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Sympathetic Activity in Patients With Secondary Symptomatic Mitral Regurgitation or End-Stage Systolic Heart Failure

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ABSTRACT

OBJECTIVES This study shows the impact of secondary mitral regurgitation (sMR) and transcatheter mitral valve repair (TMVR) with the MitraClip system on sympathetic nerve activity (SNA).

BACKGROUND An increase in SNA is associated with worse outcomes and limited survival in patients with chronic heart failure (CHF).

METHODS Twenty CHF-patients without relevant sMR and 30 CHF patients with symptomatic sMR were enrolled prospectively. All patients underwent standardized laboratory testing and microneurography. Sixteen patients from the sMR group underwent the MitraClip procedure; 10 patients after TMVR and 9 untreated sMR patients completed 6 months of follow-up.

RESULTS Comparing groups according to presence of sMR, we found no differences in left ventricular dimensions, and serum levels of N-terminal pro-brain natriuretic peptide (NT-proBNP) and noradrenaline; sMR was associated with increased MSNA (106 ± 60 burst/min vs. 74 ± 48 burst/min, d = 0.58), an impaired sympathetic baroreflex gain (10 ± 7 burst/mm Hg vs. 5 ± 5 burst/mm Hg, d = 0.61), and a higher heart rate (90 ± 27/beats/min vs. 78 ± 12/beats/min, d = 0.58). TMVR led to improved New York Heart Association functional class (d > 0.05), reduced levels of NT-proBNP (5,251 ± 3,760 pg/ml vs. 3,710 ± 2,464 pg/ml; d = 0.58) improvement in 6-minute walk test (204 ± 33 m vs. 288 ± 45 m, d = 0.64), but unchanged levels of noradrenaline. TMVR decreased MSNA burst-frequency (130 ± 78 bursts/min vs. 74 ± 21 bursts/min; d = 0.58) and baroreflex gain (7 ± 4 burst/mm Hg vs. 4 ± 1 burst/mm Hg; d = 0.61).

CONCLUSIONS In patients with CHF, concomitant sMR is associated with increased sympathetic nerve activity, which was independent from measured levels of NT-proBNP, noradrenaline, and left ventricular dimensions. Reduction of sMR with the MitraClip procedure reduced SNA and improved baroreflex gain, in line with improvements of functional capacity. (J Am Coll Cardiol Intv 2016;9:2050–7) © 2016 by the American College of Cardiology Foundation.

In patients with severe chronic heart failure (CHF) low cardiac output triggers an increase in sympathetic nerve activity (SNA) to maintain sufficient circulation. Increased SNA, on the other hand, has been shown to be associated with worse prognosis in CHF patients (1,2). SNA stimulates the production of renin, which leads to increased natrium retention from the renal tubuli. It induces systemic vasoconstriction leading to arterial hypertension and impaired peripheral perfusion. This effect potentially promotes hydropic decompensation, pulmonary congestion, and progressive left ventricular (LV) dilation. SNA can be determined by measurement of muscle SNA (MSNA), and baroreflex gain.

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Both parameters have been proven to be independent markers for adverse outcomes in different patient populations with CHF (3–5). An activated SNA has been shown of prognostic relevance in patients and animals with isolated primary mitral regurgitation (MR) (6,7).

Secondary MR (sMR) is a common finding in CHF patients with ischemic or nonischemic cardiomyopathy. The presence of sMR in heart failure patients is associated with poor prognosis (8) and the impact of surgical treatment of MR on SNA has been shown previously (9,10). It is unclear whether interventional reduction of sMR impacts on patient's prognosis and the effects of MitraClip procedure on SNA are unknown. Because SNA is an established independent risk marker for adverse outcome in CHF patients, we hypothesized that the presence of MR in CHF patients deteriorates SNA in CHF patients and that interventional reduction of MR might lead to amelioration of SNA. The objectives of this study were to: 1) compare SNA in CHF patients with and without sMR; and 2) examine the impact of transcatheter mitral valve repair (TMVR) on SNA.

