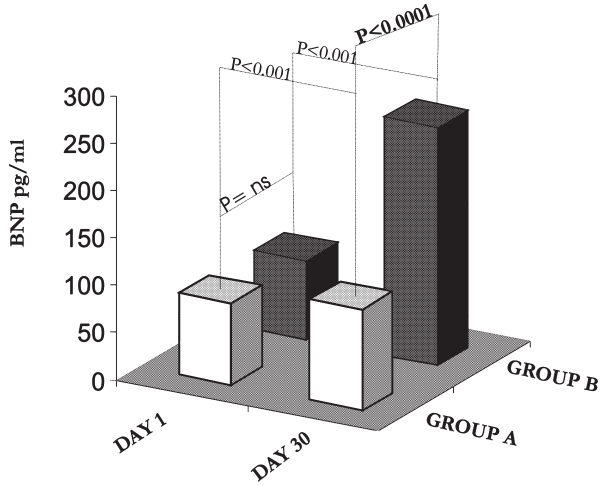

Fig. 1 BNP plasma levels before pacemaker implantation and on day 30, in two different pacing modes.

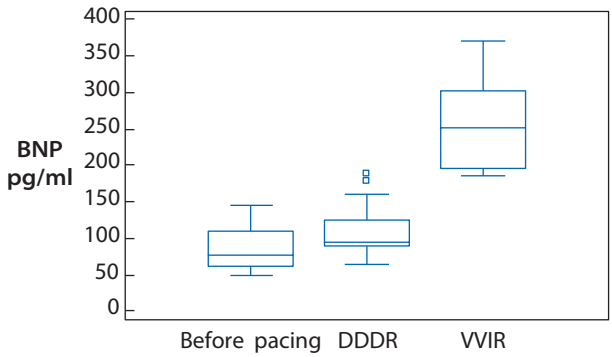

Fig. 2 The box-and-whisker diagram of BNP plasma levels in the two groups.

focused on restoring heart rate and usually ignore ventricular asynchrony.

Pacing from the right ventricular apex is particularly prevalent because the fixing site is steady and easily accessible to the pacemaker leads. Also good trigger points for pacing and sensing can be obtained. Nevertheless, from a haemodynamic point of view, it is the least satisfying position[20]. A pacing mode, whatever its pacing site, disturbs the normal excitation sequence, which is from the base to the apex and from the endocardium to the epicardium through the Purkinje fibres. This results into ventricular asynchrony.

During pacing from the right apex, dp/dt diminishes and the end-systolic volume-pressure curve shifts to the right. As a result, the left ventricle functions with increased volume and reduced contractility, resulting in ejection fraction decay[21]. Conventional RV apical pacing may have detrimental effects on cardiac structure and left ventricular function. These detrimental effects may be related to the abnormal electrical and mechanical activation pattern of the ventricles (or ventricular dyssynchrony) caused by RV apical pacing. Still, it remains uncertain whether the deterioration of left ventricular function with RV apical pacing, is directly related to acutely induced left ventricular dyssynchrony[22].

In our study we did not establish any statistically significant deterioration of the ejection fraction of the left ventricle. This can be explained by the small monitoring period and by the speculation that the ejection fraction at rest does not reveal the left ventricular performance of active patients in a 24-hour period.

In single-ventricular pacing, the loss of the atrioventricular synchronization leads to an increase of cardiac diastolic pressure. Increased wall stress triggers secretion of the natriuretic peptides.

Moreover, some studies suggest that long-term pacing from the RV apex induces histopathologic changes and cardiac remodelling: (i) changes in the dimensions and the architecture of the muscle fibres; (ii) increased apposition of adipose tissue; (iii) dystrophic disorders; (iv) calcification of the mitochondria[23]; (v) hypertrophy and dilatation of the left ventricle[24]. All these changes are related to myocardial dysfunction, which is the main cause of the BNP secretion. In our study there was no difference, neither in the dimensions of the ventricles nor in the left ventricular ejection fraction or fractional shortening. Thus, the significant elevations in BNP values were not associated with overt differences in ventricular performance. This must be attributed to the short follow-up period.

