Pathomorphological and physiological characteristics of coronary artery disease
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The association between coronary lesion severity and distal microvascular resistance in patients with coronary artery disease
ABSTRACT

Background
Homogeneity of microvascular resistance in different perfusion areas of the same heart is generally assumed, regardless the extent of coronary artery disease. The aim of the study was to investigate the effect of the severity of an epicardial stenosis on microvascular resistance in patients with coronary artery disease.

Methods and Results
Twenty-seven patients with stable angina and coronary narrowings eligible for angioplasty were analyzed. All patients had an angiographically normal coronary artery (Artery 1), one intermediate lesion (Artery 2) and one severe lesion (Artery 3), the latter was treated with angioplasty. In each patient, distal blood flow velocity and pressure were measured during baseline and maximal hyperemia (induced by i.c. adenosine), using a Doppler and pressure guidewire, respectively. The ratio of mean distal pressure to average peak blood flow velocity was used as an index for the microvascular resistance (MRv). The MRv was significantly lower during hyperemia as compared to baseline conditions for all three vessels (median values for: Artery 1, 1.7 versus 6.5, \( p < 0.001 \); Artery 2, 2.1 versus 6.4, \( p < 0.001 \); Artery 3, 2.6 versus 4.9, \( p < 0.001 \); respectively). A statistically significant difference was found between the hyperemic MRv of the different arteries (Page test: Z score 2.041; \( p = 0.021 \)). After angioplasty, the hyperemic MRv decreased towards the value of the reference artery (pre PTCA, 2.6 vs. post PTCA, 1.9, \( p < 0.01 \)).

Conclusions
There is a positive association between coronary lesion severity and variability of distal microvascular resistance that normalizes after angioplasty. This study challenges the concept of uniform distribution of microvascular resistance that is relevant for the interpretation of both non-invasive and invasive diagnostic tests.
INTRODUCTION

In recent years, research on the clinical aspects of the coronary microcirculation has made substantial advances, due to developments in non-invasive and invasive diagnostic techniques. [1] It has been proposed that the severity of coronary artery disease can be more accurately described by maximal flow capacity and coronary flow reserve, rather than angiographic findings. [2] Apart from stenosis characteristics, these indices are influenced by the behaviour of the downstream microvascular resistance. [3] It is unknown whether this resistance depends on the epicardial stenosis degree.

Several intracoronary derived physiological parameters have been introduced to characterize functional stenosis severity in patients with coronary artery disease, allowing clinical decision-making during cardiac catheterization. These parameters are based on intracoronary pressure measurements (fractional flow reserve, FFR) or intracoronary derived Doppler flow velocity measurements (coronary flow velocity reserve, CFVR). [4] Recently, we have shown that variability in microvascular resistance between patients is responsible for discordant results between FFR and CFVR. [8] High microvascular resistance was associated with a low CFVR and a high FFR, while a low microvascular resistance was associated with a high CFVR and low FFR in patients with intermediate coronary lesions. Furthermore, homogeneity in the behavior of the myocardial resistance beds of the major perfusion areas within the same heart is assumed. This is of importance for the concept of relative CFVR. This assumption conflicts with the heterogeneity of myocardial blood flow found in different coronary perfusion areas in healthy volunteers. [5] Recently, a paradoxical increase of microvascular resistance downstream of a severe coronary narrowing during tachycardia was reported, that was abolished after angioplasty. [6] These findings challenge the concept that microvascular resistance is uniformly distributed that is a generally accepted assumption for the interpretation of non-invasive diagnostic stress tests. The ratio of mean distal pressure to average peak blood flow velocity can be used as an index of microvascular resistance (MRv). [7, 8] The purpose of this study was to investigate the influence of epicardial stenosis on the resistance of the downstream microcirculation assessed by intracoronary derived pressure and Doppler flow velocity measurements in patients with coronary artery disease.

METHODS

Study population

Patients with two-vessel coronary artery disease and angina (class 1-4 according to the Canadian Cardiovascular Society; CCS) were eligible for inclusion in this study. All patients were referred to our center for a PTCA procedure. Both intracoronary pressure and Doppler
flow velocity data were obtained in all three main coronary arteries. Exclusion criteria were: factors precluding assessment of intracoronary measurements (e.g. occlusions, coronary anatomy); factors influencing coronary hemodynamic parameters (insulin dependent diabetes, Q-wave myocardial infarction, previous coronary bypass grafting, left ventricular hypertrophy, moderate or severe left ventricular dysfunction, severe valvular heart disease).

