SPECT Myocardial Perfusion Reserve in Patients with Multivessel Coronary Disease: Correlation with Angiographic Findings and Invasive Fractional Flow Reserve Measurements

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ABSTRACT

Quantification of myocardial perfusion reserve is an emerging topic in nuclear cardiology with an expected diagnostic and prognostic incremental value, especially for patients with severe coronary artery disease (CAD). The advent of new dedicated solid-state cameras have opened new perspectives for perfusion quantitation in SPECT. We appraised the feasibility of perfusion reserve estimations using a CZT camera in a cohort of multivessel patients and its pertinence with respect to angiographic data.

Methods: Twenty-three patients with known multivessel CAD were prospectively enrolled. Dynamic SPECT acquisitions using $^{99m}$Tc-tetrofosmin at rest and after vasodilator stress were performed using a dedicated CZT camera. Reconstructed frames were automatically segmented to extract the vascular input function and the myocardial uptake curve. A one-compartment kinetic modelling was employed to estimate global and regional uptake values ($K_1$), then myocardial blood flow was derived using Renkin-Crone’s equation. Global and regional myocardial perfusion reserve (MPR) was assessed using flow difference (stress – rest) and flow ratio (stress / rest). All patients underwent a control coronary angiography within four weeks which served as reference for MPR indices assessment. Relevant angiographic findings included maximal stenosis and (for a subgroup of 26 vessels) invasive measurement of fractional flow reserve (FFR). A stenosis was considered obstructive if greater than 50% and an FFR abnormal if lower than 0.8.

Results: Global MPR was well correlated with the number of obstructed vessels ($p<0.001$). After multivariate analysis, both regional flow ratio and flow difference were significantly associated with maximal stenosis ($p<0.001$) and FFR ($p<0.001$). Regional MPR indices were significantly different in obstructed and non-obstructed vessels ($p<0.001$) and in vessels with normal and abnormal FFR ($p<0.001$). With a cut-off value set at 2, the sensitivity, specificity, and accuracy of regional flow ratio were respectively 80%, 85%, and 81% for the detection of obstructed vessels, and 89%, 82%, and 85% for the detection of abnormal FFR.

Conclusion: Scintigraphic estimations of global and regional myocardial perfusion reserve in multivessel patients using a CZT camera appear to correlate well with invasive angiographic findings including maximal stenosis and FFR measurements.

Key Words: multivessel coronary artery disease, myocardial perfusion reserve, dynamic SPECT, CZT camera, fractional flow reserve.
INTRODUCTION

Owing to its wide availability, non-invasiveness, and high diagnostic performance, myocardial perfusion imaging (MPI) using SPECT has become a common practice for coronary artery disease (CAD) screening, characterization, and follow-up (1-2). The standard semi-quantitative approach based on the analysis of reversible perfusion defects between stress and rest images has excellent sensitivity and negative predictive value for ischemic lesion detection (3). However, due to the relative nature of the reconstructed activity maps, it may underestimate the extent of the disease, particularly in patients with balanced multivessel CAD (4-5). Quantitative perfusion assessment in terms of myocardial flow or myocardial perfusion reserve, a measure of coronary vasodilator capacity (6), have already been developed using cardiac PET with various tracers such as $^{82}$Rb (7) and shown to provide incremental diagnostic and prognostic information (8-10). Still, since PET tracers production requires high start-up costs, PET flow imaging has not been embraced by many healthcare systems to date, and SPECT with $^{99m}$Tc-labeled tracers remains the clinical standard for MPI worldwide. SPECT perfusion quantitation has long been hampered by the difficulty to achieve dynamic acquisitions using classical Anger cameras. With the advent of novel solid-state detectors with improved sensitivity (11-12) allowing list-mode recording and multi-frame dynamic reconstructions with sufficient temporal resolution, myocardial perfusion reserve (MPR) estimation has become feasible (13). Recent results reported a good correlation between global MPR and CAD severity expressed as stress total perfusion deficit. Global and regional MPR were also predictive of the extent of CAD as assessed angiographically (14).

