

Is contrast echocardiography safe and useful for the assessment of left ventricular function in the perioperative period after cardiac surgery? A pilot study

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Abstract

Background: Myocardial contrast echocardiography (CE) improves the quality of standard echocardiography. The value of CE during the early post-operative period after coronary artery bypass grafting (CABG) has not yet been well established.

Aim: To evaluate the accuracy and safety of CE used for the assessment of left ventricular (LV) function in patients after CABG in the setting of a cardiosurgery post-operative unit (CPU) in comparison with conventional transthoracic echocardiography (TTE).

Methods: Echocardiographic contrast agent Sono-Vue (Bracco, Italy) was administered in 30 consecutive patients with technically difficult TTE, after CABG treated in the CPU. Improved quality of echocardiographic imaging was assessed by the number of analysable LV segments. The LV end-diastolic and end-systolic volume (LVEDV, LVESV) and LV ejection fraction (LVEF) were calculated before and after contrast administration.

Results: There were no side effects after contrast administration. The mean number of LV segments visualised after CE increased from 8.0 ± 4 to 16.9 ± 0.1 in all patients (52.4% of improvement); 272 (52.3%) out of 510 segments were described as poorly visible using standard TTE while only four (0.8%) segments were not visible after contrast administration. Out of all visible hypokinetic, akinetic and dysketic segments, 63 (12%) segments were classified wrongly. The LV volumes were smaller and LVEF significantly higher after CE compared to standard TTE (LVEDV 127 mL vs 98 mL; LVESV 65 mL vs 45 mL; $p = 0.0002$ and $p = 0.0016$, respectively). In all methods used: visual, Simpson's method and biplane method, LVEF was significantly higher compared to standard TTE ($p = 0.012$, $p = 0.0088$, $p = 0.00065$, respectively). In patients after surgical LV restoration, CE enabled the assessment of LV geometry, patch localisation and the exclusion of the presence of LV thrombus.

Conclusions: Contrast echocardiography is a rapid, simple and safe technique when performed at bedside in a cardiosurgery post-operative unit setting, permitting accurate both segmental and global wall motion analysis. The use of contrast echocardiography could help to identify causes leading to LV systolic dysfunction immediately after CABG surgery.

Key words: contrast echocardiography, CABG surgery, left ventricular systolic function

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INTRODUCTION

Systolic function of the left ventricle (LV) is a powerful predictor of morbidity and mortality in patients undergoing coronary artery by-pass (CABG) surgery [1]. In the early post-operative period, LV function remains critical for patient management and preventative treatment strategies [2]. The echocardiographic evaluation of LV function is qualitative, subjective, and experience-dependent, because it is mostly based on visual interpretation of grey-scale two-dimensional images. Adequate endocardial visualisation is essential for the accurate interpretation of regional wall thickening abnormalities which contribute to LV dysfunction and for reproducible assessment of LV ejection fraction (LVEF) [3, 4]. Studies performed in the last decade have estimated the percentage of patients with suboptimal endocardial delineation by fundamental imaging at 30% [5]. Poor image quality is a major limitation of transthoracic echocardiography (TTE) in patients immediately after CABG surgery.

Real-time myocardial contrast echocardiography (CE), which enables reproducible and reliable LV opacification, improves the quality of standard echocardiography [6]. The role of CE in the setting of critically ill patients is well established. However, the value of CE during the early post-operative period after CABG surgery has yet to be evaluated.

We aimed to evaluate the accuracy and safety of CE used for the assessment of LV systolic function in patients after CABG surgery in the setting of a cardiosurgery post-operative unit (CPU) in comparison with conventional TTE.

METHODS

Between January and July 2008, 30 patients (21 men, nine women, mean age 64.3 ± 8.4 years), hospitalised in a CPU after elective CABG surgery with technically difficult TTE, were prospectively enrolled into this open-label study. Exclusion criteria were: age less than 18 or more than 80 years, previous cardiac surgery, haemodynamic instability, emergent CABG, severe pulmonary hypertension, and pregnancy or lactation. The baseline characteristics of the study group are set out in Table 1.

