

Original  
Article

# Evaluation of Left Ventricular Myocardial Work Performance in Patients Undergoing On-Pump and Off-Pump Coronary Artery Bypass Surgery

Konstantina Spetsotaki, Rashad Zayat, MD, PhD, Srinath Donuru, Ruediger Autschbach, PMD, PhD, Heike Schnoering, MD, PhD, and Nima Hatam, MD, PhD

**Purpose:** Benefits of off-pump coronary bypass (OPCAB) over on-pump (ONCAB) remain controversial. We aimed to evaluate the early impacts of OPCAB vs ONCAB for varying left ventricular (LV) function baselines by applying the non-invasive myocardial work (MW) analysis, which enables further insights in cardiac mechanics, contractility, and efficacy.

**Methods:** We retrospectively analyzed 98 patients (55 ONCAB vs 43 OPCAB). Transthoracic echocardiography (TTE) and concurrent arterial blood pressure measurements taken at rest, prior to, and early after surgery were performed. Global myocardial work index (GMWI), global constructive work (GCW), and global work efficiency (GWE), inter alia, were quantified.

**Results:** Preoperatively, OPCAB patients had significantly lower values than ONCAB patients in terms of GMWI ( $1404.33 \pm 585.41$  mmHg% vs  $1619.07 \pm 535.42$  mmHg%,  $p = 0.039$ ), GWE (90% (60%, 96%) vs 93% (74%, 98%),  $p = 0.028$ ). After surgery, GMWI was reduced in both groups. However, a more significant GMWI impairment occurred early after ONCAB than after OPCAB ( $-343.14 \pm 35.20$  mmHg%,  $p < 0.001$  vs  $-224.04 \pm 120.91$  mmHg%,  $p = 0.042$ ).

**Conclusion:** Despite lower preoperative LV function in OPCAB patients, GMWIs after OPCAB were superior to ONCAB, indicating better preservation of systolic LV function early after OPCAB by means of contractility compared to ONCAB. Further studies should investigate the long-term course of MW response and their clinical impact.

**Keywords:** echocardiography, non-invasive, global myocardial work, off-pump coronary surgery, left ventricular systolic function

Department of Thoracic and Cardiovascular Surgery, RWTH University Hospital Aachen, Aachen, Germany

Received: March 19, 2020; Accepted: June 7, 2020

Corresponding author: Nima Hatam, MD, PhD. Department of Thoracic and Cardiovascular Surgery, RWTH University Hospital, Pauwelsstr. 30, 52074 Aachen, Germany

Email: nhatam@ukaachen.de

Konstantina Spetsotaki and Rashad Zayat contributed equally first to this study.

Heike Schnoering and Nima Hatam contributed equally last to this study.

Abstract was presented at EuroEcho, December, 2019, Vienna, Austria.



This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives International License.

©2020 The Editorial Committee of *Annals of Thoracic and Cardiovascular Surgery*

## Introduction

The effectiveness of coronary artery bypass grafting (CABG) for the prognosis of multivessel and left main coronary artery disease has been proven.<sup>1,2</sup> Conventional, aortocoronary bypass (ONCAB) technique has been performed with the use of cardiopulmonary bypass (CPB). To minimize postoperative complications induced by CPB and cardioplegia, off-pump coronary artery bypass (OPCAB) grafting was introduced three decades ago.<sup>3–8</sup> However, the myocardial protection benefits of OPCAB and its impacts on early postoperative left ventricular (LV) performance remain controversial. Moreover, only few studies analyzed and compared changes in systolic left ventricular function (sLVF) after OPCAB and ONCAB.<sup>9,10</sup> Most commonly, biplane volumetric left ventricular ejection

fraction (LVEF) is solely used to define sLVF. However, the accuracy and reproducibility of biplane-LVEF measurement remain dependent on image quality/acquisition, operator skills, and loading conditions.<sup>11,12</sup> The assessment of myocardial function by means of speckle tracking has been proposed to overcome these problems but is still has load dependency as a major limitation.<sup>13,14</sup> Invasively obtained LV pressure–volume loops provide accurate assessment of hemodynamic parameters of myocardial performance by evaluating contractility, elastance, and efficiency.<sup>15</sup> Recently, Russell et al.<sup>16</sup> introduced a novel non-invasive method to measure myocardial work (MW) using two-dimensional speckle tracking echocardiography (2D-STE) strain and non-invasively estimated LV pressure curves. Russel et al. demonstrated the validity of non-invasive MW based on LV pressure–strain loop with the invasive measured MW estimated from pressure–volume loop.<sup>16,17</sup> MW measurements take myocardial deformation as well as afterload into account; therefore, it is superior to 2D-STE and EF methods and provides additional information about myocardial functionality.<sup>16,18,19</sup>

In the present study, we used this novel non-invasive method to assess myocardial performance and LV contractility, comparing preoperative and postoperative changes in two different operative strategies, OPCAB and ONCAB, for myocardial revascularization.

## Materials and Methods

### Data source

Patient's data including demographics, clinical outcome, perioperative process, postoperative course, imaging, and laboratory data were retrospectively collected from our institutional database. The study was approved by the local ethical board (Ethikkommission-RWTH Aachen, IRBP 10/2014, EK151/09-Version-1.3). Due to the retrospective nature of our study, informed consent was waived by our institutional ethical board.

### Study cohort

In this single-center, retrospective, observational study, adult patients (>18 years) who underwent isolated, elective CABG in our department between January 1, 2018 and March 30, 2019 were screened. Exclusion criteria included the following: combined procedures, emergency or urgent procedures, arrhythmia, pacemaker, aortic or mitral valve disease, hypertrophic cardiomyopathy with obstruction of LV outflow tract, history of prior cardiac surgery, severe peripheral artery disease and

inaccurate acoustic window resulting in poor transthoracic echocardiography (TTE) image quality preoperatively or postoperatively. TTEs were performed by qualified echocardiographers.

The study cohort was divided into two groups. The ONCAB group consisted of 55 patients and the OPCAB group of 43 patients, respectively.