Invasive fractional flow reserve (FFR) measurement is performed during coronary catheterization using a pressure sensor, and is defined as the ratio of hyperaemic pressure downstream the lesion to mean aortic pressure. FFR is an index of the functional significance of a coronary stenosis and have been shown to improve outcome when taken into account to guide revascularization in patients with multivessel CAD (15-16).

The aim of the present study was to evaluate the feasibility of MPR estimations in routine clinical settings using a CZT camera in a cohort of multivessel patients, and to assess its pertinence with respect to the results of coronary angiography in terms of maximal stenosis and fractional flow reserve.

MATERIALS AND METHODS

Study Population

The study was conducted from January 2014 to March 2015 at Montpellier University Hospital, France. It was designed as an ancillary study to the FUTURE cohort evaluating the place of FFR measurements in therapeutic decision making. Twenty three patients were prospectively enrolled and included in the analysis. All patients had been diagnosed with multivessel CAD during a scheduled coronary angiography 2 days to 6 weeks before MPI and were referred to the nuclear medicine department for assessment.
of myocardial ischemia before revascularization. The study was approved by the local ethics committee. All procedures were in accordance with institutional guidelines and a requirement for individual informed consent was waived. Clinical and anthropomorphic characteristics documented using the patient’s record were sex, age, body mass index (BMI), and cardiovascular risk factors (diabetes, hypertension, dyslipidaemia, smoking, personal or familial history of CAD).

**Myocardial Perfusion SPECT Protocol**

Patients were imaged using a solid-state dedicated cardiac camera (Discovery NM530c; General Electrics). They refrained from caffeine and methylxanthine-containing substances and drugs for at least 24 hours before their scans. All patients underwent a 1-day rest–stress protocol. MPI was performed at rest and at peak vasodilator stress using $^{99m}$Tc-tetrofosmin (Fig 1). To enable positioning of the heart in the field of view, a test dose of $^{99m}$Tc-tetrofosmin (35–60 MBq) was first injected at rest for a prescan of 60 s. Concomitantly to the intravenous bolus administration of the resting $^{99m}$Tc-tetrofosmin dose (185–220 MBq), a list-mode acquisition was started for 6 minutes. With the patient positioned in the scanner, pharmacologic stress was then performed using an intravenous infusion of 0.75 mg/kg dipyridamole over 4 minutes (17). At peak vasodilation, a second dose of $^{99m}$Tc-tetrofosmin (645–730 MBq) was injected and list-mode data recording was started at the time of injection for 6 minutes. The average effective dose per patient was 8.4 mSv (18).

**Myocardial Perfusion Reserve Quantification**

List-mode dynamic acquisition data were reformatted and reconstructed into 48 frames. The frame duration was 3 seconds for the first 30 frames and 15 seconds for the 18 last frames (Supplemental Fig. 1). Images were reconstructed using a MAP-EM algorithm (19) following the manufacturer specifications (30 iterations, $\alpha=\beta=0.4$, Butterworth post-filter with order 10 and cut-off frequency 0.4/cm), without correcting for attenuation or scatter. Rest and stress reconstructed images were processed using in-house software (Supplemental Fig. 2). The voxels inside the ellipsoid and above the valve plane but outside the myocardial ROI were affected to the vascular (left ventricular) ROI whose time–activity curve (TAC) served as input function in kinetic analysis. Residual activities from the positioning dose (on rest images) and rest injection (on stress images) were corrected for using the early images before the first pass of the tracer bolus. The global myocardial ROI was divided into three regional ROIs corresponding to main coronary territories (left anterior descending, right coronary artery and left circumflex coronary artery), using the standard 17-segment polar map (20). Regional and global TACs were fitted to a kinetic model using a weighted linear least-squares method in order to estimate tracer exchange rates and spill-over coefficients. A one-compartment model was implemented that takes into account the tracer...
uptake ($K_1$) and wash-out ($K_2$). Regional and global myocardial flows were derived from the corresponding $K_1$ values using the Renkin-Crone equation for tetrofosmin (21-22).