The study complied with the Declaration of Helsinki. The study protocol was approved by the local Ethics Committee and informed consent was obtained from all participants.

Transthoracic echocardiography

All studies were performed using the Vivid i (GE machine) equipped for harmonic imaging and 3.6 MHz transducer. Basic measurements, including LV size, left atrium (LA) size, interventricular septum thickness, posterior wall LV thickness and right ventricular size, were taken in every patient. Baseline harmonic imaging, including two parasternal (long and short axis) and two apical views, were used to evaluate baseline global and regional wall motion score indices using the 17 segment model prior to myocardial contrast echocardiography according to the recommendations of the European Society of Echocardiography [7]. For each wall seg-

Table 1. Patient characteristics (n = 30)

Female gender	9 (30%)
Age [years]	64.3 ± 8.4 (56–72)
BMI [kg/m ²]	29.4 ± 3.9 (25–33)
BMI > 30 kg/m ²	5 (16.6%)
Hypertension	24 (80%)
Diabetes mellitus	5 (16.6%)
Hyperlipidaemia	16 (53.3%)
Multivessel coronary artery disease	30 (100%)
History of myocardial infarction	15 (50%)
Atrial fibrillation	3 (10%)
Aneurysm of the left ventricle	3 (10%)
Chronic kidney disease	4 (13.3%)
Other cardio-vascular diseases (history of cardiac arrest, pulmonary oedema)	4 (13.3%)
Pulmonary diseases (asthma, COPD)	7 (23.3%)
Hospitalisation [days]	13.4 ± 4.3 (9–17); 13 median
Cardiosurgery post-operative unit [days]	2.9 ± 1.6 (1–5); 3 median
Aortic clamping time [min]	81.8 ± 35.9 (46–118); 66.5 median
Cardio-pulmonary by-pass time [min]	130.7 ± 43.7 (87–175); 113 median

BMI — body mass index; COPD — chronic obstructive pulmonary disease

ment, motion was scored as 1 (normal), 2 (hypokinetic), 3 (akinetic), or 4 (dyskinetic). Left ventricular ejection fraction and wall motion score index (WMSI) were obtained for all echo scans. The WMSI was obtained by dividing the sum of the segment scores by the number of segments scored. Apical two- and four-chamber views of LV were acquired using meticulous care to avoid apical foreshortening and to maximise LV length from base to apex. The LV volumes were determined using the recommended biplane summation of discs method [7].

Left ventricular end-diastolic (LVEDV), end-systolic (LVESV) volumes and LVEF were calculated in every patient. In this study, to obtain end-systolic and end-diastolic area, end-systolic and end-diastolic endocardial borders were manually traced with and without contrast enhancement, and then compared.

The LVEF was derived using the visual method, Simpson's method and also the bi-plane method, from orthogonal apical long-axis projections (four- and two-chamber views). All measurements were derived in a blind fashion by two experienced operators. The mean three measurements of the best visualised cardiac cycles were calculated for each study.

Technically difficult studies were defined as inadequate endocardial visualisation involving 50% of ventricular segments with harmonic imaging from any transthoracic imaging window.

Contrast echocardiography

Echocardiographic examinations with echocardiographic intravenous contrast agent (EICA) were performed early after CABG surgery in the setting of the CPU. Instrument setting for myocardial CE was optimised in order to have maximum sensitivity and ideal conditions for visual myocardial contrast detection. The recommended dynamic range was in the medium or mid range (45–55 dB); focal zone depth was set at approximately two thirds of the image; gain was adjusted so that myocardial tissue speckle details could be seen on baseline images (this resulted in homogenous grey backscatter throughout the entire wall of LV). Thereafter, all settings were kept constant during the acquisition of the images. The heart was visualised using harmonic imaging in either the four or two-chamber view.

