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Impact of transient decrease in mixed venous oxygen saturation on prognosis in off-pump coronary artery bypass surgery: a retrospective cohort study

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Background: The prognostic consequences of transient hemodynamic deterioration due to cardiac displacement, which is most severe during left circumflex artery (LCX) grafting in off-pump coronary artery bypass surgery (OPCAB) are unknown. This study aimed to investigate the association between mixed venous oxygen saturation (SvO_2) < 60% during LCX grafting and the occurrence of composite of morbidity endpoints.

Methods: Data of patients who underwent elective OPCAB between January 2010 and December 2019 were reviewed. Logistic regression analysis was performed to detect risk factors for the composite of morbidity endpoints, defined as 30-day or in-hospital mortality, postoperative myocardial infarction, prolonged mechanical ventilation > 24 h, cerebrovascular accident, and acute kidney injury.

Results: Among 1,071 patients, the composite of morbidity endpoints occurred in 303 (28%) patients. SvO_2 < 60% during LCX grafting was significantly associated with the composite of morbidity (OR: 2.72, 95% CI [1.60, 4.61], P < 0.001) along with advanced age, chronic kidney disease, ratio of early mitral inflow velocity to mitral annular early diastolic velocity, and EuroSCORE II. Other major hemodynamic variables including the cardiac index were not associated with the outcome. Additional regression analysis revealed pre-operative anemia as a predictor of SvO_2 < 60% during LCX grafting (OR: 2.09, 95% CI [1.33, 3.29], P = 0.001).

Conclusions: A decrease in SvO_2 < 60%, albeit confined to the period of cardiac displacement, was associated with a 2.7-fold increased risk of detrimental outcomes after OPCAB, implying the prognostic importance of this transient deterioration in oxygen supply-demand balance.

Keywords: Cardiac surgical procedures; Hemodynamic monitoring; Off-pump coronary artery bypass; Oxygen saturation; Prognosis; Retrospective study.

Introduction

Evidence suggests that the theoretical advantage of evading cardiopulmonary bypass in off-pump coronary artery bypass surgery (OPCAB) leads to outcome benefits in terms of attenuated risk of stroke, renal failure, and bleeding complications when compared with on-pump coronary artery bypass graft surgery (CABG) [1–3].

Nonetheless, OPCAB requires mechanical cardiac displacement for exposure of target vessels, which results in alterations to cardiac geometry and motion [4]. Manifested as impaired filling and diastolic dysfunction of the ventricles, these modifications inevitably

induce hemodynamic instability, which may complicate the perioperative course [5–7].

Although hemodynamic instability induced by mechanical cardiac displacement is transient and well tolerated in most patients, previous studies have indicated its potential adverse influence on post-operative outcomes [8,9]. As it is essential to provide sufficient cardiac output against mechanical constraints during OPCAB, it is reasonable to hypothesize that the resultant hemodynamic instability, when severe enough to jeopardize global oxygen supply-demand balance (manifested as severe decline in mixed venous oxygen saturation [SvO_2]), could adversely affect outcomes. This is of particular clinical importance in patients receiving multivessel OPCAB, including grafting at the lateral wall when hemodynamic instability is most severe [4]; however, this has not yet been comprehensively scrutinized. A hemodynamic management goal of $SvO_2 \geq 60\%$ has been advocated in cardiothoracic and vascular surgeries, including on-pump CABG [10–12], without any pertinent evidence related to OPCAB.

Therefore, this study aimed to examine the association between significant cardiac displacement-induced hemodynamic instability, reflected by $SvO_2 < 60\%$ during left circumflex artery (LCX) grafting, and the clinical outcomes of patients who underwent isolated multivessel OPCAB.

Materials and Methods

The present study was a retrospective review of a cohort of patients who underwent elective, isolated OPCAB between January 2010 and December 2019 in Severance Hospital, Seoul, Republic of Korea. The study was approved by the Institutional Review Board (IRB no. 4-2021-1412) of Yonsei University Health System (Seoul, Republic of Korea) in November 2021 and the requirement for written informed consent was waived. The study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines, and was conducted in accordance with the Ethical Principles for Medical Research Involving Human Subjects as outlined in the Helsinki Declaration of 1975 (revised 2013).