In order to minimize the potential biases arising from differential photon attenuation between vascular and myocardial activities, an original technique was implemented for the normalization of rest and stress arterial input functions (AIF). The rest AIF was normalized so that the global rest flow was equal to 1 mL·g$^{-1}$·min$^{-1}$, which is easily achievable since multiplying the vascular TAC by a constant amounts to dividing $K_1$ by the same constant. The assumption seems acceptable since rest flow is not expected to vary much from one individual to another and 1 mL·g$^{-1}$·min$^{-1}$ is a commonly accepted normal value in the elderly (10, 23-25). The stress AIF was normalized using the same normalization coefficient as the rest AIF postulating that the degrading factors were similar under rest and stress conditions. Myocardial flows were also computed using the standard approach without normalization.

Myocardial perfusion reserve (MPR) was assessed using two indices: flow difference (stress flow – rest flow, in mL·g$^{-1}$·min$^{-1}$) and flow ratio (stress flow / rest flow, dimensionless). Cut-off values were set at 2 for normal flow ratio (10) and 1 mL·g$^{-1}$·min$^{-1}$ for normal flow difference. Standard semi-quantitative analysis was also performed using QPS/QGS software based on a late stationary image corresponding to the last 4 minutes of the dynamic acquisition (20). Global and regional total perfusion deficit (TPD), reflecting the extent and severity of the perfusion defect, was computed. A global TPD score of 5% or greater was defined as abnormal and fixed defects were defined as a global TPD stress – TPD rest score of 3% or less. Left ventricular ejection fractions (LVEF) and end-diastolic volumes (EDV) at stress were also computed. All the scintigraphic images were processed and interpreted blind to the angiographic data.

Reference Coronary Angiography

All the patients underwent a control coronary angiography (CAG) within four weeks (5+/-8 days) after MPI that was considered as the reference exam for further assessment of MPR estimations. Each of the three coronary vessels was characterized with its maximal stenosis (0% = free; 25% = non-significant; 50% = intermediary; 60% = significant; 80% = very tight; 95% = sub-occlusive; 100% = occlusive). A vessel was considered obstructed if its maximal stenosis was strictly greater than 50%.

For 12 patients (determined by randomization inside the FUTURE cohort) and 26 vessels, invasive FFR measurements were performed as follows. A guide wire with a mounted pressure sensor (St. Jude Medical) was placed across the lesion. To induce a maximal hyperaemic vascular response, 1 mg of isosorbide dinitrate and 150 µg of adenosine were injected into the studied artery. Under conditions of maximum hyperaemia, simultaneous recording of aortic pressure and distal coronary pressure was performed. FFR was calculated as the ratio of hyperaemic mean distal coronary pressure to mean aortic pressure. An FFR lower than 0.8 was considered abnormal (15-16).
Statistical Analysis

Continuous values are given as mean ± standard deviation, eventually as median [interquartile range (IQR)] for the sake of comparison with previous studies. Categorical variables are described as number (percentage). Correlation between quantitative variables was assessed using Pearson’s coefficient and Student’s t test. Independent distributions were compared using Mann-Whitney U test. A two-sided p-value smaller than 0.05 was regarded as statistically significant. To evaluate the independent predictors of MPR indices, forward-stepwise linear regression was performed with an entry criterion of p<0.1 and a removal criterion of p>0.05. The tested predictors were: the number of obstructed vessels (for global MPR), maximal stenosis or FFR (for regional MPR), age, sex, BMI, number of cardiovascular risk factors, stress TPD, stress LVEF, and stress EDV.

