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Sympathetic Nerve Activity After Thoracoscopic Cardiac Resynchronization Therapy in Congestive Heart Failure

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ABSTRACT

Background: Sympathetic benefits of thoracoscopic cardiac resynchronization therapy (TCRT) in congestive heart failure (CHF) are unknown. We determined cardiac hemodynamics, functional status, and muscle sympathetic nerve activity (MSNA) in a group of TCRT patients. We aimed to compare these patients with CHF patients with cardiac asynchrony (ASY) to substantiate the beneficial effects of TCRT.
Methods and Results: Eleven patients resynchronized by TCRT 6 $\pm$ 1 months before study inclusion (SYN) and 10 matched ASY patients underwent blood pressure, heart rate, and MSNA recordings. All underwent functional status, cardiac index, and left ventricular ejection fraction (LVEF) assessments. SYN patients had shorter QRS duration and interventricular mechanical delays, longer 6 minute walking distance and lower New York Heart Association class (all $P < .05$) than ASY patients. MSNA of 56 $\pm$ 2 bursts/min in ASY patients was higher than in SYN patients (48 $\pm$ 3 bursts/min, $P < .05$). Cardiac index was higher in SYN patients than in ASY patients (2.8 $\pm$ 0.2 versus 1.9 $\pm$ 0.2 $L \cdot min \cdot m^2$, $P < .05$, respectively). MSNA was highest in the patients with the lowest LVEF ($r = -0.49$, $P < .05$), cardiac index ($r = -0.48$, $P < .05$) and 6-minute walking distance ($r = -0.50$, $P < .05$).
Conclusion: Lower sympathetic nerve activities in TCRT patients are related to more favorable cardiac indexes and six minute walking distances suggesting a sympathetic, hemodynamic, and functional improvement by TCRT.
Key Words: Autonomic nervous system, heart failure, microneurography, robotics.

Intraventricular conduction delay is associated to a dyssynchronous contraction of the left ventricle, a reduced systolic function, an altered clinical status, and an increased mortality in severe congestive heart failure (CHF).[1,2] Conventional cardiac resynchronization therapy (CRT) achieves right atrial and ventricular chamber stimulation through endocardial stimulation, whereas the left ventricle is activated by a lead placed in a posterolateral coronary vein. The hemodynamic, clinical, and prognostic benefits of conventional CRT are well documented in selected CHF patients.[3–11]

Peripheral sympathetic activation is a hallmark of the physiopathology of heart failure.[12] Microneurographic recordings allow direct determination of postganglionic sympathetic traffic directed to muscle blood vessels (muscle sympathetic nerve activity, MSNA), which is not affected by modifications in catecholamine clearance in severe CHF.[13] Systemic blood pressure increases when conventional CRT is performed acutely in the cardiac catheterization laboratory.[14,15] This increase activates the baroreceptors that, in turn, reduce sympathetic nerve hyperactivity.[14,15] It has been recently shown that the acute beneficial sympathetic effects of conventional CRT persists on the long term.[16]

A high nonresponder rate to conventional CRT remains, however, a significant problem.[17] Moreover, even in experienced departments, limitations in coronary vein access prevent left ventricular CRT in 5% to 10% of patients.[11,18] A new, minimally invasive, alternative surgical technique was therefore implemented in which cardiac resynchronization is achieved by conventional endocardial leads in the right

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cardiac chambers and a left ventricular epicardial lead implanted by thoracoscopic cardiac surgery (TCRT).[19,20] The main advantage of TCRT is that coronary vein anatomy does not hinder left ventricular lead placement.[19,20] Previous studies have shown the feasibility of TCRT[19,20] and subsequent improvements in exercise tolerance, left ventricular ejection fraction (LVEF), and QRS duration.[20] Sympathetic effects of TCRT are unknown.

We tested the hypothesis that TCRT induces chronic clinical and hemodynamic improvements while decreasing sympathetic activation in CHF patients. We determined MSNA, exercise tolerance, and noninvasive cardiac hemodynamics in a group of TCRT patients. These values were compared with those of closely matched asynchronous patients (ASY).

Methods

The study was approved by the Ethical Committee of the Erasme Hospital, Brussels. Each subject signed an informed consent prior to inclusion in the study.