Intraoperative management

All patients received standardized anesthetic and surgical management, which was as follows: upon arrival in the operating room, standard monitoring devices were set up, including a pulmonary artery catheter (Swan-Ganz CCOmbo CCO/SvO_2™, Edwards Lifesciences LLC, USA) to monitor cardiac index and SvO_2. Anesthesia was maintained with sevoflurane and sufentanil, and rocuronium was used for neuromuscular blockade. Mechanical ventilation was adjusted to maintain normocapnia and partial pressure of arterial oxygen ≥ 100 mmHg, with a tidal volume of 8 ml/kg, an I : E ratio of 1 : 2, and 40% oxygen with air at a positive end-expiratory pressure of 5 cmH_2O.

All surgical procedures were performed through a median sternotomy, and the heart was displaced using a posterior pericardial stitch, large gauze (12 × 70 cm) swabs, and tissue stabilizer (Octopus Tissue Stabilization Systems®, Medtronic Inc., USA). During the cardiac displacement period, a crystalloid solution was infused at a fixed rate of 6 ml/kg, and an additional colloid solution was infused to compensate for blood loss. Intraoperative blood loss was collected by a cell salvage device (Cell Saver® Elite™, Haemonetics, USA), which was re-infused into the patient after grafting was completed. Hemodynamic management during the period of cardiac displacement and grafting was as follows: (1) maintenance of a mean systemic arterial pressure (MAP) above 70 mmHg either with infusion of norepinephrine or vasopressin (up to 0.3 μg/kg/h and 4 IU/h, respectively) and (2) infusion of milrinone in patients with $SvO_2 < 60\%$ for 10 min or development of mitral regurgitation grade ≥ 3. Transfusion was performed when the hematocrit level was < 25%.

Study protocol

The assessed pre-operative variables included age, sex, body mass index, presence of anemia, hypertension (HTN), diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), cerebrovascular accident (CVA), myocardial infarction (MI) within one month, congestive heart failure (CHF, defined as New York Heart Association function classification ≥ 3), EuroSCORE II, and data derived from transthoracic echocardiography. Transthoracic echocardiography was performed 1–3 days before surgery by cardiologists, and the parameters included in the analysis were left ventricular ejection fraction (LVEF), ratio of early mitral inflow velocity to mitral annular early diastolic velocity (E/e'), and left ventricular end-diastolic diameter (LVEDD). Anemia was defined as hemoglobin concentration < 12.0 g/dl in women and < 13.0 g/dl in men [13].

All intraoperative variables were prospectively recorded according to the standardized prearranged format of our institution. Hemodynamic variables including heart rate (HR), MAP, central venous pressure (CVP), mean pulmonary arterial pressure (mPAP), cardiac index, and SvO_2 were recorded at the following five time points: after the induction of anesthesia; 10 min after stabilizer application for grafting on the left anterior descending artery (LAD), LCX, and right coronary artery (RCA); and 10 min after

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sternal closure, with additional recordings of the lowest cardiac index and SvO_2 between the time points. In addition, the exact duration of each grafting procedure was recorded.

The retrieved post-operative variables included length of stay in the intensive care unit (ICU) and hospital along with a composite of major morbidity endpoints, including 30-day or in-hospital mortality, post-operative MI, prolonged mechanical ventilation (> 24 h), CVA, and acute kidney injury (AKI). Post-operative MI was defined as an elevation of creatinine kinase-MB level ≥ 50 ng/ml (10-fold more than the upper reference limit) during the first 48 h after surgery and at least one of the following: symptoms of MI, new ischemic changes on electrocardiogram, development of pathological Q waves, or imaging evidence of new loss of viable myocardium or new regional wall motion abnormality [14]. AKI was defined as acute post-operative renal insufficiency resulting in one or more of the following: increase in serum creatinine by 50% within 7 days, increase in serum creatinine by 0.3 mg/dl (26.5 μmol/L) within 2 days, or oliguria [15]. A composite of morbidity endpoints was defined as the presence of at least one of the major morbidity endpoints described above.

Study endpoints

The primary endpoint of this study was to investigate the association between SvO_2 < 60% during LCX grafting and the occurrence of the composite of morbidity endpoints. The secondary endpoints were to assess the association of SvO_2 as a continuous variable with the composite of morbidity endpoints and identify the risk factors for SvO_2 < 60% during LCX grafting when adjusted for well-known, conventional risk factors.

