REVIEW ARTICLE

MYOCARDIAL DYNAMIC CONTRAST-ENHANCED MR: VASCULAR DISEASES AND BEYOND

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Contrast-enhanced cardiac magnetic resonance imaging allows the evaluation of both myocardial perfusion and myocardial tissue characteristics. This paper reviews different microvascular and non-vascular conditions that can cause abnormal findings on contrast-enhanced myocardial magnetic resonance imaging. Knowledge of their characteristics can avoid misinterpretation and avoid inappropriate referral for further invasive imaging in patients suspected of myocardial vascular disease.

Key-word: Myocardium, MR.

Due to an unprecedented combination of spatial resolution, temporal resolution and tissue contrast differentiating properties, unenhanced magnetic resonance imaging (MRI) is in many instances considered a reference standard for assessment of cardiac morphology, function and mass. Using dynamic and delayed contrast-enhancement techniques after intravenous injection of a T1-shortening contrast agent allows further evaluation of myocardial signal intensity changes, additionally helping to assess myocardial vascular supply and tissue composition. Cardiac dynamic contrast-enhanced magnetic resonance (DCEMR) imaging is as such increasingly used as an alternative technique to nuclear isotope studies in the evaluation of myocardial perfusion (1-3), while late contrast-enhanced MR (LCEMR) imaging has been established as a reference standard in the assessment of myocardial viability (4). Nevertheless, a large number of microvascular and non-vascular diseases are important to recognize, as their may both clinically and on imaging studies mimic vascular diseases that require revascularization. The purpose of this paper is to describe these abnormal myocardial findings on DCEMR, correctly assess their significance, and consequently avoid misinterpretation and incorrect referral for further diagnostic procedures.

Imaging principles and analysis

Electrocardiographically-triggered T1-weighted images are acquired across the heart during the circulation of a bolus of a contrast agent at typical doses of 0.025-0.2 mmol of gadolinium/kg of body weight, injected intravenously at a rate of 2-3 ml/sec. At least three slice positions should be acquired in the left-ventricle's short axis (5). Several saturation recovery images can be obtained within a single heartbeat using fast low-angle spin echo, echo-planar or steady-state free precession acquisition protocols, hereby aided by technical advances such as parallel imaging (6). To lower the threshold for vascular disease detection, data should be acquired after adenosine or dipirydamole administration (stress-DCEMR), with territories supplied by diseased arteries failing to display blood flow increase (the so-called perfusion reserve) under vasodilatation (7).

On DCEMR, normal myocardial enhancement is homogenous and occurs nearly simultaneously with contrast arrival in the epicardial arteries (Fig. 1). Time-resolved signal intensity curves in any region of interest can be extracted from these frames, allowing a semi-quantitative or a quantitative assessment of myocardial blood flow.

A relatively hypointense myocardial area during DCEMR is the elementary abnormal finding, which can be detected either visually or by a observing a defect in the ascending portion of the time-signal intensity curve.

Across the literature, these hypo-intensities are better specified as:

– Showing no spatial variation with time (8, 9);
– Involving the subendocardium, with a variable extent; as coronary obstruction initially decreases blood flow to the subendocardial circulation, only afterwards extending deeper towards the epicardial circulation (10);
– Showing temporal persistence (9, 11-13).

The diagnostic accuracies using these criteria for the diagnosis of significant coronary disease were all above 88% (8-13). Their importance was further stressed by Lubbers et al. (14) who observed a decrease of the interobserver variability with the use of these criteria for the diagnosis of myocardial perfusion abnormalities.

Finally, delayed-enhancement techniques are used for a comprehensive assessment of myocardial vascular disease. Through an inversion pulse, the normal myocardial signal on a T1-weighted sequence is nulled in order to better detect pathological areas where the contrast agent accumulates in excess.