Studies have been attempted to determine the effect of atrial and atrioventricular pacing on the fractional shortening of the left ventricle in patients with SSS. A statistically significant reduction of the fractional shortening in the DDDR group with short AV-delay, was observed after 2.9 ± 1.1 years of monitoring, when compared with the AAIR pacing group[5]. Also, a recent study has shown that in patients with SSS there is no statistically significant difference in death from any cause between AAIR pacing and DDDR pacing programmed with a moderately prolonged atrioventricular delay, resulting in less ventricular pacing[25]. However, in general, it has been proved that in patients with SSS, DDDR-pacing but not AAIR-pacing induces significant LV desynchronization and reduction of LVEF[16].

These studies seem to agree with our conclusions, based on BNP values, that any ventricular pacing from the apex of the right ventricle could exert deleterious effects on cardiac function.

Regarding the secretion of BNP/NT-proBNP, it has been shown that in patients with high-grade atrioventricular block, single-lead ventricular pacing from the apex of the right ventricle elicits the increase of BNP and NT-proBNP levels, while atrioventricular pacing does not provoke such an increase[26]. Our results are in accordance with the above study regarding the effect of single-chamber pacing but opposed to it as far as atrioventricular pacing is concerned. This disagreement can be justified by two structural differences between these two studies: (i) in our study the measurement of BNP levels was done with the patient on a pacing mode for 30 days, while in the other study the pacing period was 15 days. This can make a difference as other studies[15] have shown that chronic dual-chamber pacing promotes ventricular dysfunction; (ii) in the other study, 25 out of the 41 patients (60%) suffered from an atrioventricular conduction disorder before pacemaker implantation, which means that they had already lost their atrioventricular synchronization and, concomitantly, they could already have an increase in their BNP levels. So after they were in atrioventricular pacing, they failed to exhibit a further BNP level raise. No significant differences in echocardiographic parameters were registered in both studies. Also they had a short follow-up period, of about 30 days, as opposed to previously mentioned studies[5,14-16].

CONCLUSION

According to our observations, pacing from the apex of the right ventricle provokes an increase in BNP levels regardless of pacing mode (DDDR or VVIR), exerting an adverse effect on the myocardium. Furthermore, VVIR pacing mode compared with DDDR, evokes a higher raise in BNP levels suggesting a more detrimental effect. Several previous studies have demonstrated a worsening of left ventricular function after a long period of right ventricular apical pacing[15-18]. With this argument

in mind, we concluded that BNP is a very early marker, predicting structural and/or functional heart changes, after long-term pacing from the right ventricular apex. We believe that, even though early post-implantation functional heart changes are not apparent, pacing from the apex of the right ventricle should be avoided mainly by appropriate pacemaker adjustments.

LIMITATIONS

The study was performed using a single-blind design and had a short monitoring period. Nevertheless, other studies with different populations have shown that the levels of natriuretic peptides may change even in shorter monitoring periods and these changes have, indeed, a prognostic value. Also, most surveys on the effect of pacing and natriuretic peptides usually last only 15 days.

The 80% pacing that we have chosen as an inclusion criterion, was in a way arbitrary. This cut-off value was chosen as this percentage of pacing is considered as sufficient to reveal any difference in haemodynamics or ventricular performance.

Our conclusion that the elevation of BNP levels is an early marker of left ventricular dysfunction is based on other studies having demonstrated a detrimental effect of long-term right ventricular apex pacing on left ventricular function.

BNP is a marker of ventricular dysfunction with a high sensitivity and a lower specificity.

CONFLICT OF INTEREST: none declared.