**Study protocol**

Twenty-seven patients underwent routine coronary angiography, during which intracoronary measurements were performed. Coronary lesion severity was determined by quantitative coronary angiography (QCA). Main coronary arteries (i.e. right coronary artery, RCA; left anterior descending coronary artery, LAD; and the left circumflex artery, LCx) were functionally divided per patient into: an angiographically normal reference artery (Artery 1); an artery with the less severe narrowing (Artery 2); and an artery with the more severe narrowing (Artery 3). Thus, measurements in each artery represented a different myocardial perfusion area. Flow velocity and pressure were measured sequentially distal to the coronary narrowings, and in the reference artery in all patients. Furthermore, all lesions in Artery 3 (with a severe coronary narrowing) were treated with PTCA; Doppler flow measurements were repeated afterwards. The Medical Ethics Committee of our institution approved the study protocol; all patients gave written informed consent.

**Quantitative coronary angiography (QCA)**

Coronary angiography was performed according to standard procedure, as previously described. [9] Coronary lesion severity was measured by QCA, using the CMS-QCA software version 3.32 (MEDIS, Leiden, The Netherlands). [10] Coronary lesion severity was expressed as the percent diameter stenosis (%DS) and minimal lumen diameter (in mm; MLD) using an automated contour detection algorithm, and the reference diameter were measured (in mm). Coronary lesion severity was assessed on an end-diastolic frame in two, if possible, orthogonal views. The projection showing the most severe coronary narrowing in %DS was used.

**Intracoronary hemodynamic measurements**

Measurements were performed in all patients in the LAD, LCx and RCA. An intracoronary bolus of 0.1 mg nitroglycerin was administered every 30 minutes to ensure maximal epicardial vasodilation. All measurements were performed at baseline and during hyperemia, and repeated to assess variability of the pressure and flow velocity measurements. Hyperemia was induced by administering an intracoronary bolus of adenosine (15 µg in the right coronary artery and 20 µg in the left coronary artery).

Translesional blood flow velocity was measured with a 0.014-in Doppler guidewire (FloWire®, JOMED, Rancho Cordova, CA). The Doppler guidewire was advanced distal to the stenosis; care
was taken to avoid post-stenotic turbulent flow and the distal tip was not placed adjacent to side branches. Distal baseline and hyperemic blood flow velocity data were obtained and a real time spectral analyzer processed the Doppler signals. [11]

Intracoronary pressure was measured with a 0.014" pressure guide wire, connected to the pressure console (RAI Medical Systems, Uppsala, Sweden). After calibration with the pressure console, the accuracy of the signal was verified using the aortic pressure as measured through the guiding catheter. The wire was advanced with the pressure sensor at least 3 cm distal to the lesion. No pressure wire was introduced in the reference vessels and post PTCA; the pressure as measured through the guiding catheter was used to calculate the MRv.

An index of minimal microvascular resistance (in mmHg/cm/sec) during baseline (b-MRv) and maximum hyperemia (h-MRv) was defined as the ratio of mean distal pressure to average peak blood flow velocity. [8] Pressure and blood flow velocity data were obtained sequentially using two guidewires. The ability of the resistance vessels to dilate under maximal hyperemic conditions was expressed as b-MRv minus h-MRv; this ability was also expressed as a percentage of baseline.

The coronary circulation was modeled as a series of three of resistances, each reflecting a certain behavior: the stenosis resistance (Rs) in the epicardial conduit artery, the variable arteriolar resistance vessels (Rres), and the minimal microvascular resistance (Rmin) present during maximal hyperemia. [12] By definition, the microvascular resistance is defined as the sum of the 2 resistances present distal of an epicardial coronary narrowing. Therefore, as indicated in Figure 1, b-MRv represents the sum of the latter two, whereas h-MRv is minimum microvascular resistance during hyperemia (assuming that the resistance vessels are maximally dilated), and thus, b-MRv - h-MRv represents the resistance vessels during baseline conditions.

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**Figure 1** Model of the coronary circulation with 3 resistances each reflecting a certain behavior: the stenosis resistance (Rs), the variable arteriolar resistance vessels (Rres), and the minimal microvascular resistance (Rmin).