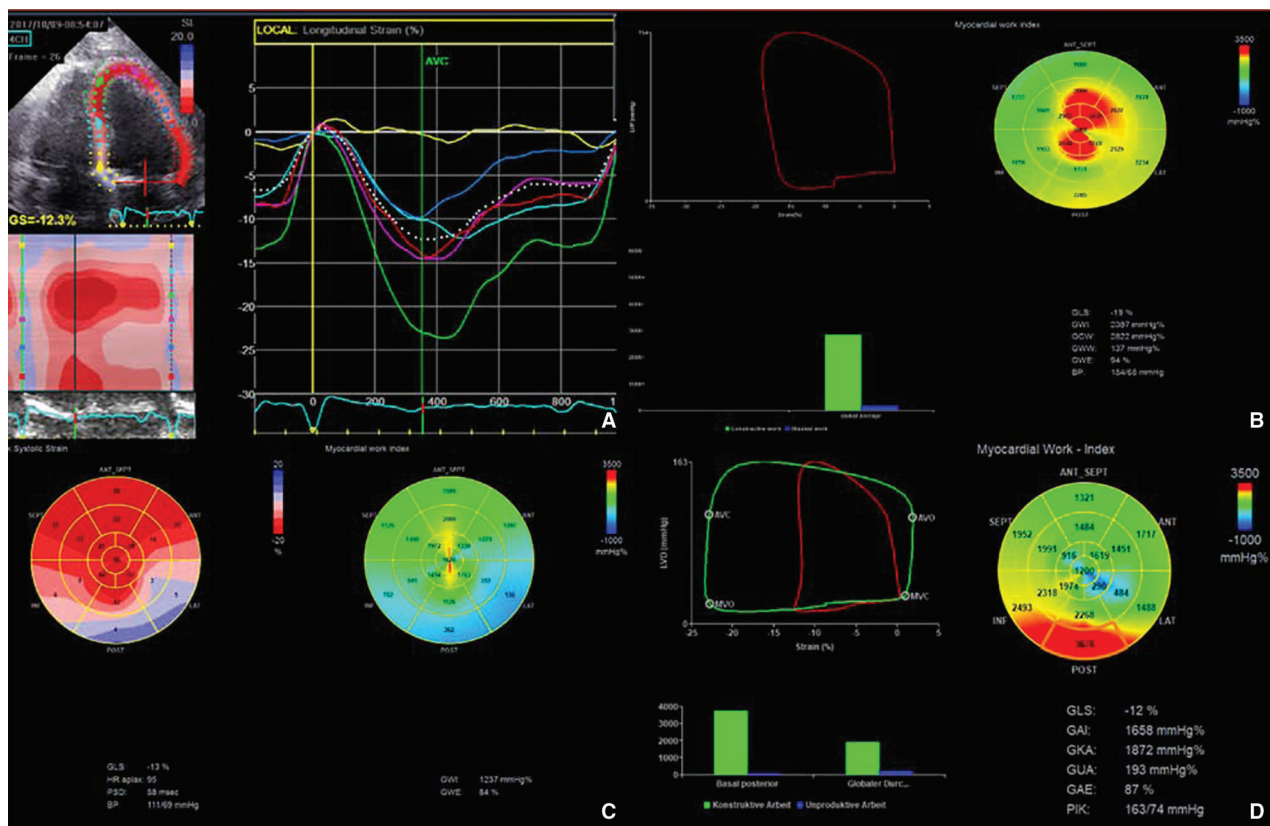
### Echocardiographic analysis and measurements of LV parameters

TTE is routinely performed for all our patients. All patients underwent preoperative and postoperative standardized TTE according to American Society of Echocardiography (ASE) and the European Association of Cardiovascular Imaging (EACVI).<sup>14,20</sup> TTE was performed the day before operation and early after surgery at a median of 7 days postoperatively. Patients were scanned in the left lateral decubitus position with standard 2D images consisting of three cardiac cycles triggered to the QRS complex saved in cine-loop digital format for offline analysis. All echocardiography studies were performed using the Vivid E9 (GE Vingmed Ultrasound AS, Horton, Norway) and the measurements were done with EchoPAC version BT 202 (GE Vingmed Ultrasound AS).

Complete offline analysis for the assessment of the LV was performed accordingly by an expert. These included M-mode, 2D and tissue-Doppler imaging (TDI) as well as 2D-STE. Biplane EF of the LV was measured using the Simpsons method from apical four-chamber (A4C) and apical two-chamber (A2C) views. Peak systolic global longitudinal strain (GLS) of the LV was indicated as an average value from the three standard apical views. The timing of aortic and mitral valve opening and closure were determined by continuous wave Doppler. The brachial-cuff systolic pressure was measured immediately prior to each patient echocardiographic process. Global myocardial work index (GMWI), global constructive work (GCW), global wasted work (GWW), myocardial work efficiency ( $MWE = GCW/(GCW + GWW)$ ) were calculated using a specific commercially available processing software package (GE Vivid E90 with the EchoPAC workstation) (**Fig. 1**) based on the described method by Russell et al.<sup>16</sup> TTE studies and analyses were performed by experienced and certified physicians.

### Surgical technique

Decision on operative technique was made after team evaluation of the cases in our daily departmental



**Fig. 1** Exemplary demonstration of selected echocardiography deformation imaging analysis. (A) GLS of LV, measured in 4CH view, (B) GMWI estimation (bull's eye), (C) peak systolic strain and GMWI bull's eye, and (D) regional and global MWI estimation. The GMWI bull's eye shows areas of negative work as blue, green indicates normal values while red shows areas of high work. GLS: global longitudinal strain; GMWI: global myocardial work index; LV: left ventricle; MWI: myocardial work index

meeting. Our practice is to perform OPCAB surgery, if deemed possible, in all multimorbid patients with prior cerebrovascular events, porcelain aorta, or severely reduced LV systolic function, presumed that the anatomy and quality of the target vessels, and the intraoperative tolerance of hemodynamic changes induced by heart positioning permit OPCAB performance. The final decision-making was left to the surgeon's preference. In both strategies, OPCAB and ONCAB, left internal mammary artery was used to bypass the left descending artery and vein grafts to bypass all other targets.

