



Safety of dobutamine or adenosine stress cardiac magnetic resonance imaging in patients with left ventricular thrombus

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Abstract

Background Left ventricular (LV) thrombus formation is a common but potentially serious complication, typically occurring after myocardial infarction. Due to perceived high thromboembolic risk and lack of safety data, stress cardiac magnetic resonance (CMR) imaging especially with dobutamine is usually avoided despite its high diagnostic yield. This study aimed to investigate the characteristics, safety and outcome of patients with LV thrombus undergoing dobutamine or vasodilator stress CMR.

Methods Patients undergoing stress CMR with concomitant LV thrombus were retrospectively included. Risk factors, comorbidities, and previous embolic events were recorded. Periprocedural safety was assessed for up to 48 h following the examination. Major adverse cardiac events (MACE) 12 months before the diagnosis were compared to 12 months after the exam and between patients and a matched control group. Additionally, patients were followed up for all-cause mortality.

Results 95 patients (78 male, 65 ± 10.7 years) were included. Among them, 43 patients underwent dobutamine (36 high-dose, 7 low-dose) and 52 vasodilator stress CMR. Periprocedural safety was excellent with no adverse events. During a period of 24 months, 27 MACE (14.7%) occurred in patients and controls with no statistical difference between groups. During a median follow-up of 33.7 months (IQR 37.6 months), 6 deaths (6.3%) occurred. Type of stress agent, thrombus mobility, or protrusion were not correlated to embolic events or death.

Conclusion The addition of a stress test to a CMR exam is safe and does increase the generally high cardioembolic event rate in LV thrombus patients. Therefore, it is useful to support reperfusion decision-making.

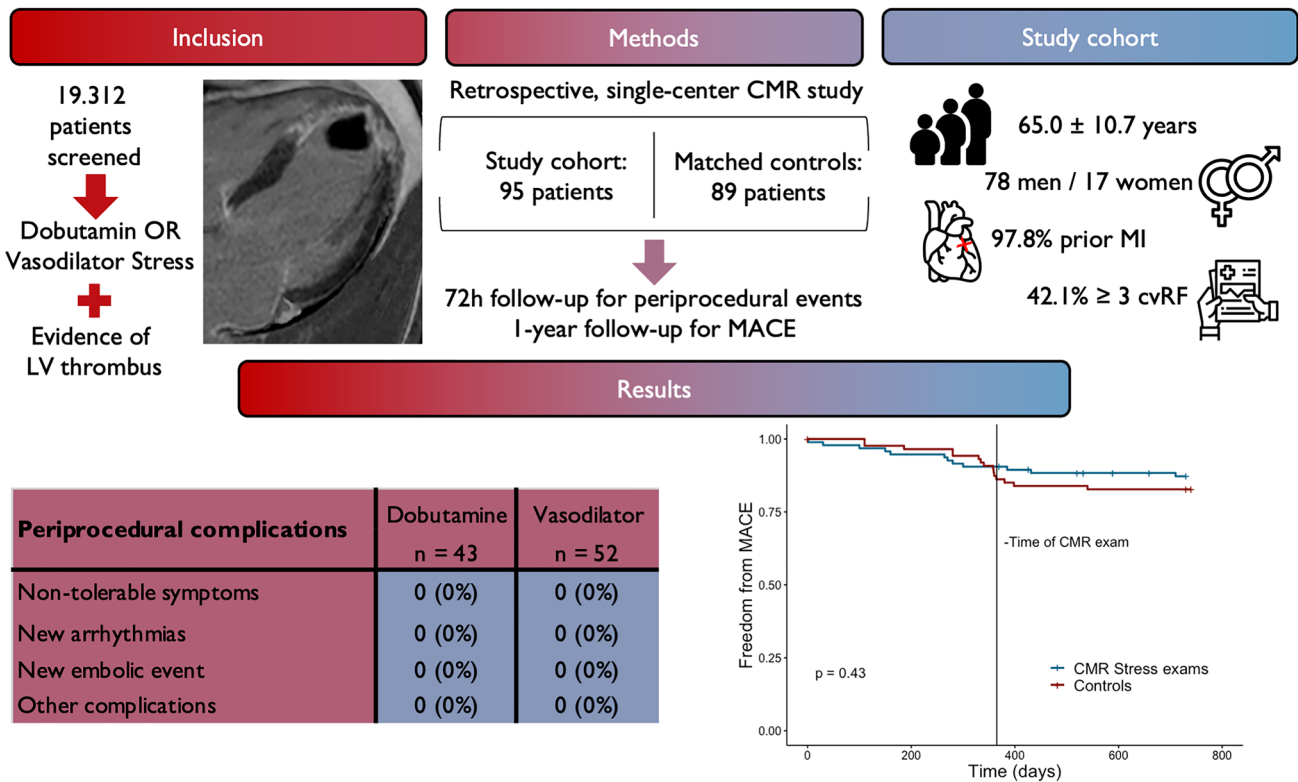
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Graphical Abstract



Keywords CMR · Cardiovascular imaging · Adenosine · Dobutamine · LV thrombus · Stroke

Abbreviations

- CAD Coronary artery disease
- CMR Cardiac magnetic resonance imaging
- LV Left ventricular
- MACE Major adverse cardiovascular event
- SD Standard deviation
- PCI Percutaneous coronary intervention

Background

The formation of a left ventricular (LV) thrombus is a common but often undetected phenomenon following myocardial infarction. Despite significant advancements in primary percutaneous coronary intervention (PCI) treatment, the incidence of LV thrombus after ST elevation myocardial infarction still ranges from 2.7% to 6.3% of all patients [1–5]. Studies utilizing routine cardiac magnetic resonance (CMR) imaging have reported prevalence rates of 8% to 15%, suggesting that many patients with LV thrombi are discharged undiagnosed [6, 7]. Cardiac magnetic resonance (CMR) is considered the gold standard for detecting LV thrombi due to its excellent sensitivity (88%) and specificity (99%), whereas

detection with standard transthoracic echocardiography is challenging due to a low sensitivity of 29% to 35% [2, 6, 8, 9].