The CE was performed using a modality of real-time perfusion imaging with low mechanical index (0.1). A Sono-Vue (Bracco, Italy) contrast agent was administered via a peripheral vein. A dose of 1 mL for each echocardiographic view was followed by 10 mL of saline flushed through.

Echocardiographic images were digitally stored in a cine loop format for off-line analysis by two experienced observers. Discrepancies were resolved by consensus.

Improvement of the quality of echocardiographic imaging was assessed by the number of LV segments it was possible to evaluate after contrast injection. The LVEDV, LVESV and LVEF were calculated with standard TTE and compared to the results obtained after contrast administration.

CABG

The CABG surgery was done using cardio-pulmonary by-pass. All patients underwent a revascularisation through a midline sternotomy.

Statistical analysis

Descriptive statistics (percentages for discrete variables and mean \pm SD for continuous variables) was done for baseline characteristics. Student *t* test was performed to reveal possible differences in data between groups. The χ^2 test was used to analyse the differences between the group with and without perfusion defects on CE. A *p* value \leq 0.05 was considered statistically significant. A NCSS 2007 statistical software was used.

RESULTS

Thirty consecutive patients after CABG surgery with a poor acoustic window were enrolled into the trial. Half of the patients had a history of myocardial infarction and 10% had LV aneurysm. All patients underwent CABG surgery, and 17 (56.6%) also had either valve replacement or valve repair. Thirty patients were operated using cardio-pulmonary by-pass. Types of operations are set out in Table 2. Duration of cardio-pulmonary by-pass, aortic clamping time, hospitalisation in the CPU, and the whole hospitalisation duration are set out in Table 1.

Table 2. Types of surgical procedures (patients: *n* = 30)

CABG only	13 (43.4%)
CABG + valve replacement or valve repair	17 (56.6%)
CABG + aortic valve replacement	4 (13.2%)
CABG + mitral valve repair	4 (13.2%)
CABG + mitral valve replacement	11 (36.6%)
CABG + tricuspid anuloplasty	2 (6.6%)
CABG + left ventricular reconstruction	3 (10%)

CABG — coronary artery by-pass graft

Table 3. Assessment of left ventricular segmental contractility with and without contrast agent

ECHO	Without contrast agent	With contrast agent
Segments with poor visualisation	272	4
Hypokinetic segments	58	27
Akinetic segments	32	10
Dyskinetic segments	14	4
Segments classified wrongly	63	–

There were no side effects after intravenous contrast administration. The total number of segments analysed was 510. The number of LV segments visualised after CE increased from 8.0 ± 4 to 16.9 ± 0.1 segments in all patients (52.4% of improvement); 272 (52.3%) segments were described as poorly visible, while only four (0.8%) segments were not visible after contrast administration. Moreover, 63 (12%) segments from visible hypokinetic, akinetic and dyskinetic segments were classified wrongly (Table 3). The LVEDVs were significantly smaller after contrast injection both in four- and two-chamber views ($p = 0.0002$ and $p = 0.00052$, respectively; Table 4). The LVESVs were also significantly smaller compared to standard TTE in both apical views ($p = 0.0016$, $p = 0.000004$, respectively, Table 4). As a consequence of significant differences in LV volumes, we also found differences in LVEF. In all methods used: visual, Simpson's and biplane, LVEF was significantly higher compared to standard TTE ($p = 0.011$, $p = 0.0088$, $p = 0.00065$, respectively; Fig. 1).

In three patients after the surgical LV restoration, CE enabled the assessment of LV geometry, patch localisation, and let us exclude LV thrombus. Examples of LV images using standard TTE and CE are presented in Figures 2 and 3.