REFERENCES

1. Connolly SJ, Kerr CR, Gent M, Roberts RS, Yusuf S, Gillis AM, Sami MH, Talajic M, Tang AS, Klein GJ, Lau C, Newman DM. Effects of physiologic pacing versus ventricular pacing on the risk of stroke and death due to cardiovascular causes. Canadian Trial of Physiologic Pacing Investigators. *N Engl J Med* 2000; **342**: 1385-91.
2. Lammas GA, Lee KL, Sweeney MO, Silverman R, Leon A, Yee R Marinchak RA, Flaker G, Schron E, Orav EJ, Hellkamp AS, Greer S, McAnulty J, Ellenbogen K, Ehlert F, Freedman RA, Estes NA 3rd, Greenspon A, Goldman L; Mode Selection Trial in Sinus-Node Dysfunction. Ventricular pacing or dual-chamber pacing for sinus-node dysfunction. *N Engl J Med* 2002; **346**: 1854-62.
3. Toff WD, Camm AJ, Skehan JD; United Kingdom Pacing and Cardiovascular Events (UKPACE) Trial Investigators. Single-chamber versus dual-chamber pacing for high-grade atrioventricular block. *N Engl J Med* 2005; **353**: 145-55.
4. Andersen HR, Nielsen JC, Rhomsen PEB, Mortensen PT, Vesterlund T, Pendersen AK. Long-term follow-up of patients from a randomised trial of atrial versus ventricular pacing for sick-sinus syndrome. *Lancet* 1997; **350**: 1210-6.
5. Nielsen JC, Kristensen L, Andersen HR, Mortensen PT, Pedersen OL, Pedersen AK. A randomized comparison of atrial and dual-chamber pacing in 177 consecutive patients with sick sinus syndrome: echocardiographic and clinical outcome. *J Am Coll Cardiol* 2003; **42**: 614-23.
6. Sweeney MO, Bank AJ, Nsah E, Koullick M, Zeng QC, Hettrick D, Sheldon T, Lamas GA; Search AV Extension and Managed Ventricular Pacing for Promoting Atrioventricular Conduction (SAVE PACe) Trial. Minimizing ventricular pacing to reduce atrial fibrillation in sinus-node disease. *N Engl J Med* 2007; **357**: 1000-8.
7. Sweeney MO, Hellkamp AS, Ellenbogen KA, Greenspon AJ, Freedman RA, Lee KL, Lamas GA; MOde Selection Trial Investigators. Adverse effect of ventricular pacing on heart failure and atrial fibrillation among patients with normal baseline QRS duration in a clinical trial of pacemaker therapy for sinus node dysfunction. *Circulation* 2003; **107**: 2932-7.
8. Yasue H, Yoshimura M, Sumida H, Kikuta K, Kugiyama K, Jongasaki M, Ogawa H, Okumura K, Mukoyama M, Nakao K. Localisation and mechanism of secretion of B-type natriuretic peptide in comparison with those of A-type natriuretic peptide in normal subjects and patients with heart failure. *Circulation* 1994; **90**: 195-203.
9. Lubien E, DeMaria A, Krishnaswamy P, Clopton P, Koon J, Kazanegra R, Gardetto N, Wanner E, Maisel AS. Utility of B-natriuretic peptide in detecting diastolic dysfunction: comparison with Doppler velocity recordings. *Circulation* 2002; **105**: 595-601.
10. Mueller C, Scholer A, Laule-Kilian K, Martina B, Schindler C, Buser P, Pfisterer M, Perruchoud AP. Use of B natriuretic peptide in the evaluation and management of acute dyspnea. *N Engl J Med* 2004; **350**: 647-54.
11. Cheng V, Kazanagra R, Garcia A, Lenert L, Krishnaswamy P, Gardetto N, Clopton P, Maisel A. A rapid bedside test for B-type peptide predicts treatment outcomes in patients admitted for decompensated heart failure: a pilot study. *J Am Coll Cardiol* 2001; **37**: 386-91.
12. Latini R, Masson S, Anand I, Salio M, Hester A, Judd D, Barlera S, Maggioni AP, Tognoni G, Cohn JN; Val-HeFT Investigators. The comparative prognostic value of plasma neurohormones at baseline in patients with heart failure enrolled in Val-HeFT. *Eur Heart J* 2004; **25**: 292-9.
13. De Lemos JA, Morrow DA, Bentley JH, Omland T, Sabatini MS, McCabe CH, Hall C, Cannon CP, Braunwald E. The prognostic value of B-type natriuretic peptide in patients with acute coronary syndromes. *N Eng J Med* 2001; **345**: 1014-21.
14. Thambo JB, Bordachar P, Garrigue S, Lafitte S, Sanders P, Reuter S, Girardot R, Crepin D, Reant P, Roudaut R, Jaïs P, Haïssaguerre M, Clementy J, Jimenez M. Detrimental ventricular remodeling in patients with congenital complete heart block and chronic right ventricular apical pacing. *Circulation* 2004; **110**: 3766-72.
15. Zhang XH, Chen H, Siu CW, Yiu KH, Chan WS, Lee KL, Chan HW, Lee SW, Fu GS, Lau CP, Tse HF. New-onset heart failure after permanent right ventricular apical pacing in patients with acquired high-grade atrioventricular block and normal left ventricular function. *J Cardiovasc Electrophysiol* 2008; **19**: 136-41.
16. Albertsen AE, Nielsen JC, Poulsen SH, Mortensen PT, Pedersen AK, Hansen PS, Jensen HK, Egeblad H. DDD(R)-pacing, but not AAI(R)-pacing induces left ventricular desynchronization in patients with sick sinus syndrome: tissue-Doppler and 3D echocardiographic evaluation in a randomized controlled comparison. *Europace* 2008; **10**: 127-33.
17. Ten Cate TJ, Scheffer MG, Sutherland GR, Verzijlbergen JF, van Hemel NM. Right ventricular outflow and apical pacing comparably worsen the echocardiographic normal left ventricle. *Eur J Echocardiogr* 2008; **9**: 672-7.
18. Muto C, Ascione L, Canciello M, Carreras G, Iengo R, Ottaviano L, Calvanese R, Accadia M, Celentano E, Ciardiello C, Tuccillo B. Effect of right ventricular apical pacing in survivors of myocardial infarction. *Pacing Clin Electrophysiol* 2009; **32**(Suppl 1): S173-6.
19. Stewart WJ, Dicola VC, Harthorne JW, Gillam LD, Weyman AE. Doppler ultrasound measurements of cardiac output in patients