There is limited data to support prophylactic anticoagulation, even in high-risk patients, due to the associated risk of bleeding [9, 10]. For treating a diagnosed LV thrombus, American and European guidelines recommend oral anti-coagulation for 3 to 6 months guided by repeated imaging [11, 12]. This recommended treatment is successful in 62% to 92% of patients [2, 13–15]. While not explicitly stated in the American Guidelines, a majority of recent studies indicate that direct oral anticoagulants are equally effective [11, 13, 15–24].

Systemic embolism is a severe complication of LV thrombus formation with an annual embolic rate of approximately 3.7% [2, 15, 25, 26]. Simultaneously, non-invasive stress testing methods are necessary to assess the hemodynamic relevance of residual coronary stenoses following myocardial infarction [27–32]. Stress CMR using dobutamine or a vasodilator (i.e. adenosine) is an established diagnostic modality recommended by the current guidelines [33, 34]. It possesses both a high diagnostic accuracy non-inferior to invasive fractional flow reserve and an excellent safety

profile in the general population [33, 35–37]. Paradoxically, whilst regular exercise generally protects against atherosclerosis, acute exercise is associated with a significant increase in thromboembolic risk for up to 2 h [38]. However, it is unclear how this relates to the periprocedural thromboembolic risk of stress CMR, particularly with high-dose dobutamine infusion. In practice, although not explicitly advised against in the current guidelines, stress CMR in general and dobutamine stress in particular is avoided in patients with LV thrombus [39, 40]. Hence, no data exists on the periprocedural risk and long-term outcome of patients with LV thrombus undergoing stress CMR.

Therefore, this study sought to investigate the characteristics, anticoagulation efficacy, safety, and outcome of patients with LV thrombus undergoing dobutamine or vasodilator stress CMR.

Methods

Study population and design

The clinical database was searched for patients undergoing stress CMR (adenosine, dobutamine, or regadenoson) with concomitant LV thrombus between February 2015 and September 2022.

If available, it was noted whether the transthoracic echocardiography reports at the time of CMR (or up to 30 days before or after) detected the LV thrombus. Cardiovascular risk factors such as arterial hypertension, current or former smoking habit, hypercholesterolemia, diabetes mellitus, obesity, and family history of cardiovascular disease were assessed using medical reports. Comorbidities including prior myocardial infarction, prior venous thrombosis, prior arterial embolism, active malignant disease, and known thrombophilia were also assessed. For arterial embolisms, the timing of occurrence relative to the CMR was recorded: > 12 months prior to CMR (no assumed correlation to LV thrombus) or < 12 months before CMR (assumed correlation to LV thrombus). As a control, a sex-, age- and LV ejection fraction-matched control group of patients undergoing a stress-free CMR with concomitant LV thrombus was retrospectively identified in our database. Likewise, prior arterial embolisms < 12 months before CMR (assumed correlation to LV thrombus) were assessed for this group.

CMR acquisition protocol

CMR imaging was performed at a 1.5 Tesla or a 3 Tesla MRI scanner (Ingenia and Ingenia CX, Philips Healthcare, Best, The Netherlands). Cine images were obtained with a steady-state free precession sequence using retrospective electrocardiographic gating in at least three long-axis planes

(two, three, and four-chamber views), as well as a short-axis stack of the whole left ventricle (slice thickness 8 mm) during breath-hold with 35 phases per cardiac cycle. For dobutamine stress, CMR, three long axis and three short-axis planes (basal, midventricular, apical) were acquired before and during dobutamine infusion starting at 10 µg/kg/min and increased by 10 µg/kg/min every step to a maximum of 40 µg/kg/min (20 µg/kg for low-dose vitality testing). In case of an insufficient heart rate response, additional medication with up to 2 mg atropine intravenously was used in the absence of contraindications. For vasodilator stress CMR, an intravenous infusion of 140 or 210 µg/kg/min adenosine for three minutes or a 0.4 mg single injection of regadenoson was followed by a gadolinium-based contrast agent bolus and a three-slice turbo field gradient echo-echo-planar imaging sequence. Patients were able to communicate with the technician or doctor during the exam via intercom and were regularly asked about the occurrence of symptoms like shortness of breath or angina. Late gadolinium enhancement images were acquired 10 min after the contrast agent injection. We used the contrast agent Gadovist™ (Bayer AG, Leverkusen, Germany) at a dose of 0.1–0.2 mmol/kg. Image analysis was performed using the IntelliSpace Portal (Philips Healthcare) and cvi42 (Circle Cardiovascular Imaging, Calgary, Canada). Images were verified for the presence of an LV thrombus and analyzed by two independent readers with more than 3 years of clinical CMR experience each. LV wall motion including the presence of a local akinesia or aneurysm (defined qualitatively as an abnormality in the diastolic contour with systolic dyskinesis) was assessed [41]. Each thrombus was classified as either mural (flat and parallel to the endocardial surface) or protruding (projecting into the left ventricular cavity) and mobile (motion of the thrombus independently of surrounding myocardial wall) or non-mobile as described earlier [41]. Global and regional (at the site of thrombus) longitudinal strain was calculated using the feature tracking module of cvi42.

This retrospective study was approved by the ethical commission of our institution (S-151/2019) and followed the declaration of Helsinki.

Adverse events and follow-up

During the CMR scans, the occurrence of moderate or severe symptoms as well as the occurrence of minor or major adverse events was noted. A minor adverse event was defined as persisting severe symptoms or arrhythmias needing therapy. Major adverse cardiovascular events (MACE) were defined as cardiovascular death or non-fatal thromboembolic event such as stroke, transient ischemic attack, myocardial infarction, or other arterial embolism.

Patients' follow-up was conducted by telephone interview, hospital follow-up or at their outpatient cardiologist

for the occurrence of death from any cause and, limited to 12 months, for the occurrence of MACE. Controls were followed up for 12 months for the occurrence of MACE. Medication with oral anticoagulant before and after CMR was registered for both patients and controls.

Statistical analysis

Analyses were carried out using the R language and environment for statistical computing (version 4.2.1) with the user interface R Studio (version 2023.06.0/421) [42].

Normal distribution was assessed by using the Shapiro–Wilk test. Parametric variables are given as mean \pm standard deviation and non-parametric variables as median with interquartile range.

For the comparison of normally distributed parameters between two groups, the Welch two-sample t-test was used. Non-parametric parameters were tested for differences using the Wilcoxon rank-sum test. A Pearson's Chi-squared test of independence was employed to test for a correlation between two variables. A Kaplan–Meier estimator was calculated to visualize survival probability. The a priori significance level was set to $p < 0.05$.