Monitoring, induction, and anesthesia were standardized for all patients. This included the use of transesophageal echocardiography (TEE). In both groups, patients received a complete revascularization and a transit-time flowmeter was used for the intraoperative control of the quality of the target vessel coronary anastomosis. All patients received the same postoperative intensive and intermediate care management.

### ONCAB Group

Under weight-adjusted full heparinization, CPB was instituted using standard cannulation techniques (single-arterial and two-stage venous). Systemic temperature was kept between 34 °C and 36 °C. After aortic cross-clamping, myocardial protection was achieved using a cold single shot of antegrade Bretschneider crystalloid cardioplegia, with a doses of 1mL/minutes per gram of myocardium, in a temperature between 5 °C and 8 °C, at an initial perfusion pressure of 80–100 mmHg (perfusion pressure was maintained at 80–90 mmHg after diastolic arrest induction), over 6–8 minutes in all patients.

### OPCAB Group

For OPCAB, all the patients received the same techniques for the exposure and lifting of the heart, and the stabilization and shunting of the target coronary vessel. Visualization, target vessel exposure, and hemostasis as well as coronary anastomosis were enhanced with the use of the same technique. An intracoronary shunt was

used in all distal anastomosis. The order of revascularization was LIMA to LAD grafting, followed by inferior and marginal coronary branches.

### Statistical analysis

All statistical analyses were performed using SPSS statistical software, version 25.0 (SPSS Inc., Chicago, IN, USA). Figures were made using Graph Pad Prism version 7.0a for MAC OS X (Graph Pad Software, La Jolla, CA, USA). The Kolmogorov–Smirnov test was used to assess the normal distribution of the continuous variables. Continuous variables are expressed as the means  $\pm$  standard deviations (SDs) or as medians (minimum, maximum) if they were non-normally distributed. Categorical variables are expressed as absolute numbers and percentages. Comparisons between groups were performed with two-tailed Student's *t*-tests for normally distributed non-repeated continuous variables and with the Mann–Whitney *U* test for non-normally distributed continuous variables. Continuous repeated variables were analyzed with the two-way analysis of variance (ANOVA) test for the comparison between and within groups. Categorical variables were analyzed with a chi-square test or, if appropriate, Fisher's exact test. *p* values were reported as three-digit numbers or with at least one nonzero digit. A *p* value  $< 0.05$  was considered statistically significant.

## Results

### Baseline, procedural, and clinical characteristics

In all, 324 patients were screened and 226 patients had to be excluded due to the following reasons: 76 patients had atrial fibrillation postoperatively, 6 patients had pacemaker implanted postoperatively, 38 patients had severe peripheral disease, 17 patients had prior cardiac surgery, preoperative TTE performed in our department revealed moderate aortic stenosis in 31 patients and moderate aortic regurgitation in 9 patients, 12 patients had moderate mitral regurgitation, and 37 patients had inaccurate image quality. The final cohort comprised of 98 patients.

All patients had an uneventful surgery. No conversion from OPCAB to ONCAB or other procedures occurred. Among the 98 studied patients in our cohort, 55 (56.1%) underwent ONCAB, and 43 (43.9%) underwent OPCAB surgery. The mean age of all patients was  $67.28 \pm 9.4$  years. The detailed data for the entire cohort

are included in **Table 1**. The two groups were well matched by means of age, body mass index (BMI), gender, and preoperative comorbidities. As expected, patients in the OPCAB group had higher European system for cardiac operative risk evaluation (EuroSCORE) II compared to ONCAB group ( $2.27 [1.10, 26.69]$  vs  $1.10 [0.54, 3.15]$ ,  $p = 0.003$ ).

In the ONCAB group, the total bypass duration time was  $98.64 \pm 24.22$  minutes, and the average cross-clamp time was  $62.62 \pm 18.54$  minutes.

All patients were clinically and hemodynamically stable and received evidence-based medical therapy in their early phase after surgery. No instances of acute myocardial infarction (MI) or neurological injury occurred. Regarding the immediate postoperative complications, there was one case of re-exploration surgery due to bleeding in each group. Maximal creatine kinase myocardial band (CK-MB) peak activity within the first 24 hours after surgery showed no significant differences between the groups. Duration of mechanical ventilation did not differ between ONCAB and OPCAB groups ( $6 \pm 2$  hr. vs  $5.5 \pm 1.5$  hr,  $p = 0.175$ , respectively). Intra-aortic balloon pump was required in one patient in the OPCAB group postoperatively, due to cardiogenic shock. In both groups, no patient required extracorporeal membrane oxygenator treatment (**Table 1**). There were no differences in the incidence of major adverse cerebral and cardiovascular events (MACCEs), acute kidney injury (AKI), sepsis, or 30-day mortality (**Table 1**).

### Echocardiographic findings

Summary of all preoperative and postoperative changes in echocardiographic measurements between and within the groups are presented in **Table 2** and **Fig. 2**

### Comparison of baseline (OPCAB vs ONCAB)

Preoperatively, OPCAB patients had significantly lower values than the ONCAB patients in terms of the GMWI ( $1404.33 \pm 585.41$  mmHg% vs  $1619.07 \pm 535.42$  mmHg%,  $p = 0.039$ ), global work efficiency (GWE; 90% [60%, 96%] vs 93% [74%, 98%],  $p = 0.028$ ), LVEF ( $47.52 \pm 14.00\%$  vs  $55.72 \pm 10.23\%$ ,  $p = 0.004$ ) and stroke volume index (SVI;  $21.94 \pm 7.39$  mL/m<sup>2</sup> vs  $27.31 \pm 9.93$  mL/m<sup>2</sup>,  $p = 0.026$ ) (**Table 2** and **Fig. 2**). Additionally, OPCAB patients had significantly higher GWW compared to ONCAB group ( $169.92 \pm 95.12$  mmHg%, vs  $109.37 \pm 64.65$  mmHg%,  $p = 0.006$ ).