Statistical analysis

Statistical analyses were performed using SPSS 23.0 (IBM Corp., USA). The results are expressed as the median (Q1, Q3) or number of patients (percentage). Patients were allocated to either the SvO_2 ≥ 60% group or SvO_2 < 60% group according to their nadir SvO_2 values measured in the LCX grafting period. Continuous variables were first assessed for normality using the Kolmogorov-Smirnov test, and the Wilcoxon signed-rank test was used to analyze those variables that did not meet normality. The Chi-square or Fisher's exact tests were used to compare categorical variables between the groups. Additionally, comparisons of hemodynamic variables with their corresponding baseline values were performed using repeated-measures analysis of variance with post-hoc tests using Bonferroni's correction. To investigate the association between SvO_2 < 60% and the composite of morbidity endpoints, variables that showed significant differences between the groups, along with variables regarding SvO_2, were included in the logistic regression analysis, and multicollinearity was checked by using the variance inflation factors. The optimal cutoff values for continuous variables were determined using receiver operating characteristic (ROC) curve analysis.

Additionally, a comparison of the intraoperative hemodynamic variables between patients without any morbidity complications (non-morbidity group) and patients with at least one of the major morbidity endpoints (morbidity group) was performed in the same manner to further illustrate the hemodynamic trends of patients who exhibited morbidities afterwards. To identify risk factors for SvO_2 < 60%, the following variables were introduced a priori to the logistic regression analysis: age, HTN, DM, COPD, CKD, old CVA, MI within one month, CHF, pre-operative anemia, LVEF, E/e', and LVEDD. Statistical significance was set at $P < 0.05$.

Results

We retrospectively reviewed the electronic medical records of 1,182 patients who underwent elective multivessel OPCAB between January 2010 and December 2019. Patients with atrial septal defects or patent foramen ovale inducing left-to-right shunts (n = 78) or inadequate hemodynamic data due to failure of pulmonary artery catheter insertion were excluded (n = 33). Data from the remaining patients (n = 1,071) were analyzed (Fig. 1).

Among the assessed 1,071 patients, the composite of morbidity endpoints occurred in 303 (28.3%) patients (Supplementary Table 1). Intergroup comparisons of pre-operative variables between the SvO_2 ≥ 60% group and SvO_2 < 60% group are listed in Table 1. The SvO_2 < 60% group exhibited advanced age, higher E/e' and EuroSCORE II, and higher incidences of CKD and anemia.

The intraoperative hemodynamic data of the SvO_2 ≥ 60% group and SvO_2 < 60% group are presented in Table 2. The SvO_2 < 60% group exhibited lower cardiac index and SvO_2 values at all assessed time points when compared to those of the SvO_2 ≥ 60% group. Decline in SvO_2 below 60% was most frequently observed at the period of LCX grafting (93 patients), followed by periods of RCA grafting (23 patients) and LAD grafting (11 patients). The majority of patients who exhibited nadir SvO_2 < 60% during LAD and RCA grafting also exhibited SvO_2 < 60% during LCX grafting, with the exception of four patients whose incidence of SvO_2 < 60% was confined to the LAD (3 patients) or RCA grafting period (1 patient). None of the patients exhibited SvO_2 < 60% at baseline or after sternal closure. Supplementary Table 2 shows the hemodynamic data of the patients grouped into either the mor-