Results

Study population

19,312 patients in our databank were screened and 95 (78 male/17 female, 65 ± 10.7 years) fulfilled the inclusion criteria. Cardiovascular risk factors were frequent, 40 patients (42.1%) exhibited ≥ 3 risk factors. 93 patients (97.8%) had a history of a prior myocardial infarction, which occurred in the last 6 months before the CMR in 35 (36.8%) of those. In 68 of those patients (73.1%), initial reperfusion therapy had been successful (TIMI 2 in 7 patients, TIMI 3 in 61 patients). In another 15 (16.1%), reperfusion had been attempted but ultimately failed (TIMI 0 in 14 patients, TIMI 1 in 1 patient). After the myocardial infarction diagnosis, of those 83 patients 61 were treated in the form of dual therapy and 22 in the form of triple therapy. Ultimately, in 11 patients (11.8%) a myocardial infarction had not been noticed or diagnosed before, but invasive coronary angiography showed a total (9 patients, TIMI 0) or near total (2 patients, TIMI 1) occlusion of a coronary artery and CMR showed late gadolinium enhancement suggestive of past myocardial infarction. Since troponin values were inconspicuous, no reperfusion therapy was attempted, and no new medication was started in those 11 patients. A relevant portion of patients had an active malignant disease (10.5%), a known thrombophilia (3.2%), or a history of previous arterial (24.2%) or venous (12.6%) thrombosis. For all patients, a complete medical history with

all events prior to and up to 48 h after the CMR exam was available. For MACE, a 30 day and 12 month follow-up was available for 94 (98.9%) and 89 (93.7%) patients, respectively. All patient characteristics are given in Table 1.

For the matched control group, 89 patients were identified to match the 89 patients of the study group for whom a 12 month follow-up was available. A 12-month follow-up

Table 1 Overview of the characteristics of all included patients

Total number of patients	95
Men/Women	78/17 (82.1%/17.9%)
Age (years)	65 ± 10.7
New York Heart Association class	
I	19 (20.0%)
II	49 (51.2%)
III	26 (27.4%)
IV	1 (1.1%)
Canadian Cardiovascular Society grading	
0	24 (25.3%)
1	38 (40.0%)
2	23 (24.2%)
3	10 (10.5%)
4	2 (2.1%)
Cardiovascular risk factors for CAD	
Hypertension	67 (70.5%)
Smoking habit	45 (47.4%)
Hypercholesterolaemia	54 (56.8%)
Diabetes	26 (27.4%)
Family history	31 (32.6%)
Obesity	18 (18.9%)
Medical history	
Prior MI	93 (97.8%)
Culprit lesion: LAD	78 (83.9%)
Culprit lesion: LCX	7 (7.5%)
Culprit lesion: RCA	9 (9.7%)
Peak high sensitivity Troponin T	3095 ng/l (1434; 7797)
MI in the last 6 months	35 (36.8%)
No prior venous or arterial thrombosis	63 (66.3%)
Prior TIA ^a	3 (3.2%)
Prior stroke ^a	8 (8.4%)
Prior LV thrombus ^b	11 (11.6%)
Prior other arterial embolism ^a	4 (4.2%)
Prior pulmonary embolism	5 (5.3%)
Prior deep vein thrombosis	10 (10.5%)
Active malignant disease	10 (10.5%)
Known thrombophilia	3 (3.2%)

MI myocardial infarction, LAD left anterior descending artery, RCA right coronary artery, LCX circumflex artery, TIA transient ischemic attack

^aOver 12 months before the current LV thrombus diagnosis

^bWith evidence of disappearance > 12 months prior to current CMR

after CMR and details about embolic events prior to the CMR were available for all controls. As per matching, sex [72 male, 17 female], age (62 ± 13.3 years) and LV ejection fraction ($36.7 \pm 13.4\%$) did not differ between the study group and controls. Neither did the rate of anticoagulation prior to ($p=0.84$) or after the CMR exam ($p=0.77$). The underlying cardiac pathology was an ischemic cardiomyopathy in 61 (68.5%), a dilated cardiomyopathy in 14 (15.7%) and another non-ischemic cardiomyopathy in 14 (15.7%). Cardiovascular risk factors were equally common with hypertension in 51 (57.3%), a smoking habit in 50 (56.2%), hypercholesterolaemia in 35 (39.3%), diabetes in 15 (16.9%), family history in 15 (16.9%) and obesity in 18 patients (20.2%), respectively.

CMR results

CMR showed a reduced ejection fraction in most patients (89.5%), with 46.3% of patients exhibiting an ejection fraction of $<40\%$, a known precipitator of thrombus development [43]. Global longitudinal strain was $-9.3 \pm 2.2\%$, whereas regional longitudinal strain at the thrombus location was significantly lower ($-2.8 \pm 2.6\%$, $p < 0.001$). In 87.4% of patients, the thrombus was located in the apex and local akinesia was present at the site of the thrombus in nearly all patients (98.9%). 83.2% had an aneurysm at the site of the thrombus. Multiple thrombi were present in 12.6% and protruding thrombi in 51.6%. The mean thrombus size (2D) was $1.6 \pm 1.6 \text{ cm}^2$. 43 patients underwent dobutamine stress (36 high-dose, 7 low-dose) whereas 52 underwent vasodilator stress CMR. Heart rate increased in all groups, most notably during high-dose dobutamine stress ($\Delta 68/\text{min}$). The dobutamine stress CMR was positive in 3 cases and vasodilator stress CMR in 9 cases. The positive stress CMR lead to a successful revascularization of the affected coronary via PCI in 7 patients and via Bypass in 2 patients. In 1 patient, a coronary artery bypass surgery was initiated but ultimately failed. In 4 patients (2 of those with negative stress CMR but persisting symptoms) a revascularization via PCI was planned but estimated as technically infeasible during invasive diagnostic angiography. CMR data is given in Tables 2, 3 and exemplary cases are shown in Fig. 1.

Safety of stress CMR in LV thrombus patients

Only three patients (3.1%) experienced moderate or severe symptoms during high-dose dobutamine stress, which completely resolved without medication. There were no minor or major complications during and up to 48 h after the CMR stress exam, and no examination had to be aborted. No patient in the control group experienced symptoms or complications during CMR and up to 48 h after the exam. Details on periprocedural safety data are given in Table 4.