Abnormalities on DCEMR are artefactual until proven otherwise

Meta-analyses have shown variations in sensitivity and specificity of DCEMR in the detection of coronary artery disease requiring revascularization, in the ranges of 88-94%, and 77-85% respectively (15, 16), showing that myocardial revascularization
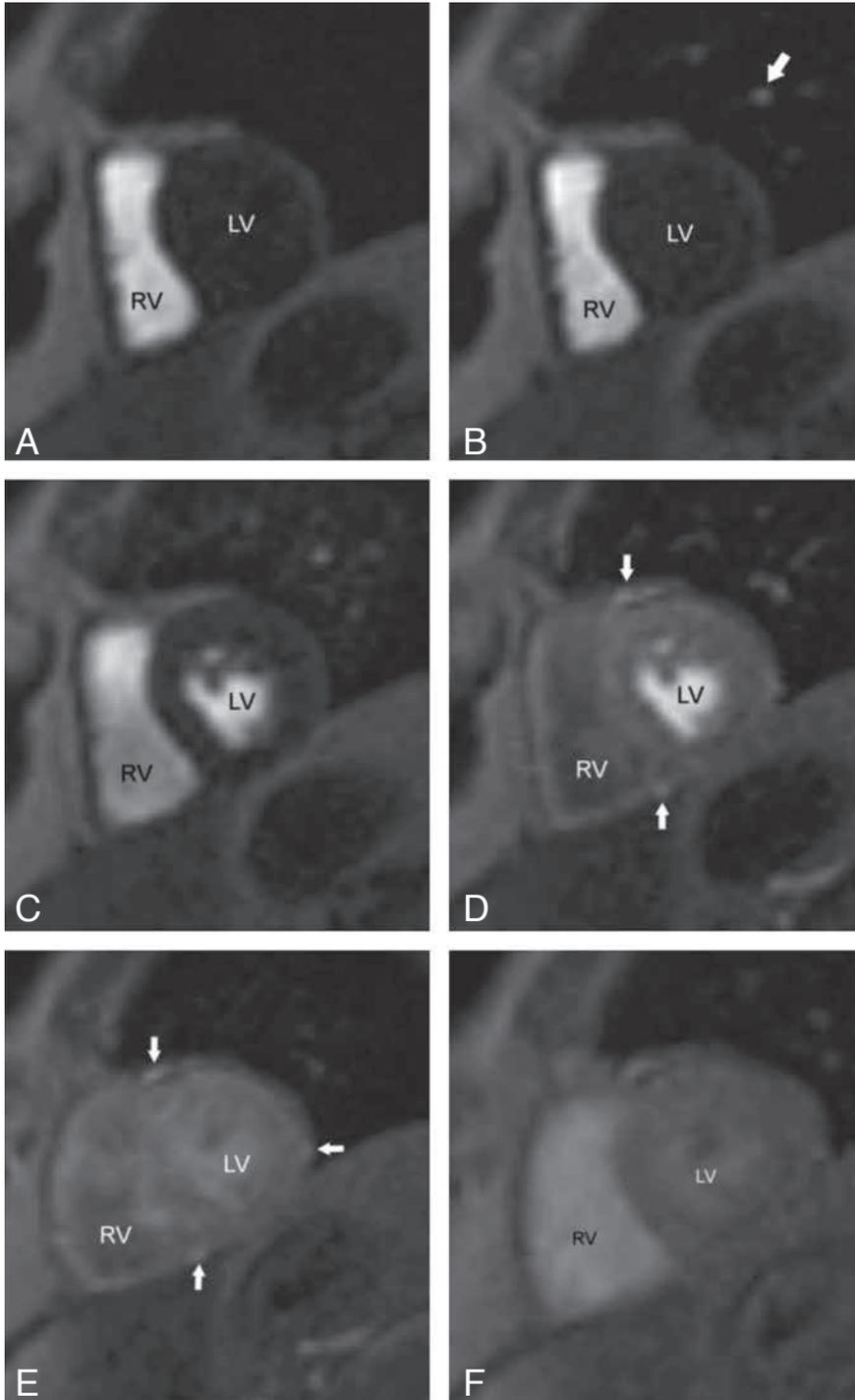
Fig. 1. — Normal findings on DCEMR. On short-axis DCEMR in normal subjects, the contrast agent bolus first arrives into the right ventricle (RV), with a strong enhancement (A). Shortly after, the pulmonary vasculature also becomes enhanced (arrow, B). Then the contrast agent bolus returns to the heart and starts to enhance the left ventricle (LV) chamber (C), with the RV enhancement being progressively washed by the saline flush (D). At this time, the myocardium also begins to enhance progressively, while epicardial vessels may appear in both interventicular grooves and on the posterior and lateral faces of the LV (D, E, arrows). Epicardial vessels visualization is an inconsistent figure, but these vessels appear nearly simultaneously at all locations. The myocardium reaches homogenous enhancement shortly after the LV's peak. Thereafter, all cardiac chambers appear fugaciously at equilibrium enhancement, before the contrast recirculation occurs (F).

solely based on DCEMR findings may actually lack accuracy in some cases.

The main pitfalls of DCEMR are artefacts caused by the technical constraints to produce several images in less than a second. Among these, the so-called "dark-rim artifact" (DRA) or banding artifact is the most challenging. DRA is a generic name for a myocardial rim-like hypointensity that may occur with a subendocardial predominance as a result of multiple causes, leading in some cases to major challenges in differentiating it from a true perfusion abnormality.

Susceptibility effects may cause DRA as a result of field distortion (B0) during the first-pass of a contrast agent leading to dephasing of individual voxels around boundaries (17, 18).

Partial volume effects causes DRA by contribution of different compartments (blood pool versus myocardium) within voxels of interest; similar to k-space weighting heterogeneity by distortion of the point spread function (16). These effects are enhanced by cardiac motion, causing oscillations in the voxel values along the borders of different tissues with different signal intensities (19). Lastly, the finite nature of the spatial resolution causes DRA due to Gibbs ringing artifacts or truncation of the high k-space frequencies (20).

