Assessment of myocardial adrenergic innervation with a solid-state dedicated cardiac cadmium–zinc–telluride camera: first clinical experience

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Aims

To investigate the relationships between regional adrenergic innervation heterogeneity, myocardial perfusion, and contractile function obtained by means of a low-dose imaging protocol with a cadmium–zinc–telluride (CZT) dedicated camera.

Methods

Twenty-eight patients with or without ischaemic heart disease underwent 123I-metaiodobenzylguanidine (MIBG) planar scintigraphic and CZT early and delayed evaluations followed by 99mTc-tetrofosmin rest gated CZT with a single-day protocol. The heart-to-mediastinum ratio and the washout rate were computed from planar 123I-MIBG images. The summed 123I-MIBG defect scores (SS-MIBG) were semi-quantitatively assessed from CZT images. The summed rest score (SRS), summed motion score (SMS), and summed thickening score (STS) were quantitated from 99mTc-tetrofosmin images.

Results

Sixteen patients showed a depressed left ventricular systolic function [ejection fraction (EF) ≤ 50%]. They presented higher SRS (P = 0.007), SMS (P < 0.001), STS (P < 0.001), and early SS-MIBG (P = 0.007) values than those with normal contractile function. Interestingly, higher early SS-MIBG values, index of regional sympathetic innervation heterogeneity, clustered with more elevated SRS (P = 0.023), and more impaired measures of regional and global left ventricle systolic function, i.e. SMS (P = 0.046), STS (P = 0.014), and EF (P = 0.027). At multivariate analysis, a higher SRS (P = 0.039) remained the only independent predictor of more elevated early SS-MIBG values. In the 20 of 28 ischaemic patients, the correlations between early SS-MIBG and SMS (P = 0.017) and also STS (P = 0.036) were further confirmed. The effective dose of the investigation was 4.2 ± 0.72 mSv.

Conclusions

An altered early SS-MIBG, assessed with a low-dose imaging protocol and a CZT cardiac camera, identifies patients with more impaired myocardial perfusion and contractile function.

Keywords 123I-MIBG • CZT camera • Heart-to-mediastinum ratio • Cardiac innervation

Introduction

The scintigraphic evaluation of myocardial adrenergic activity has become feasible after the introduction of 123I-metaiodobenzylguanidine (123I-MIBG) as a dedicated tracer. 1-3 123I-MIBG is a norepinephrine analogue, whose reuptake and retention into cardiac sympathetic terminals reflect neuronal integrity.4 Interestingly, different indexes derived from the analysis of 123I-MIBG kinetics, such as the heart-to-mediastinum (H/M) ratio and the myocardial washout rate,1-5 have been consistently associated with heart failure progression, arrhythmic events, and cardiac death.3,6,7 However, despite these parameters have gained diffuse clinical application,1,6,7 they can only give a picture of the overall cardiac adrenergic activity and are unable to assess the presence of regional differences in myocardial innervation, which may characterize specific cardiac pathologies, such as ischaemic heart disease (IHD).

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Evidences have been accumulating on the possibility to compare, by the use of single-photon emission computed tomography (SPECT), cardiac sympathetic activity, and myocardial perfusion on a regional basis, deriving indexes of cardiac innervation that might be superior to the standard H/M ratio in predicting patients’ morbidity.

Nevertheless, the combined assessment of myocardial innervation and perfusion has never gained wide clinical application, possibly due to the high radiation exposure and long acquisition time of this integrated imaging protocol. The use of new solid-state cardiac cameras with cadmium–zinc–telluride (CZT) detectors, characterized by a higher photon sensitivity and spatial resolution than standard cameras, could overcome these limitations and allow the assessment of myocardial innervation and perfusion in a single imaging session and with a limited radiation burden, possibly guiding clinical decision-making.

We sought to investigate the relationships between measures of regional myocardial adrenergic innervation heterogeneity, cardiac perfusion, and mechanical function, obtained by means of a low-dose imaging protocol with a dedicated CZT cardiac camera and a reduced acquisition time, in a series of consecutive patients with or without IHD.

**Methods**

**Patient population**

Twenty-eight consecutive subjects underwent a combined evaluation of myocardial resting perfusion, with gated $^{99m}$Tc-tetrofosmin tomographic acquisitions on a dedicated CZT camera, and cardiac adrenergic innervation, by means of $^{123}$I-MIBG CZT scintigraphy followed by standard planar acquisition. Specifically, 20 of 28 patients with a history of myocardial infarction were submitted to this functional evaluation because of cardiovascular risk stratification. All these patients had been submitted to coronary angiography for clinical reasons. The remaining 8 patients without a history of IHD underwent a combined evaluation of cardiac function and adrenergic innervation because of suspected primary autonomic dysfunction. 