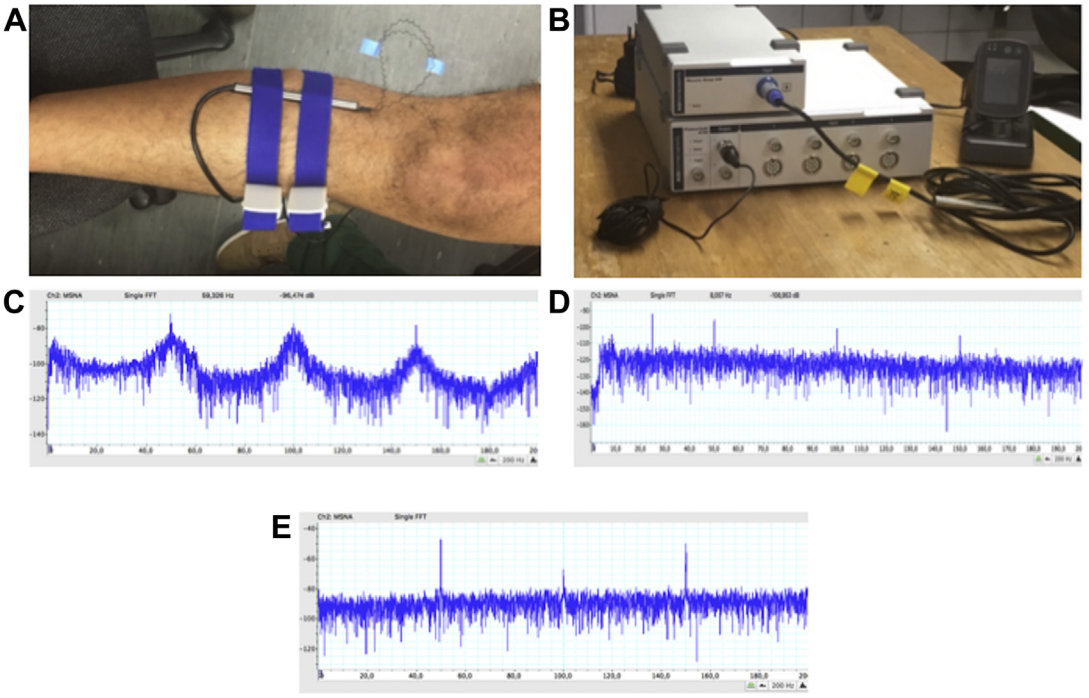
METHODS

PATIENTS. Thirty consecutive patients presenting with symptomatic moderate to severe MR (MR grade >II) and 20 controls with CHF due to LV systolic dysfunction (left ventricular ejection fraction [LVEF] <40%) were prospectively enrolled to the study. Patients with CHF and without relevant MR were matched to sMR patients concerning baseline characteristics (age, sex, and body mass index), functional capacity, and cardiovascular comorbidities. All patients underwent standardized transthoracic echocardiography, clinical examination, 6-min walk test, routine laboratory testing, and microneurography. N-terminal pro-brain natriuretic peptide (NT-proBNP) and noradrenaline levels were determined from blood

ABBREVIATIONS AND ACRONYMS

CHF = chronic heart failure
LV = left ventricular
LVEF = left ventricular ejection fraction
MR = mitral regurgitation
MSNA = muscle sympathetic nerve activity
NT-proBNP = N-terminal pro-brain natriuretic peptide
sMR = secondary mitral regurgitation
SNA = sympathetic nerve activity
TMVR = transcatheter mitral valve repair

FIGURE 1 Microneurography



(A) Setting of MSNA assessment. Two tungsten microelectrodes are inserted at the caput fibuli and 1 reference electrode is attached to the skin. **(B)** Setup of ADInstruments neuroamplifier and SomnoMedics finometer. **(C)** MSNA recording example of a patient with secondary mitral regurgitation before MitraClip implantation. **(D)** MSNA recording example of a control patient with chronic heart failure. **(E)** MSNA recording of the MitraClip patient 6 months after clip procedure with normalized MSNA values. MSNA = muscle sympathetic nerve activity.