The intra-reader reliability was assessed using type 1 intraclass correlation coefficients, which were 94% for global MPR indices and 92% for regional MPR indices.

RESULTS

The clinical and anthropometric characteristics of the study population as well as the results of semi-quantitative analysis of SPECT data are summarized in Table 1. Standard semi-quantitative analysis was abnormal in 21 (91%) with 10 (43%) having reversible perfusion defects and 11 (48%) having fixed perfusion defects.

Global and regional kinetic parameters, myocardial blood flow, and perfusion reserve estimates resulting from the processing of the dynamic SPECT images are detailed in Table 2. The corrective factor for the normalization of the AIFs amounted 1.49 ± 0.35 (range 1.00–2.40). Mean rest and stress flows amounted respectively 2.58 mL.g⁻¹.min⁻¹ and 4.01 mL.g⁻¹.min⁻¹ using the standard approach, and 1 mL.g⁻¹.min⁻¹ and 1.96 mL.g⁻¹.min⁻¹ using the normalization technique described above. The sequel of this section focuses on the results obtained using the AIF normalization technique. The results obtained using the conventional approach (without normalization) are not detailed for the sake of concision. Their pertinence in terms of correlation with angiographic findings was highly similar.

Multivariate regression analysis revealed that the number of obstructed vessels was the sole significant predictor for global MPR (r=0.70; p<0.001) (Figure 2). Furthermore, flow ratio was significantly reduced in patients with (n=9) three-vessel CAD compared to those without (n=14) three-vessel CAD (1.57 ± 0.41 vs 2.17 ± 0.50; p=0.01) while stress global TPD and LVEF were not.

Regional MPR indices were first compared to angiographic findings in terms of maximal stenosis. Multivariate regression analysis showed statistically significant association of both flow difference and flow ratio with age (p=0.02). Sex, BMI, stress TPD, LVEF and EDV were not significant predictors. The correlation with maximal stenosis (Fig. 3 & Supplemental Fig. 3) was highly significant for both flow ratio (r=0.51; adjusted p<0.001) and flow difference (r=0.47; adjusted p<0.001). Regional MPR indices were
significantly lower in obstructed (n=49) vessels than in non-obstructed (n=20) vessels (Fig. 4), both in terms of flow difference (0.71 ± 0.54 mL.g⁻¹.min⁻¹ vs 1.40 ± 0.71 mL.g⁻¹.min⁻¹; p<0.001) and flow ratio (1.72 ± 0.52 vs 2.51 ± 0.66; p<0.001). Flow ratio was a slightly better predictor of vessel obstruction than flow difference with respective c-statistics (i.e., AUC of the ROC curve) of 0.85 and 0.78. By comparison, the ROC curve AUC of regional stress TPD was 0.55. The diagnostic performances in terms of sensitivity, specificity and accuracy were respectively 80%, 85% and 81% for flow ratio with a cut-off value set at 2, and 76%, 60% and 71% for flow difference with a cut-off value set at 1 mL.g⁻¹.min⁻¹.

Regional MPR indices were then compared to FFR in the subgroup of 26 vessels for which FFR measurements were available. After multivariate regression analysis, FFR remained a highly significant predictor for regional MPR (Fig. 5 & Supplemental Fig. 4) both in terms of flow ratio (r=0.73; adjusted p<0.001) and flow difference (r=0.69; adjusted p<0.001). Regional MPR indices were significantly lower in vessels with abnormal (n=10) FFR than in vessels with normal (n=16) FFR (Fig. 6), both in terms of flow difference (0.41 ± 0.47 mL.g⁻¹.min⁻¹ vs 1.45 ± 0.52 mL.g⁻¹.min⁻¹; p<0.001) and flow ratio (1.48 ± 0.37 vs 2.49 ± 0.58; p<0.001). Flow ratio was a slightly better predictor of FFR alteration than flow difference (ROC curve AUC = 0.97 vs 0.92). The diagnostic performances in terms of sensitivity, specificity and accuracy were respectively 89%, 82% and 85% for flow ratio with a cut-off value set at 2, and 89%, 76% and 81% for flow difference with a cut-off value set at 1 mL.g⁻¹.min⁻¹.