Table 2 Overview of the Cine-derived cardiac measurements of all patients

	Unit	Mean	SD
LVEDD	mm	56.4	7.9
LVESD	mm	40.4	10.0
LVEDV/BSA	ml/m ²	107.9	30.1
LVESV/BSA	ml/m ²	67.0	28.7
LV-EF	%	39.6	9.4
Global longitudinal strain	-%	9.3	2.2
Regional longitudinal strain on thrombus location	-%	2.8	2.6
MAPSE	mm	9.2	2.5
Septal wall thickness	mm	12.0	2.1
Lateral wall thickness	mm	7.2	1.6
LV mass/BSA	g/m ²	69.0	15.3
RVEDD	mm	43.9	6.9
TAPSE	mm	18.5	5.0

LV left ventricle, LVEDD LV end-diastolic diameter, LVESD LV end-systolic diameter, LVEDV LV end-diastolic volume, BSA body surface area, LVESV LV end-systolic volume, LV-EF LV ejection fraction, MAPSE mitral annular plane systolic excursion, RVEDD right ventricular end-diastolic diameter, TAPSE tricuspid annular plane systolic excursion

Sensitivity of echocardiography and thrombus resolution rates

In 61 patients, multimodality imaging with an additional transthoracic echocardiography within 30 days was available. The LV thrombus was only found in 17 cases (27.9%) by echocardiography. As a results of the newly diagnosed LV thrombus, anticoagulation was initiated in 65 patients. Of those, only 11 LV thrombi would have been diagnosed with echocardiography alone and the diagnosis and treatment decision were solely dependent on CMR imaging in the other 54.

Follow-up imaging (echocardiography or CMR) was conducted for 74 patients at least 3 months after the initial CMR exam. A thrombus resolution was observed in 55 cases (74.3%). In the subgroup of patients undergoing CMR as follow-up, thrombus resolution was observed in 27 of 42 patients (64.3%). There was no significant correlation between the type of anticoagulant and thrombus resolution ($p=0.299$). Data is displayed in Fig. 2.

Outcome and embolic events before vs. after CMR

In total, 27 patients and controls experienced a MACE during the follow-up period (14.7%). There was no statistical difference between the occurrence of MACE between patients and controls ($p=0.45$). Of those, 20 (9 in the study group, 11 in the control group) had occurred in the

Table 3 Overview of the performed stress exam including the type of stress agent, dosis of stress agent and vital signs before and during peak stress

	High-dose dobutamine	Low-dose dobutamine	Vasodilator stress
Number of patients	36	7	52
Stress medication	Dobutamine/atropine	Dobutamine	Adenosine ^a
Vital parameters at rest			
Heart rate (min)	67 ± 9	64 ± 13	67 ± 11
Systolic blood pressure (mmHg)	123 ± 17	118 ± 25	123 ± 16
Diastolic blood pressure (mmHg)	71 ± 12	68 ± 12	71 ± 9
Vital parameters at peak stress			
Heart rate (/min)	135 ± 14	84 ± 19	84 ± 13
Systolic blood pressure (mmHg)	129 ± 27	119 ± 19	115 ± 16
Diastolic blood pressure (mmHg)	68 ± 17	64 ± 9	61 ± 12
Stress result positive	3	n.a	9

^a 1 patient received vasodilator stress using a 0,4 mg single injection of regadenoson

Fig. 1 Image examples of six patients (1–6) with an LV thrombus on cine images (arrows) or late gadolinium enhancement images (white arrowheads). Detection of a thrombus may be difficult on cine images in some cases but is much easier on Late Gadolinium Enhancement images. Extensive transmural myocardial scar can be seen (red arrowheads) as predisposing factor for thrombus development. Patients either received high-dose dobutamine (1,3,6), low-dose dobutamine (2), or vasodilator stress with adenosine (4,5)

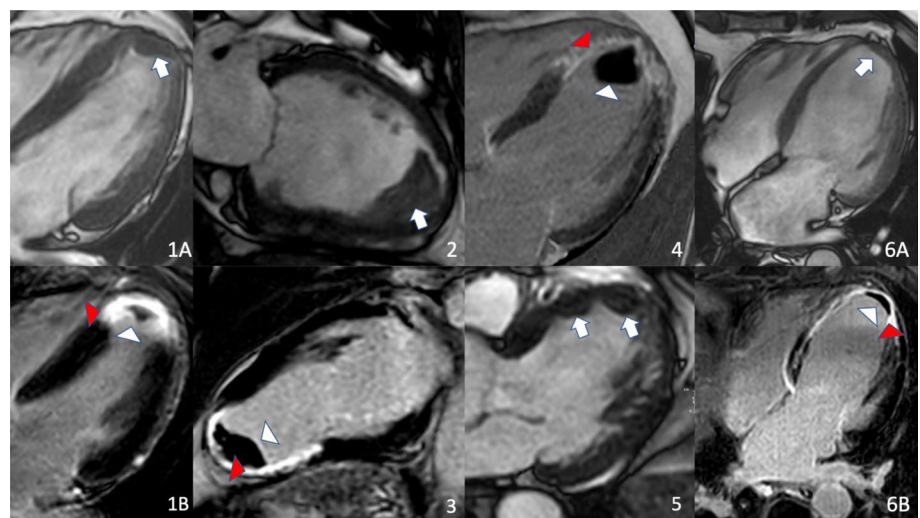


Table 4 Overview of the periprocedural safety of stress CMRs and thrombus characteristics

Periprocedural complications	
Occurrence of symptoms alone (shortness of breath or angina)	3 (3.2%)
Non-tolerable symptoms with or without need for medication	0 (0%)
New arrhythmias	0 (0%)
New embolic event	0 (0%)
Other complications	0 (0%)
LV thrombus characteristics	
Size (2D), cm ²	1.6 ± 1.6
Mobile	12 (12.6%)
Multiple thrombi	12 (12.6%)
Protruding into LV cavum	49 (51.6%)
Local acinesia	94 (98.9%)
Local aneurysm	79 (83.2%)
Apical location	83 (87.4%)