DRAs are commonly perpendicular to the phase-encoding direction and are transient, lasting a few heartbeats and displaying little spatial persistence (18). Although the criteria of temporal and spatial persistence may allow in most cases to distinguish DRA from a true perfusion abnormality, the presence of a strong enhancement and challenging technical demands – leading to a compromised image quality caused by e.g. respiratory motion, poor electrocardiographic synchronization, tachycardia or delayed intracardiac conduction – can further trigger or enhance these artifacts to a point where they may be undistinguishable from true perfusion defects. In such circumstances, evaluating to which extend the myocardial hypointensities actually don't correspond to an artery distribution territory may provide a clue to differentiation, since the segmental perfusion abnormalities can be anticipated a priori for a given artery (21, 22) (Fig. 2). Strategies for DRA reduction include: (i) administration of a lower dose of contrast agent (0.025-0.05 instead of 0.1 mmol of gadolinium per

kg of body weight) to decrease the level of enhancement, (ii) oxygen administration to decrease respiratory motion, and (iii) repetition time reduction to shorten image acquisition time. Other strategies are more controversial and require trade-offs. For example, Gibbs ringing and partial volume artifacts may be reduced by increasing image resolution, although at the cost of longer acquisition times that may conversely increase motion artifacts (18).

Other technical artifacts may cause false low signal intensity on DCEMR. They pose less serious interpretation challenges, as they are easily recognizable, distorting the normal anatomy or extending into tissues surrounding the heart. These artifacts include off-resonance ghosting, chemical shift and aliasing artifacts.

