Artificial Intelligence-based Fully Automated Global Circumferential Strain in a Large Cohort of Patients Undergoing Stress CMR

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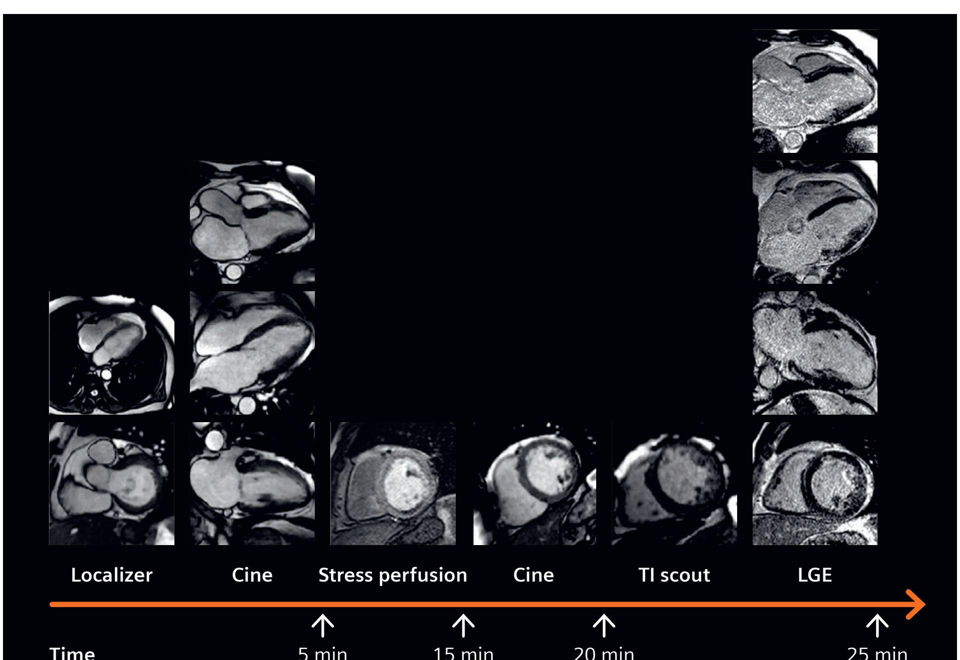
Introduction

Stress cardiovascular magnetic resonance (CMR) imaging has emerged as a very accurate modality for the diagnosis of obstructive coronary artery disease (CAD) without ionizing radiation [1]. Several studies have shown the strong prognostic value of both inducible ischemia and myocardial infarction (MI) above traditional cardiovascular risk factors in patients with suspected or known CAD [1, 2].

Recent studies have also underlined the potential prognostic value of global longitudinal strain (GLS) using feature-tracking imaging (FTI) assessed during vasodilator stress. In particular, perfusion abnormalities on stress CMR are associated with a significant decrease in GLS [3]. Recent data suggest that circumferential strain could be more effective than longitudinal strain in detecting myocardial ischemia [4]. Although recent FTI techniques allow measurement of strain using standard cine CMR images [3], post-processing and inter-observer reproducibility of FTI strain measurements [8], limit their widespread use in clinical routine. Artificial intelligence (AI)-based algorithms can compute left ventricular (LV) strain fully automatically. However, the prognostic value of AI-based fully automated global circumferential strain (GCS) determined during stress CMR is not well established. Therefore, our working group aimed to determine whether AI-based fully automated GCS assessed during vasodilator stress could provide additional prognostic value beyond traditional cardiovascular risk factors to predict cardiovascular events. The aim of this article is to review our experience of more than 15 years with stress CMR in patients using a dedicated workflow, and to present the main findings of a recent work supported by a collaboration with Siemens Healthineers to assess the clinical interest of a new, full-AI automated algorithm[1] for assessing LV strain during a stress CMR exam.

