Myocardial Imaging of Sympathetic Nervous Function by Radiolabelled Metaiodobenzylguanidine

Radiolabelled MIBG (metaiodobenzylguanidine) was first developed by Wieland et al as a candidate of agents to make it possible to evaluate the in vivo function of sympathetic nerve (1). It is one of the analogs of guanethidine which is an adrenergic blocking agent. It has been known to be stored in the storage vesicle of the sympathetic nerve endings by reuptake as well as noradrenalin and is mainly excreted by exocytosis, and a part of this excreted MIBG is reuptaken into presynapse of sympathetic nerve ending but does not bind to the postsynaptic receptor of the target organs. Furthermore it is not metabolized by monoamine oxidase or catechol-o-methyl transferase differently from noradrenalin. Recently developed radiolabelled MIBG (123I-MIBG) has a high specific radioactivity; early images after administration are thought to reflect the specific uptake (uptake 1). Therefore it is thought possible to detect the distribution of catecholaminergic nerve and the function of the sympathetic nervous system by 123I-MIBG imaging.

It has not been possible to date to evaluate the in vivo kinetics of noradrenaline because of its technical difficulties except for by histochemical study or dynamic change of its plasma levels. On the meanwhile it is known that the sympathetic nervous function may play an important role in the pathophysiology of organ functions, and its functional disorders are closely related to the pathogenesis of many cardiovascular diseases. 123I-MIBG imaging provides quantitative information on catecholamine content, and myocardial imaging has been used to visualize the myocardium in normal and pathological conditions (2). Therefore it has been used for the imaging of myocardium for the analysis of sympathetic nervous function and the myocardial morphology (3). The clinical applications of 123I-MIBG have been expanded to the evaluation of not only myocardial sympathetic nervous functions on ischemic myocardium or heart failure, but also to adrenomedullary imaging.

The myocardial uptake of 123I-MIBG is heterogenous and is decreased in the inferior wall of the ventricle and its clearance is rather slow in normal subjects. The changes of MIBG images may reflect the physiological variations of sympathetic nervous function in humans and these findings are pronounced in the elderly. A decreased 123I-MIBG uptake or defect of the 123I-MIBG images is observed in patients with myocardial ischemia as well as on the 201Thalium images, however the dissociation between these two images is magnified when the coronary flow is recovered by recanalization in the patients with a reperfused coronary. These findings suggest that the sympathetic nervous function is attenuated in those patients or that they are in the state of denervation. The decreased myocardial 123I-MIBG uptake suggests an area at risk in the myocardium, and the discrepancy between 123I-MIBG and 201Thalium images may reflect the area of myocardium which was salvaged by reperfusion. A combination with 201Thalium scintigram can detect the denervated but viable area of myocardium, and the detecting power of 123I-MIBG on the ischemic myocardium is to be higher than 201Thalium. As was mentioned above, the dual application of different nuclides may provides the further informations not only on the dynamic change of tissue damages but also the functional aspect of myocardium.

An interesting finding on the myocardial sympathetic nervous function is disclosed by an application of 123I-MIBG in the cases of hypertrophic cardiomyopathy. Scintigram shows the higher clearance and the decreased uptake of 123I-MIBG especially in the inferoposterior wall of left ventricle and apex of myocardium, and this decreased uptake is wide-spread especially in the patients with chest symptoms. In these patients with hypertrophic cardiomyopathy the disordered noradrenalin uptake into sympathetic nerve endings is one of the possible mechanisms for the decreased uptake, although the other mechanism is also posturated to be due to overexcretion of noradrenalin or myocardial ischemia. On the other hand in the cases of dilated cardiomyopathy, the typical findings are the decreased uptake in the whole hart and the rapid clearance of 123I-MIBG. It indicates the decrease in the noradrenalin concentration in the myocardium and these findings might have prognostic value as an indicator of failing hearts (4).

Cause of cardiac hypertrophy and its regression observed in hypertensive patients is one of the topics which has been focused on in the treatment of hypertension to prevent the cardiac complications. The improvement of cardiac hypertrophy and the recovery of abnormal MIBG images have recently been reported with antihypertensive treatment, and it is indicated that the cardiac sympathetic nervous dysfunction might have been related to the regression of left ventricular hypertrophy because the abnormality in MIBG images is improved by the treatment (5). 123I-MIBG imaging may be applied for clarifying the mechanism of regression of cardiac hypertrophy.

Generalized autonomic neuropathy is known to be present in the diabetic patients or Shy-Drager syndrome, and the clearance of 123I-MIBG from the myocardium of these patients is fast...
and the decreased uptake or diffuse defect of $^{123}$I-MIBG is common findings in these situations. It is also reported that a patient with diabetic autonomic neuropathy whose $^{123}$I-MIBG imaging shows the broad defect of uptake developed a sudden cardiac death in spite of typical $^{201}$Thallium imaging (6). The association between the lack of adrenergic symptoms during hypoglycemia and myocardial $^{123}$I-MIBG is evaluated in the insulin-treated noninsulin-dependent diabetes mellitus (NIDDM) patients, and it is reported that the lack of adrenergic symptoms during hypoglycemia might be associated with cardiac sympathetic nervous dysfunction and that this dysfunction is mainly due to cardiac sympathetic denervation in insulin-treated NIDDM patients (7). These experimental studies have accumulated and have provided new information on the role of sympathetic nervous function in the myocardium; further studies are expected for the evaluation of its clinical applications.

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References