DISCUSSION

Contrast echocardiography

The EICA is nowadays widely used in cardiology, especially following the publication of evidence-based recommendations by the European Association of Echocardiography [8]. According to the recommendations, CE significantly impro-

Table 4. Echocardiographic parameters with and without contrast agent

Echocardiographic parameters	Without contrast agent	With contrast agent	P <
EDV: 4-chamber view [mL]	127 ± 60.3	98 ± 40.5	0.0002
ESV: 4-chamber view [mL]	64.9 ± 35.7	45.1 ± 30.2	0.0016
LVEDV: 2-chamber view [mL]	121.0 ± 51.7	98.6 ± 34.3	0.00052
LVESV: 2-chamber view [mL]	62.2 ± 35.3	40.4 ± 27.9	0.000004
LVEF: Simpson’s method [%]	47.5 ± 13.1	52.1 ± 17.1	0.012
LVEF: visual method [%]	45.0 ± 18.4	55.0 ± 16.6	0.0088
LVEF: biplane method [%]	46.71 ± 12.8	58.5 ± 14.7	0.00065

LVEDV — left ventricular end-diastolic volume; LVESV — left ventricular end-systolic volume; LVEF — left ventricular ejection fraction

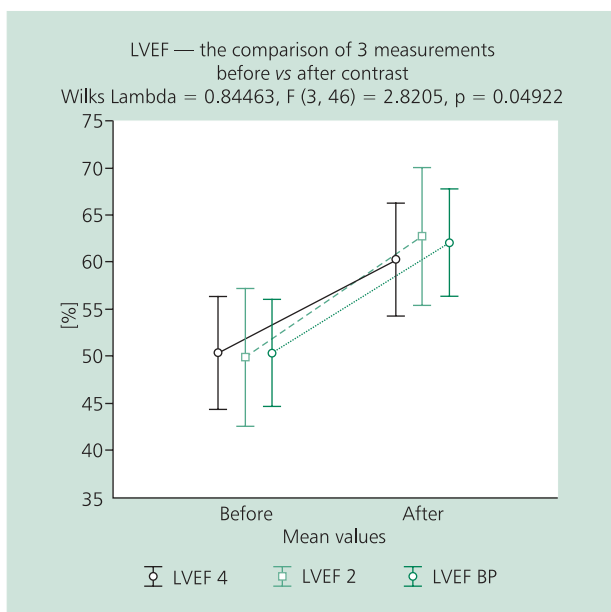


Figure 1. Comparison of left ventricular ejection fraction by various methods (visual, Simpson’s and biplane); LVEF — left ventricular ejection fraction

ves the image quality during rest and stress echocardiography (LV opacification, endocardial border delineation) and at the same time provides additional information on myocardial perfusion. Furthermore, CE reduces the need for additional, costly, and more hazardous invasive tests [9]. We worked on a widely used echo machine without specific contrast visualisation modalities (i.e. power Doppler ultraharmonics, power pulse inversion, coherent contrast imaging techniques). We would like to emphasise that good results are possible even if the echo machine does not have (relatively costly) imaging options.

The EICA contains gas microbubbles which cross pulmonary circulation, have similar properties to blood cells and may be assumed to be blood flow tracers. In our study, we used SonoVue containing sulphur hexafluoride encapsulated in a phospholipid shell. Such contrast agents, poorly soluble, not undergoing metabolism, and remaining totally in the intravascular space, are eliminated during expiration, thus

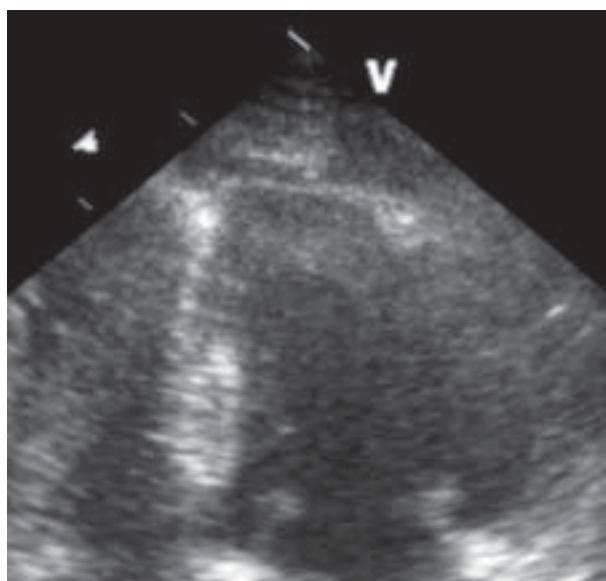


Figure 2. Echocardiographic image of left ventricle without contrast agent (four-chamber view)