DISCUSSION

In this paper, we demonstrated the feasibility of myocardial perfusion quantitation using a novel semi-conductor dedicated SPECT camera, automated extraction of vascular and myocardial TACs, and full compartmental modelling of tracer kinetics. To our knowledge, this is the first study assessing the pertinence of MPR estimations with regards to angiographic findings in terms of both maximal vessel stenosis and fractional flow reserve. We also proposed a simple method for AIF normalization based on a priori knowledge regarding normal rest flow in an elderly population, in order to compensate for the differential photon attenuation between myocardial and vascular ROIs. The normalization technique efficiently constrained absolute myocardial flows to physiological values (1 mL.g⁻¹.min⁻¹ at rest, 2–3 mL.g⁻¹.min⁻¹ at stress) hence allowing to rely on established cut-off values for flow ratio and flow difference interpretation.

The acquisition workflow was compatible with routine practice and remains consistent with clinical guidelines since it allows for both conventional and quantitative MPI while keeping constant the protocol duration (about 20 minutes) and the radiation exposure (below 9 mSv). Although quantitative perfusion protocols using classical Anger cameras have been recently described and validated (26-27), state of the art dedicated cardiac cameras, which clinical performances have clearly been demonstrated (28-30), appear as the natural tool for the development of steady myocardial perfusion quantitation in SPECT.
The data processing has been largely automated in order to ensure the robustness of the quantitative analysis. Intra-reader reliability was satisfying. Inter-operator variability has not been tested but is expected to be moderate since the only steps requiring manual adjustment were the re-orientation of the reconstructed slices into canonical axes and the position of the valve plane delimiting the basis of the myocardium and left ventricular cavity. Besides, as already pointed out by Murthy et al (10), most of the variability in kinetic parameter estimation is linked to the definition of the vascular input function. Preliminary experiments that we have carried out using various semi-automated ROI approaches for the extraction of the AIF have confirmed this observation and led us to implement the robust normalization method exposed above. Using a linear attenuation coefficient in water of 0.16 cm\(^{-1}\) for 140 KeV photons, the normalization factors can be considered to account for an additional attenuation of the vascular signal corresponding to 2.3 ± 1.4 cm, consistent with basic anatomical considerations.

The results obtained using our methodology in terms of stress flow and flow reserve were consistent with the many reference values available in the literature. As expectable, mean stress flow in our population (1.96 mL.g\(^{-1}\).min\(^{-1}\)) was lower than previously reported values of about 2.8–3.4 mL.g\(^{-1}\).min\(^{-1}\) measured using \(^{82}\)Rb PET in healthy volunteers (7, 25), and MPR was reduced accordingly (1.96 vs 3.5–4.2). In the study by Lortie et al (7) comparing MPR estimation with \(^{13}\)NH\(_3\) and \(^{82}\)Rb PET, the mean stress flow in CAD patients was around 2 mL.g\(^{-1}\).min\(^{-1}\) with a flow ratio around 2.4, which is close to our values albeit slightly higher likely due to a lesser prevalence of severe CAD. In the case of SPECT imaging, K\(_1\) ratio has sometimes been used as a surrogate for MPR characterization. In our study, the global K\(_1\) ratio was 1.30 [1.15 1.41] which is comparable to global K\(_1\) ratios of 1.46 [1.22 1.79] measured in the cohort studied by Ben-Haim et al (14). The highest median and wider IQR are easily explained by the higher variety of the study population in terms of CAD severity and the lower prevalence of severe CAD. Our results were also consistent with those of Klein et al (27) regarding patients with known or suspected CAD, in terms of mean blood flow (1.82 mL.g\(^{-1}\).min\(^{-1}\)) and K\(_1\) ratio (1.17 [0.96 1.48]). Of note, our mean rest and stress K\(_1\) values (respectively 0.25 and 0.32) were in close agreement with the recent results of Wells et al using tetrofosmin in a porcine model (respectively 0.25 and 0.33).