Both planar and tomographic acquisition were performed on a 1-day protocol.

The exclusion criteria were haemodynamic instability, severely symptomatic heart failure (New York Heart Association (NYHA) Class IV), and active or known myocardial inflammatory/infective disease.

The study was approved by the local Ethical Committee and conformed to the Declaration of Helsinki on human research. Written informed consent was obtained from every patient after complete explanation of the protocol, its aim and potential risks.

**Acquisition protocol**

Patients underwent a $^{123}$I-MIBG CZT scintigraphic evaluation followed by a planar acquisition on a standard camera and subsequently a $^{99m}$Tc-tetrofosmin rest gated CZT acquisition using a single-day protocol (74–111 MBq for innervation and 222–259 MBq for perfusion scan).

**$^{123}$I-MIBG imaging**

Patients were pre-treated with sodium or potassium perchlorate to block thyroid uptake of free iodine. Fifteen minutes after the administration of the $^{123}$I-MIBG dose, a scintigraphic acquisition, lasting 10 min, was performed using a dedicated CZT cardiac camera (Discovery NM 530c; GE Healthcare; Haifa, Israel) equipped with a multiple-pinhole collimator and 19 stationary CZT detectors, simultaneously imaging 19 cardiac views. Each detector comprised a $32 \times 32$ pixelated 5-mm thick (2.46 × 2.46 mm) elements. The design of the system enabled a high-quality imaging of a three-dimensional volume where the patient’s heart was to be positioned. A 10-min planar image of the anterior thorax was then acquired using a dual-headed gamma camera (E.Cam; Siemens Medical Solution; Hoffman Estates, IL, USA), equipped with a low-energy all-purpose parallel-hole collimator. All images were acquired with a $128 \times 128$ matrix and a 20% energy window centred at the 159 keV photopeak of $^{123}$I. Repeat planar and CZT studies were acquired 4 h after injection.

**$^{99m}$Tc-tetrofosmin imaging**

Thirty minutes after the delayed $^{123}$I-MIBG acquisition, all patients underwent the $^{99m}$Tc-tetrofosmin CZT scan, lasting 8 min. Acquisitions were anticipated, when necessary, by the administration of sublingual nitrates.

Patients were imaged in the supine position with arms placed over their head. Once acquisition was started there was no detector or collimator motion. List mode files were acquired and stored. Images were reconstructed on a standard workstation (Xeleris II; GE Healthcare) using a previously validated dedicated iterative algorithm with 50 iterations. A Butterworth post-processing filter (frequency 0.37, order 7) was applied to the reconstructed slices. The tomographic studies were also re-projected into 60 planar projections to emulate a standard SPECT layout. Images were reconstructed without scatter or attenuation correction.

**Image quality and dosimetry**

Image quality for planar and CZT images was assessed with a four-point scale ($1 = $ poor, $2 = $ fair, $3 = $ good, and $4 = $ very good) by a consensus of two experienced nuclear cardiologists. The residence time values needed for the dosimetric evaluation were taken from published reports and entered into the OLINDA software. Adult phantoms for either men or women were taken into account in order to evaluate the average committed effective dose in relation to our diagnostic investigation.

