Supplementary material

Sokolska JM, von Spiczak J, Gotschy A, et al. Cardiac magnetic resonance imaging to detect ischemia in chronic coronary syndromes: state of the art. Kardiol Pol. 2019; 77: 1123-1133. doi:10.33963/KP.15057

STUDY, YEAR	**BRIEF NAME OF THE CLINICAL TRIAL**	**STUDIED STRATEGIES**	**TYPE OF THE STUDY**	**PATIENTS INCLUDED**	**PATIENTS EXCLUDED**	**REFERENCE (GOLD STANDARD)**	**RESULTS/ CONCLUSIONS**
MR-IMPACT 2008 [ref. 13]	**M**agnetic **R**esonance **I**maging for **M**yocardial **P**erfusion **A**ssessment in **C**oronary Artery Disease **T**rial	**CMR adenosine stress** (*with randomized 5 doses of CM: 0.01, 0.025, 0.05, 0.075, or 0.1 mmol/kg*, 1.5 T scanners) **vs. SPECT** (^{99m}Tc- or ^{201}Tl-tracers, 1- or 2-day protocol, adenosine/ physical stress, gated/ungated image acquisition)	prospective; randomized; multi-centre (18 in Europe and in the USA); multivendor, double-blind	**234 pts** who underwent CXA or positive SPECT with scheduled CXA	- AMI 1 week prior to study enrollment; - history of CABG; - UA; - AHF; - any intervention on the coronary arteries in the time period between CXA, SPECT and CMR; - arrhythmias (AFib or >20 ectopic beats/min).	**CXA** CAD= quantitative assessment of ≥50% diameter stenosis in 2 orthogonal planes in ≥1 vessel with ≥2 mm diameter. * All pts underwent CXA, SPECT, and CMR within 4 wks.	**● the optimal CM dose was 0.1 mmol/kg** **● superiority of CMR perfusion over SPECT for CAD detection** ● also in MVD: perfusion-CMR was superior vs. SPECT ● in the head-to-head comparison: CMR (CM dose of 0.1 mmol/kg) was equal to SPECT
MR-IMPACT II 2012	**M**agnetic **R**esonance **I**maging for **M**yocardial **P**erfusion **A**ssessment in **C**oronary	**CMR adenosine stress** (1.5 T scanners) **vs. SPECT and gated SPECT** (^{99m}Tc- or ^{201}Tl-	prospective; randomized; multi-centre (33 in Europe and in the USA); multivendor	**533 pts** scheduled for CXA and/or a SPECT for clinical reasons	- AMI <2 weeks prior to study enrollment; - history of CABG; - UA; - AHF; - any intervention	**CXA** CAD= quantitative assessment of ≥50% diameter stenosis (i.e. ≥75% area reduction) in 2 orthogonal planes in ≥1 vessel with ≥2 mm	**● the sensitivity of perfusion-CMR was superior to SPECT, whereas its specificity was inferior to SPECT.** * *Analysis of secondary*

[ref. 14-15]	Artery Disease **T**rial II	tracers, 1- or 2-day protocol, adenosine/ physical stress)			on the coronary arteries in the time period between CXA, SPECT and CMR; - arrhythmias (AFib, bigeminus, >15 extrasystoles/min).	diameter OR history of previous AMI without significant stenosis on current CXA. * All pts underwent CXA, SPECT, and CMR within 4 wks.	*endpoints:* ● superiority of CMR perfusion over gated- SPECT for CAD detection; ● superiority of CMR perfusion over SPECT in MVD, in men and in women, as well as in the non-infarct patients; ● no severe adverse effects occurred in pts who received the CM during CMR.
CE-MARC 2012 [ref. 16-17]	The **C**linical **E**valuation of **MA**gnetic **R**esonance imaging in **C**oronary heart disease	**multiparametric CMR** (adenosine stress, coronary angiography, LGE; 1.5 T scanner) **vs.** **gated SPECT** (^{99m}Tc tetrofosmin, 2-day protocol)	prospective; randomized; single center; one vendor	**752 pts** with suspected stable angina pectoris and ≥1 CVRF, needed further investigation (628 pts completed all 3 tests)	- previous CABG; - crescendo angina; - ACS.	**CXA** clinically significant CAD= quantitative assessment of ≥70% stenosis in LAD/Cx/RCA with ≥2 mm diameter, or ≥50% stenosis of LMS. * All pts underwent CXA, SPECT, and CMR within 4 wks.	**● superiority of CMR perfusion over gated- SPECT** ● higher sensitivity (87 vs. 67%) and negative predictive value (91 vs. 79%) in CMR than in SPECT; ● similar specificity (83 vs. 83%) and positive predictive value (77 vs. 71%); ● CMR offers an accurate assessment of 1-vessel and MVD, irrespective of the cutoff used for severity of clinically significant angiographic stenosis (50 vs. 70%).
CE-MARC 2 2016 [ref.18-19]	The **C**linical **E**valuation of **MA**gnetic **R**esonance imaging in **C**oronary heart disease- 2	**CMR** **adenosine stress** (3 T scanners) **vs.** **SPECT** (^{99m}Tc tetrofosmin or ^{99m}Tc-sestamibi, 1- or 2-day protocol) **vs.** **NICE GL***	prospective; randomized; multi-centre (6 in the UK); multivendor	**1202 pts** ≥30 years old, with suspected stable angina pectoris (PTL 10-90%), suitable for revascularization	- nonanginal chest pain; - normal SPECT/CCT within the last 2 years; - previous AMI; - previous coronary revascularization (PCI or CABG).	**CXA ± FFR** FFR in all coronary vessels ≥2.5 mm diameter with a 40-90% stenosis, when FFR was not possible quantitative assessment of CXA was performed. (unnecessary angiogram defined as: normal FFR >0.8 or quantitative CXA showing no percentage diameter stenosis ≥70%	**● CMR- and SPECT- guided strategies (equally) significantly reduced unnecessary CXA within 12 months compared with NICE GL strategy;** ● unnecessary angiography occurred in 8% in the CMR, 7% in the SPECT group and 29% in the NICE GL group; ● there was no difference in major cardiovascular event rates at 12 months between the 3 groups.