Always confront DCEMR to LCEMR

Klem et al and Cury et al (9, 23) have proposed to compare stress- and rest-DCEMR to differentiate "reversible" from "fixed" abnormalities that respectively represent true perfusion deficits versus changes in tissue properties (scars) or artifacts. They subsequently identify artifacts as abnormalities which are further unmatched to findings on LCEMR. Nevertheless, caution is advised when applying this approach. First, it is debatable whether only "reversible" hypointensities should be considered perfusion abnormalities, since severe vascular lesions may cause perfusion alterations even at rest. Second, myocardial signal intensities on rest-DCEMR may be different than expected in some instances. Indeed, differences in heart rate induced by refractory tachycardia to pharmacological vasodilatation makes the exact duplication of a given heart rate unpredictable, leading to a different amount of heart-rate related DRA during stress- and rest-DCEMR. Moreover, in clinical protocols rest-DCEMR is usually performed after vasodilatation-DCEMR. In such instances, the expected hypointensity of altered tissues on rest-DCEMR may be overshadowed by contrast staining. Furthermore, given the small risk of nephrogenic systemic fibrosis, the additional dose of contrast agent administered for rest-DCEMR may come under debate, especially in patients with altered or unknown renal function. Finally, some DCEMR hypointensities may match imperfectly with scars detected on LCEMR, since myocar-
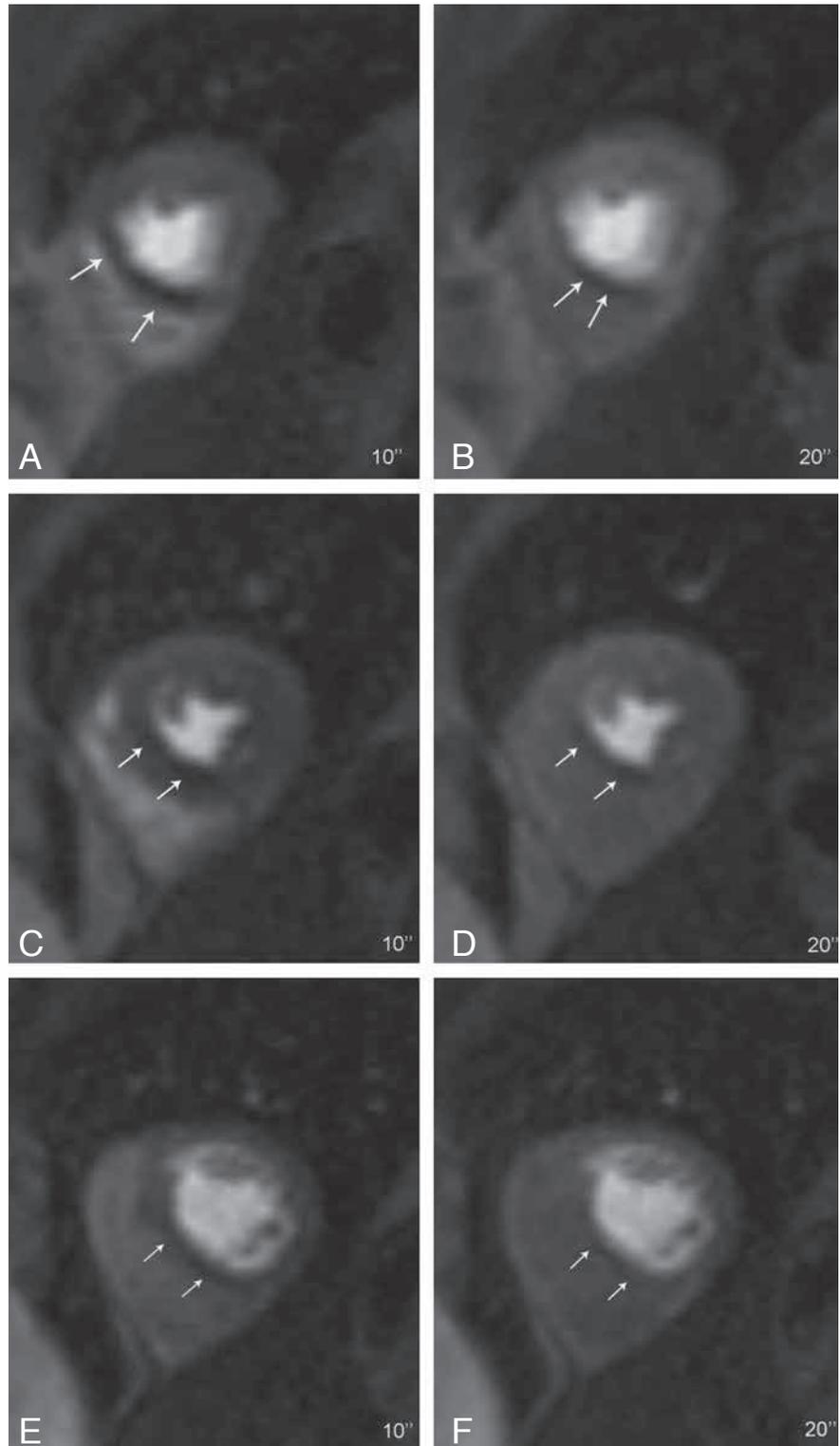
Fig. 2. — An asymptomatic 51-year-old man with diabetes mellitus. Post-adenosine apex- (A, B), mid- (C, D) and basal- left ventricle (E, F) short-axis slices 10'' and 20'' after contrast agent injection to exclude silent myocardial ischemia showed a subendocardial hypointensity involving the interventricular septum (arrows). These findings are suggestive of a dark-rim artifact (DRA), since an epicardial coronary artery stenosis causing such a large perfusion deficit is likely to involve either the anterior or the inferior wall, respectively in case of obstruction of left anterior descending artery or posterior descending artery.
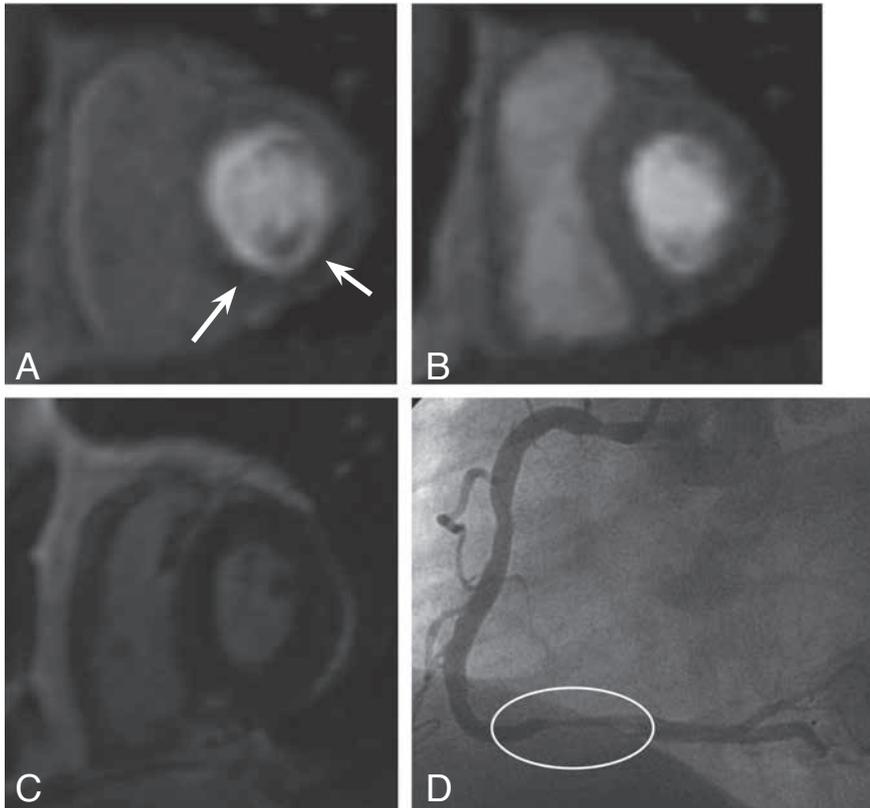
Fig. 3. — A 68-year old male with epigastralgia and normal gastrointestinal endoscopy. Peak enhancement post-adenosine basal left ventricle short-axis view (A) showed inferior myocardial hypointensity (arrows), with normal LCEMR (B) and rest DCEMR (C), consistent with *reversible abnormalities*, suggesting a right coronary artery stenosis that was evidenced on catheter coronary angiography (D, circled area).

– Insufficient spatial resolution may be cause for false-positive DCEMR in myocardial thinning. Indeed, the presence of a subendocardial DRA may actually involve a much larger proportion of the myocardial thickness. Conversely, unmatched demands in coverage caused by increased heart volume may result into failed depiction of small vascular territories, especially when the number of frames is reduced.
– Decrease in blood flow demand is proportional to the alteration of systolic function. This phenomenon is common during the course of several cardiomyopathies and may cause diffusely prolonged DCEMR hypointensities.
– Myocardial tissue alterations are common in inflammatory, infiltrative and scar processes that cause changes in the microvasculature (Fig. 5) and replacement by abnormal extracellular matrix (Fig. 6). These processes may cause hypointensities on DCEMR, but are depicted on LCEMR.