with physiologic pacemakers. Effects of left ventricular function and retrograde ventriculoatrial conduction. *Am J Cardiol* 1984; **54**: 308-12.
20. Prinzen FW, Peschar M. Relation between the pacing induced sequence of activation and left ventricular function in animals. *Pacing Clin Electrophysiol* 2002; **25**: 484-98.
21. Simantirakis EN, Vardakis KE, Kochiadakis GE, Manios EG, Igoumenidis NE, Brignole M, Vardas PE. Left ventricular mechanics during right ventricular apical or left ventricular-based pacing in patient with chronic atrial fibrillation after atrioventricular based ablation. *J Am Coll Cardiol* 2004; **43**: 1013-8.
22. Tops LF, Schalij MJ, Bax JJ. The effects of right ventricular apical pacing on ventricular function and dyssynchrony implications for therapy. *J Am Coll Cardiol* 2009; **54**: 764-76.
23. Spragg DD, Leclercq C, Loghmani M, Faris OP, Tunin RS, DiSilvestre D, McVeigh ER, Tomaselli GF, Kass DA. Regional alterations in protein expression in the dyssynchronous failing heart. *Circulation* 2003; **108**: 929-32.
24. Van Oosterhout MFM, Prinzen FW, Arts T, Schreuder JJ, Vanagt WY, Cleutjens JP, Reneman RS. Asynchronous electrical activation induces asymmetrical hypertrophy of the left ventricular wall. *Circulation* 1998; **98**: 588-95.
25. Nielsen JC, Thomsen PE, Højberg S, Møller M, Vesterlund T, Dalsgaard D, Mortensen LS, Nielsen T, Asklund M, Friis EV, Christensen PD, Simonsen EH, Eriksen UH, Jensen GV, Svendsen JH, Toff WD, Healey JS, Andersen HR; DANPACE Investigators. A comparison of single-lead atrial pacing with dual-chamber pacing in sick sinus syndrome. *Eur Heart J* 2011; **32**: 686-96.
26. Naegeli B, Kurz DJ, Koller D, Straumann E, Furrer M, Maurer D, Minder E, Bertel O. Single-chamber ventricular pacing increases markers of left ventricular dysfunction compared with dual-chamber pacing. *Europace* 2007; **9**: 194-9.