

CMR AND OTHER IMAGING MODALITIES

Adjunctive role of cardiovascular magnetic resonance in the assessment of patients with inferior attenuation on myocardial perfusion SPECT

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Purpose: Inferior attenuation is a common problem in the interpretation of myocardial perfusion SPECT. We explored whether cardiovascular magnetic resonance (CMR) was a useful adjunct in differentiating between artifactual attenuation of the inferior wall and the presence of myocardial infarction and/or ischemia. **Methods:** We used CMR to assess resting wall motion, myocardial perfusion, and the presence of infarction with late gadolinium enhancement in 30 patients with presumed inferior attenuation on ungated myocardial perfusion SPECT, but where uncertainty was present over interpretation of the inferior wall. Perfusion CMR was analyzed visually and quantitatively. **Results:** In 23 patients (77%), CMR excluded infarction or ischemia in the inferior wall. The myocardial perfusion reserve index (MPR_I) was the same in the inferior and remote myocardium (1.74 ± 0.43 vs. 1.77 ± 0.50 , $p = 0.61$). Coronary angiography was performed in 11 of these patients, and was normal in all cases. In the remaining seven subjects (23%), significant abnormality was detected by CMR (infarction, 5; wall motion abnormality, 3; perfusion defect, 5). In these patients, the MPR_I was reduced in the inferior myocardium compared with remote (1.07 ± 0.19 vs. 1.74 ± 0.49 , $p = 0.04$). Coronary angiography was performed in three of these patients, revealing significant coronary disease in the artery supplying the inferior territory in all patients. **Conclusion:** Approximately one-quarter of patients with inferior attenuation on ungated, nonattenuation corrected myocardial perfusion SPECT have abnormalities on CMR. CMR can readily distinguish between artifact, ischemia, and infarction in these cases and in some cases might obviate the need for diagnostic coronary angiography.

Key Words: Magnetic resonance imaging; Inferior attenuation; Nuclear medicine; Artifact

1. Introduction

Attenuation artifacts in myocardial perfusion SPECT, in particular inferior wall attenuation, can lead to diagnostic uncertainty. Inferior attenuation is the result of the blood pool and other soft tissue between the camera and the inferior myocardium, and may be exaggerated depending on the shape of the chest wall, and the position and shape of the diaphragm (1, 2). Inferior attenuation is more common in males, with inferior wall counts typically up to 30% lower than the anterior wall (3). However, in one study, the investigators showed that males with a flat, wide chest as assessed

on chest films, were also prone to inferior myocardial attenuation irrespective of the characteristics of the diaphragm (4). The adverse effect on the diagnostic accuracy of myocardial perfusion SPECT has led to many adaptations in the acquisition, postprocessing, and interpretation of images, all aimed at minimizing the effects of attenuation (5, 6).

The technetium-based perfusion tracers emit higher energy photons than thallium, and these are less susceptible to attenuation. ECG-gated imaging is also useful because of the simultaneous assessment of myocardial motion and thickening (5, 7). This aids the distinction between attenuation artifact and myocardial infarction (8, 9), but the resolution of the technique remains insufficient to reliably visualize limited subendocardial infarctions (10). These may not be associated with wall motion abnormality if the distribution is less than 25% of the transmural extent (11). In addition, the technetium perfusion agents may lead to additional difficulty in interpreting the inferior wall because of high counts from subdiaphragmatic structures such as the liver and intestine.

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More recently, methods of correcting for attenuation and other artifacts have become available. Attenuation and scatter correction increases specificity without significantly affecting sensitivity (6, 12, 13), but the techniques are not perfect. Hendel et al. showed higher normalcy with attenuation and scatter correction, but reduced sensitivity for disease of the right coronary artery and multivessel disease (12). More recently, Links et al. showed a similar improvement in overall sensitivity and specificity without affecting sensitivity for multivessel disease (13). Therefore, the value of attenuation correction and its limitations remain an area of debate. Certainly an understanding of the range of normal appearances for a given system and a confidence in the robustness of the attenuation correction methods employed is needed (14).