Our results showed a clear correlation between the MPR indices and the extent and severity of the coronary disease. First, global MPR was significantly associated with the extent of CAD in terms of number of obstructed vessels, and global MPR was significantly reduced in patients with 3-vessel disease compared to patients without 3-vessel disease (1.57 vs 2.17 for flow ratio, and trivially 0.57 vs 1.17 mL.g\(^{-1}\).min\(^{-1}\) for flow difference). These values were quite close to those already obtained by Ziadi et al (8) using \(^{82}\)Rb perfusion PET for the detection of 3-vessel disease (1.3 vs 2.2 for flow ratio, and 0.3 vs 1.0 mL.g\(^{-1}\).min\(^{-1}\) for flow difference). Second, regional MPR was significantly associated with both anatomical (maximal stenosis) and functional (FFR) severity of CAD on a per-vessel basis. As expected, regional MPR indices (flow ratio and difference) allowed efficient discrimination between normal and pathological vessels, from both an anatomical and functional point of view. As appreciable from the ROC curves, flow ratio was a slightly better predictor of obstructive CAD than flow difference, with fairly good diagnostic performances in terms of sensitivity...
and specificity using the commonly employed cut-off value of 2 (8,10,31-32). The incremental diagnostic information over classical semi-quantitative processing clearly appears on the ROC curve in Figure 4. The c-statistic derived here (0.85 for regional flow ratio vs 0.55 for regional stress TPD in the detection of obstructive stenosis) were in agreement with previously reported values. In (26), the c-statistic of regional flow ratio and summed stress score (SSS) for the detection of obstructive stenosis were respectively 0.81 and 0.62. In (8), the c-statistic of global MPR and SSS for the detection of 3-vessel disease were respectively 0.82 and 0.68.

The main original contribution of the present paper lies in the assessment of scintigraphic flow reserve estimations with comparison to invasive flow reserve measurements which pertinence for patient workup and risk stratification has already been established (15-16). Previous studies demonstrated moderate adequacy between classical semi-quantitative SPECT perfusion analysis and FFR (33-35). Classical MPI mostly underestimated the extent and severity of CAD (33), with a subsequent fall in terms of sensitivity estimated around 60–65% (specificity 80%) on a per-vessel basis (34-35) to be compared with the 90% (specificity 80%) obtained here using fully quantitative modelling. The preliminary results presented here (Fig. 5 and 6) on a relatively small sample of measures require further confirmation on a larger cohort with long term follow-up but seem to indicate a close agreement between the invasive and the non-invasive indicators of the functional burden characterizing a coronary artery stenosis.

CONCLUSION

We described a method to derive myocardial flow reserve estimates using dynamic SPECT images from a solid state dedicated camera. The acquisition workflow was compatible with routine practice and consistent with current clinical guidelines for MPI. The results in terms of myocardial stress blood flow and flow reserve were in agreement with the recent literature related to PET and SPECT MPR. Global and regional MPR indices were highly correlated with the anatomical extent and severity of CAD and demonstrated increased diagnostic performances compared to classical semi-quantitative analysis. Most importantly, regional flow ratios were in close agreement with the functional characterization of perfusion impairment obtained with invasive FFR measurements. SPECT MPR quantification, as a non-invasive and cost-effective procedure, appears as a promising tool for routine assessment of coronary artery disease in complement to classical MPI.
REFERENCES


FIGURES

FIGURE 1. Myocardial perfusion SPECT workflow.