See text for explanation of different MRv values. Pa and Pv refers to the arterial and venous pressure, respectively. Q indicates the flow.
Statistical considerations

Data were expressed as mean ± standard deviation (SD). Skewed data distributions were presented as median and range, and non-parametric statistical tests were performed: the Wilcoxon signed ranks test was used for paired comparisons within patients, i.e. comparison of baseline and hyperemic MR\textsubscript{V} values in all 3 arteries, and pre PTCA and post PTCA comparison of MR\textsubscript{V} in Artery 3. The Page test for ordered alternatives [13] was applied to compare the MR\textsubscript{V} value for the three different perfusion areas within patients, based on their division in Artery 1, Artery 2, and Artery 3. Data analysis was performed using the SPSS 10.0.5 software package for Windows (SPSS Inc. 1999, Arlington, VA). A p-value of less than 0.05 was considered statistically significant.

RESULTS

Study population and QCA results

The baseline characteristics of the 27 patients are depicted in Table 1. The division of RCA/LAD/LCx was 2/7/18 for Artery 1, 11/11/5 for Artery 2, and 14/9/4 for Artery 3, respectively. In Figure 2, the classification in perfusion areas is expressed in terms of %DS, MLD and diameter of the reference locations. The stenosis degree was most severe in Artery 3, as illustrated by QCA analysis: median diameter stenosis for Artery 1 was 16% (range: 7-35%); for Artery 2, 54% (range: 39-68%), and for Artery 3, 70% (range: 54-85%). It should be noted that there was some overlap in stenosis degree, especially between Artery 2 and Artery 3, because the most severe lesion of one heart (per definition in Artery 3) may be comparable in severity with a stenosis in Artery 2 of a different heart. There was no difference between the average diameters of the reference locations between the three groups (median reference diameter: 2.90, 2.76, and 2.94 mm, respectively) and therefore the groups are not differentiated by this parameter. Accordingly, the MLD significantly decreased from Artery 1 to Artery 2 to Artery 3 (median MLD: 2.33, 1.37, and 0.85 mm, respectively).
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Table 1 Baseline Characteristics of the 27 Patients.

<table>
<thead>
<tr>
<th>Patients</th>
<th>Male</th>
<th>18 (67%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age in years (range)</td>
<td>62 (43-78)</td>
<td></td>
</tr>
<tr>
<td>History</td>
<td>Previous MI</td>
<td>10 (37%)</td>
</tr>
<tr>
<td></td>
<td>Previous PTCA</td>
<td>4 (15%)</td>
</tr>
<tr>
<td>Risk factors</td>
<td>Smoking</td>
<td>20 (74%)</td>
</tr>
<tr>
<td></td>
<td>Hypertension</td>
<td>10 (37%)</td>
</tr>
<tr>
<td></td>
<td>Hypercholesterolaemia</td>
<td>18 (67%)</td>
</tr>
<tr>
<td></td>
<td>Non-insulin dependent diabetes mellitus</td>
<td>3 (11%)</td>
</tr>
<tr>
<td></td>
<td>Positive family history</td>
<td>17 (63%)</td>
</tr>
<tr>
<td>Medication</td>
<td>Beta-blockers</td>
<td>23 (85%)</td>
</tr>
<tr>
<td></td>
<td>Calcium-antagonists</td>
<td>11 (41%)</td>
</tr>
<tr>
<td></td>
<td>Nitrates</td>
<td>20 (74%)</td>
</tr>
<tr>
<td></td>
<td>Lipid lowering</td>
<td>18 (67%)</td>
</tr>
<tr>
<td>Anginal complaints</td>
<td>CCS class 2</td>
<td>7 (26%)</td>
</tr>
<tr>
<td></td>
<td>CCS class 3</td>
<td>13 (48%)</td>
</tr>
<tr>
<td></td>
<td>CCS class 4</td>
<td>7 (26%)</td>
</tr>
</tbody>
</table>

Data are expressed as n (%). CCS = Canadian Cardiovascular Society; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty.