**Table 1** Baseline and procedural characteristics of ONCAB and OPCAB groups

Variables	ONCAB (n = 55)	OPCAB (n = 43)	p value
Age (years)	66.23 ± 9.13	69.08 ± 8.04	0.217
Male sex	46.00 (83.63)	33.00 (76.74)	0.990
BMI	26.14 (19.25, 45.00)	26.18 (19.81, 35.43)	0.901
BSA	1.96 ± 0.19	1.90 ± 0.16	0.301
Hypertension	36.00 (65.45)	34 (79.06)	0.243
Diabetes	15.00 (27.27)	12.00 (27.9)	0.561
Current smoker	12.00 (21.81)	22 (51.16)	<b>0.003</b>
COPD >II	1.00 (1.81)	2.00 (4.65)	0.408
Stroke	0.00	0.00	–
Peripheral vascular disease	7.00 (12.72)	11.00 (25.58)	0.116
Cerebral vascular disease	11.00 (20.00)	6.00 (13.95)	0.593
STEMI	4.00 (7.27)	3.00 (6.97)	1.000
NSTEMI	15.00 (27.27)	21.00 (48.83)	<b>0.034</b>
NYHA >II	20.00 (36.36)	15.00 (34.88)	1.000
Previous cardiac surgery	2.00 (3.63)	0 (0)	0.505
Previous stent implantation	11.00 (20.00)	1.00 (2.32)	0.081
Single vessel disease	2.00 (4.65)	6.00 (13.95)	0.073
Double vessels disease	9.00 (16.36)	14.00 (32.55)	0.059
Triple vessels disease	44.00 (80.0)	22.00 (51.16)	0.005
EuroSCOREII II	1.10 (0.54, 3.15)	2.27 (1.10, 26.69)	<b>0.003</b>
CPB time, in minutes	98.64 ± 24.22	–	–
Clamp time, in minutes	62.62 ± 18.54	–	–
All cause death	0 (0)	0 (0)	–
Reintubation	1.00 (1.81)	1.00 (2.32)	1.000
MV duration in hours	6 ± 2	5.5 ± 1.5	0.175
Re-exploration	1.00 (1.81)	1.00 (2.32)	1.000
MACCE	0.00 (0)	0.00 (0)	–
Cardiogenic shock	0.00 (0)	2.00 (4.65)	0.180
Sepsis	2.00 (3.63)	2.00 (4.65)	1.000
need of IABP	0	1 (2.3)	0.431
AKI	2.00 (3.63)	1.00 (2.32)	1.000
AV-Block	0	1.00 (2.32)	0.481
CK-MB peak activity (U/L)	43.67 ± 30.23	30.49 ± 45.03	0.100
Postoperative ICU stay (days)	2.00 (0.00, 21.00)	2.00 (1.00, 112.00)	0.670

\*Categorical data are presented as number (%). Continuous data are presented as median (interquartile range), and year is shown also with the standard deviation. Plus, minus values are means ± SD. Percentages may not sum to 100 because of rounding. AKI: acute kidney injury; BMI: body mass index; BSA: body surface area; CK-MB: creatine kinase myocardial band; COPD: chronic obstructive pulmonary disease; ECMO: extra corporeal membrane oxygenation; IABP: intra-aortic balloon pump; ICU: intensive care unit; MACCE: major adverse cerebral and cardiovascular events; MV: mechanical ventilation; NSTEMI: non-ST-elevation myocardial infarction; NYHA: New York Heart Association; ONCAB: on-pump coronary artery bypass grafting; OPCAB: off-pump coronary artery bypass grafting; STEMI: ST-elevation myocardial infarction

Neither GLS ( $-13.54 \pm 5.14\%$  vs  $-15.48 \pm 4.62\%$ ,  $p = 0.055$ ) nor GCW ( $1648.92 \pm 658.75$  mmHg% vs  $1808.60 \pm 551.60$  mmHg%,  $p = 0.240$ ) did differ between the two groups preoperatively.

### Echocardiographic changes within each group

In the ONCAB group, significant reduction in GMWI GCW, SVI, GLS, and LVEF was documented postoperatively ( $p < 0.001$ ,  $p < 0.001$ ,  $p = 0.016$ ,  $p < 0.001$ ,  $p = 0.023$ ) (Table 2, Fig. 2). Postoperatively, GWW did not increase

significantly ( $p = 0.078$ ) within the ONCAB group (Table 2, Fig. 2).

In the OPCAB group, postoperative values of GWE, GCW, SVI, and left ventricular end-diastolic index (LVEDVi) did not differ significantly compared to the baseline (Table 2). While GMWI and GLS decreased significantly after surgery (mean difference  $-224.04 \pm 120.91$  mmHg%,  $p = 0.042$ ;  $-1.79 \pm 1.09\%$ ,  $p = 0.016$ , respectively), and the GWW value increased significantly ( $p = 0.028$ ) (Table 2, Fig. 2).