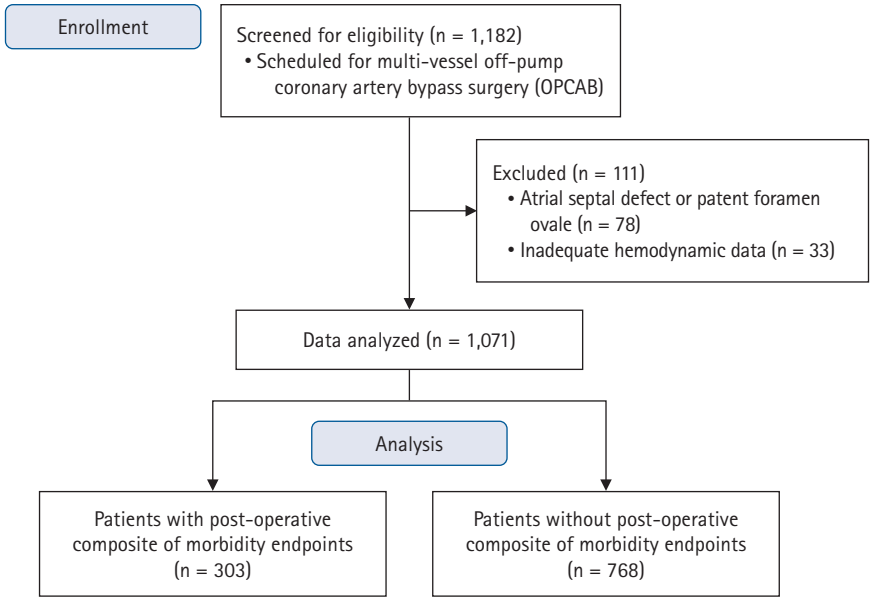

Fig. 1. Flowchart of patient enrollment.

Table 1. Pre-operative Data of Patients Classified by Nadir SvO_2 during Grafting of LCX

Variable	$SvO_2 \geq 60\%$ (n = 978)	$SvO_2 < 60\%$ (n = 93)	P value
Age (yr)	66.1 (59.2, 72.0)	69.4 (64.6, 73.2)*	0.021
Sex (M/F)	763 (78.0)/215 (22.0)	67 (72.0)/26 (28.0)	0.187
BMI (kg/m^2)	24.3 (22.3, 26.4)	24.0 (22.3, 25.5)	0.215
HTN	698 (71.4)	66 (71.0)	0.935
DM	514 (52.6)	53 (57.0)	0.413
COPD	43 (4.4)	1 (1.1)	0.123
CKD	105 (10.7)	17 (18.3)*	0.029
CVA	134 (13.7)	11 (11.8)	0.614
MI within one month	259 (26.5)	28 (30.1)	0.451
CHF	104 (10.6)	13 (14.0)	0.323
Anemia	405 (41.4)	58 (62.4)*	< 0.001
Ejection fraction (%)	58 (46, 67)	57 (46, 68)	0.999
E/e'	12.0 (9.8, 16.0)	13.0 (11.0, 16.5)*	0.026
LVEDD (mm)	51 (47, 54)	51 (47, 54)	0.413
EuroSCORE II	1.15 (0.79, 1.92)	1.51 (0.97, 2.88)*	< 0.001

Values are presented as median (Q1, Q3) or number of patients (%). SvO_2: mixed venous oxygen saturation, LCX: left circumflex artery, $SvO_2 \geq 60\%$ group: patients whose nadir SvO_2 during LCX grafting was more than or equal to 60%, $SvO_2 < 60\%$ group: patients whose nadir SvO_2 during LCX grafting was less than 60%, BMI: body mass index, HTN: hypertension, DM: diabetes mellitus, COPD: chronic obstructive pulmonary disease, CKD: chronic kidney disease, CVA: cerebrovascular accident, MI: myocardial infarction, CHF: chronic heart failure, E/e': early mitral inflow velocity/mitral annular early diastolic velocity, LVEDD: left ventricular end-diastolic diameter. *P < 0.05, compared with the $SvO_2 \geq 60\%$ group.

bidity or non-morbidity group. The morbidity group exhibited lower SvO_2 values at all assessed time points than the non-morbidity group, while no significant differences in HR, MAP, CVP, mPAP, or cardiac index were observed. The incidence of $SvO_2 < 60\%$ during the three grafting periods was significantly higher in the morbidity group.

In the multivariable logistic regression analysis, $SvO_2 < 60\%$ during LCX grafting was identified as an independent risk factor for the composite of morbidity (odds ratio [OR]: 2.72, 95% CI [1.60, 4.61], P < 0.001), along with age, CKD, E/e', and EuroSCORE II (Table 3). When introduced as a continuous variable, nadir SvO_2 during LCX grafting remained an independent risk

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Table 2. Intraoperative Hemodynamic Data of Patients Classified by Nadir SvO_2 during Grafting of LCX