Left ventricular pressure overload

Increased left ventricle diastolic pressure overload, such as in aortic valve stenosis or systemic hypertension, potentially decreases the subendocardial myocardial perfusion, resulting into diffuse subendocardial hypointensities on DCEMR, even with normal epicardial vasculature.
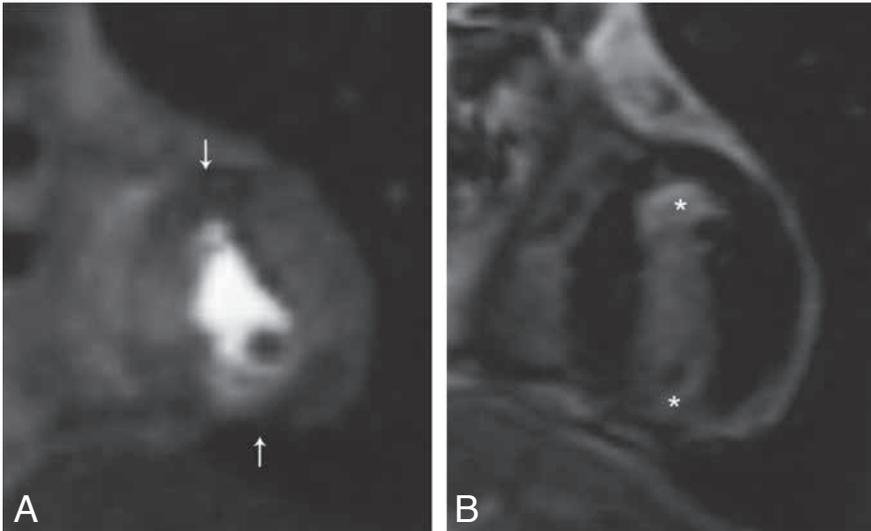
Flow competition

Left main coronary artery and multiple vessel disease cause challenges to DCEMR, although the latter has a higher accuracy than single photon emission computed tomography (31, 32).
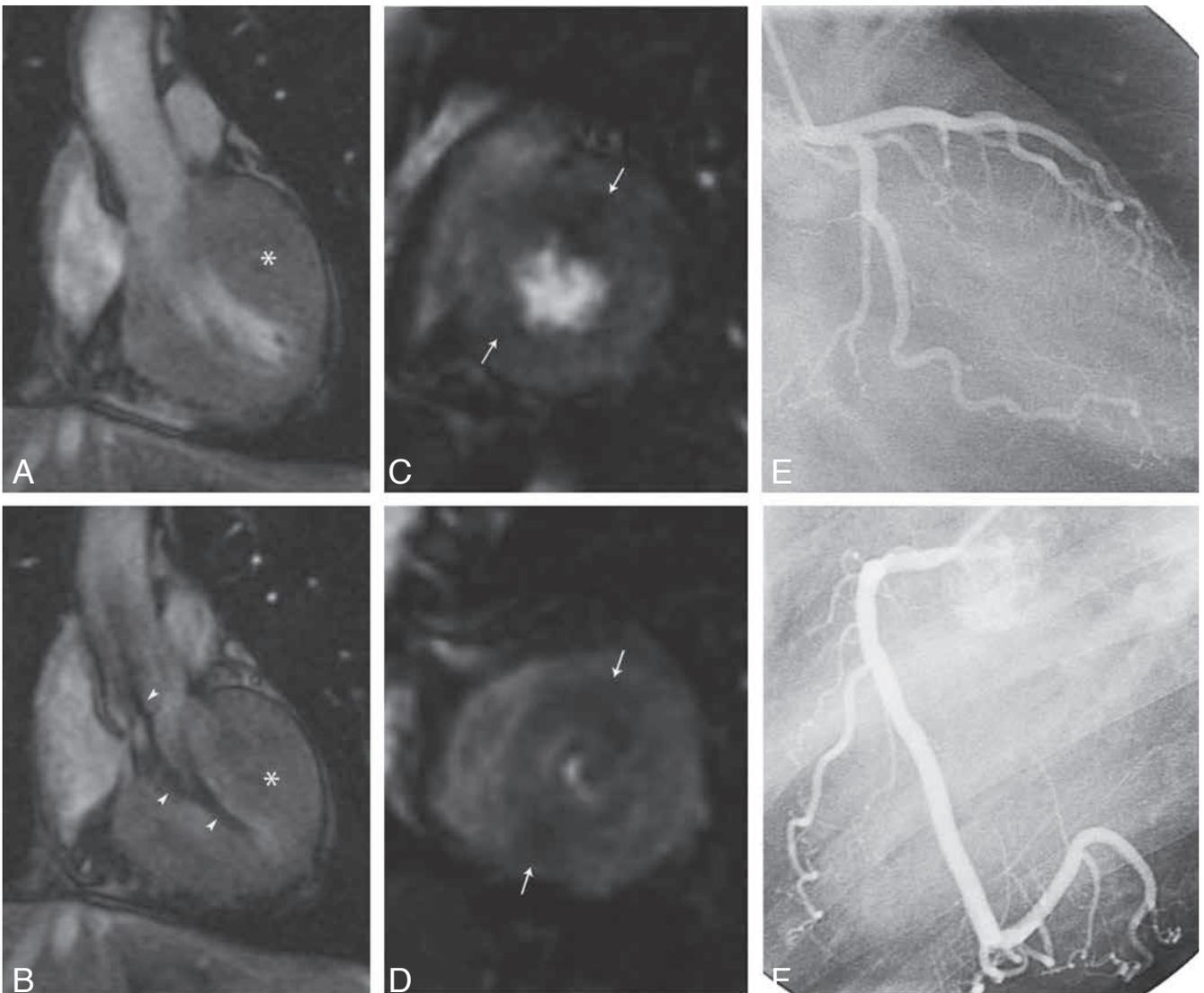
Indeed, when a single epicardial artery disease is narrowed, the imaging contrast between normal and underperfused myocardium is caused by the differences in perfusion reserve. Unfortunately, this contrast is decreased to a variable extent – with regard to the level of collateral flow compensation – when multiple epicardial arteries are occluded.