Table 2 Comparison of echocardiographic changes between and with the groups

	Pre-op		Post-op		OPCAB		ONCAB		OPCAB		ONCAB	
	OPCAB	ONCAB	OPCAB	ONCAB	OPCAB	ONCAB	OPCAB	ONCAB	OPCAB	ONCAB	OPCAB	ONCAB
GMWI	1619.07 ± 535.42	1404.33 ± 585.41	0.039	1275.93 ± 570.65	1180.29 ± 464.50	0.421	1619.07 ± 535.42	1312 ± 576	<0.001	1404.33 ± 585.41	1180.29 ± 464.5	0.042
GCW	1808.06 ± 551.60	1648.92 ± 658.75	0.240	1513.08 ± 608.79	1524.70 ± 497.82	0.988	1808.60 ± 551.60	1553 ± 604	0.004	1648.92 ± 658.75	1524.70 ± 497.82	0.473
GWW	109.37 ± 65.65	169.92 ± 95.12	0.006	164.81 ± 111.66	228.24 ± 168.13	<0.01	109.37 ± 64.65	164 ± 107	0.078	169.92 ± 95.12	228.24 ± 168.13	0.028
GWE	93 (74, 98)	90 (60, 96)	0.028	88 (31, 99)	85 (55, 96)	0.498	93 (74, 98)	88 (31, 99)	<0.001	90 (60, 96)	85.00 (55, 96)	0.111
SVI	27.31 ± 9.93	21.94 ± 7.39	0.026	25.16 ± 7.10	20.50 ± 6.48	0.941	27.31 ± 9.93	25.16 ± .10	0.016	21.94 ± 7.39	20.50 ± 6.48	0.964
LVEDVi	50.74 ± 13.78	50.52 ± 12.87	0.557	48.32 ± 12.95	50.42 ± 14.30	0.687	50.74 ± 13.78	48.32 ± 12.95	0.038	50.52 ± 12.87	50.42 ± 14.30	0.889
LVEF	50.77 ± 11.34	47.55 ± 12.24	0.004	50.77 ± 11.34	47.55 ± 12.24	0.498	55.72 ± 10.23	50.77 ± 11.34	0.023	47.52 ± 14.00	47.55 ± 12.24	0.972
GLS	-15.48 ± 4.62	-13.54 ± 5.14	0.055	-12.64 ± 4.09	-11.75 ± 4.05	0.588	-15.48 ± 4.62	-12.64 ± 4.09	<0.001	-13.54 ± 5.14	-11.75 ± 4.05	0.023

GCW: global constructive work (%mmHg); GLS: global longitudinal strain (%); GMWI: global myocardial work index (%mmHg); GWW: global wasted work (%mmHg); GWE: global work efficiency (%); LVEDi: left ventricular end-diastolic index; LVEF: left ventricular ejection fraction (%); Pre-op: preoperative; Post-op: postoperative; SVI: stroke volume index

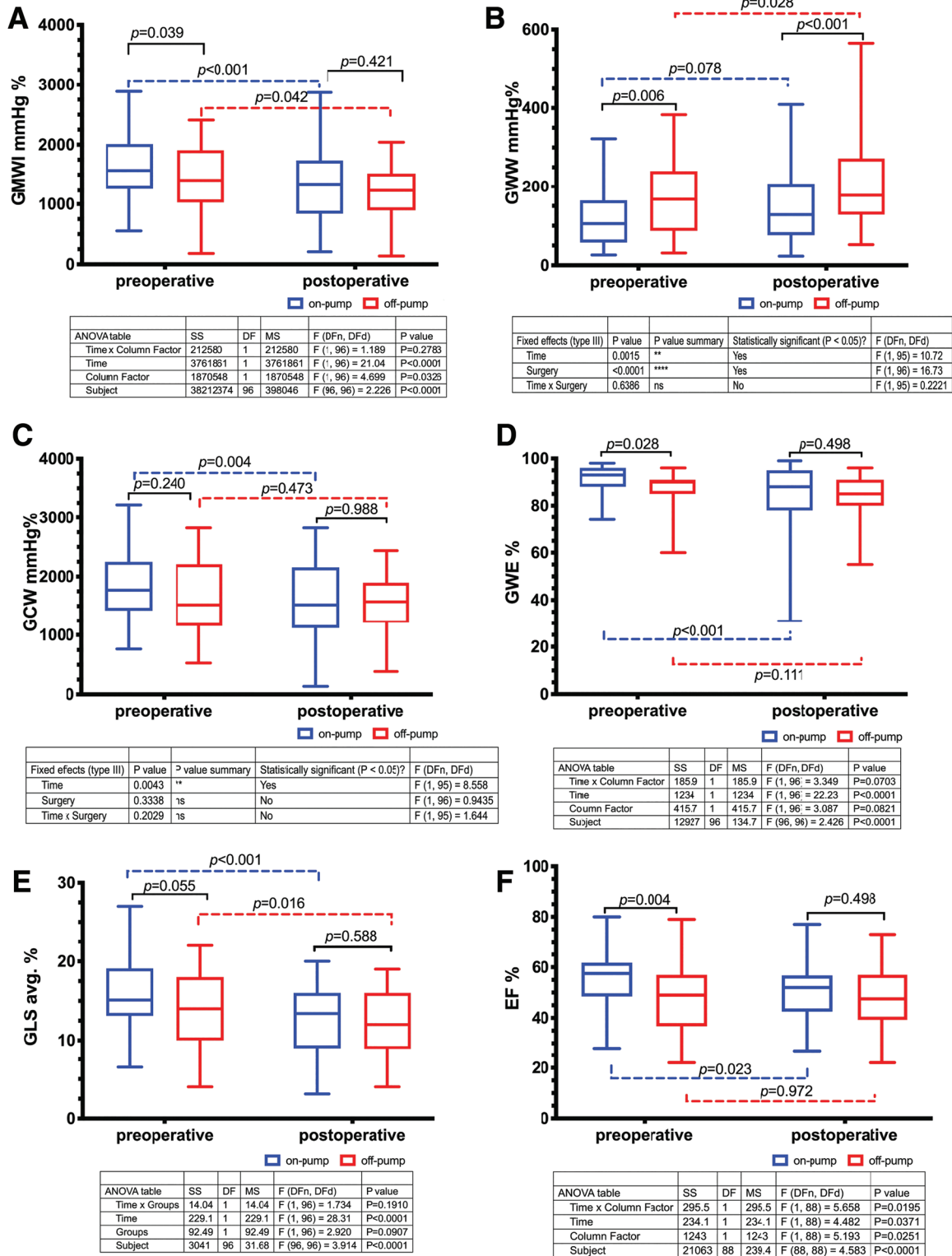
### Comparison between the groups (OPCAB vs ONCAB)