Microvascular resistance index (MRv)

Hemodynamic data of all patients during baseline and hyperemic conditions are summarized in Table 2. Variability of the repeated measurements of the indices was 2-5% for pressure, 8-10% for Doppler flow velocity measurements and 7-13% for the hyperemic MRv. The MRv was significantly lower during hyperemia as compared to baseline conditions for all three vessels (median values for: Artery 1, 1.69 versus 6.50, p < 0.001; Artery 2, 2.08 versus 6.38, p < 0.001; Artery 3, 2.56 versus 4.94, p < 0.001; respectively). The mean ability of resistance vessels (expressed as percentage decrease of baseline value) to reduce microvascular resistance during maximal hyperemia was for Artery 1: 74 %, for Artery 2: 67 %, and for Artery 3: 48 %. MRv data for Artery 2 and Artery 3 are compared to those of the respective Artery 1 in Figure 3. No significant trend was detected between the baseline MRv of the three arteries (Page test: Z score -1.225; p = 0.1093). However, it can be appreciated that the b-MRv of Artery 3 is lower than for Artery 1 (p = 0.078) and for Artery 2 (p = 0.022) [Figure 3a]. In contrast, a statistically significant difference was found between the hyperemic MRv’s of the different arteries (Page test: Z score 2.041; p = 0.0207), which was confirmed by pair wise comparisons [Figure 3b]; h-MRv of Artery 3 is significantly higher than the h-MRv of Artery 1 (p = 0.001) and Artery 2 (p = 0.029). The difference between b-MRv and h-MRv, representing the resistance of the arte-
Figure 2 Box-Whisker plots of QCA data of the 3 Arteries. * p < 0.0001, † p = 0.5
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rioles at baseline ($R_{res}$), was significantly higher for Artery 1 and Artery 2 than for Artery 3 (Page test: Z score -3.402; $p < 0.0001$), which was confirmed by pair wise comparisons ($b$-$MR_v - h$-$MR_v$ of Artery 3 is significant lower than for Artery 1 ($p = 0.001$) and for Artery 2 ($p = 0.001$), as illustrated in Figure 3c). Hence, the effect of the compensatory vasodilatation at baseline induced by the pressure drop resulting from a stenosis was noticeable in this patient group. Furthermore, from Figures 3a, 3b and 3c it can be appreciated that the frequency distributions of the resistances in the different perfusion areas show a considerable variation within each group but also between groups at the same conditions of baseline versus hyperemia.

**MRv pre and post PTCA**

All lesions in Artery 3 underwent a PTCA procedure. In 2 patients, no flow velocity measurements were performed post PTCA because the PTCA procedure was not successful. Therefore, the MRv post PTCA of Artery 3 was calculated in 25 patients (93%). The median MRv value declined from 2.56 pre PTCA to 1.85 post PTCA ($p < 0.009$). In total, 19 out of 25 patients (76%) showed a decline of the MRv. There was no statistical difference between the MRv value of Artery 1 and post PTCA in Artery 3 (median value 1.69 and 1.85, respectively; $p = 0.671$, suggesting that treating the epicardial stenosis influences the microvascular resistance.

**DISCUSSION**

This study demonstrates that there was a statistical significant increase of hyperemic MRv of diseased arteries. The severity of coronary artery disease was associated with significantly higher values of the hyperemic microvascular resistance that normalized after angioplasty of the epicardial narrowing. Hence, coronary artery disease not only induces a reduction of tone at baseline, as is to be expected from a normal physiological response, but also increases the hyperemic microvascular resistance. Furthermore, this study showed that a large heterogeneity of microvascular resistance was present between different perfusion areas in patients with coronary artery disease.

**Relation between severity of coronary artery disease and microvascular resistance**

The present results demonstrate that minimal microvascular resistance is higher distal to hemodynamically significant stenosis in comparison with vessels without stenosis in the same patient. These results are in accordance with the work of Sambuceti and others, who found also a paradoxical increase in microvascular resistance during tachycardia downstream from a severe stenosis in patients with coronary artery disease that was reversed by angioplasty. [6] Several explanations for the higher h-MRv distally of epicardial narrowings are possible. First, we hypothesize that the pressure dependence of the microvascular resistance vessels could play a
It is obvious that the distal pressure depends on the severity of coronary narrowing in the epicardial conduit artery [see Table 2]. A higher MRV can be explained by a paradoxical vasoconstriction as a result of passive collapse of larger sized (> 100 μm) arterial microvessels due to reduced distending pressure. This suggestion is supported by the effect of angioplasty, resulting in MRV values that did not significantly differ from values in the reference vessels without focal coronary narrowings (Artery 1). Second, regional differences of the extent of atherosclerotic disease can be present within the coronary artery tree. The observed increased hyperemic microvascular resistance distal to severe narrowings may be due to more extensive diffuse atherosclerotic disease, in contrast to an angiographically normal artery. Finally, it has been suggested that several growth factors (e.g., endothelin, heparin, fibroblast growth factor) may influence vascular tone, resulting in spatial heterogeneity. Further research is mandatory to elucidate the underlying mechanism.