**Semi-quantitative analysis of CZT images**

Two experienced nuclear cardiologists independently performed the semi-quantitative analyses, and consensus was reached in cases of disagreement. Rest myocardial perfusion images and $^{123}$I-MIBG innervation images obtained by CZT acquisitions were semi-quantitatively scored using a 17-segment model of the left ventricle (LV) and a five-point scale ($0 = $ normal, $1 = $ mild, $2 = $ moderate, $3 = $ severe reduction of radioisotope uptake, and $4 = $ absence of detectable tracer uptake), as previously reported. Reproducibility of the $^{123}$I-MIBG scoring system was evaluated by the assessment of intra- and interobserver variabilities. To determine the interobserver variability, myocardial segments were scored twice by the same observer in two different sessions. To assess interobserver variability, the scores of the two independent readers were compared. The summed rest score (SRS) and the summed $^{123}$I-MIBG defect score (SS-MIBG) were calculated by adding the segmental scores in the perfusion and innervation images, respectively. Similarly, the H/M ratios were computed by the same nuclear cardiologists from early and delayed planar $^{123}$I-MIBG scintigraphic images as previously reported. Finally, the percentage of myocardial washout rate was calculated as follows: $\left(\text{Heart counts (early)} - \text{Heart counts (late)}\right) / \text{Heart counts (early)} \times 100\%$; no background correction was performed.
Analysis of gated images
LV volumes, ejection fraction (EF), and the peak filling rate were automatically measured from gated 99mTc-tetrofosmin images using a commercially available software (Corridor4DM, Invia, Ann Arbor, MI, USA).19,20 LV systolic dysfunction was diagnosed in the presence of an LVEF of <50%. LV volumes were further indexed for patients body surface area. Moreover, from 99mTc-tetrofosmin gated images, the summed motion score (SMS) and the summed thickening score (STS) were calculated using the same software package, according to a previously validated method.21,22

Statistical analysis
Continuous variables were expressed as mean ± 1 SD, and categorical variables as percentages. Groups were compared for categorical data using Fisher’s exact test and for continuous variables using the analysis of variance followed by Fisher’s protected least significant difference for multiple comparisons. All tests were two-sided; a P-value of <0.05 was considered to be statistically significant. Logistic regression models were used to identify the determinants of the presence of a more altered SS-MIBG (above the median value of patients’ distribution; >23) at univariate and multivariate analyses. A similar cut-off value of SPECT-derived summed MIBG defect score has been already associated with patients adverse prognosis.11 Only variables with a P-value of <0.05 at univariate analyses were included in the multivariate models. The predictive value of a variable was expressed as odds ratio (OR) with corresponding 95% confidence interval (CI); the Wald test was used for significance. A P-value of <0.05 was considered significant. Intra- and interobserver agreements were assessed by calculating the respective intraclass correlation coefficients (ICCs). Excellent agreement was defined as an ICC of >0.8.

Statistical analyses were performed using the JMP statistical software, SAS Institute, Inc., version 4.0.0, and Stata software (Stata Statistical Software: Release 10, StataCorp. 2007, College Station, TX, USA).

Results
Characterization of the study population
Of the 28 patients studied, 16 (57%) showed a preserved LV systolic function, and 12 (43%) a reduced LV systolic function. The characteristics of the whole patients’ population, and of the two groups with preserved or reduced systolic function as to demographics, clinical presentation, cardiovascular risk factors, as well as perfusion, functional and innervation parameters are summarized in Tables 1 and 2. Patients with overt LV dysfunction were more frequently symptomatic for effort dyspnoea (P = 0.017). Interestingly, no difference in the prevalence of major cardiovascular risk factors nor in age and sex distribution was observed between the two groups. As expected, the presence of LV systolic dysfunction associated with significantly more altered indexes of regional myocardial perfusion (SRS, P = 0.007) and contractile function (STS, P < 0.001 and SMS, P < 0.001). Moreover, it also associated with a more impaired LV diastolic function, as indicated by a significantly reduced PRF (P < 0.001). Interestingly, while the presence of a depressed LV systolic function did not correlate with more altered measures of global cardiac adrenergic innervation, i.e. the H/M ratio and the washout rate, it was significantly associated with a more impaired early SS-MIBG (P = 0.007), as an indicator of regional sympathetic heterogeneity.

Image quality and dosimetry
The intraobserver reproducibility for both early and delayed 123I-MIBG CZT defect scores was excellent (ICC: 0.97, 95% CI: 0.95–0.99 and ICC: 0.98, 95% CI: 0.97–0.99, respectively). Similarly, both readers showed an excellent agreement for early and delayed 123I-MIBG CZT defect scores (ICC: 0.98, 95% CI: 0.97–0.99 and ICC: 0.97, 95% CI: 0.94–0.99, respectively). 123I-MIBG images were graded good or better for planar and CZT acquisitions in 20 of 28 (71%) and in 24 of 28 (85%) patients, respectively (P = 0.205). 99mTc-tetrofosmin perfusion images were graded good or better in 26 of 28 (93%) patients. Representative images of a good and poor quality 123I-MIBG CZT studies are reported in Figure 1.