Heart positioning

Rest dynamic acquisition

Dipyridamole 0.75 mg/kg

Stress dynamic acquisition

\[ ^{99m} \text{Tc-tetrofosmin} \quad 35–60 \text{ MBq} \]

\[ ^{99m} \text{Tc-tetrofosmin} \quad 185–220 \text{ MBq} \]

\[ ^{99m} \text{Tc-tetrofosmin} \quad 645–730 \text{ MBq} \]
FIGURE 2. Correlation between global flow ratio and the number of obstructed vessels.

$r = 0.70$
$P = 0.0002$
FIGURE 3. Correlation between regional MPR indices and maximal stenosis.
FIGURE 4. Regional MPR indices in obstructed vessels (n=49) and non-obstructed vessels (n=20).

Boxes: interquartile range, whiskers: mean ± 1.5 std. dev. Right: ROC curves (circles stand for optimal cut-off values).

$P < 0.0001$

Flow ratio

Sensitivity

1 - Specificity
FIGURE 5. Correlation between regional MPR indices and invasive fractional flow reserve (FFR) measurements.
FIGURE 6. Regional MPR indices in normal (n=16) and abnormal (n=9) vessels in terms of FFR.

Boxes: interquartile range, whiskers: mean ± 1.5 std. dev. Right: ROC curves (circles stand for optimal cut-off values).
## TABLE 1

Clinical and SPECT characteristics of the study population (n=23).

Continuous values are given as mean ± std dev.

<table>
<thead>
<tr>
<th>Sex</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>19 (83%)</td>
</tr>
<tr>
<td>Female</td>
<td>4 (17%)</td>
</tr>
</tbody>
</table>

| Age (years)    | 66 ± 12 |

Cardiovascular risk factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>4 (17%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>7 (30%)</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>12 (52%)</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>12 (52%)</td>
</tr>
<tr>
<td>Body mass index (kg.m⁻²)</td>
<td>26 ± 4</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>7 (30%)</td>
</tr>
<tr>
<td>Familial CAD disease history</td>
<td>2 (9%)</td>
</tr>
</tbody>
</table>

| Number of cardiovascular risk factors | 2.5 ± 1.5 |

SPECT data

<table>
<thead>
<tr>
<th>Data</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal exam</td>
<td>2 (9%)</td>
</tr>
<tr>
<td>Global stress TPD (%)</td>
<td>14 ± 10</td>
</tr>
<tr>
<td>Stress ejection fraction (%)</td>
<td>47 ± 11</td>
</tr>
</tbody>
</table>

BMI: body mass index; TPD: total perfusion deficit.
TABLE 2
Global and regional kinetic parameters and MPR indices

<table>
<thead>
<tr>
<th></th>
<th>Global (n=23)</th>
<th>Regional (n=69)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest $K_1$ (min$^{-1}$)</td>
<td>0.25</td>
<td>0.24 ± 0.04</td>
</tr>
<tr>
<td>Stress $K_1$ (min$^{-1}$)</td>
<td>0.32 ± 0.04</td>
<td>0.32 ± 0.07</td>
</tr>
<tr>
<td>$K_1$ ratio</td>
<td>1.31 ± 0.18</td>
<td>1.31 ± 0.20</td>
</tr>
<tr>
<td>Rest flow (mL.g$^{-1}$.min$^{-1}$)</td>
<td>1.00</td>
<td>1.00 ± 0.38</td>
</tr>
<tr>
<td>Stress flow (mL.g$^{-1}$.min$^{-1}$)</td>
<td>1.96 ± 0.57</td>
<td>1.92 ± 0.87</td>
</tr>
<tr>
<td>Flow difference (mL.g$^{-1}$.min$^{-1}$)</td>
<td>0.96 ± 0.57</td>
<td>0.93 ± 0.69</td>
</tr>
<tr>
<td>Flow ratio</td>
<td>1.96 ± 0.57</td>
<td>1.97 ± 0.67</td>
</tr>
</tbody>
</table>
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