						in 1 view or ≥50% in 2 orthogonal views in all coronary vessels ≥2.5 mm diameter within 12 months).	▪ *mean PTL in studied population was 50%.*
MR-INFORM 2019 [ref. 20-21]	MR perfusion imaging to guide management of patients with stable coronary artery disease	**CMR adenosine stress** (1.5 T scanners) **vs. CXA with FFR** (to guide decision about the need of revascularization)	prospective; randomized; multi-centre; international (UK, Germany, Portugal); unblended; multivendor	**918 pts** with typical angina (CCS II-III) and either ≥2 CVRF or positive exercise treadmill/ bicycle test.	- PCI within the last 6 months; - previous CABG; - LVEF <30%; - NYHA class III or IV; - cardiac arrhythmias (AFib, >20 ectopic beats/min).	none [*direct comparison of outcomes in two study strategies to guide revascularization according to either presence of ischemia in ≥ 6% of the myocardium in the CMR- group or FFR ≤0.8 in the FFR- guided group*].	● **CMR-guided strategy noninferior to invasive FFR;** ● index revascularization was performed in 36% of the pts in CMR- group and 45% of those in FFR- group; ● MACE (death from any cause, nonfatal MI, target-vessel revascularization) occurrence at 1 year was similar in studied groups (4% vs. 4%); ● The percentage of pts free from angina after 1 year did not differ significantly between CMR and FFR-group (49% vs. 44%). ▪ *mean PTL in MR group was 75±14% and 74±13% in FFR group.*

Table S1. Summarize of the most important randomized prospective clinical trials in the perfusion cardiovascular magnetic resonance.

Abbreviations: AFib- atrial fibrillation; AHF, decompensated heart failure; AMI, acute myocardial infarction; CABG, coronary artery bypass surgery; CCS, Canadian Cardiovascular Society Angina Grade; CCT, cardiac computed tomography; CM, contrast media; CVRF, cardiovascular risk factors; Cx, left circumflex coronary artery; CXA, invasive coronary x-ray angiography; LAD, left anterior descending coronary artery;

LMS, left main stem; MACE, major adverse cardiac events; MI- myocardial infarction; MR- magnetic resonance; MVD, multivessel disease; NICE GL*, National Institute for Health and Care Excellence guidelines [CG95]: management according to patients pre-test likelihood of having CHD: 10-29% - CT calcium score +/- CT coronary angiography; 30-60% - SPECT; 61-90% - X-Ray coronary angiography; NYHA, New York Heart Association Functional Classification of heart failure; PCI- percutaneous coronary intervention; PTL, pre-test likelihood; pts., patients; RCA, right coronary artery, ref., reference; UA, unstable angina pectoris; UK, United Kingdom; USA, United States of America; wks, weeks.

Abbreviations: ACS; CAD; CMR; FFR; LGE; LVEF; SPECT - see the main text of the review.