The radiation exposure of the study protocol was calculated. The total committed effective dose related to the entire diagnostic investigation (99mTc-tetrofosmin and 123I-MIBG scans) was 4.2 ± 0.72 (range 3.2–5.1) mSv. Patients individual radiation exposures, regarding both 99mTc-tetrofosmin and 123I-MIBG scans, are reported in Figure 2.

Relationship between cardiac innervation, myocardial perfusion, and mechanical function
In our study population, CZT-derived measures of myocardial innervation, perfusion, and contractile functional clustered together. Early SS-MIBG moderately correlated with indexes of regional myocardial perfusion and contractile function, SRS (R = 0.43), SMS (R = 0.38), and STS (R = 0.46) (Figure 3). Moreover, as shown in Figure 4, an early SS-MIBG defect score significantly correlated with measures of LV volumetric overload and systolic function. On the contrary, although early and delayed SS-MIBG scores were strongly inter-related (R = 0.72), the latter did not associate with any of the measures of LV perfusion and function. Finally, at multivariate logistic analysis, an elevated SRS remained the only independent predictor of more altered SS-MIBG (Table 3). Images of representative patients with innervation–perfusion regional myocardial match (Figure 5) and mismatch (Figure 6) are further shown.

In the overall population, neither measures of global adrenergic innervation (H/M ratios and washout rate) correlated with CZT-derived indexes of LV contractile function. However, when the analysis was limited to patients with depressed LV systolic function, a significant, albeit weak, correlation between early H/M ratio and LVEF (R = 0.58; P = 0.047) was evident.

Cardiac innervation and LV systolic function in patients with ischaemic heart disease
In the subgroup of patients with IHD, the relationships between depressed LV systolic function and more altered measures of regional myocardial adrenergic innervation, i.e early SS-MIBG, were confirmed (Table 4). Moreover, as in the overall population, significant correlations between early SS-MIBG and CZT-derived measures of regional LV contractile function, such as SMS (R = 0.53; P = 0.017) and STS (R = 0.47; P = 0.036), were further demonstrated. Interestingly, the relationship between early H/M ratio, as a measure of global
adrenergic innervation, and LVEF was maintained only in patients with depressed LV systolic function ($R = 0.61; P = 0.043$).

**Discussion**

The present study represents the first clinical experience of the assessment of myocardial adrenergic innervation with a low-dose CZT imaging protocol. The obtained results show that a more impaired early regional adrenergic innervation heterogeneity correlates with abnormal myocardial perfusion and contractile function. Therefore, CZT-derived indexes of cardiac regional sympathetic derangement could be used to evaluate the physiological effects and the clinical role of denervated, but viable myocardium in order to improve the risk stratification of high-risk patients.

**Regional evaluation of adrenergic innervation**

An alteration of myocardial sympathetic activity is a prominent feature of different cardiac pathologies, such as heart failure or IHD. Specifically, in patients with LV systolic dysfunction, an increased cardiac adrenergic activity, as shown by a reduced H/M ratio, has been associated with heart failure progression and cardiac mortality.

As SPECT technology was applied to $^{123}$I-MIBG imaging, it became evident how the new measures of regional adrenergic heterogeneity...
**Figure 1** Good quality (left) and poor quality (right) early $^{123}$I-MIBG images.
that could be obtained might allow a more complete functional assessment and better predict patients morbidity than standard planar measures.5,9–11

In the present study, a combined evaluation of cardiac adrenergic innervation and myocardial perfusion was performed with an elevated image quality and a limited radiation burden. In particular, our results demonstrated how CZT-derived measures of adrenergic innervation heterogeneity could better identify, if compared with the classical planar indexes, patients at higher cardiovascular risk, adding relevant regional information on cardiac adrenergic nerve activity. CZT-derived early 123I-MIBG defect score is a semi-quantitative, reproducible, measure of cardiac denervation that correlates with major indicators of myocardial perfusion, contractile function, and volume overload, independently of patients clinical presentation. Therefore, the regional evaluation of sympathetic innervation seems to better unmask, if compared with the standard planar assessment, patients with significantly impaired myocardial perfusion and contractile function, both in the overall population and in the subgroup of ischaemic patients. Accordingly, the tomographic evaluation of cardiac adrenergic activity, initially performed in conjunction with the standard planar assessment, might represent an interesting way for clinical stratification high-risk patients.

