in-stent restenosis, and we think that further investigations are needed.

Daiju Fukuda, MD
The Department of Internal Medicine and Cardiology
Graduate School of Medicine
Osaka City
University Medical School, Osaka, Japan
1-4-3, Asahimachi, Abenoku, Osaka 545-8585, Japan
E-mail: daiju@qg7.so-net.ne.jp

Kenei Shimada, MD
Atsushi Tanaka, MD
Takahiko Kawarabayashi, MD
Minoru Yoshiyama, MD
Junichi Yoshikawa, MD, FACC

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Prognostic Value of Left Ventricular Dyssynchrony in Patients With Heart Failure

Bader et al. (1) in a recent issue of the *Journal* reported on the value of left ventricular (LV) dyssynchrony for the prognostification of patients with severe heart failure (HF). A large group of HF patients (n = 104) with depressed left ventricular ejection fraction (LVEF) (<45%) was followed up for one year. During this one-year period, 83% of the patients were hospitalized for decompensated HF. Based on multivariate Cox regression analysis, three variables predicted HF hospitalization: QRS width >140 ms, LVEF <25%, and LV dyssynchrony (the mean LV dyssynchrony was 68 ± 44 ms). The patients included in the study by Bader et al. (1) represent typical patients who may benefit from cardiac resynchronization therapy (CRT). Recent studies on CRT have shown improvement in symptoms, quality-of-life score, exercise capacity, and LV systolic function after CRT (2). Current selection criteria for CRT include: severe HF (New York Heart Association functional class III or IV), depressed LVEF (<35%), and wide QRS complex (>120 ms). Careful analysis of the large clinical trials, however, has revealed that 20% to 30% of patients do not respond to CRT. Based on these observations, emphasis has shifted toward a better selection of patients who may benefit from CRT (3). Various studies have demonstrated that LV dyssynchrony may predict response to CRT and, therefore, the findings of Bader et al. (1) are of great importance. Eventually, the identification of patients with dyssynchrony may not only allow for optimal selection for CRT but also may favorably affect the prognosis of these patients. On the basis of their findings, do the authors feel that the presence of dyssynchrony should be used to identify patients who may benefit from CRT? And, if so, should the region of latest activation before CRT be the preferred location for the LV lead? This is of interest because substantial percentage of patients in the study by Bader et al. (1) exhibited other regions than the lateral wall as the latest activation. This may then in turn raise the question whether a surgical approach may sometimes be preferred rather than transvenous implantation of the LV lead.

Jeroen J. Bax, MD
Department of Cardiology
Leiden University Medical Center
Albinusdreef 2
2333 ZA Leiden, The Netherlands
E-mail: jbax@knoware.nl

Ernst E. van der Wall, MD
Martin J. Schalij, MD

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REPLY

We thank Dr. Bax and colleagues for their interest in our study (1) and, above all, for raising several important issues. As they mentioned in their letter, various studies have demonstrated or at least suggested that left ventricular (LV) dyssynchrony might predict response to cardiac resynchronization therapy (CRT). A recent study published in the *Journal* (2) has showed that patients with a narrow QRS complex and with LV electromechanical dyssynchrony could benefit from CRT (even with a larger pacing-induced QRS width compared with spontaneous rhythm) at the same level of hemodynamic and clinical improvement than patients with large QRS complexes (>120 ms). These new data can at least suggest that, independent of the QRS

width, the presence of dyssynchrony is likely to be the key point for selecting candidates to CRT. However, one issue still remains: what is the best predictive echocardiographic method (among the different Doppler tissue imaging techniques) for selecting those patients? This requires larger studies comparing the positive and negative predictive values of several techniques already published.

From this point, it can be emphasized that heart failure patients (New York Heart Association functional class III or IV) with mechanical LV dyssynchrony should systematically benefit from CRT. So far, no study has clearly demonstrated that medical treatment by itself could reduce the level of ventricular dyssynchrony. If the future confirms that drugs have no significant effect on ventricular dyssynchrony, CRT should be applied systematically in such patients.

Concerning the absence of relationship between the QRS complex morphology and region of latest activation, we fully agree with Bax et al. Ansalone et al. (3) already have demonstrated that placing the LV pacing lead in regard to the region of latest activation could further improve patients benefiting from CRT. However, we think that this might be suitable only in patients with primitive dilated cardiomyopathy. Indeed, by considering patients with severe ischemic heart disease, regions with the latest activation could be highly ischemic, so that pacing from such ventricular areas could be first, potentially arrhythmogenic and second hemodynamically detrimental because it might induce a new dyssynchrony resulting from the low conduction velocity in such regions. For that reason, further studies are crucially needed to definitely state on this point.

Finally, we also agree that the best way to reach optimal LV pacing sites should be the epicardial surgical approach via thoracoscopy or mini-thoracothomy procedures. The transseptal approach with endocardial LV pacing could also be considered with the advantage of preserving the endovenous approach and permitting free access to the four ventricular walls.

Stephane Garrigue, MD, PhD
Hopital Cardiologique du Haut-Leveque
University of Bordeaux
19, avenue de Magellan
Pessac 33600, France
E-mail: stephane.garrigue@chu-bordeaux.fr

Hugues Bader, MD

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Serum Potassium Level and Risk of Postoperative Atrial Fibrillation in Patients Undergoing Cardiac Surgery

We read with great interest the article by MacDonald and Struthers (1) in a recent issue of the *Journal*. The article reports that potassium depletion is important in the pathogenesis of cardiovascular disease and sudden cardiac death. The authors suggest that avoiding hypokalemia is beneficial in several cardiovascular disease states, including acute myocardial infarction, heart failure, and hypertension. The data linking hypokalemia with arrhythmia and cardiac arrest in acute myocardial infarction are fairly strong (2–4).

We want to add atrial fibrillation (AF) after cardiac surgery to the list of cardiovascular diseases where electrolyte imbalance may play an important pathogenetic role. Although the etiology of AF after heart surgery is incompletely understood, stimuli and triggers such as pre-existing structural changes of the atria related to hypertension, mechanical damage, volume overload, age, intraoperative atrial ischemia, and pericardial lesions are thought to play a role in the pathogenesis (5). Additionally, there seems to be a significant increase in sympathetic tone in the postoperative period in those patients who subsequently develop AF (6). Hypokalemia causes cellular hyperpolarity, increases resting potential, hastens depolarization, and increases automaticity and excitability (7). Thus, electrolyte imbalances and hypokalemia may contribute to the etiology of postoperative AF (5,8). To test this hypothesis, we analyzed data from the Study of Prevention of Postoperative Atrial Fibrillation (SPPAF), a randomized, double-blind, placebo-controlled trial at a single tertiary care center of 253 patients undergoing cardiac surgery. The study was designed to test whether each of three active oral drug regimens—amiodarone plus metoprolol, metoprolol alone, and sotalol—is superior to placebo for prevention of AF after cardiac surgery (9). Overall, 39.1% of the total study population developed AF during the postoperative period. Advanced age and surgery for heart valve disease increased, and use of antiarrhythmic drugs, including beta-adrenergic blockers, decreased the risk of postoperative AF by multivariate analysis ($p < 0.05$). The rate of postoperative AF in patients with serum potassium levels of 3.9 mmol/l or less, compared with those with serum potassium levels of 4.4 mmol/l or greater were 50.7% and 32.9%, respectively ($p < 0.05$).

Thus, AF after cardiovascular surgery should be added to a group of cardiovascular disease that may be adversely influenced by low serum potassium concentrations. Additionally, potassium replacement may reduce the risk of postoperative AF and should be tested prospectively in a controlled clinical trial.