On the other hand, a vessel obstruction with excellent collateral flow may exhibit normal DCEMR findings. In some cases, only a delayed epicardial vessel enhancement may help suspecting multiple vessel or collateralized vessel obstruction (Fig. 7).

When applicable, flow competition between coronary bypass grafts and native coronary vessels may oc-

dial scars may be surrounded to a variable extent by tissues with impaired microvasculature (24, 25). There is, to the best of our knowledge, no available data in the literature evaluating specifically how to differentiate microvascular from macrovascular obstruction in a LCEMR-DCEMR mismatch, resulting into systematic and potentially excessive referrals to catheter coronary angiography. In our experience, macrovascular obstruction causes larger mismatches than microvascular obstruction, the latter typically producing rim-like, sharp and strong hypointensities on DCEMR.

In summary, in order to correctly characterize abnormal findings on vasodilatation-DCEMR we recommend additionally performing only LCEMR. It may help to report myocardial appearances requiring no revascularization, ie: (i) matching and (ii) rim-mismatching LCEMR abnormalities; and those potentially requiring revascularization ie: (iii) largely mismatching LCEMR abnormalities (Fig. 3 and 4).

Beware of other special conditions

Other vascular conditions and myocardial diseases that cause morphologic and functional alterations to the vessels or myocardial tissue are important to recognize, as they all impact DCEMR interpretation.

Cardiomyopathies

The total prevalence of cardiomyopathies is unknown; they include a wide range of diseases, from primary cardiomyopathies (ie: genetic, mixed, and acquired cardiomyopathies) to cardiomyopathies caused by either another organ or a systemic disease (26). Although overlaps are common, it is important to understand that cardiomyopathies can be the cause for one of the following:

– Microvascular obstruction occurring either in acute primary cardiac syndromes like cardiac syndrome X and Takotsubo disease (27-29), or in vasculitis involving small vessels, like Kawasaki disease (30).

Fig. 4. — A 65-year old male with clinical suspicion of coronary vascular disease. Post-adenosine mid- ventricle short-axis DCEMR (A) showed both anterior and inferior transmural hypointensities (arrows). LCEMR (B) showed hyperenhancement in these segments (asterisks), consistent with matching DCEMR abnormalities caused by myocardial scars.