**Relationship between cardiac innervation and myocardial perfusion**

As previously documented, sympathetic terminals are more sensitive than normal myocytes to the effects of ischaemia,27 which may induce damage to sympathetic neurons resulting in decreased 123I-MIBG uptake.9,27 In particular, Marini et al.9 demonstrated a close relationship between early 123I-MIBG myocardial distribution and regional myocardial perfusion. Moreover, while measures of delayed

![Image](https://example.com/image.png)

**Figure 2** Individual radiation dose of 123I-MIBG and 99mTc-tetrofosmin scans.

![Image](https://example.com/image.png)

**Figure 3** Relationships between the early ‘SS-MIBG’ and CZT-derived measures of resting myocardial regional perfusion and contractile function.
123I-MIBG distribution are believed as more accurate indicators of neuronal activity,\textsuperscript{5,10} abnormalities of early 123I-MIBG kinetics have been consistently associated with regional myocardial contractile impairment.\textsuperscript{28} Interestingly, despite delayed 123I-MIBG distribution has been proposed to give information on the extent of inducible ischaemia in patients with IHD,\textsuperscript{29} the evaluation of early 123I-MIBG kinetics, joining perfusion, and neuronal data may allow a more accurate risk stratification of patients referred to myocardial innervation imaging. To this respect, the combined assessment of early 123I-MIBG distribution and regional myocardial perfusion in the same imaging session may give important information on adrenergic neuronal activity and myocardial viability, allowing an integrated evaluation of these two distinct myocardial functional parameters. In our study, early SS-MIBG significantly correlated with regional myocardial perfusion abnormalities, indicated by SRS, and also with other measures of myocardial functional impairment, identifying patients at higher cardiac risk. Interestingly, a higher SRS remained the only predictor of regional sympathetic heterogeneity, overwhelming the effects of the other parameters. Nevertheless, due to the only moderate correlation between early SS-MIBG and SRS, our data suggest that, in selected patients with IHD, 123I-MIBG imaging could be coupled with myocardial perfusion imaging in order to obtain a more

**Table 3  Predictors of severely impaired myocardial innervation**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate OR (95% CI)</th>
<th>P-value</th>
<th>Multivariate OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.98 (0.91 – 1.06)</td>
<td>0.688</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Male sex, 1–0</td>
<td>0.11 (0.02 – 0.61)</td>
<td>0.012</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Summed rest score</td>
<td>0.88 (0.79 – 0.97)</td>
<td>0.012</td>
<td>0.86 (0.76 – 0.97)</td>
<td>0.039</td>
</tr>
<tr>
<td>Summed thickening score</td>
<td>0.91 (0.84 – 0.99)</td>
<td>0.025</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Summed motion score</td>
<td>0.95 (0.89 – 1.00)</td>
<td>0.050</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>LVEF &lt;50%, 1–0</td>
<td>0.15 (0.03 – 0.81)</td>
<td>0.028</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Peak filling rate, EDV/s</td>
<td>2.09 (0.50 – 8.68)</td>
<td>0.313</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

**Figure 4** Relationships between the early ‘SS-MIBG’ and CZT-derived parameters of left ventricular global systolic function and volumetric overload.
complete functional characterization of those category of patients at increased cardiovascular risk.

**Cardiac innervation and LV contractile function**

An alteration of cardiac sympathetic activity has been demonstrated in patients with depressed LV systolic function, independently from the aetiology of cardiac disease. Specifically, previous data have reported the existence of a significant correlation between measures of global adrenergic denervation, i.e. the H/M ratio, and LV contractile impairment mainly in patients with LV systolic dysfunction. Moreover, in heart failure, the improvement in LV systolic function parameters has been associated with parallel modifications of global and regional $^{123}$I-MIBG distribution.

Our study demonstrates that CZT-derived indexes of regional sympathetic heterogeneity better correlate, if compared with planar measures, with indicators of regional and global LV contractile function. These results suggest that the relationship between measures of regional sympathetic heterogeneity and myocardial functional impairment is independent of patient baseline systolic function and clinical presentation. Conversely, the correlation between depressed H/M ratio and impaired LV contractile function was limited to patients with overt systolic dysfunction.

While the causal relationship between these variables cannot be assessed by the present study, our data suggest the importance of
the evaluation of adrenergic nerve activity on a regional basis as a measure of integrated cardiac functional impairment.