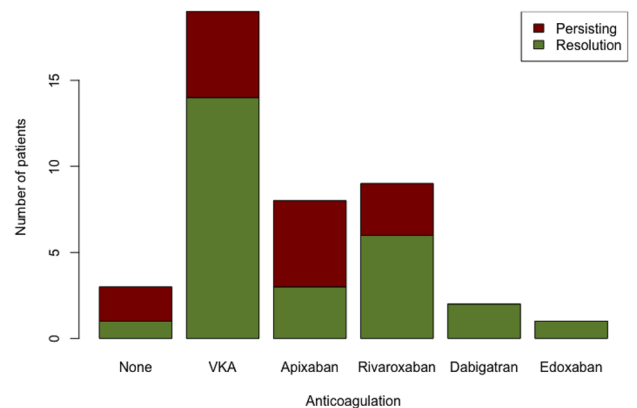


Fig. 2 Thrombus resolution and choice of contrast agent in the study group. No statistical significance between choice of contrast agent and thrombus resolution was found

12 months prior to the initial CMR exam with 12 strokes, 3 myocardial infarctions and 5 other arterial embolisms. During that time, only 29 (15.3%) of the study patients and controls were on permanent oral anticoagulation (12 on vitamin K antagonists (VKA) and 17 on direct oral anticoagulants). Among the 20 patients who experienced MACE before CMR, 15 were not receiving any anticoagulation.

The thrombus characteristics size, mobility and protrusion did not correlate with the occurrence of embolic events in the study group ($p=0.625$, $p=0.988$, $p=0.848$) or death ($p=0.329$, $p=1$, $p=0.236$). Likewise, embolic events were independent of the chosen anticoagulant ($p=0.883$ before CMR, $p=0.146$ after CMR) and stress agent ($p=0.437$) for the study group. During a median follow-up of 33.7 months, 6 deaths (6.3%) occurred in the study group with no correlation observed to the choice of stress agent or thrombus characteristics. The outcomes of the study group and controls are displayed in Fig. 3.

Discussion

In a group of 95 patients with LV thrombi at a moderate to high cardiovascular risk, this study is the first to demonstrate a high periprocedural safety of dobutamine and adenosine stress CMR in the evaluation of CAD. No adverse event occurred during and up to 48 h after the exam. Nonetheless, patients were found to be at an overall high risk as 12 patients experienced a MACE during a follow-up of 24 months. However, this risk was not associated with the stress exam since no difference in outcome was observed when compared to a sex-, age- and left ventricular ejection fraction-matched control group without a stress exam. The

addition of a stress test brought significant benefits to the patients, as 12 patients were scheduled for revascularization due to the stress exam results. In addition, there is less use of invasive diagnostic approaches after negative stress exams.

Our study reports an annual embolic event rate of 6.7% and an average annual mortality rate of 1.5%, which emphasizes the importance of thorough screening in high-risk patients [44]. Standard echocardiography alone demonstrated limited sensitivity detecting only 27.9% of LV thrombi in this study. Therefore, the identification of precipitating factors such as local wall akinesia or aneurysms through echocardiography should merit further investigations such as the use of ultrasound contrast agents or conduction of a CMR, if available [45]. In addition, cardiac computed tomography has been shown to possess high diagnostic accuracy and is widely available [46–50]. In patients with an indication for a contrast CT due to other comorbidities, cardiac CT may replace additional CMR imaging for further thrombus assessment.

A successful thrombus resolution after guideline-adherent therapy was observed in 64.3% to 74.3% of the study group, which underlines the importance of repeated imaging to adjust therapy [51]. The choice of anticoagulant did not affect resolution rates, adding evidence to previous data and current discussions about a comparable efficacy of direct oral anticoagulants and vitamin K antagonists [9, 21–24].

A higher rate of thrombus resolution might have been achieved through longer anticoagulation or by switching between anticoagulants in selected patients [2, 18, 21]. In this context it is of interest that 16.8% of the study patients were already receiving anticoagulation for other indications at the time of LV thrombus diagnosis, a fact that is not well established in the literature [52, 53].

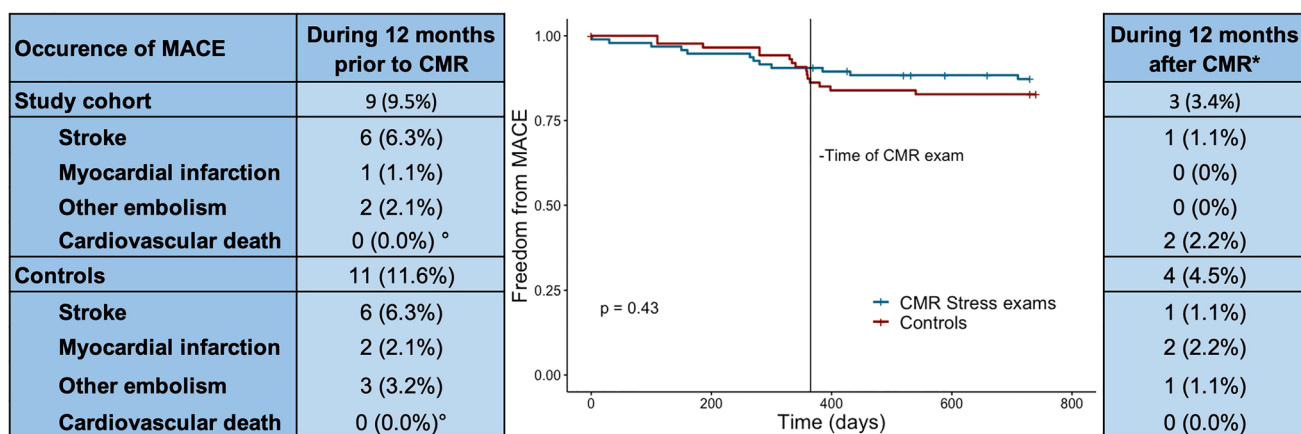


Fig. 3 Event rates of MACE of the study group and an age-, sex- and ejection fraction-matched control group in the 12 months prior compared to 12 months after CMR. A Kaplan–Meier curve shows a graphical illustration of event rates for MACE with the vertical line indicating the time of CMR with subsequent diagnosis of LV throm-

bus and (in many cases) therapeutic changes. *Data available for 89 patients. ^oPer study design patients with death before CMR were not included in the study, therefore they are underrepresented and cannot be compared between groups

Although the annual embolic event rate of 6.7% in our study is comparable to previous CMR studies, the reported annual embolic risk of previously published echocardiography studies on LV thrombus patients was higher at around 10% [25]. This difference may be attributed to the lower sensitivity of echocardiography in detecting thrombi, and therefore generally larger thrombus sizes in those studies [17, 18].