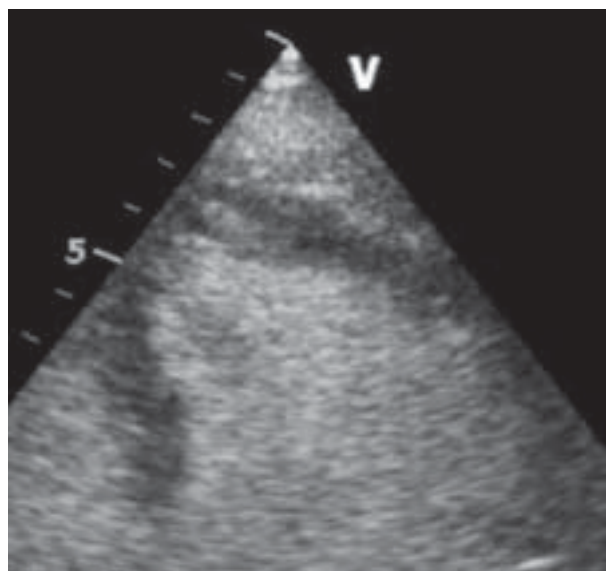


Figure 3. Echocardiographic image of left ventricle with contrast agent (four-chamber view)

not contraindicated in patients with renal failure. In the literature, the incidence of side effects is low (0.01%), mainly limited to allergic reactions [9, 10].

Value and safety of contrast echocardiography in a cardiosurgery post-operative unit

Elective CABG surgery is associated with in-hospital mortality rates of 2.03% to 5.20% with major perioperative morbidity [11]. The mortality is even higher (10.8%) when, apart from CABG, valve repair or valve replacement is necessary [12]. The mortality rate can be attributed to the recent trend of providing CABG surgery to older and sicker patients who often have compromised LV systolic function. Such older patients, with many comorbidities such as obesity, chronic obstructive pulmonary disease and emphysema, often have very difficult echocardiographic windows.

Moreover, TTE frequently provides suboptimal information immediately after CABG due to reasons such as mechanical ventilation, presence of subcutaneous emphysema and chest tubes. Most patients are unable to co-operate with the cardiologist and cannot be adequately positioned.

In these patients, EICA capable of producing LV cavity opacification can be helpful in detecting the endocardial border [4]. In a large group of patients with poor images, Spencer et al. [13] reported that contrast enhancement resulted in a significantly higher segmental salvage rate compared to harmonic imaging alone. We selected our patients on the basis of the adequacy of their baseline echocardiographic images. Our intent was to not to include patients with good images.

Few studies have examined the impact of CE in the very early period after cardiac surgery. However, the method has already been validated according to various methods such as transoesophageal echocardiography (TEE), three-dimensional echocardiography and magnetic resonance imaging (MRI). To the best of our knowledge, this is the first study in Polish literature concerning CE in the very early period after cardiac surgery.

Reilly et al. [14] and Yong et al. [15] demonstrated that the use of EICA improved the delineation of the endocardial border, the interpretation of segmental wall motion and LVEF in unselected intensive care unit patients. Contrast echocardiography provided an alternative to TEE, which is a standard, but relatively invasive technique that requires sedation and carries a risk of complications, including aspiration and laryngeal or oesophageal rupture [16]. The latter study also proved that CE is cost-effective in this setting [15].