After surgery, GMWI values were reduced in both groups. However, a more significant GMWI impairment was detected early after ONCAB than after OPCAB (mean differences preoperative vs postoperative:  $-343.14 \pm 35.20$  mmHg%,  $p < 0.001$  vs  $-224.04 \pm 120.91$  mmHg%,  $p = 0.042$ ) (Table 2, Fig. 2). The GWE, GCW, SVI, and LVEF values were significantly preserved after OPCAB but reduced significantly after ONCAB ( $-5\%$  [ $-5\%$ ,  $0\%$ ],  $p = 0.111$  vs  $-5\%$  [ $-1\%$ ,  $-43\%$ ]  $p < 0.001$ ,  $-124.22 \pm 160.93$  mmHg%  $p = 0.473$  vs  $-295.52 \pm 57.19$  mmHg%,  $p = 0.004$ ,  $-1.44 \pm 0.91$  mL/m<sup>2</sup>,  $p = 0.964$  vs  $-2.15 \pm 0.07$  mmHg%,  $p = 0.016$ ,  $-0.03 \pm 1.76\%$ ,  $p = 0.972$  vs  $-5.05 \pm 1.11\%$ ,  $p = 0.023$ ). Interestingly, the GWE and SVI values were proven to be maintained after OPCAB, even with the significantly inferior baseline values.

Despite significant difference in baseline MW parameters and conventional echocardiographic measurements (Table 2, Fig. 2), postoperatively only GWW values remained significantly higher in the OPCAB group than in the ONCAB group ( $228.24 \pm 168.13$  mmHg%, vs  $164.81 \pm 111.66$  mmHg%,  $p < 0.001$ ), while GMWI, GCW, GWE, GLS, and EF remained similar between the two groups.

### Discussion

The utility of OPCAB has been well described, but its effects on sLVF have not been thoroughly investigated. To the best of our knowledge, our study is the first based on the non-invasive MW method to evaluate the early effects of ONCAB and OPCAB surgery on sLVF in patients with both normal and abnormal baseline LV function. Non-invasive assessment of myocardial performance remains a challenging topic. Deformation imaging using 2D-STE myocardial is a valuable tool, enabling extensive quantitative assessment of myocardial function far beyond EF.<sup>21,22</sup> Nonetheless, a major limitation of STE is its load dependency, which affect the accuracy of myocardial function evaluation.<sup>23</sup> Contrarily, the novel non-invasive MW measurement takes into account both deformation changes and afterload, therefore offers potentially incremental value to myocardial function evaluation.<sup>16,24</sup> Non-invasive GMWI did find clinical implications in many areas. Edwards et al.<sup>25</sup> found that non-invasive GMWI is sensitive to metabolic adaptation of the myocardium in the presence of CAD. Findings by Edwards et al.<sup>25</sup> are promising and demonstrated the possible use of non-invasive MW analysis as clinical



**Fig. 2** Comparison of echocardiographic values between the groups and within each group, before and after surgery. Two-way ANOVA table: Each F ratio is computed by dividing the MS value by another MS value. The MS value for the denominator depends on the experimental design. ANOVA: analysis of variance; DF: degrees of freedom; F: ratio; MS: mean square; PI: pulse index; rpm: revolution per minute; SS: the sum-of-squares

diagnostic utility for early detection of CAD. Previous study by Chan et al.<sup>26)</sup> demonstrated the use of non-invasive MW measurements as diagnostic tool in ischemic and non-ischemic cardiomyopathies. Non-invasive MW analysis has been used in resynchronization therapy to predict responders, who would benefit from resynchronization device therapy.<sup>27)</sup>

In our study, MW assessment revealed differences in both baseline and postoperative sLVF that even SVI and GLS failed to detect.

In summary, OPCAB proved to preserve sLVF postoperatively, despite lower baseline sLVF compared to ONCAB. The combination of the unchanged sLVF after OPCAB and the significantly reduced sLVF after ONCAB eliminated the sLVF baseline disadvantage of OPCAB patients, resulting in a similar postoperative LV performance for both groups. Our findings confirm the hypothesis that OPCAB surgery provides better preservation of sLVF compared to ONCAB early after surgery.

In our study, the two groups were well matched in terms of the preoperative and perioperative characteristics. Patients in the OPCAB group had a significantly higher EuroSCOREII than patients in the ONCAB group, mainly due to the high outlier scoring rather than to the mean. Within the ONCAB group, all patients received the same cardioplegic agent administered by the same technique. Within the OPCAB group, the same surgical technique was applied. Myocardial injury biomarkers (CK-MB) showed no significant differences between the two groups. This suggests that our results reflect real differences between ONCAB and OPCAB surgery more than patient heterogeneity of the two groups despite the small sample numbers.

GWE reflects the energy consumed by LV and is reduced in cases of reduced sLVF.<sup>18)</sup> GCW estimation allows the assessment of sLVF during the systolic and isovolumic relaxation phase. GWW reflects the energy loss, by means of work that is being produced by the ventricle, but does not contribute to LV ejection and represents a measure of contractile reserve.<sup>28)</sup>

There was a significant alter in MW indices in both groups postoperatively. Baseline GWW values proved to be higher within the OPCAB group than in the ONCAB group and continued to extend significantly after OPCAB, while no significant difference occurred after ONCAB. Hence, consequently, as GWW reflects the viable myocardium, it is possible that the higher viable myocardial reserve within the OPCAB group than within the ONCAB group might explain in part the better

preservation of LV contractility.<sup>17)</sup> In contrast, any such advantage of myocardial recovery may be temporary outweighed by the myocardial changes induced by cardioplegia during ONCAB surgery. There is evidence that cardioplegic arrest, perioperative ischemia, reperfusion injury, myocardial stunning, and hibernation trigger ultrastructural and biochemical myocardial changes that persist for hours, days, or even weeks.<sup>29)</sup> There is a variable recovery time course of the viable myocardium because dysfunctional segments can demonstrate different stages of structural abnormalities.<sup>30,31)</sup>

Only few preexisting studies have thoroughly inspected sLVF changes early after revascularization. Diller et al.<sup>32)</sup> showed that sLVF was not affected within the first 5 days after CABG, even in patients with preserved preoperative myocardial function and independently of the surgical technique (ONCAB and OPCAB). This was a small study based only on tissue Doppler imaging, which is an angle-dependent method necessitating apnea during recording.<sup>32)</sup> Letsou et al. proved that sLVF, as assessed by LVEF, improved early after OPCAB and beating heart on-pump surgery.<sup>33)</sup> Koene et al. were the first to prove a significant decrease in sLVF by means of LVEF after ONCAB in patients with normal preoperative LVEF and an increase in those with poor baseline LVEF 3 months after surgery.<sup>34)</sup> These studies lacked comparison data between ONCAB and OPCAB and referred to another follow-up period.