Subjects

Resynchronized heart failure patients. Eleven consecutive heart failure patients who had undergone TCRT 6 ± 1 months before study inclusion (synchronous patients, SYN) were compared to ASY patients. The indications for TCRT were (1) patients in New York Heart Association (NYHA) class ≥III despite maximal medical therapy, including, if tolerated, a converting enzyme inhibitor (or an angiotensin antagonist), a diuretic, a β-blocker, spironolactone, and other vasodilators; (2) a left bundle branch block with a QRS duration >120 ms; (3) LVEF assessed by echocardiography <35%; (4) left ventricular end-diastolic diameter >55 mm; and (5) an interventricular asynchrony (difference between aortic and pulmonary pre-ejection time delay >40 ms, interventricular mechanical delay) or an intraventricular asynchrony (septal to posterior wall motion delay >130 ms).[21] These patients had similar LVEF (28 ± 2%) and NYHA functional class (3.2 ± 0.1) before TCRT than the ASY patients.

All the biventricular pacemakers implantations were made according to the operative technique previously described.[19] We used steroid-eluting epicardial leads, which are associated with a better stability and pacing thresholds that conventional epicardial leads (Medtronic, Minneapolis, MN, epicardial leads, 4968).[21]

As a result, all SYN patients were taking an angiotensin-converting enzyme inhibitor or an angiotensin antagonist (all except 1 at maximal recommended daily dosage), 9 took a β-blocker (all but 2 at maximal dosage), and all received diuretics. The cause of CHF was coronary artery disease in 6 patients, previously operated valvular heart disease in 2 patients, and idiopathic dilated cardiomyopathy in 3 patients.

Asynchronous heart failure patients. Ten consecutive heart failure patients scheduled for TCRT participated in the study before the procedure (ASY). Their indications for TCRT were identical to those of the SYN patients. All patients were receiving an angiotensin-converting enzyme inhibitor or an angiotensin antagonist (all but 1 at maximal recommended daily dosage), 6 took a β-blocker (all except 2 at maximal dosage), and all were treated with diuretics. The etiology of CHF was coronary artery disease (n = 5), valvular (n = 2) (both had previously undergone valve replacement surgery), or idiopathic cardiopathy (n = 3).

Measurements

Multiunit recordings of postganglionic MSNA were obtained in all patients with an unipolar tungsten electrode inserted selectively into a nerve fascicle of the right or left peroneal nerve, posterior to the fibular head. Acceptable recordings met the following 4 criteria: spontaneous bursts of neural discharge synchronous with heart rate, no response to arousal stimuli or skin stroking, an increase in nerve burst frequency with apnea, a signal to noise ratio of 3:1. MSNA recordings were acquired and analyzed on a MacLab 8/s data acquisition system (AD Instruments, Castle Hill, Australia).

All also underwent continuous recording of heart rate (Siemens Medical, ECG Monitoring, Erlangen, Germany), oscillometric blood pressure measurements every 2 minutes with a Physiocontrol Colin BP-880 sphygmomanometer (Colin Press Mate, Colin Corp, Japan), and continuous oxygen saturation determinations (Nellcor, Pleasanton, CA, N-100 C pulse oximeter).

An electrocardiogram (Hewlett Packard, Palo Alto, CA, XLS electrocardiograph) was performed to determine the QRS duration.

Standard echocardiography (Vivid 7-General Electric, Horten, Norway) was performed in patients according to the American Society of Echocardiography recommendations.[22] Three consecutive beats were measured and averaged. Left ventricular end-systolic diameter and left ventricular end-diastolic diameter were measured by M-mode echocardiography. Left ventricular end-diastolic volume and left ventricular end-systolic volume were measured by the biplane Simpson method and were used for LVEF determinations. Aortic and pulmonary pre-ejection times were derived from continuous wave Doppler measurements allowing to calculated interventricular mechanical delay. Doppler echocardiography allowed measurements of cardiac output (CO) and cardiac index at the level of the left ventricular outflow tract.

The patients underwent a functional evaluation by a 6-minute walking test conducted according to Bittner.[23] One ASY patient could not perform the 6-minute walking test because of severe dyspnea. All completed the self-administered Minnesota Living with Heart Failure questionnaire for scoring quality of life on a scale from 0 (best) to 105 (worst).

Statistical Analysis

Analysis of MSNA recordings was blinded according to the clinical status of the subjects. Results are expressed as mean ± SEM. Comparison between ASY and SYN patients were made with unpaired 2-tailed Student's *t*-test (Statview 5.0, SAS, Cary, NC). Relations between parameters were assessed by regression analysis. Six-minute walking distances were compared by Mann-Whitney and Spearman correlation coefficients because these data were not distributed normally. Comparison of nominal data (medication and NYHA class) was performed with a chi-square test. Significance was assumed at $P < .05$.

Results

Differences Between SYN and ASY Patients

There were no differences in the treatment regimen between SYN and ASY patients (chi-square $P = 0.46$). The SYN and ASY groups had similar age, body mass index, gender, heart rate, blood pressure, and oxygen saturation