Cardiac Sympathetic Activity and Left Ventricular Dyssynchrony

– An Old and New Issue –

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Cardiac sympathetic activity in the failing heart is both an old and a new issue. Classically in the heart, sympathetic activation results in an increased heart rate, more forceful contraction, and enhanced atrioventricular conduction, whereas the primary effect of the parasympathetic system is on heart rate regulation. Patients with heart failure show activation of the sympathetic nerve system, as reflected by increased plasma norepinephrine levels. As a consequence, a higher concentration of norepinephrine is present in the sympathetic cleft, leading to chronic stimulation and downregulation of myocardial β -adrenoceptors. Many studies^{1–3} have shown that the loss of normal sympathetic control over myocardial function is associated with an increased incidence of adverse outcomes such as the development and progression of heart failure and the occurrence of critical arrhythmias that often cause sudden cardiac death. In general, neuronal uptake of norepinephrine is impaired in the failing myocardium. ¹²³I-MIBG has become known as a reliable indicator of cardiac sympathetic activity and in this issue of the Journal, Tanaka et al clearly show that decreased uptake of MIBG is associated with dyssynchrony and successful response to cardiac resynchronization therapy (CRT).⁴

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Dyssynchrony is associated with not only the electrical conduction system but also myocardial mechanical contraction. In that sense, patients in the study by Tanaka et al had wide QRS duration (>120ms). I suppose that this is a very important point because those patients must have electromechanical dyssynchrony in their myocardial cells. Xiao et al previously reported that patients with dilated cardiomyopathy (DCM) show prolonged QRS activation time on signal-averaged ECG, with a long PR interval, and these findings are closely associated with their prognosis.^{5,6} Underlying low-voltage contraction activity, previously referred to as “early potential”, causes a prolonged PR interval, because ventricular activation under low-voltage conditions is cut out by the filter function of the ECG. Dyssynchrony is also related to a prolonged QRS activation time. Therefore, dyssynchrony on echocardiography in DCM is also a phenomenon of prolonged electromechanical, nonuniform ventricular activation. This nonuniform ventricular activation may be caused by myo-

cardial injury, showing as decreased sympathetic activity on MIBG scintigraphy in the report by Tanaka et al.⁴

On the other hand, contraction delay leads to low cardiac output, and may also increase systemic sympathetic activity and cause downregulation of myocardial cells. This must cause the reduced sympathetic activity in the myocardium on MIBG. We cannot distinguish such an effect using Doppler echocardiography. This is also an unsolved problem.

For CRT in DCM, dyssynchrony in the ventricle is estimated as the electromechanical coupling time by Doppler echocardiography.⁷ But such time intervals include delays in both electrical conduction time and myocardial mechanical contraction. An MIBG scintigraphic abnormality may reflect both phenomena. When considering the conduction delay in the dyssynchrony observed in DCM, we need to adjust not only the electrical delay caused by CRT, but also the mechanical contraction delay caused by medical treatment.^{8–12}

LV filling time is also an important factor for dyssynchrony. Brecker et al reported that patients with a short filling time are good candidates for CRT.¹³ We need to emphasize more the importance of the LV filling time in DCM as an indication for CRT.

As the next step, we need to investigate the recovery of sympathetic activity on MIBG scintigraphy after CRT and medical treatment.

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