Our study proved an acute impairment of sLVF by terms of GMWI and MWE reduction early after both ONCAB and OPCAB surgery, tended, however, to be significantly extended after ONCAB. Substantial improvements in sLVF are often noted as early as 3–5 days after OPCAB revascularization techniques.<sup>33,35)</sup> One explanation for sLVF recovery was described by Letsou et al.,<sup>33)</sup> and they showed that CABG did increase the myocardial oxygen supply to formerly ischemic myocardial, while having no further damage to non-ischemic well-perfused myocardium.<sup>33)</sup> The avoidance of ischemic myocardial arrest (and possibly the resultant myocardial edema) might be the most essential factor in the early regeneration of myocardial function after OPCAB.

Our findings support the advantages of OPCAB over ONCAB in the sLVF preservation, in the absence of clinical impact at this early stage.

### Limitations

Due to the retrospective nature of our study, our analysis was prone to potential bias in patient selection and data acquisition. As a notable limitation, myocardial



protection was performed with crystalloid cardioplegia in this study. The postoperative differences documented in our study between the groups may considerably be lower using intermittent blood cardioplegia in the ONCAB cohort, although there were no significant postoperative differences in myocardial injury by means of enzyme profiles.

LV pressure estimation based on the arterial systolic pressure measured by the brachial-cuff sphygmomanometer might be imprecise due to variation in the arterial tree. Central systolic pressure is lower than peripheral systolic pressure due to aortic augmentation. However, in our study, we already excluded all patients with aortic stenosis, LV outflow-tract hypertrophy with obstruction, and any other cardiac pathologies that could induce a pressure gradient between aorta and LV. A further important limitation is the effect of heart rate variability and arrhythmia on MW measurements, significant beat-to-beat variability, can lead to an inaccurate assessment of GLS by 2D-STE, therefore making MW estimation questionable in such patients. In our study, we also did exclude patients with atrial fibrillations and other arrhythmias. After cardiac surgery with sternotomy, it is difficult to obtain enough acoustic window. Other factors such as obesity and pulmonary emphysema also limit the quality of TTE imaging. Reduction of ultrasound frequency to 1.5 Mhz or lower increased image quality in patients with poor acoustic windows, but at the cost of lateral resolution. Interestingly, sufficient speckle-tracking can be achieved even in med-quality TTE images, as commercial algorithms are able to resort to variability of spline smoothing using available information from the strongest ultrasound signals. Myocardial recovery appears at various stages; hence, our findings exhibit the evaluation of the sLVF at the early postoperative period, no long-term conclusion, can be drawn based on our results. Further studies of the regional and global MW parameters in larger cohorts with long-term follow-up are required.

## Conclusion

Despite lower preoperative LV function in OPCAB patients, GMWIs after OPCAB were greater compared to ONCAB patients. Our finding indicates the superiority of OPCAB in sLVF preservation over ONCAB. Further studies should investigate the long-term changes in global and regional MW parameters and their clinical impact.

## Acknowledgment

We thank Ms. Giulia Musseti (GE, Healthcare, Germany) for providing technical assistance with EchoPac and the integrated Myokardial work software.

## Disclosure Statement

All authors have declared no conflicts of interest.

## References

- 1) Stone GW, Sabik JF, Serruys PW, et al. Everolimus-eluting stents or bypass surgery for left main coronary artery disease. *N Engl J Med* 2016; **375**: 2223–35.
- 2) Park SJ, Ahn JM, Kim YH, et al. Trial of everolimus-eluting stents or bypass surgery for coronary disease. *N Engl J Med* 2015; **372**: 1204–12.
- 3) Ankeny JL. Editorial: To use or not to use the pump oxygenator in coronary bypass operations. *Ann Thorac Surg* 1975; **19**: 108–9.
- 4) Laborde F, Abdelmeguid I, Piwnica A. Aortocoronary bypass without extracorporeal circulation: why and when? *Eur J Cardiothorac Surg* 1989; **3**: 152–4; discussion 154–5.
- 5) Abu-Omar Y, Taggart DP. The present status of off-pump coronary artery bypass grafting. *Eur J Cardiothorac Surg* 2009; **36**: 312–21.
- 6) Puskas JD, Williams WH, Duke PG, et al. Off-pump coronary artery bypass grafting provides complete revascularization with reduced myocardial injury, transfusion requirements, and length of stay: a prospective randomized comparison of two hundred unselected patients undergoing off-pump versus conventional coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2003; **125**: 797–808.
- 7) Parissis H, Lau MC, Parissis M, et al. Current randomized control trials, observational studies and meta analysis in off-pump coronary surgery. *J Cardiothorac Surg* 2015; **10**: 185.
- 8) Rastan AJ, Bittner HB, Gummert JF, et al. On-pump beating heart versus off-pump coronary artery bypass surgery-evidence of pump-induced myocardial injury. *Eur J Cardiothorac Surg* 2005; **27**: 1057–64.
- 9) Ngu JMC, Ruel M, Sun LY. Left ventricular function recovery after revascularization: comparative effects of percutaneous coronary intervention and coronary artery bypass grafting. *Curr Opin Cardiol* 2018; **33**: 633–7.
- 10) Tannvik TD, Rimehaug AE, Skjaervold NK, et al. Post cardiac surgery stunning reduces stroke work, but leaves cardiac power output unchanged in patients with normal ejection fraction. *Physiol Rep* 2018; **6**: e13781.
- 11) Baron T, Berglund L, Hedin EM, et al. Test-retest reliability of new and conventional echocardiographic