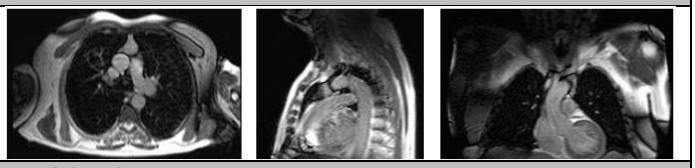
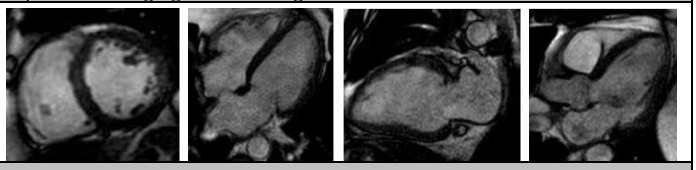
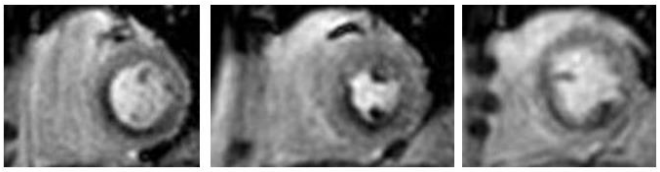
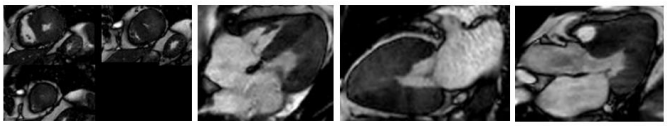
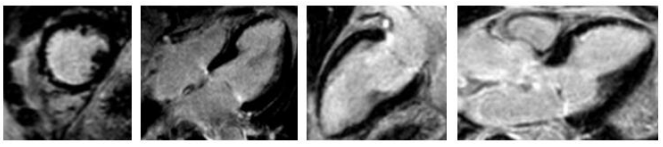
Duration	CMR sequences	Diagnostic Information	Example of images
SURVEY, LOCALIZER			
< 1 minute	**scout images: transaxial, coronal, sagittal** *(SSFP or fast spin echo)*	extracadiac findings, measurement of aorta ascendens	
CINE IMAGING long axis views can be performed after perfusion imaging if time saving is needed			
~ 10 minutes	**cine images: SA, 4CH, 2CH, 3CH** *(SSFP; SR:* ~1.8 mm*)*	anatomy and function (LV, LA, RV, RA), regional wall motion abnormalities, pericardial effusion	
• **PERFUSION IMAGING WITH VASODILATOR AND GADOLINIUM**			
*** ADENOSINE** (140-210 μg/kg/min i.v. infusion for at least 3 minutes) ****** or **REGADENOSONE** (0.4 mg i.v. bolus for > 10 seconds, followed by injection of 5 ml 0.9% NaCl) ******* or **DIPYRIDAMOLE** (0.56 mg/kg i.v. infusion for 4 minutes; if needed 2nd dose: 0.28 mg/kg for 2 minutes or 0.86 mg/kg for 6 minutes)			**+ gadolinium** (0.05-0.1 mmol/kg; 3-4 ml/second) +30 ml saline flush (3-4 ml/second)
2-8 minutes (depends on the type of vasodilator)	**test-** *"dummy" scan*	to check position and detect potential artefacts	
	STRESS: 3 SA slices (basal-midventricle- apex) *(saturation recovery imaging with GRE-EPI, hybrid, GRE or SSFP readout; SR* <3 mm*)*	presence and location of perfusion defect	Stress: 
< 1 minute (~ 5 minutes after stress, when heart rate decreased) **+ second dose of gadolinium** (0.05-0.1 mmol/kg; 3-4 ml/second) +30 ml saline flush	**REST** ***(optional)*** **3 SA slices** *(saturation recovery imaging with GRE-EPI, hybrid, GRE or SSFP readout; SR:* <3 mm*)*	rest perfusion deficits, artefacts	Rest: 
• **DOBUTAMINE STRESS** (10- 20- 30- 40 μg/kg/min i.v. infusion for 3-5 minutes per stage until 85% of the maximal predicted HR is reached. **+ ATROPINE** (0.5- 2 mg i.v.) if HR is inadequate			
12-20 minutes	**SA (basal-midventricle-apex), 4CH, 2CH, 3CH** *(SSFP; SR:* <3 mm*)*	stress induced regional wall motion abnormalities	
LATE GADOLINIUM ENHANCEMENT- VIABILITY IMAGING			
~ 5-10 minutes	**Look- Locker**	to find an optimal time to null the normal myocardium	
(~ 10-20 minutes after administration of total dose of CM)	**LGE: SA, 3CH, 4CH, 2CH** (IR GRE; *SR*: 1.4- 1.8 mm*)*	presence, pattern, location and transmural extent of scar (≤25%, 26-50%, 51-75%, 76-100%)- viability of the myocardium. Correlation between infarct scar and perfusion defect.	