In contrast to previous data, protrusion and mobility of thrombi were not associated with an increased embolic risk. However, these studies were based on echocardiography at a time when PCI was not available as a treatment for myocardial infarction. Therefore, the comparability of these studies to our current findings may be limited [41, 54]. In agreement with our study, Cusick et al. reported no complications during moderate dobutamine stress echocardiography in 55 LV thrombus patients. However, the study fails to achieve an adequately high heart rate response (peak heart rate 114/min) and does not include postprocedural observations or outcome [55, 56].

Due to the design of our study, several limitations must be considered. Firstly, the retrospective and monocentric design of the study is a significant limitation. Together with the moderate-sized sample size it limits the generalizability and rare complications might be underrepresented. However, the study serves as an important initial investigation for the clinical use of stress CMR in appropriate LV thrombus patients and provides a basis for future prospective studies on this topic. Secondly, the embolic event rates of the study might be underestimated as small events might go unnoticed by the patients and treating physicians. Nonetheless, that is also applicable to most studies on the topic. Thirdly, the study only analysed CMR patients, which is not universally and timely available. Therefore, a selection bias needs to be considered when interpreting the data. Fourthly, the assessment of anticoagulation efficacy and an intramodality comparison to echocardiography were not the primary endpoints and thus, the statistical power is limited. In addition, the sensitivity of echocardiography might have been partly improved by the use of ultrasound contrast agents. However, the use of contrast agents is not part of a clinical routine in our hospital and was not done in our study patients. Lastly, our study only assessed drug-induced stress tests and new stressors like dynamic handgrip exercises or hyperventilation were not analysed [57–60].

Conclusions

Despite a high risk of thromboembolic events in patients diagnosed with a LV thrombus, no periprocedural adverse events occurred during CMR stress testing with dobutamine

or vasodilators. During a 12 month follow-up, the occurrence of MACE was not statistically different to a control group.

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Author contribution Conceptualization: LDW, FA, HS; study design: LDW; data acquisition: LDW, SS; data interpretation: LDW; first manuscript draft: LDW, HS, FA; manuscript revision: LDW, SS, JS, AO, JH, ACH, DS, HS, NF, FA.

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Availability of data and materials The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest The authors declare that they have no conflict of interests.

Ethical approval The ethical committee of the University of Heidelberg (S-151/2019) approved this study. Additional informed consent was waived. The study followed the 1964 Declaration of Helsinki and its later amendments.

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References

1. Robinson AA, Jain A, Gentry M, McNamara RL (2016) Left ventricular thrombi after STEMI in the primary PCI era: a systematic review and meta-analysis. *Int J Cardiol* 221:554–559
2. Bulluck H, Chan MHH, Paradies V, Yellon RL, Ho HH, Chan MY et al (2018) Incidence and predictors of left ventricular thrombus by cardiovascular magnetic resonance in acute ST-segment elevation myocardial infarction treated by primary percutaneous coronary intervention: a meta-analysis. *J Cardiovasc Magnetic Resonance Off J Soc Cardiovasc Magnetic Resonance* 20(1):72
3. Keren A, Goldberg S, Gottlieb S, Klein J, Schuger C, Medina A et al (1990) Natural history of left ventricular thrombi: their appearance and resolution in the posthospitalization period of acute myocardial infarction. *J Am Coll Cardiol* 15(4):790–800