- parameters of left ventricular systolic function. *Clin Res Cardiol* 2019; **108**: 355–65.
- 12) Medvedofsky D, Kebed K, Laffin L, et al. Reproducibility and experience dependence of echocardiographic indices of left ventricular function: Side-by-side comparison of global longitudinal strain and ejection fraction. *Echocardiography* 2017; **34**: 365–70.
  - 13) Brown J, Jenkins C, Marwick TH. Use of myocardial strain to assess global left ventricular function: a comparison with cardiac magnetic resonance and 3-dimensional echocardiography. *Am Heart J* 2009; **157**: 102.e101–5.
  - 14) Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2015; **28**: 1–39.e14.
  - 15) Suga H, Sagawa K. Instantaneous pressure-volume relationships and their ratio in the excised, supported canine left ventricle. *Circ Res* 1974; **35**: 117–26.
  - 16) Russell K, Eriksen M, Aaberge L, et al. A novel clinical method for quantification of regional left ventricular pressure-strain loop area: a non-invasive index of myocardial work. *Eur Heart J* 2012; **33**: 724–33.
  - 17) Russell K, Eriksen M, Aaberge L, et al. Assessment of wasted myocardial work: a novel method to quantify energy loss due to uncoordinated left ventricular contractions. *Am J Physiol Heart Circ Physiol* 2013; **305**: H996–1003.
  - 18) El Mahdiui M, van der Bijl P, Abou R, et al. Global left ventricular myocardial work efficiency in healthy individuals and patients with cardiovascular disease. *J Am Soc Echocardiogr* 2019; **32**: 1120–7.
  - 19) Hubert A, Le Rolle V, Leclercq C, et al. Estimation of myocardial work from pressure-strain loops analysis: an experimental evaluation. *Eur Heart J Cardiovasc Imaging* 2018; **19**: 1372–9.
  - 20) Mitchell C, Rahko PS, Blauwet LA, et al. Guidelines for performing a comprehensive transthoracic echocardiographic examination in adults: recommendations from the American Society of Echocardiography. *J Am Soc Echocardiogr* 2019; **32**: 1–64.
  - 21) Chan J, Shiino K, Obonyo NG, et al. Left ventricular global strain analysis by two-dimensional speckle-tracking echocardiography: the learning curve. *J Am Soc Echocardiogr* 2017; **30**: 1081–90.
  - 22) Mignot A, Donal E, Zaroui A, et al. Global longitudinal strain as a major predictor of cardiac events in patients with depressed left ventricular function: a multicenter study. *J Am Soc Echocardiogr* 2010; **23**: 1019–24.
  - 23) Dandel M, Hetzer R. Echocardiographic strain and strain rate imaging—clinical applications. *Int J Cardiol* 2009; **132**: 11–24.
  - 24) Boe E, Russell K, Eek C, et al. Non-invasive myocardial work index identifies acute coronary occlusion in patients with non-ST-segment elevation-acute coronary syndrome. *Eur Heart J Cardiovasc Imaging* 2015; **16**: 1247–55.
  - 25) Edwards NFA, Scalia GM, Shiino K, et al. Global myocardial work is superior to global longitudinal strain to predict significant coronary artery disease in patients with normal left ventricular function and wall motion. *J Am Soc Echocardiogr* 2019; **32**: 947–57.
  - 26) Chan J, Edwards NFA, Khandheria BK, et al. A new approach to assess myocardial work by non-invasive left ventricular pressure-strain relations in hypertension and dilated cardiomyopathy. *Eur Heart J Cardiovasc Imaging* 2019; **20**: 31–9.
  - 27) Galli E, Leclercq C, Hubert A, et al. Role of myocardial constructive work in the identification of responders to CRT. *Eur Heart J Cardiovasc Imaging* 2018; **19**: 1010–8.
  - 28) Russell K, Eriksen M, Aaberge L, et al. Assessment of wasted myocardial work: a novel method to quantify energy loss due to uncoordinated left ventricular contractions. *Am J Physiol Heart Circ Physiol* 2013; **305**: H996–1003.
  - 29) Selvanayagam JB, Petersen SE, Francis JM, et al. Effects of off-pump versus on-pump coronary surgery on reversible and irreversible myocardial injury: a randomized trial using cardiovascular magnetic resonance imaging and biochemical markers. *Circulation* 2004; **109**: 345–50.
  - 30) Chowdhury UK, Malik V, Yadav R, et al. Myocardial injury in coronary artery bypass grafting: on-pump versus off-pump comparison by measuring high-sensitivity C-reactive protein, cardiac troponin I, heart-type fatty acid-binding protein, creatine kinase-MB, and myoglobin release. *J Thorac Cardiovasc Surg* 2008; **135**: 1110–9, 1119.e1111-1110.
  - 31) Vanoverschelde JL, Dépre C, Gerber BL, et al. Time course of functional recovery after coronary artery bypass graft surgery in patients with chronic left ventricular ischemic dysfunction. *Am J Cardiol* 2000; **85**: 1432–9.
  - 32) Diller GP, Wasan BS, Kyriacou A, et al. Effect of coronary artery bypass surgery on myocardial function as assessed by tissue Doppler echocardiography. *Eur J Cardiothorac Surg* 2008; **34**: 995–9.
  - 33) Letsou GV, Wu YX, Grunkemeier G, et al. Off-pump coronary artery bypass and avoidance of hypothermic cardiac arrest improves early left ventricular function in patients with systolic dysfunction. *Eur J Cardiothorac Surg* 2011; **40**: 227–32.
  - 34) Koene RJ, Kealhofer JV, Adabag S, et al. Effect of coronary artery bypass graft surgery on left ventricular systolic function. *J Thorac Dis* 2017; **9**: 262–70.
  - 35) Eryilmaz S, Corapçio lu T, Eren NT, et al. Off-pump coronary artery bypass surgery in the left ventricular dysfunction. *Eur J Cardiothorac Surg* 2002; **21**: 36–40.