Fig. 5. — A 49-year-old heavy smoker female was evaluated for atypical chest pain and left ventricle outflow tract obstruction caused by myocardial hypertrophy at echocardiography (not shown). Diastolic (A) and systolic (B) LV outflow tract outflow views showed a localized anteroseptal myocardial hypertrophy (asterisk) causing flow acceleration signal voids (arrowheads), consistent with obstructive hypertrophic cardiomyopathy. Post-adenosine basal- (C) and mid-left ventricle (D) short-axis DCEMR showed anterior and inferoseptal segmental hypointensities (arrows). LCEMR was unremarkable, as catheter coronary angiograms of both the left (E) and right (F) coronary arteries.
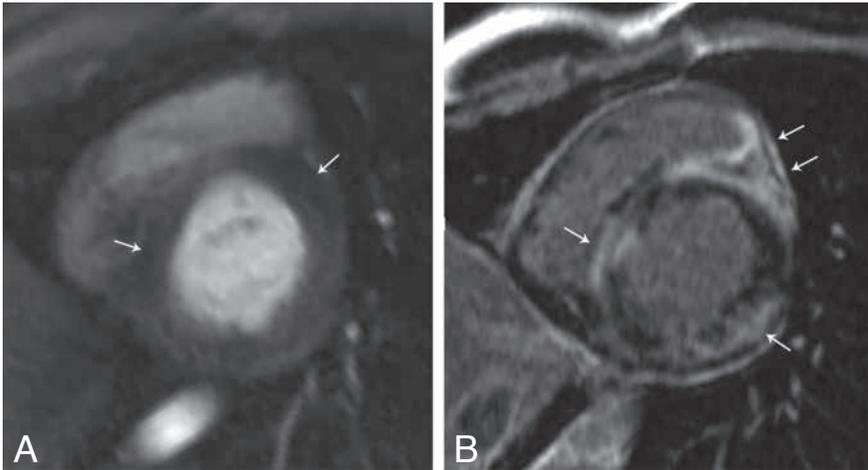
Fig. 6. — A 35-year-old male with a re-
cently diagnosed pulmonary sarcoidosis
experienced an episode of malignant
tachyarrhythmia. Left ventricle basal
short-axis DCEMR (A) showed persistent
patchy hypointensities (arrows), involv-
ing intramyocardial subendocardial and
subpericardial areas, caused by inflam-
mation and/or necrosis, as demonstrated
by hyperenhancement on LCEMR (B, ar-
rows).
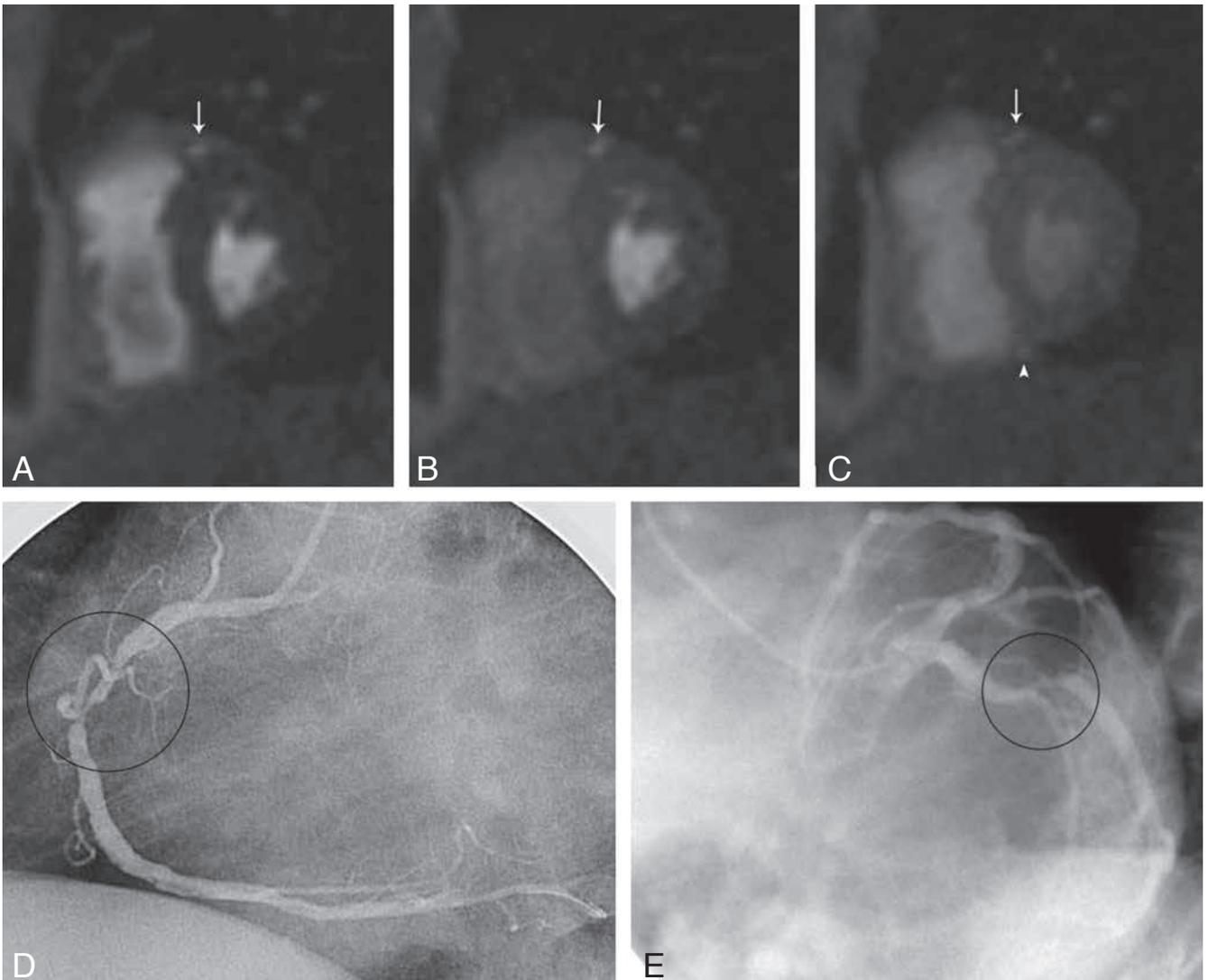
Fig. 7. — A 63-year old male with thoracic angina underwent post-adenosine DCEMR (A-C). On left ventricle basal slices, the myo-
cardial enhancement was homogenous. The anterior interventricular groove vasculature enhancement coincides with the peak left
ventricle cavity enhancement (arrows), while the posterior interventricular groove vasculature started to enhance only at the end of
the myocardial first-pass (C, arrowheads). The patient remained symptomatic and underwent eventually a catheter coronary angiog-