4. Boivin-Proulx LA, Ieroncig F, Demers SP, Nozza A, Soltani M, Ghersi I et al (2023) Contemporary incidence and predictors of left ventricular thrombus in patients with anterior acute myocardial infarction. *Clin Res Cardiol Off J German Cardiac Soc* 112(4):558–565
5. Hemetsberger R, Mankerious N, Toelg R, Abdelghani M, Farhan S, Garcia-Garica HM et al (2023) Patients with higher-atherothrombotic risk vs lower-atherothrombotic risk undergoing coronary intervention with newer-generation drug-eluting stents: an analysis from the randomized BIOFLOW trials. *Clin Res Cardiol*. <https://doi.org/10.1007/s00392-023-02205-4>
6. Weinsaft JW, Kim J, Medicherla CB, Ma CL, Codella NC, Kukar N et al (2016) Echocardiographic algorithm for post-myocardial infarction LV thrombus: a gatekeeper for thrombus evaluation by delayed enhancement CMR. *JACC Cardiovasc Imaging* 9(5):505–515
7. Solheim S, Seljeflot I, Lunde K, Bjornerheim R, Aakhus S, Forfang K et al (2010) Frequency of left ventricular thrombus in patients with anterior wall acute myocardial infarction treated with percutaneous coronary intervention and dual antiplatelet therapy. *Am J Cardiol* 106(9):1197–1200
8. Srichai MB, Junor C, Rodriguez LL, Stillman AE, Grimm RA, Lieber ML et al (2006) Clinical, imaging, and pathological characteristics of left ventricular thrombus: a comparison of contrast-enhanced magnetic resonance imaging, transthoracic echocardiography, and transesophageal echocardiography with surgical or pathological validation. *Am Heart J* 152(1):75–84
9. Camaj A, Fuster V, Giustino G, Bienstock SW, Sternheim D, Mehran R et al (2022) Left ventricular thrombus following acute myocardial infarction: JACC state-of-the-art review. *J Am Coll Cardiol* 79(10):1010–1022
10. van Rein N, Heide-Jorgensen U, Lijfering WM, Dekkers OM, Sorensen HT, Cannegieter SC (2019) Major bleeding rates in atrial fibrillation patients on single, dual, or triple antithrombotic therapy. *Circulation* 139(6):775–786
11. O’Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA et al (2013) 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American college of cardiology foundation/american heart association task force on practice guidelines. *Circulation* 127(4):e362–425
12. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H et al (2018) 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the task force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European society of cardiology (ESC). *Eur Heart J* 39(2):119–177
13. Lattuca B, Bouziri N, Kerneis M, Portal JJ, Zhou J, Hauguel-Moreau M et al (2020) Antithrombotic therapy for patients with left ventricular mural thrombus. *J Am Coll Cardiol* 75(14):1676–1685
14. Tomasoni D, Sciatti E, Bonelli A, Vizzardi E, Metra M (2020) Direct oral anticoagulants for the treatment of left ventricular thrombus—a new indication? A meta-summary of case reports. *J Cardiovasc Pharmacol* 75(6):530–534
15. McCarthy CP, Murphy S, Venkateswaran RV, Singh A, Chang LL, Joice MG et al (2019) Left Ventricular thrombus: contemporary etiologies, treatment strategies, and outcomes. *J Am Coll Cardiol* 73(15):2007–2009
16. Fleddermann AM, Hayes CH, Magalski A, Main ML (2019) Efficacy of direct acting oral anticoagulants in treatment of left ventricular thrombus. *Am J Cardiol* 124(3):367–372
17. Ali Z, Isom N, Dalia T, Sami F, Mahmood U, Shah Z et al (2020) Direct oral anticoagulant use in left ventricular thrombus. *Thromb J* 18:29
18. Daher J, Da Costa A, Hilaire C, Ferreira T, Pierrard R, Guichard JB et al (2020) Management of left ventricular thrombi with direct oral anticoagulants: retrospective comparative study with vitamin K antagonists. *Clin Drug Investig* 40(4):343–353
19. Guddeti RR, Anwar M, Walters RW, Apala D, Pajjuru V, Kousa O et al (2020) Treatment of left ventricular thrombus with direct oral anticoagulants: a retrospective observational study. *Am J Med* 133(12):1488–1491
20. Iqbal H, Straw S, Craven TP, Stirling K, Wheatcroft SB, Witte KK (2020) Direct oral anticoagulants compared to vitamin K antagonist for the management of left ventricular thrombus. *ESC Heart Fail* 7(5):2032–2041
21. Jones DA, Wright P, Alizadeh MA, Fhadil S, Rathod KS, Guttman O et al (2021) The use of novel oral anticoagulants compared to vitamin K antagonists (warfarin) in patients with left ventricular thrombus after acute myocardial infarction. *Eur Heart J Cardiovasc Pharmacother* 7(5):398–404
22. Abdelnabi M, Saleh Y, Fareed A, Nossikof A, Wang L, Morsi M et al (2021) Comparative study of oral anticoagulation in left ventricular thrombi (No-LVT Trial). *J Am Coll Cardiol* 77(12):1590–1592
23. Bass ME, Kiser TH, Page RL 2nd, McIlvennan CK, Allen LA, Wright G et al (2021) Comparative effectiveness of direct oral anticoagulants and warfarin for the treatment of left ventricular thrombus. *J Thromb Thrombolysis* 52(2):517–522
24. Robinson AA, Trankle CR, Eubanks G, Schumann C, Thompson P, Wallace RL et al (2020) Off-label use of direct oral anticoagulants compared with warfarin for left ventricular thrombi. *JAMA Cardiol* 5(6):685–692
25. Velangi PS, Choo C, Chen KA, Kazmirczak F, Nijjar PS, Farzaneh-Far A et al (2019) Long-Term Embolic outcomes after detection of left ventricular thrombus by late gadolinium enhancement cardiovascular magnetic resonance imaging: a matched cohort study. *Circ Cardiovasc Imaging* 12(11):e009723
26. Maniwa N, Fujino M, Nakai M, Nishimura K, Miyamoto Y, Kataoka Y et al (2018) Anticoagulation combined with antiplatelet therapy in patients with left ventricular thrombus after first acute myocardial infarction. *Eur Heart J* 39(3):201–208
27. Kwong RY, Ge Y, Steel K, Bingham S, Abdullah S, Fujikura K et al (2019) Cardiac magnetic resonance stress perfusion imaging for evaluation of patients with chest pain. *J Am Coll Cardiol* 74(14):1741–1755
28. Baessato F, Guglielmo M, Muscogiuri G, Baggiano A, Fusini L, Scafuri S et al (2021) Stress CMR in known or suspected CAD: diagnostic and prognostic role. *Biomed Res Int* 2021:6678029
29. Weberling LD, Lossnitzer D, Frey N, Andre F (2022) Coronary computed tomography vs cardiac magnetic resonance imaging in the evaluation of coronary artery disease. *Diagnostics* 13(1):125
30. Kelle S, Chiribiri A, Vierecke J, Egnell C, Hamdan A, Jahnke C et al (2011) Long-term prognostic value of dobutamine stress CMR. *JACC Cardiovasc Imaging* 4(2):161–172
31. Lipinski MJ, McVey CM, Berger JS, Kramer CM, Salerno M (2013) Prognostic value of stress cardiac magnetic resonance imaging in patients with known or suspected coronary artery disease: a systematic review and meta-analysis. *J Am Coll Cardiol* 62(9):826–838
32. Schwitter J, Wacker CM, van Rossum AC, Lombardi M, Al-Saadi N, Ahlstrom H et al (2008) MR-IMPACT: comparison of perfusion-cardiac magnetic resonance with single-photon emission computed tomography for the detection of coronary artery disease in a multicentre, multivendor, randomized trial. *Eur Heart J* 29(4):480–489
33. Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C et al (2020) 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. *Eur Heart J* 41(3):407–477