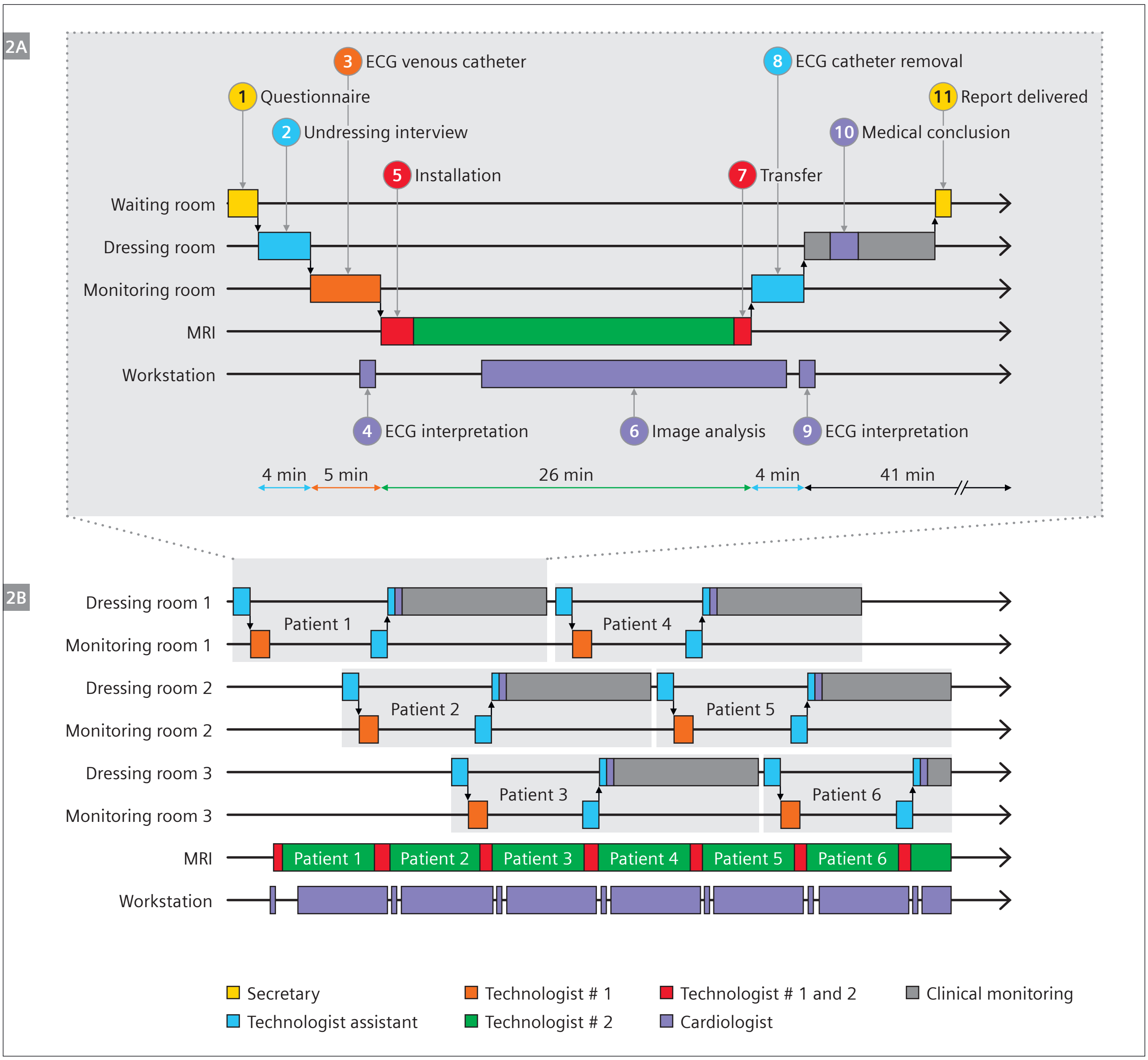
[1]Work in progress. The application is currently under development and is not for sale in the U.S. and in other countries. Its future availability cannot be ensured.