raphy few weeks later, where a low-grade stenosis of the left circumflex artery and high-grade stenoses of both the right coronary
(D, circled area) and left anterior descending (E, circled area) arteries were found.
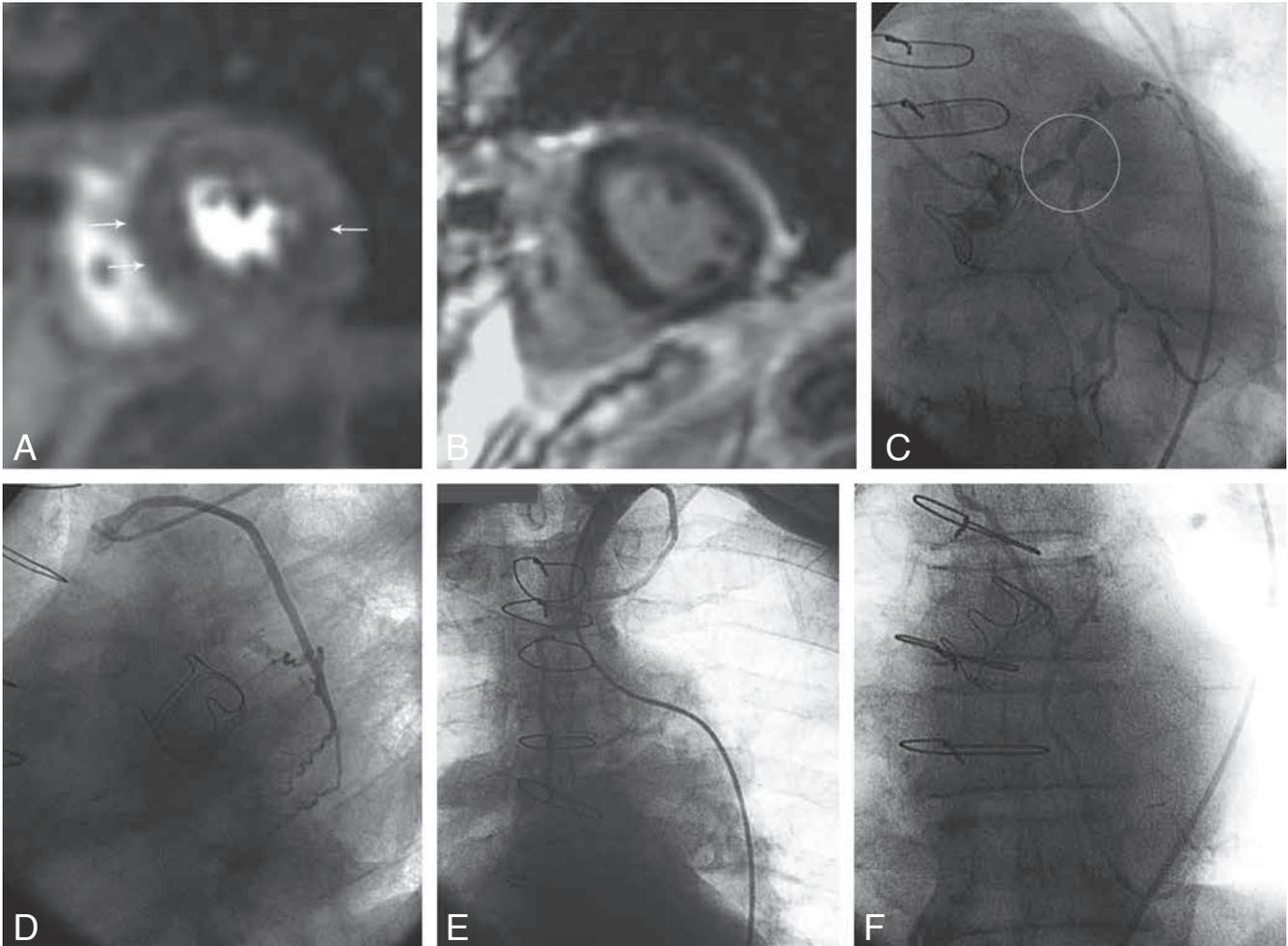
Fig. 8. — An 83-year old male experiencing an increasing chest pain was evaluated by DCEMR. His medical records were positive for aortic valve replacement and coronary grafts to the distal left anterior descending and circumflex arteries to bypass stenosis of the left main coronary artery, 11 years earlier. Post-adenosine mid-LV short-axis DCEMR images showed transient anteroseptal and lateral segmental myocardial hypointensities (A, arrows). Catheter coronary angiography was performed to exclude grafts stenosis, since LCEMR was normal (B). It actually showed a narrowed but still-patent left main artery (C, circled area), and no stenosis of both the venous (D) and left internal mammary artery (E) bypass grafts. DCEMR hypointensities were therefore attributable to blood flow competition between the grafts and the native arteries.

cur. It results into transient myocardial hypointensities on DCEMR, potentially leading to inappropriate referrals to diagnostic catheter coronary angiography (Fig. 8).

Conclusion

Signal distortions and a large variety of pathological conditions may either mimic or overshadow treatable myocardial vascular disease on DCEMR. Nevertheless, knowledge of both the origins of technical pitfalls and the presence of particular patient conditions can in many instances strongly help to provide appropriate recommendation and a correct stratification of patients for catheter coronary angiography.

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