Table 2 Physiological Data of all Patients (n = 27) During Baseline and Hyperemic Conditions.

<table>
<thead>
<tr>
<th>Artery</th>
<th>Parameter</th>
<th>Median</th>
<th>(range)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Baseline</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Artery 1</td>
<td>$P_d$</td>
<td>87'</td>
<td>(67-128)</td>
</tr>
<tr>
<td></td>
<td>APV</td>
<td>18.0</td>
<td>(5.6-26.0)</td>
</tr>
<tr>
<td></td>
<td>MRV</td>
<td>6.50</td>
<td>(3.32-13.21)</td>
</tr>
<tr>
<td>Artery 2</td>
<td>$P_d$</td>
<td>91'</td>
<td>(65-113)</td>
</tr>
<tr>
<td></td>
<td>APV</td>
<td>15.0</td>
<td>(4.3-40.0)</td>
</tr>
<tr>
<td></td>
<td>MRV</td>
<td>6.38</td>
<td>(6.68-17.91)</td>
</tr>
<tr>
<td>Artery 3</td>
<td>$P_d$</td>
<td>71'</td>
<td>(23-118)</td>
</tr>
<tr>
<td></td>
<td>APV</td>
<td>14.0</td>
<td>(7.5-37.0)</td>
</tr>
<tr>
<td></td>
<td>MRV</td>
<td>4.94</td>
<td>(2.21-9.10)</td>
</tr>
<tr>
<td><strong>Hyperemia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Artery 1</td>
<td>$P_d$</td>
<td>84'</td>
<td>(62-118)</td>
</tr>
<tr>
<td></td>
<td>APV</td>
<td>49.0**</td>
<td>(25.0-84.0)</td>
</tr>
<tr>
<td></td>
<td>MRV</td>
<td>1.69**</td>
<td>(0.94-3.16)</td>
</tr>
<tr>
<td>Artery 2</td>
<td>$P_d$</td>
<td>78'</td>
<td>(47-102)</td>
</tr>
<tr>
<td></td>
<td>APV</td>
<td>37.0**</td>
<td>(17.0-76.0)</td>
</tr>
<tr>
<td></td>
<td>MRV</td>
<td>2.08**</td>
<td>(0.85-4.24)</td>
</tr>
<tr>
<td>Artery 3</td>
<td>$P_d$</td>
<td>46'</td>
<td>(20-107)</td>
</tr>
<tr>
<td></td>
<td>APV</td>
<td>21.0**</td>
<td>(9.0-56.0)</td>
</tr>
<tr>
<td></td>
<td>MRV</td>
<td>2.56**</td>
<td>(0.75-4.67)</td>
</tr>
</tbody>
</table>

* * p < 0.0001 (Page test from Artery 1 to Artery 2 to Artery 3), * p < 0.05 as compared to baseline value $P_d$ = distal pressure (mm Hg); APV = average peak velocity (cm/sec); MRV = microvascular resistance index (mmHg/cm/sec).
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Figure 3 Results of MR_v depicted per vessel. First, Box-Whisker plots are shown (left panel; top and bottom of box: 25th and 75th percentile; horizontal line in box: median). Individual data are plotted in the right panel; for each measured MR_v in the reference vessel (Artery 1) (x-axis), the MR_v in both Artery 2 and Artery 3 are depicted for the same heart (n = 27), the line of identity is shown.

(A) There was no significant decrease of the of the b-MR_v from Artery 1-Artery 2-Artery 3 (p = 0.1093). There was no significant deviation of the line of identity for the b-MR_v values of both Artery 2 and Artery 3.

(B) There was a significant increase in the h-MR_v from Artery 1-Artery 2-Artery 3 (p = 0.021). The h-MR_v values of Artery 3 were significantly higher than the line of identity (mean difference value -0.71, 95% CI: -1.03, -0.38, p < 0.025).