34. Writing Committee M, Gulati M, Levy PD, Mukherjee D, Amsterdam E, Bhatt DL et al (2021) 2021 AHA/ACC/AASE/CHEST/SAEM/SCCT/SCMR guideline for the evaluation and diagnosis of chest pain: a report of the American college of cardiology/american heart association joint committee on clinical practice guidelines. *J Am Coll Cardiol* 78(22):e187–e285
35. Monmeneu Menadas JV, Garcia Gonzalez MP, Lopez-Lereu MP, Higuera Ortega L, Maceira Gonzalez AM (2022) Safety and tolerability of regadenoson in comparison with adenosine stress cardiovascular magnetic resonance: data from a multicentre prospective registry. *Int J Cardiovasc Imaging* 38(1):195–209
36. Wahl A, Paetsch I, Gollesch A, Roethemeyer S, Foell D, Gebker R et al (2004) Safety and feasibility of high-dose dobutamine-atropine stress cardiovascular magnetic resonance for diagnosis of myocardial ischaemia: experience in 1000 consecutive cases. *Eur Heart J* 25(14):1230–1236
37. Nagel E, Greenwood JP, McCann GP, Bettencourt N, Shah AM, Hussain ST et al (2019) Magnetic resonance perfusion or fractional flow reserve in coronary disease. *N Engl J Med* 380(25):2418–2428
38. Olsen LN, Fischer M, Evans PA, Gliemann L, Hellsten Y (2021) Does exercise influence the susceptibility to arterial thrombosis? An Integrative Perspective *Front Physiol* 12:636027
39. Geleijnse ML, Krenning BJ, Nemes A, van Dalen BM, Soliman OI, Ten Cate FJ et al (2010) Incidence, pathophysiology, and treatment of complications during dobutamine-atropine stress echocardiography. *Circulation* 121(15):1756–1767
40. Kramer CM, Barkhausen J, Bucciarelli-Ducci C, Flamm SD, Kim RJ, Nagel E (2020) Standardized cardiovascular magnetic resonance imaging (CMR) protocols: 2020 update. *J Cardiovasc Magnet Resonan Off J Soc Cardiovasc Magnet Reson* 22(1):17
41. Haugland JM, Asinger RW, Mikell FL, Elsparger J, Hodges M (1984) Embolic potential of left ventricular thrombi detected by two-dimensional echocardiography. *Circulation* 70(4):588–598
42. R Core Team. R (2022) A Language and environment for statistical computing. R Foundation for Statistical Computing, Vienna
43. Chiarella F, Santoro E, Domenicucci S, Maggioni A, Vecchio C (1998) PredischARGE two-dimensional echocardiographic evaluation of left ventricular thrombosis after acute myocardial infarction in the GISSI-3 study. *Am J Cardiol* 81(7):822–827
44. Esteban-Fernández A, Anguita-Sánchez M, Bonilla-Palomas JL, Anguita-Gómez M, Rosillo N, Del Prado N et al (2023) One-year readmissions for circulatory diseases and in-hospital mortality after an index episode of heart failure in elderly patients: a nationwide data from public hospitals in Spain between 2016 and 2018. *Clin Res Cardiol Off J German Cardiac Soc* 112(8):1119–28
45. Vij V, Cruz-González I, Galea R, Piayda K, Nelles D, Vogt L et al (2023) Symptomatic vs non-symptomatic device-related thrombus after LAAC: a sub-analysis from the multicenter EUROC-DRT registry. *Clin Res Cardiol Off J German Cardiac Soc.* <https://doi.org/10.1007/s00392-023-02237-w>
46. Beavers DL, Ghannam M, Liang J, Cochet H, Attili A, Sharaf-Dabbagh G et al (2021) Diagnosis, significance, and management of ventricular thrombi in patients referred for VT ablation. *J Cardiovasc Electrophysiol* 32(9):2473–2483
47. Cox M, Balasubramanya R, Hou A, Deshmukh S, Needleman L (2015) Incidental left atrial and ventricular thrombi on routine CT: outcome and influence on subsequent management at an urban tertiary care referral center. *Emerg Radiol* 22(6):657–660
48. Barnea R, Agmon IN, Shafir G, Peretz S, Mendel R, Naftali J et al (2022) Cardiac CT for intra-cardiac thrombus detection in embolic stroke of undetermined source (ESUS). *Eur Stroke J* 7(3):212–220
49. Bittencourt MS, Achenbach S, Marwan M, Selmann M, Muschiol G, Ropers D et al (2012) Left ventricular thrombus attenuation characterization in cardiac computed tomography angiography. *J Cardiovasc Comput Tomogr* 6(2):121–126
50. Korosoglou G, Thiele H, Baldus S, Boehm M, Frey N (2023) Lessons learned from SCOT-HEART, DISCHARGE, and PRECISE: a patient-centered perspective with implications for the appropriate use of CCTA. *Clin Res Cardiol Off J German Cardiac Soc.* <https://doi.org/10.1007/s00392-023-02277-2>
51. Dissabandara T, Lin K, Forwood M, Sun J (2023) Validating real-time three-dimensional echocardiography against cardiac magnetic resonance, for the determination of ventricular mass, volume and ejection fraction: a meta-analysis. *Clin Res Cardiol Off J German Cardiac Soc.* <https://doi.org/10.1007/s00392-023-02204-5>
52. Weberling LD, Steen H, Frey N, Andre F (2022) Large mobile left ventricular thrombi formation in a 32-year-old despite direct oral anticoagulation with dabigatran. *JACC Case Rep* 4(16):1015–1019
53. Knaepen L, Delesie M, Vijgen J, Dendale P, Ector J, Desteghe L et al (2023) Adherence to oral anticoagulation measured by electronic monitoring in a Belgian atrial fibrillation population. *Clin Res Cardiol Off J German Cardiac Soc.* <https://doi.org/10.1007/s00392-023-02261-w>
54. Stratton JR, Resnick AD (1987) Increased embolic risk in patients with left ventricular thrombi. *Circulation* 75(5):1004–1011
55. Cusick DA, Bonow RO, Chaudhry FA (1997) Safety of dobutamine stress echocardiography in patients with left ventricular apical thrombus. *Am J Cardiol* 80(9):1252–1254
56. Cusick DA, Bonow RO, Chaudhry FA (2000) Left ventricular apical thrombus and myocardial viability: a dobutamine stress echocardiographic study. *Echocardiography* 17(6 Pt 1):547–554
57. Ochs A, Nippes M, Salatzki J, Weberling LD, Riffel J, Muller-Hennessen M et al (2021) Dynamic handgrip exercise: feasibility and physiologic stress response of a potential needle-free cardiac magnetic resonance stress test. *Front Cardiovasc Med* 8:755759
58. Siry D, Riffel JH, Salatzki J, Andre F, Ochs M, Weberling LD et al (2022) Hyperventilation strain CMR imaging in patients with acute chest pain. *Sci Rep* 12(1):13584
59. Weberling LD, Friedrich MG (2022) Oxygenation-sensitive cardiac magnetic resonance imaging. *Radiologie* 62(11):971–976
60. Ochs MM, Kajzar I, Salatzki J, Ochs AT, Riffel J, Osman N et al (2021) Hyperventilation/breath-hold maneuver to detect myocardial ischemia by strain-encoded CMR: diagnostic accuracy of a needle-free stress protocol. *JACC Cardiovasc Imaging* 14(10):1932–1944