The purpose of this study was to explore whether cardiovascular magnetic resonance (CMR) of myocardial perfusion, wall motion, and late gadolinium enhancement performed as a single scan might clarify the diagnosis in patients with inferior attenuation, potentially avoiding the need for invasive investigations.

2. Methods

2.1. Patients

We studied 30 consecutive male subjects (mean age 60 ± 13 years) who had been reported to have inferior attenuation on routine ungated myocardial perfusion SPECT, which was sufficiently marked to raise clinical doubt in the reporting of the scan. CMR was performed at a mean of 4 ± 3 months after scintigraphy, and there were no clinical events in the intervening period. Informed, written consent was obtained and the study was approved by the institutional ethics committee. The only exclusion criteria were those pertinent to CMR safety, such as the presence of a pacemaker.

2.2. Myocardial perfusion SPECT

All patients received adenosine stress (140 ug/kg/min) for 6 minutes combined with bicycle exercise ranging from 0 to 75 watts according to capability, as previously validated at our institution (15). Thallium (80 MBq) was given to 25 patients with immediate stress imaging and 4-hour redistribution imaging, and five received a technetium labeled perfusion tracer using a 1-day stress/rest protocol with $250 \text{ MBq}/750 \text{ MBq}$ of tracer and imaging 30 to 60 minutes after injection. Imaging was performed using a dual-headed gamma camera with the heads at 90° (Optima, GE Medical Systems, Milwaukee, IL). Sixty-four projections were acquired over 180° from right anterior oblique to left posterior oblique with 20 seconds per projection. Tomograms were reconstructed in vertical and horizontal long-axis planes and in the short-axis plane.

2.3. SPECT analysis

The presence and severity of inferior attenuation was assessed visually by two independent observers using a nine-segment model of the left ventricle (15). Tracer uptake in each segment was graded using a five-point scale with reference to regions of maximum uptake (0 = absent, $< 10\%$; 1 = severely reduced, $11\text{--}30\%$; 2 = moderately reduced, $31\text{--}50\%$; 3 = mildly reduced, $51\text{--}70\%$; and 4 = normal, $> 70\%$). The raw data cines were also viewed for position of the diaphragms or other causes of artifact. When judged to be present, the attenuation artifact was graded as mild, moderate, or severe. The uncertainty in the clinical report to the referring physician was recorded.

2.4. CMR

CMR was performed on a 1.5-T Siemens Sonata scanner (Siemens AG, Erlangen, Germany) using a previously reported technique (16). In brief, first-pass myocardial perfusion imaging was performed using a saturation recovery turbo FLASH (Fast Low Angle Shot) sequence (TE/TR 0.9/1.4 ms, flip angle 8° , saturation recovery time 84 ms, in-plane pixel size approximately $3 \times 3 \text{ mm}$ interpolated to $1.5 \times 1.5 \text{ mm}$, slice thickness 8–10 mm) in three short-axis planes with a full set of three short-axis images acquired every cardiac cycle. Gadolinium-DTPA (Magnevist, Schering AG, Germany) was administered using a power injector (Medrad Spectris) in an antecubital vein at 0.1 mmol/kg at 3 mL/s . Rest perfusion was performed first, and the adenosine stress study was performed after 15–20 minutes. Resting wall motion was assessed for each perfusion short-axis slice using an 8 second breath-hold TrueFISP cine sequence (TE/TR 1.6/3.2 ms, flip angle 60° , in-plane pixel size approximately $1.5 \times 2 \text{ mm}$, slice thickness 7 mm, temporal resolution 40–60 ms). Late gadolinium enhancement imaging was performed in the same three short-axis slice positions used for perfusion and in vertical and horizontal long-axis views using a 2-D inversion recovery gradient echo sequence. Imaging was started 10 minutes after the administration of gadolinium-DTPA with sequence parameters; TE 4 ms, TR 450 ms, flip angle 20° , segmentation 17 to 23, trigger 2 to 3 depending on the RR interval, and average in-plane pixel size of $1.6 \times 1.4 \text{ mm}$ and slice thickness 8 mm. Inversion times were adjusted to null the normal myocardium and ranged from 300–420 ms.