**Limitations**

This is a proof-of-concept study. Therefore, the small number of the patients studied prevents the assessment of any causal relationship between the variable explored. Moreover, the consecutive nature of the enrolment prevented the selection of a homogeneous population of patients, i.e. with or without LV dysfunction. However, due to the absence of substantial exclusion criteria, the patients analysed represent a close picture of the population of subjects that ordinarily come to our attention for myocardial innervation imaging. In the present study, a comparison of $^{123}$I-MIBG CZT with standard SPECT could not be performed. In fact, due to the low $^{123}$I-MIBG injected dose, a prolonged SPECT acquisition would have been necessary, inevitably conflicting with patients compliance.

Since the majority of the patients studied suffered from IHD, the present results should not be directly extended to different cohorts of subjects. Nevertheless, most of the studies evaluating the potentials of $^{123}$I-MIBG scintigraphy in the characterization and risk stratification of patients have been conducted in populations of mainly ischaemic subjects.
Finally, in the present study, only the measures of early adrenergic innervation derangement, i.e. early H/M ratio and early SS-MIBG defect score, correlated with myocardial functional parameters. While the indicators of delayed 123I-MIBG distribution are considered better measures of neuronal integrity and predict adverse prognosis, the existence of a strict association between early 123I-MIBG myocardial uptake, cardiac perfusion, and contractile function has been already reported.28

### Conclusions

Measures of early regional adrenergic innervation heterogeneity, as assessed by means of a low-dose imaging protocol with a CZT dedicated camera, correlate with the presence of impaired myocardial perfusion and contractile function. This study may represent the first step for the development of new protocols for the combined evaluation of cardiac innervation and perfusion in high-risk patients.

**Conflict of interest:** The authors declare no relationship with industry.

### References


### Table 4  CZT data in patients with ischaemic heart disease

<table>
<thead>
<tr>
<th>Parameter</th>
<th>LV dysfunction absent (N = 9)</th>
<th>LV dysfunction present (N = 11)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV functional data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Summed thickening score</td>
<td>7 ± 7</td>
<td>25 ± 8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Summed motion score</td>
<td>10 ± 7</td>
<td>25 ± 9</td>
<td>0.001</td>
</tr>
<tr>
<td>End-diastolic volume (EDV) index mL/m²</td>
<td>55 ± 18</td>
<td>114 ± 37</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>End-systolic volume mL/m²</td>
<td>21 ± 9</td>
<td>78 ± 28</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak filling rate, EDV/s</td>
<td>2.28 ± 0.28</td>
<td>1.49 ± 0.45</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Myocardial global innervation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early heart-to-mediastinum ratio</td>
<td>1.58 ± 0.16</td>
<td>1.53 ± 0.14</td>
<td>0.477</td>
</tr>
<tr>
<td>Delayed heart-to-mediastinum ratio</td>
<td>1.54 ± 0.17</td>
<td>1.43 ± 0.19</td>
<td>0.161</td>
</tr>
<tr>
<td>Washout rate, %</td>
<td>30 ± 10</td>
<td>40 ± 10</td>
<td>0.053</td>
</tr>
<tr>
<td>Early SS-MIBG</td>
<td>21 ± 8</td>
<td>33 ± 6</td>
<td>0.002</td>
</tr>
<tr>
<td>Delayed SS-MIBG</td>
<td>29 ± 12</td>
<td>37 ± 8</td>
<td>0.114</td>
</tr>
</tbody>
</table>
A 63-year-old man with a history of chronic kidney disease and atrial flutter status post ablation and permanent pacemaker implant presented with worsening shortness of breath. Echocardiogram revealed asymmetric left ventricular wall thickness involving the posterior wall and midventricular septum (S) with maximal thickness of 28 mm, midventricular obstruction (gradient 19 mmHg), moderate mitral regurgitation, and Grade II diastolic dysfunction. An apical aneurysm was identified using contrast echocardiography (Panels A–C, arrows) and by computed tomography (Panel D, arrows). A diagnosis of hypertrophic cardiomyopathy (HCM) phenotype was made. However, the alpha-galactosidase level was low. Genetic testing confirmed mutation of alpha-galactosidase A (alpha-Gal A) gene while genetic testing for HCM was negative. Electron microscopy of renal tissue showed hypertrophic vacuolated cells with electron-dense concentric lamellar bodies, typical for Fabry’s disease. The patient has been treated with alpha-Gal A replacement for 8 months without any side effects.

This case illustrates the formation of an apical aneurysm as a novel presentation of Fabry’s disease, akin to its HCM phenocopy. Meticulous imaging and high degree of suspicion are needed for diagnosis and may impact management decisions for HCM phenocopies.

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