Table S2. Cardiac magnetic resonance standard protocol for the stress test by myocardial perfusion with adenosine/ regadenosone/ dipyridamole or dobutamine examination.

Abbreviations: 2CH, 2-chamber view; 3CH, 3-chamber view; 4CH, 4-chamber view; EPI, echo-planar imaging; GRE, spoiled gradient echo; IR, inversion recovery; LA, left atrium; RA, right atrium; RV- right ventricle; SA, short axis*;* SR, spatial resolution; SSFP, steady state free precession.

Abbreviations: CMR; HR; LGE; LV- see the main text of the review; CM- see Supplementary Table S1; i.v.- see Table 1.

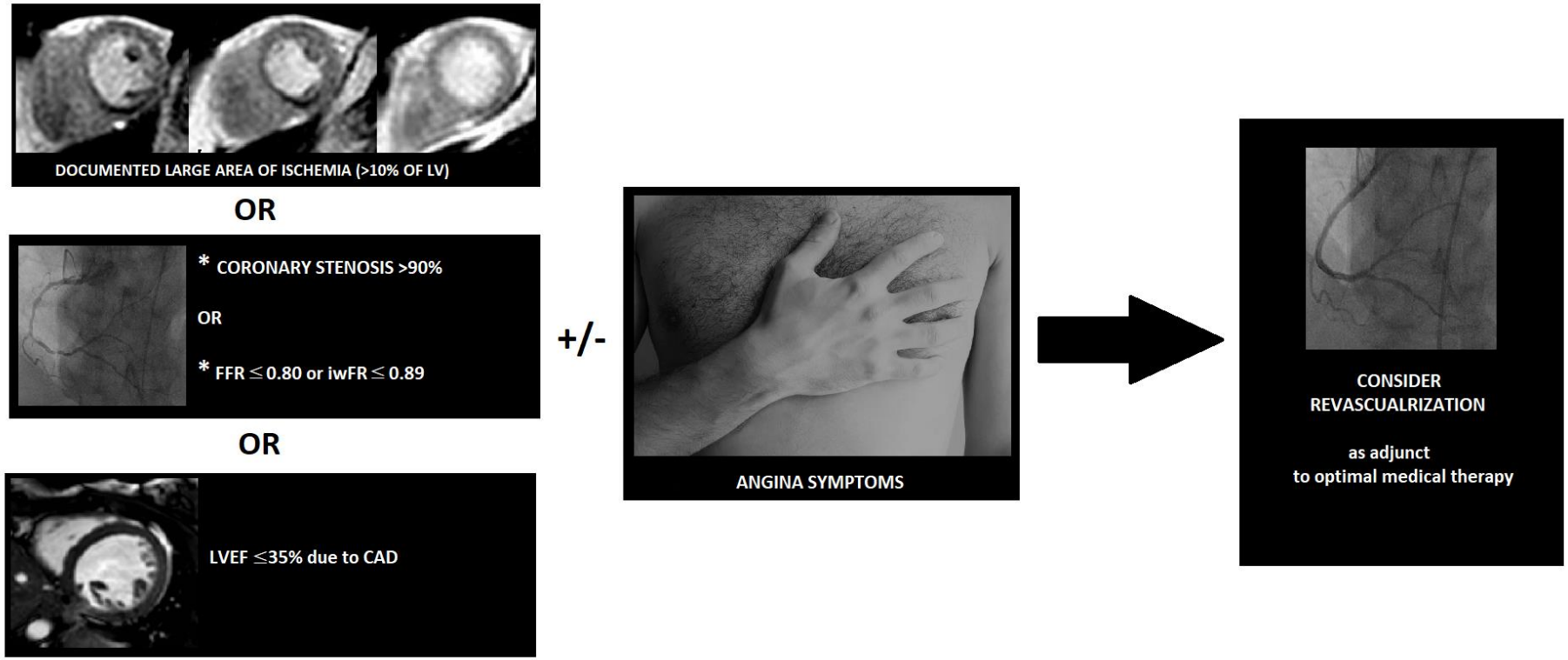


Figure S1. Revascularization in patients with chronic coronary syndromes.

Abbreviations: iwFR, instantaneous wave-free ratio; CAD; FFR; LV; LVEF - see the main text of the review.