(C) There was a significant decrease in the b-MR_v minus h-MR_v (representing R_{res}) from Artery 1-Artery 2-Artery 3 (p < 0.0001). The values of Artery 3 were significantly lower than the line of identity (mean difference value 1.49, 95% CI: 1.76, 2.22, p < 0.025).
Spatial heterogeneity of the resistance in the coronary microcirculation

The present study showed spatial heterogeneity of the microvascular resistance index during hyperemic conditions [see Figure 3b], representing Rmin. Despite the large variability between the groups, the h-MRv downstream of the most severely diseased vessel (Artery 3) was demonstrated to be significantly higher. This suggests that the differences in h-MRv are modulated by the pressure changes as a result of epicardial coronary artery disease. This finding is independent of the autoregulatory mechanism that acts solely on the Rres, represented by b-MRv - h-MRv, whose value was lower in the narrowed arteries [Figure 3c]. These results are important in view of the concepts of intracoronary derived hemodynamic parameters that assume homogeneity in the behavior of the myocardial resistance beds of the major perfusion areas within the same heart.

Comparison with other studies

In 1990, a study in dogs found that coronary flow reserve is spatially heterogeneous and determined by two distinct perfusion patterns: the resting (control) pattern and the maximal perfusion pattern. Normal hearts, therefore, contain small regions that may be relatively more vulnerable to ischemia. This may explain the patchy nature of infarction with hypoxia and at reduced perfusion pressures as well as the difficulty of using global parameters to predict regional ischemia. [18]

Recently, Chareonthaitawee et al. showed that there is variability of myocardial blood flow as measured with PET, both between and within 169 healthy volunteers. [5] They demonstrated spatial flow heterogeneity between four perfusion regions (anterior, septal, inferior and lateral) within each individual during hyperemic conditions. These data are in accordance with previous reports [19] and our results, obtained in patients with multivessel coronary artery disease.

Limitations

Flow velocity and pressure were sequentially measured after exchanging the Flowire for the pressure wire. No significant hemodynamic changes in blood pressure and heart rate occurred between the measurements. For practical reasons, we used the aortic pressure as measured through the guiding catheter to determine MRv in the reference vessel and post PTCA in Artery 3. However, an apparently angiographically normal reference artery does not exclude presence of atherosclerotic disease. [20] Our QCA data showed a median diameter stenosis of 16% in the reference vessels. It was suggested that a decline in pressure might be present in these diffusely diseased vessels without a focal stenosis. [21, 22] It was demonstrated that this decline is most likely no more than 0.12-0.25 mmHg per cm during maximal hyperemia. [23, 24] Therefore, it is conceivable that this limitation of the protocol did not influence the main conclusions, drawn from this study.
We used a Doppler guidewire to assess blood flow velocity in the three coronary arteries, whereas coronary blood flow may be dependent on arterial dimensions. All patients received an intracoronary bolus of 0.1 mg nitroglycerine, and thus, epicardial vessel diameters were maximally dilated and remained constant throughout the procedure. Variability’s in flow velocity and pressure measurements may contribute to the found heterogeneity in h-MR. However, this variability varies between 2-5% for pressure, 8-10% for flow velocity measurements and 7-13% for the hyperemic MR. This indicates that the observed heterogeneity in h-MR cannot be explained by the variability of the pressure or flow velocity measurements.

Although no visible collaterals were present in these patients (according to Rentrop classification), we cannot exclude a confounding effect of recruitable collateral flow, especially in areas supplied by the severely narrowed coronary arteries.

**Clinical implications**

For clinical practice, the fact that the spatial heterogeneity in MR exists during hyperemia indicates that the role of relative CFVR for patient management is of limited value considering the more extensive acquisition requirements (both stenotic and reference vessel must be instrumented with a Doppler guidewire), since homogeneity of microvascular resistances in the adjacent perfusion regions is a prerequisite for this index. In addition to previous reports[5], these findings are also relevant for the interpretation of the results of regional myocardial perfusion for all stress test modalities using imaging techniques in this patient cohort that warrants testing in a direct comparative study.

Our results provide novel insight into the dynamic behavior of the coronary microcirculation in the presence of epicardial narrowings that is relevant for the interpretation of diagnostic non-invasive and invasive tests as well as the evaluation of pharmacological or mechanical coronary interventions.
REFERENCES