Jenkins et al. [17] examined the accuracy of non-contrast and contrast enhanced echocardiography and three-dimensional echocardiography for calculation of LV volumes and LVEF, relative to cardiac MRI in 50 patients with past myocardial infarction who underwent echocardiographic assessment of LV volume and function. Contrast enhanced echocardiography was analogous to non-contrast three-dimensional echocardiography in accurate assessment of LV function.

Patient selection for CE in a CPU should be based not only on the adequacy of baseline images, but also on the clinical questions being asked [16, 18]. It is already known that in patients who undergo CABG surgery, the contrast opacification of Optison in the LV is not changed by cardiopulmonary bypass or alterations in fraction of inspired oxygen F(I)O₂ during intraoperative TEE. The application of Optison for enhancement of the endocardial border is not limited during cardiac surgery [17].

Aronson et al. [20] conducted intraoperative CE to determine whether the identification of regional wall motion abnormalities and myocardial flow patterns during revascularisation could predict myocardial contractile function immediately (15 min) after weaning from cardiopulmonary bypass after CABG surgery. They did not notice any serious side effects of contrast agent [20]. Eventually, safety was confirmed by recommendations of the European Association of Echocardiography in 2009 [8]. We did not observe any side effects after contrast agent application.

Left ventricular volumes and ejection fraction

To determine whether contrast echocardiography improves the evaluation of LV volumes and LVEF, Hundley et al. [21] acquired data before and after intravenous contrast injection and compared these measurements to quantitative assessments obtained by MRI. The use of contrast improved the echocardiographic assessment of LVEDV, LVESV and of LVEF. The percentage of subjects with the correct echocardiographic classification of LVEF improved significantly after contrast enhancement. These findings were striking in study subjects who had two adjacent poorly visualised segments. In our study, in which an inclusion criterion was inadequate endocardial visualisation involving at least 50% of the segments, we observed improvement in LV opacification in all patients after use of a contrast agent. According to Hundley et al. [21] Bland-Altman analysis showed that the limits of agreement (95% CI) between MRI and echocardiographic measurements of LVEDV, LVESV, and LVEF narrowed significantly after intravenous contrast injection.

Another study [22] evaluated Alunex in improving the accuracy of LV volumes and LVEF measurements which were compared to measurements taken from angiography of the LV performed within six hours of CE in 50 patients. After contrast, LV volumes were significantly more accurate than with angiography; however, there was no significant improvement in LVEF measurements. Interobserver agreement for echocardiographic measurements was also improved by CE.

In our study, manually traced end-diastolic and end-systolic areas measured after contrast injection were significantly smaller than before the use of contrast. As a consequence, both LVEDVs and LVESVs were also smaller and LVEF significantly better. We showed these differences in the group with a relatively good LV function. Such differences in LVEF may have greater clinical relevance in a population with severely injured LV. When LV volumes and function are determined by angiogra-

phy and compared to echocardiographic ones, usually the LV volumes are larger, but the LVEF is poorer by angiography than by echocardiography [23, 24]. In summary, CE spares patients further invasive and potentially hazardous diagnostics (angiographic ventriculography), semi-invasive methods like TEE or exposure to X-rays (computed tomography).

Segmental contractility disturbances

The ability to enhance endocardial border definition can also improve the accuracy of regional wall motion analysis by echocardiography. Hundley et al. [25] reported the comparison of wall motion scoring between echocardiography before and after contrast and cine MRI in 35 patients. The identification of regional wall motion abnormalities during echocardiography improved after contrast enhancement. The clinical utility of the contrast agent was greatest in the lateral and anterior walls. In these regions, the ability to distinguish normal from abnormal wall motion increased from 78% to 98% and from 65% to 88%, respectively. In our study, 52.3% of segments were not assessed at all due to a poor acoustic window, and even 12% of relatively well visible segments according to the sonographer were wrongly interpreted.