2.5. CMR analysis

Rest and stress first-pass perfusion images were analyzed visually by two experienced observers using the same nine-segment analysis used for SPECT. This was followed by quantitative analysis of perfusion using dedicated software (CMRtools, Cardiovascular Imaging Solutions, London, UK). The analysis of perfusion CMR has been described elsewhere

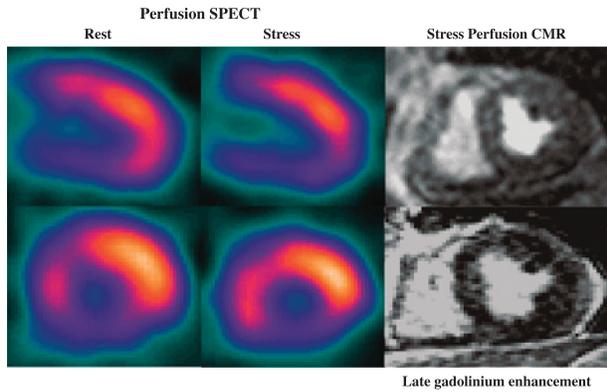


Figure 1. The myocardial perfusion SPECT study (left panels) shows a moderate fixed inferior defect and could not exclude partial thickness inferior infarction in this patient with previous LAD stenting. The stress perfusion CMR and late gadolinium enhancement scans were normal (right panel). Subsequent angiography confirmed a patient LAD stent and no evidence of coronary disease in the right coronary or circumflex arteries.

(17–19); in brief, the maximum slope in myocardial signal intensity during the first pass of gadolinium was measured, this was divided by the maximum slope of the signal in the left ventricular blood pool, which serves as an input function. This parameter is termed the myocardial perfusion index (MP_I). When this is repeated at rest and stress, the ratio is termed the myocardial perfusion reserve index (MPR_I). The inferior LV wall was compared with remote myocardium that was normal by SPECT and CMR. In two patients with a previous LAD stent, the basal lateral wall was used as the remote myocardium. Wall motion in each segment was assessed by two experienced observers using a five-point scale of 4 = dyskinesia, 3 = akinesia, 2 = severe hypokinesia,

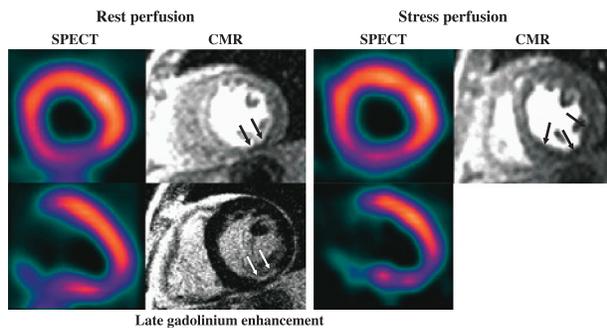


Figure 2. Comparison of rest (left panel) and stress (right panel) perfusion images in the same patient using myocardial perfusion SPECT and CMR. There is a moderate, fixed, inferior defect with SPECT. CMR shows reduced resting perfusion in the basal and mid-inferolateral wall with a larger area of abnormality during stress (arrows). Late gadolinium enhancement CMR shows inferior subendocardial infarction corresponding to the resting hypoperfusion on first-pass imaging (arrows). Subsequent coronary angiography showed an 80% stenosis of a dominant left circumflex artery.

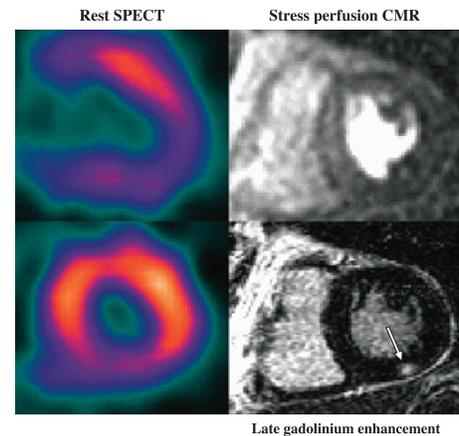


Figure 3. This patient had previously undergone angioplasty and stenting of the left anterior descending artery, and on repeat angiography there was no re-stenosis or other significant disease. Rest myocardial perfusion SPECT shows a moderate fixed inferior and apical defect, but no abnormality of the stress perfusion CMR. There is a small area of gadolinium enhancement, however (lower right), which may be due to previous infarction related to a recanalized coronary artery, embolic phenomena, or thrombus that could not be visualized angiographically.