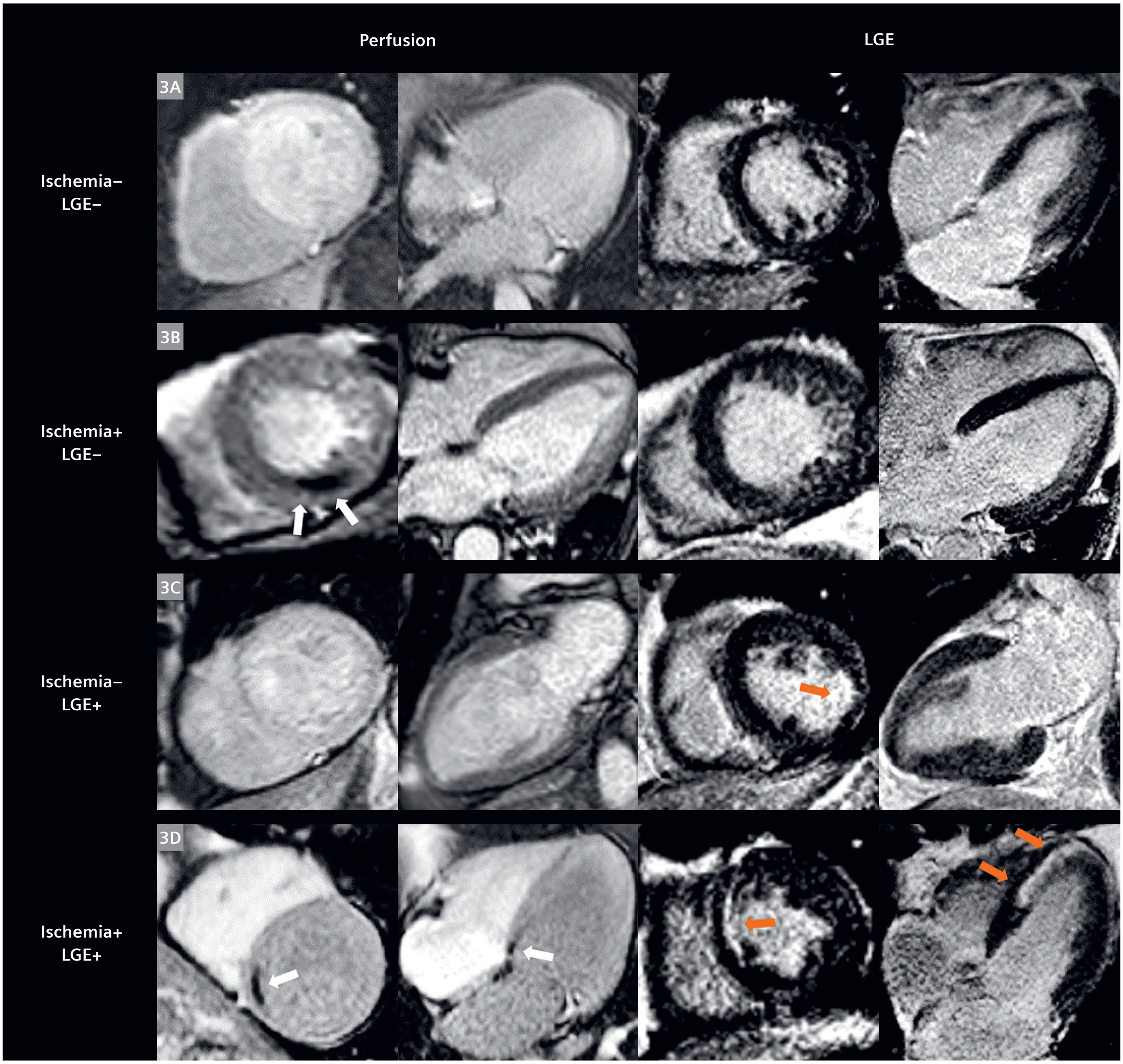
1 Perfusion stress CMR imaging protocol [9]
After individual patient planning, short- and long-axis cine images were acquired; then, intravenous dipyridamole was given at 0.84 mg/kg or 0.56 mg/kg over 3 or 4 minutes, and first-pass stress myocardial perfusion imaging was acquired in the short- and long-axis views (typically four short-axis and two long-axis views every other heart beat after 0.1 mmol/kg gadolinium contrast agent bolus through the myocardium at 5 mL/s). Ten minutes after injection, a modified Look-Locker inversion time scout was performed before late gadolinium enhancement (LGE) imaging in short- and long-axis views.