Limitations of the study

The main study limitation is the small sample size. The effects of CE on the clinical decision-making were not investigated.

CONCLUSIONS

Contrast imaging is a rapid, simple and safe technique when performed at bedside in the CPU setting, permitting accurate analysis of both segmental and global wall motion. The LVEF is significantly underestimated in echocardiography without contrast administration.

Contrast echocardiography should therefore be considered before the performance of TEE in all CPU patients in whom TTE images are inadequate for the evaluation of LV function.

Conflict of interest: none declared

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Czy kontrast echokardiograficzny jest bezpieczny i użyteczny w ocenie funkcji lewej komory w okresie okołoperacyjnym po zabiegu kardiochirurgicznym? Badanie pilotażowe

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Streszczenie

Wstęp: Kontrast echokardiograficzny poprawia jakość standardowego badania echokardiograficznego. Wartość badania kontrastowego we wczesnym okresie po operacji pomostowania aortalno-wieńcowego (CABG) nie została dotychczas dostatecznie zbadana.

Cel: Celem pracy była ocena wartości diagnostycznej i bezpieczeństwa echokardiografii kontrastowej w ocenie funkcji lewej komory u pacjentów po operacji CABG w warunkach kardiochirurgicznego oddziału pooperacyjnego w porównaniu z tradycyjną echokardiografią przezklatkową.

Metody: Kontrast echokardiograficzny Sono-Vue (Bracco, Włochy) zastosowano u 30 kolejnych pacjentów z trudnym technicznie obrazem przezklatkowym po CABG w warunkach kardiochirurgicznego oddziału pooperacyjnego. Poprawę jakości badania echokardiograficznego określano na podstawie liczby segmentów lewej komory możliwych do oceny po podaniu kontrastu. Objętość końcoworozkurczową i końcowoskurczową lewej komory (LVEDV, LVESV) oraz frakcję wyrzutową lewej komory (LVEF) oceniano przed podaniem kontrastu i po jego zastosowaniu.

Wyniki: Nie zaobserwowano skutków ubocznych podania kontrastu echokardiograficznego. Liczba segmentów lewej komory po podaniu kontrastu wzrosła z $8,0 \pm 4$ do $16,9 \pm 0,1$ (52,4% poprawy). Spośród 510 segmentów 272 (52,3%) było opisanych jako źle widoczne, podczas gdy tylko 4 (0,8%) segmenty były niewidoczne po podaniu środka kontrastowego. Spośród widocznych hipokinetycznych, akinetycznych i dyskinytycznych segmentów 63 (12%) segmenty były źle zakwalifikowane. Objętości lewej komory były mniejsze, a LVEF istotnie statystycznie wyższa po podaniu kontrastu w porównaniu ze standardowym badaniem (LVEDV 127 ml v. 98 ml; LVESV 65 ml v. 45 ml; $p = 0,0002$ i $p = 0,0016$, odpowiednio). We wszystkich metodach użytych do oceny LVEF (metodzie wizualnej, metodzie Simpsona i metodzie dwupłaszczyznowej) LVEF była istotnie wyższa w porównaniu ze standardowym badaniem ($p = 0,012$; $p = 0,0088$; $p = 0,00065$, odpowiednio). U chorych po plastyce lewej komory podanie kontrastu umożliwiło ocenę jej geometrii, lokalizację naszytej łaty oraz wykluczyło obecność zakrzepu w lewej komorze.

Wnioski: Kontrast echokardiograficzny jest szybką, prostą i bezpieczną metodą w warunkach kardiochirurgicznego oddziału pooperacyjnego, która pozwala ocenić segmentalną i globalną kurczliwość lewej komory. Zastosowanie echokardiografii kontrastowej może pomóc w różnicowaniu stanów przebiegających z dysfunkcją lewej komory tuż po operacji CABG.

Słowa kluczowe: kontrast echokardiograficzny, operacja pomostowania aortalno-wieńcowego, funkcja skurczowa lewej komory

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