1 = mild to moderate hypokinesia, and 0 = normal. Gadolinium uptake in each segment was noted as present or absent and the transmural extent measured. The average scan duration was 50 ± 6 minutes.

2.6. Statistics

All numerical values are given as mean \pm standard deviation. Comparison of proportions was performed using a chi-squared test. Myocardial perfusion indices for inferior vs. remote myocardial segments in each patient were compared using paired t-tests. The level set for statistical significance was a P value < 0.05 .

3. Results

3.1. Assessment of inferior attenuation with SPECT

Of the 30 patients with inferior attenuation, 19 (63%) had mild fixed inferior wall defects. In six of these patients, the clinical report indicated that partial thickness inferior infarction could not be excluded, and in the others, the reduction in counts was simply noted as being most likely due to inferior attenuation. In the remaining 11 patients, eight (27% of the total population) had moderate reduction in inferior wall counts (two with mild reversibility at rest), and three (10%) had severe reduction in counts. In seven of these 11 patients, the clinical report did not exclude partial thickness infarction as an explanation for the inferior wall appearance.

3.2. Coronary angiography

Invasive coronary angiography was performed in 14 patients for clinical indications. In 11 cases, angiography was normal, and in all these cases CMR was normal. Coronary disease (> 50% stenosis) was present in three cases, and CMR was abnormal in all three cases.

3.3. CMR Analysis

In 23 of the 30 patients (77%), CMR showed normal perfusion and wall motion of the inferior wall, with no late gadolinium enhancement. Of these patients, two had severe attenuation on scintigraphy (Fig. 1), and two had mild defect reversibility.

Seven of the 30 patients (23%) had an abnormality of the inferior wall by CMR. In three patients, there were combined perfusion and wall motion abnormalities, with subendocardial basal and mid inferior wall late gadolinium enhancement, indicating subendocardial infarction. In two of these three patients, there was additional inducible inferior wall ischaemia (Fig. 2), and subsequent coronary angiography revealed an 80% stenosis in a dominant left circumflex artery in one case and a 70% mid-right coronary artery stenosis in the other. In the third patient there was inducible anterior wall subendocardial ischemia in addition to the subendocardial inferior infarction. This patient had a 70% stenosis of the mid-left anterior descending artery and mild disease of both the right coronary and left circumflex arteries.

In two patients, there was a CMR stress perfusion abnormality. Gadolinium enhancement was absent in one patient, but present in the other but without wall motion abnormality. These two patients were clinically stable and have not undergone angiography.

Finally, there were two patients in which the only abnormality was late gadolinium enhancement. One had enhancement in the posteromedial papillary muscle consistent with fibrosis in the presence of posterior leaflet prolapse of the mitral valve, and the other had a discrete area of subendocardial infarction in the basal inferior wall (Fig. 3). Neither patient had wall motion abnormality.

3.4. CMR—quantitative perfusion analysis

In patients whose perfusion CMR was reported as normal ($n = 25$), there was no significant difference in myocardial perfusion index (MP_I) between the inferior wall and remote myocardium either at rest (0.11 ± 0.02 vs. 0.12 ± 0.03 , $P = 0.11$) or at stress (0.19 ± 0.05 vs. 0.2 ± 0.06 , $P = 0.12$, respectively). Furthermore, the myocardial perfusion reserve index (MPR_I) was the same between the two regions (1.74 ± 0.43 vs. 1.77 ± 0.50 , $P = 0.61$, respectively).