Description of our CMR workflow

In our CMR laboratory, which is accredited by the European Association of Cardiovascular Imaging (EACVI) for stress CMR, we perform stress CMR at 1.5 Tesla using dipyridamole as vasodilator agent following a stress CMR protocol depicted in Figure 1. Following a very standardized, published workflow [9], our CMR laboratory is dedicated to cardiovascular imaging, with designated and experienced staff (eight CMR technologists, one technologist assistant) working on two MR scanners for 55 hours per week per scanner, specifically for CMR (Fig. 2). The medical team



2 Optimized stress CMR workflow
The different steps of the final workflow were described at the patient scale **(2A)** and the CMR laboratory scale **(2B)**. On arrival in the waiting room, the patient fills in a questionnaire with the help of the administrative assistant ①. Then the patient undresses in a changing room. The technologist assistant checks the questionnaire and contraindications for CMR and perfusion stress studies, while providing explanations of the CMR study ②. The patient is brought into in a monitoring room on a stretcher, where a 12-lead pretest electrocardiogram (ECG) is performed ③ ④ and a venous catheter is inserted. Both technologists position the patient in the magnetic resonance scanner, with ECG for triggering, appropriate surface coils, and stress-test monitoring ⑤. The cardiologist is present throughout the study, analyses the images and produces a final report shortly after the end of the study ⑥. After performing the stress CMR test, the patient is transferred back to the room on a stretcher ⑦, the venous catheter is removed, and a post-test ECG is performed and interpreted ⑧ ⑨. During a 45-minute clinical monitoring period, the cardiologist provides the final conclusions of the study before discharge ⑩ ⑪.



3 Examples of inducible ischemia on stress CMR in patients suspected of CAD.
(3A) Normal: 79-year-old female presenting with atypical angina. Stress CMR revealed no perfusion defect and LGE was negative, ruling out the diagnosis of myocardial ischemia.
(3B) Inducible ischemia: 81-year-old male with diabetes and hypertension, presenting with dyspnea on exertion. First-pass myocardial stress perfusion images revealed a reversible perfusion defect of the inferior wall (white arrows) without LGE, indicative of myocardial inducible ischemia suggestive of significant RCA stenosis, confirmed by coronary angiography.
(3C) Myocardial scar without ischemia: 75-year-old female with a history of lateral STEMI treated by PCI of the Cx six years ago and a prior inconclusive stress echocardiography, presenting with atypical angina. Stress CMR showed a subendocardial lateral scar on LGE (orange arrow), without any perfusion defect and, therefore, no inducible ischemia.
(3D) Myocardial scar with additional inducible ischemia: 68-year-old male with a history of anterior STEMI treated by PCI of the LAD, presenting with dyspnea on exertion. Stress CMR showed a subendocardial scar on the antero-septo-apical wall on LGE sequences (orange arrows), and a perfusion defect of the inferior and infero-septal wall (white arrows) on first-pass perfusion images, indicative of inducible myocardial ischemia. Coronary angiography revealed high-grade stenoses of the RCA.

Abbreviations: CAD: coronary artery disease; Cx: circumflex coronary artery; ECG: electrocardiogram; LAD: left anterior descending; MI: myocardial infarction; PCI: percutaneous coronary intervention; RCA: right coronary artery; STEMI: ST-segment elevation myocardial infarction.

comprises six senior cardiologists who have over 15 years' experience in CMR and are trained in intensive cardiovascular care. Two of them have EACVI level 3 accreditation. Stress CMR sessions require two technologists (one at the CMR workstation, one for patient preparation and discharge), one technologist assistant and one physician for an optimized patient workflow. Notably, the mean duration of a stress CMR study (from the beginning of the first localizer sequence to the exit of the magnet) is 27 ± 5 minutes.

Stress CMR analysis to identify inducible ischemia

According to the current SCMR guidelines, inducible ischemia is defined as a sub-endocardial or transmural perfusion defect that

1) occurred in at least 1 myocardial segment;
2) persisted for at least 3 phases beyond peak contrast enhancement;
3) followed a coronary distribution and
4) occurred in the absence of co-location with LGE (Fig. 3) [10].

