Myocardial Iodine-123-Metaiodobenzylguanidine (\(^{123}\text{I-MIBG}\)) Imaging in Brugada Syndrome

To the Editor:

We read with interest a recent article in Circulation by Wichter et al on cardiac autonomic dysfunction in Brugada syndrome. The authors demonstrated that regionally reduced iodine-123-metaiodobenzylguanidine (\(^{123}\text{I-MIBG}\)) uptake in the inferior and septal left ventricular wall was present in 8 (47%) of 17 patients with Brugada syndrome but in none of 10 age-matched control subjects. The study may provide new insight into the pathogenesis and arrhythmogenesis of Brugada syndrome. However, we have some questions concerning other indices of \(^{123}\text{I-MIBG}\) imaging, clinical characteristics of Brugada syndrome, and sodium channel blocker loading test.

In normal subjects, regional MIBG uptake may be nonhomogeneous and apparently lower in the inferior and septal wall than in the anterior wall: 80±11% versus 95±5% (mean±SD). Additionally, a heterogeneous \(^{123}\text{I-MIBG}\) distribution in the left ventricle may be a physiological phenomenon mediated by the parasympathetic nerve fibers predominantly located in the inferior wall. Therefore, it is possible that segmental (inferior and septal) reduction of \(^{123}\text{I-MIBG}\) uptake in patients with Brugada syndrome is a normal variant.

Cardiac \(^{123}\text{I-MIBG}\) markers that have been used include not only regional uptake heterogeneity but also global myocardial uptake (heart-to-mediastinum ratio) and washout kinetics. Our recent study showed that the heart-to-mediastinum ratio has independent and incremental prognostic value. It seems essential to investigate other indices such as the heart-to-mediastinum ratio and washout kinetics in patients with Brugada syndrome.

We also think that subjects with right bundle branch block but no ST-segment elevation, or asymptomatic subjects with Brugada-type ST shift but no ST-segment augmentation by a sodium channel blocker loading test, should be enrolled as control subjects. We previously found an asymptomatic Brugada-type ST shift in 12 (0.14%) of 8612 general Japanese control subjects. We performed \(^{123}\text{I-MIBG}\) imaging in 11 of these 12 subjects. Segmental reduction of \(^{123}\text{I-MIBG}\) uptake in the inferior wall was found in 5 (45%) of those 11 subjects (unpublished data, 1999). None were patients with proven Brugada syndrome because sodium channel blocker loading tests failed to enhance ST-segment elevation. Reduced \(^{123}\text{I-MIBG}\) uptake in the inferior left ventricular wall does not necessarily explain the pathogenesis and arrhythmogenesis of Brugada syndrome.

Finally, the timing of \(^{123}\text{I-MIBG}\) imaging was not defined in the article. We speculate that \(^{123}\text{I-MIBG}\) uptake would be persistently impaired by rescue DC shock or after ventricular arrhythmia. We would like to know about the difference between acute and chronic phases, the time course, and the pharmacological change in \(^{123}\text{I-MIBG}\) uptake.

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Response

We appreciate the questions raised by Dr Furushashi and colleagues. However, most of the issues addressed in their letter have already been discussed in the original article (Discussion section). From our large experience with iodine-123-metaiodobenzylguanidine (\(^{123}\text{I-MIBG}\)–imaging (see references\(^3,4\) and others), we agree that \(^{123}\text{I-MIBG}\) uptake may be inhomogeneous (especially in inferior and septal regions) in controls as well as in disease. This finding may be attributed to inhomogeneous distribution of the regional parasympathetic innervation. However, in the 8/17 patients with Brugada syndrome and abnormal \(^{123}\text{I-MIBG}\) images, the regional uptake in inferior and septal segments was as low as 51.0±8.6% and 54.8±10.1%, respectively. This magnitude of abnormal uptake is not consistent with the heterogeneities in control subjects (80±11% in inferior and septal walls) cited by Furushashi et al. Therefore, it clearly is not a normal variant but indicates a significant reduction in \(^{123}\text{I-MIBG}\) uptake found only in disease.

In contrast to published data concerning the stability of heart-to-mediastinum ratios and washout measurements, our findings showed a significant variability of heart-to-mediastinum ratios and washout measurements highly influenced by the placement of the regions of interest (ROI) and by varying background \(^{123}\text{I-MIBG}\) uptake in the mediastinum. Therefore, we focused on quantifying regional rather than global uptake of \(^{123}\text{I-MIBG}\) in our previous as well as in the present study.\(^1,3,4\) Because this approach may potentially miss a homogeneous global reduction of \(^{123}\text{I-MIBG}\) uptake in the myocardium, it may underestimate rather than overestimate the number of patients with innervation defects. However, there is obviously a need for complementary studies on global sympathetic innervation. For this reason, our group previously concentrated on the superior technique of PET using \(^{12}\text{C-HED}\) with absolute quantification (see reference\(^5\) and others) with a future study also planned in Brugada syndrome.

The finding of abnormal \(^{123}\text{I-MIBG}\) uptake (magnitude not reported) in asymptomatic individuals with positive ECG signs but negative sodium channel blocker challenge as reported by Furushashi et al (unpublished data) may add new aspects to the controversial issue of the diagnostic value of sodium channel blocker provocation in asymptomatic individuals with ECGs suspicious for Brugada syndrome.

\(^{123}\text{I-MIBG}\) imaging was performed in the chronic state (\(>3\) months) after an episode of resuscitation or sustained ventricular tachyarrhythmia in all patients of our study. Therefore, we consider our findings not related to a transient effect in the acute phase after DC shock or ventricular tachycardia.


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