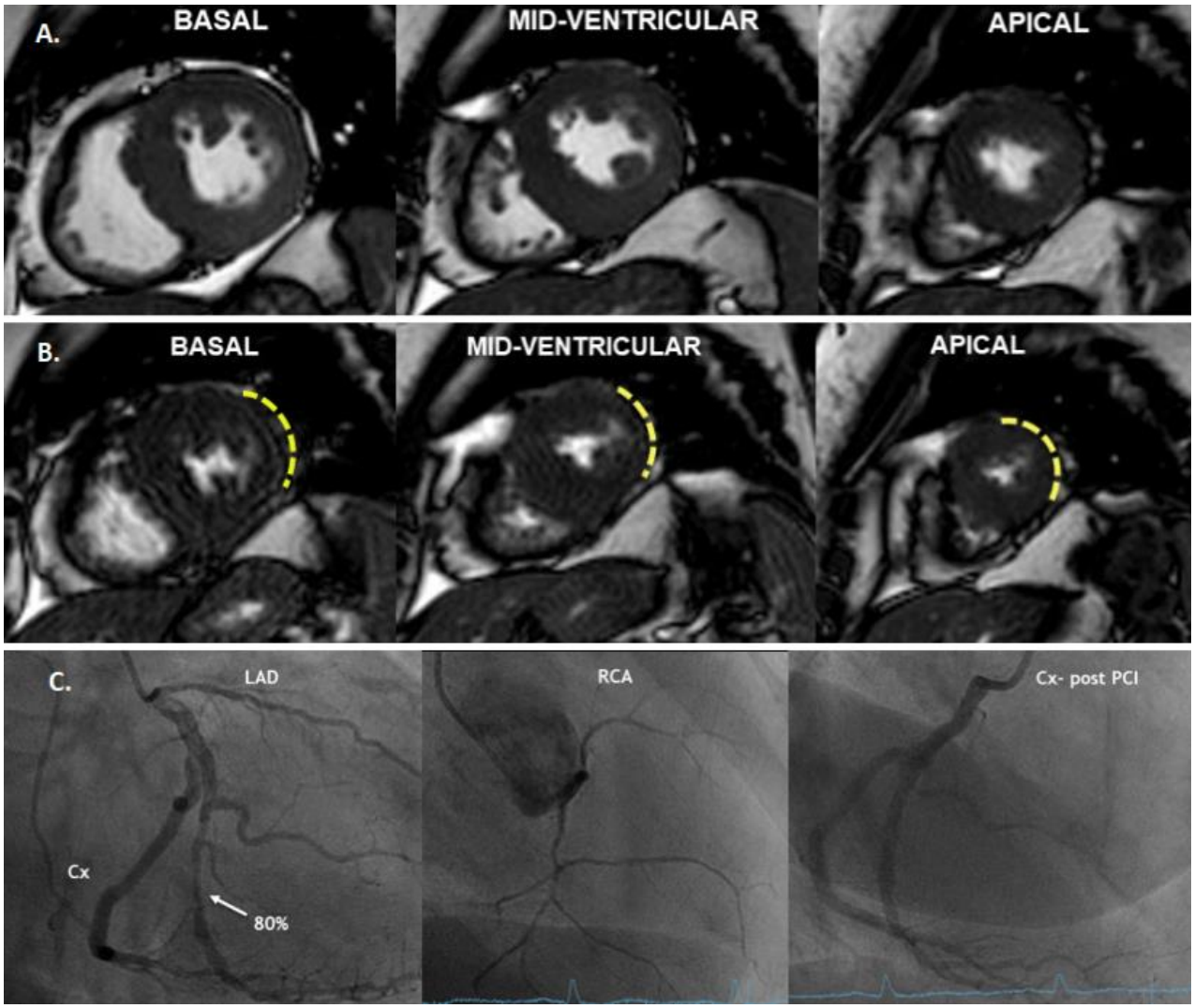


Figure S2. 63-year old female patient with cardiovascular risk factors (arterial hypertension, diabetes mellitus, hypercholesterolemie, former smoker, positive family history for CAD) and glomerulonephritis were sent to CMR for dobutamine stress (without LGE) to exclude cardiac ischemia before planned kidney transplantation.

A. Normal LV and right ventricular function without regional wall motion abnormalities at rest.

B. Dobutamine stress under dose of 40 µg/kg and 0.5 mg of atropine (cine short axis). At target heart rate wall motion abnormalities were observed in the inferolateral (basal to mid-ventricular) and lateral (apical) AHA LV segments (***yellow dashed lines***).

C. Patient was sent to coronary angiography, which revealed 80% stenosis in dominant Cx and small RCA. Lesion in Cx was successfully treated.

Abbreviations: AHA- see Figure 2; CAD; CMR; LGE; LV- see the main text of the review; Cx; LAD; PCI; RCA- see Supplementary Table S1.