AI-based fully automated global circumferential strain (GCS) at stress

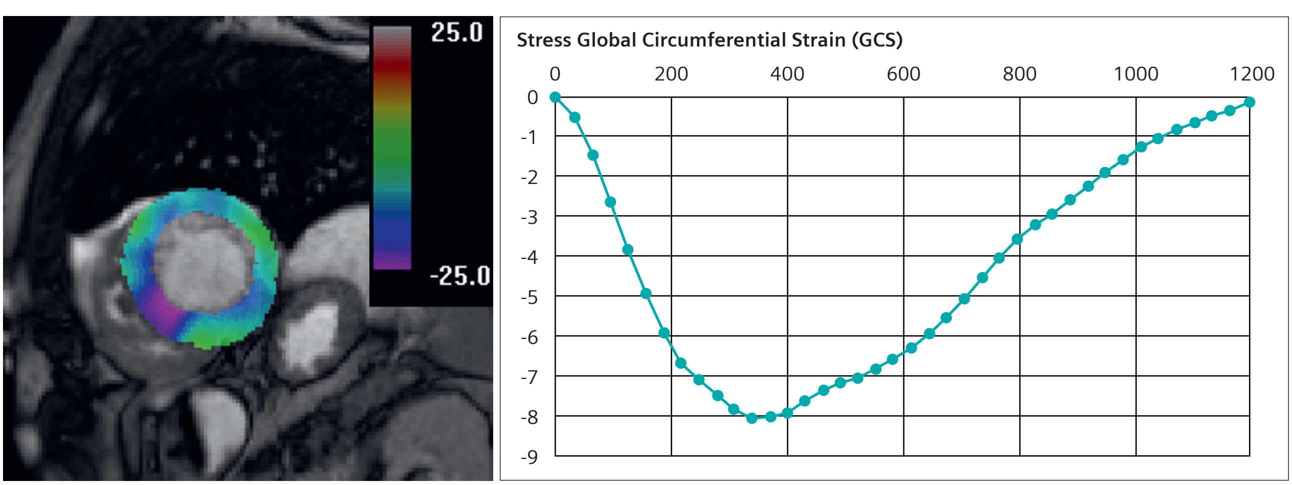
With the support of Siemens Healthineers within a strong collaboration for several years, we assessed the prognostic value of a full-AI algorithm for assessing the LV strain. Indeed, a fully automatic machine learning algorithm was developed to segment the myocardium and to assess the stress GCS from a short-axis cine stack of slices (Fig. 4). The AI-algorithm combines a deep learning network for segmentation with an active-contours approach to segment the endocardial and epicardial borders of LV into individual 2D short-axis views images [11]. A dense Unet [12] was trained on 3,000 CMR studies (10% reserved for validation) from the UK Biobank resource [13, 14]. The AI segmentation algorithm was tested on 1,719 unseen CMR studies [13], obtaining a dice score of 96.2% for the LV. The contours were automatically detected at several timepoints in the cine series and were automatically propagated to the rest of the phases, to minimize propagation errors. The strain tensors were projected in cylindrical coordinates centered with respect to the LV axes in radial, circumferential, and longitudinal directions. The global radial, circumferential, and longitudinal strain values were computed, which corresponds to the maximum strain magnitude values from the temporal series [6].

Prognostic impact of AI-based fully automated GCS measured at stress

In this study with a large cohort of consecutive patients referred for stress CMR, AI-based fully automated stress GCS measurement was feasible in 98% of patients referred for stress CMR with a good accuracy. In addition, stress GCS was independently associated with the occurrence of cardiovascular events (cardiovascular death or non-fatal myocardial infarction) during a median follow-up of five years. Our findings are in line with data by Romano et al. using GLS [3], which strongly suggests that a blunted stress GCS could impact clinical decision-making in those patients. Further clinical prospective trials are warranted to assess the clinical yield of strain imaging during stress CMR.

Conclusion

In patients referred for stress CMR, AI-based fully automated GCS assessed during vasodilator stress was a significant independent predictor of cardiovascular events.



4 Example of AI-based fully automated global circumferential strain (GCS) measurement during a stress CMR exam from cine images performed immediately after stress using vasodilator agent.

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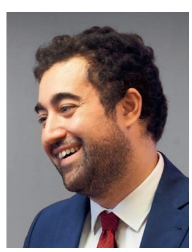

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