In the five patients with inferior perfusion defects at rest and/or stress, the MP_I at rest (0.09 ± 0.06 vs. 0.13 ± 0.07 , $p = 0.01$) and stress (0.12 ± 0.08 vs. 0.20 ± 0.1 , $p = 0.02$)

was lower in the inferior wall compared with remote myocardium. In addition, the MPR_I was reduced in the inferior wall (1.07 ± 0.19 vs. 1.74 ± 0.49 , $p = 0.04$).

3.5. Degree of attenuation vs. CMR

There was no difference in the proportion of patients with CMR abnormalities according to the severity of the inferior attenuation (mild inferior attenuation 26% compared with 18% of patients with moderate or severe attenuation, $P = ns$).

4. Discussion

Although the prevalence of attenuation artifacts in SPECT is unknown, it probably occurs in between 20–50% of studies (20, 21), with approximately one half of this being due to inferior attenuation in males, and the majority of the remainder being anterior attenuation in females (5). Doubt caused by such attenuation may lead to further investigation, including coronary angiography. The main finding in this study is that CMR may be useful for resolving doubts arising from inferior attenuation in ungated myocardial perfusion SPECT. We found normal CMR perfusion, wall motion, and no subendocardial infarction in 77% of our patients with inferior attenuation, and 10 patients in this group had normal coronary angiography. Although we do not have information on clinical outcomes, it is reasonable to suggest that this group may not have required coronary angiography as no abnormality was demonstrated by CMR. In 23% of our patients with inferior attenuation however, there were abnormalities on CMR, indicating myocardial ischemia or previous infarction, and all three patients in this group who underwent coronary angiography had significant coronary artery disease. This suggests that abnormal CMR may justifiably increase the likelihood of referral for coronary angiography. Even if angiography were not performed, the abnormalities on CMR would indicate the need for secondary preventive measures such as aspirin and modification of coronary risk factors. In addition to the need to identify ischemia, the accurate assessment of infarction is prognostically important. There is a three to 14 times greater mortality rate in survivors of infarction regardless of whether the infarction was symptomatic or not, or whether it was associated with Q-waves (22, 23). Five of our 30 patients with inferior attenuation were ultimately shown to have inferior infarction and three had subendocardial ischemia.

ECG gating of SPECT studies has helped in the assessment of attenuation artifacts and identification of infarction, but it has limitations. Recently, CMR has shown that 25% of myocardial regions with limited subendocardial infarction on late enhancement gadolinium imaging have normal contraction (24), and such infarctions may not be visualized by SPECT (10). This has been apparent in the nuclear literature as well, since a study to assess infarct size showed that 25%

of patients with infarction documented clinically showed normal SPECT (25). This changing pattern of relation between infarction and wall motion abnormalities may result from the widespread use of aspirin with spontaneous thrombolysis, the successful early use of thrombolytics or angioplasty to achieve early infarct-related artery patency limiting both infarction and remodeling (26).

4.1. Limitations

We did not collect data on the likely causes for the inferior attenuation, and therefore cannot comment on their relation to the severity of the inferior attenuation found, or the CMR findings. Neither gating nor attenuation correction technique was employed for the SPECT, and these have been used to both reduce the incidence of reporting of inferior attenuation and increase diagnostic confidence. However, neither technique is ideal, and SPECT is commonly performed without either or both of these techniques. Additionally, we did not use a quantitative SPECT analysis referenced to a database of regional normal values as is our routine clinical practice at our institution. It is not clear from our observational study as to whether the use of CMR in cases of inferior attenuation would be cost effective, but if coronary angiography could be avoided, this is entirely possible.

5. Conclusion

Perfusion CMR and late gadolinium enhancement imaging are new techniques but comparisons have been good with animal studies (27–29), clinical nuclear, echo, and PET techniques (30–31). Our data suggest that CMR may be helpful when inferior attenuation leads to doubt in the interpretation of myocardial perfusion SPECT for two main reasons: first, CMR images are not influenced by the factors that create attenuation in scintigraphy; and second, the improved resolution allows the identification of subendocardial perfusion defects (16), and infarction (10), not detectable by other techniques. CMR may therefore help in improving diagnostic confidence and preventing the need for invasive angiography in patients with inferior attenuation.

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