Variable	Baseline	LAD grafting	LCX grafting	RCA grafting	Sternal closure	$P_{group \times time}$
HR (beats/min)						0.997
$SvO_2 \geq 60\%$ group	59 (53, 65)	66 (60, 72)*	70 (63, 76)*	71 (63, 77)*	77 (71, 82)*	
$SvO_2 < 60\%$ group	59 (53, 66)	68 (61, 74)*	70 (63, 78)*	71 (65, 79)*	77 (71, 83)*	
MAP (mmHg)						0.196
$SvO_2 \geq 60\%$ group	75 (69, 81)	77 (72, 82)*	78 (72, 84)*	77 (72, 82)*	77 (70, 84)	
$SvO_2 < 60\%$ group	76 (69, 87)	76 (71, 81)	75 (68, 82)	76 (71, 82)	77 (72, 83)	
CVP (mmHg)						0.223
$SvO_2 \geq 60\%$ group	9 (8, 11)	12 (10, 14)*	17 (13, 19)*	16 (14, 18)*	10 (8, 11)	
$SvO_2 < 60\%$ group	9 (7, 11)	11 (10, 13)*	16 (12, 19)*	16 (13, 18)*	9 (8, 11)	
mPAP (mmHg)						0.148
$SvO_2 \geq 60\%$ group	17 (15, 20)	21 (19, 23)*	24 (21, 27)*	25 (22, 27)*	18 (16, 20)	
$SvO_2 < 60\%$ group	17 (15, 20)	20 (18, 22)*	22 (19, 26)*	23 (20, 27)*	18 (16, 21)	
Cardiac index ($L/min/m^2$)						0.031
$SvO_2 \geq 60\%$ group	2.3 (1.9, 2.6)	2.0 (1.7, 2.3)*	1.8 (1.6, 2.1)*	1.8 (1.6, 2.0)*	2.2 (2.0, 2.6)	
$SvO_2 < 60\%$ group	2.1 (1.7, 2.5)†	1.7 (1.5, 2.1)*†	1.6 (1.4, 1.8)*†	1.5 (1.3, 1.7)*†	1.9 (1.6, 2.2)*†	
SvO_2 (%)						< 0.001
$SvO_2 \geq 60\%$ group	80 (77, 84)	77 (73, 81)*	73 (68, 78)*	74 (69, 78)*	78 (74, 82)*	
$SvO_2 < 60\%$ group	75 (71, 80)†	67 (62, 70)*†	57 (54, 58)*†	61 (58, 66)*†	70 (65, 75)*†	
Incidence of $SvO_2 < 60\%$ (n)						N/A
$SvO_2 \geq 60\%$ group	0 (0%)	3 (0.3%)	0 (0%)	1 (0%)	0 (0%)	
$SvO_2 < 60\%$ group	0 (0%)	8 (8.6%)†	93 (100%)†	22 (23.7%)†	0 (0%)	

Values are presented as median (Q1, Q3) or number of patients (%). SvO_2: mixed venous oxygen saturation, LCX: left circumflex artery, LAD: left anterior descending artery, RCA: right coronary artery, $SvO_2 \geq 60\%$ group: patients whose nadir SvO_2 during LCX grafting was more than or equal to 60%, $SvO_2 < 60\%$ group: patients whose nadir SvO_2 during LCX grafting was less than 60%, HR: heart rate, MAP: mean systemic arterial pressure, CVP: central venous pressure, mPAP: mean pulmonary arterial pressure. *P < 0.05, compared with baseline within the $SvO_2 \geq 60\%$ group and $SvO_2 < 60\%$ group, respectively. †P < 0.01, compared with the $SvO_2 \geq 60\%$ group.

Table 3. Predictive Power of Selected Variables for Composite Morbidity according to Logistic Regression Analysis

Variable	Univariable analysis		Multivariable analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Age	1.05 (1.03, 1.06)*	< 0.001	1.03 (1.01, 1.05)*	0.008
CKD	3.28 (2.23, 4.81)*	< 0.001	2.15 (1.32, 3.51)*	0.002
Pre-operative anemia	1.96 (1.50, 2.56)*	< 0.001	1.45 (1.00, 2.12)	0.053
E/e'	1.07 (1.05, 1.10)*	< 0.001	1.05 (1.01, 1.08)*	0.005
EuroSCORE II	1.26 (1.16, 1.37)*	< 0.001	1.12 (1.01, 1.24)*	0.040
$SvO_2 < 60\%$ during LAD grafting	4.67 (1.36, 16.10)*	0.015	2.61 (0.64, 10.56)	0.180
$SvO_2 < 60\%$ during LCX grafting	3.33 (2.16, 5.13)*	< 0.001	2.72 (1.60, 4.61)*	< 0.001
$SvO_2 < 60\%$ during RCA grafting	2.55 (1.11, 5.86)*	0.028	0.46 (0.15, 1.38)	0.166

OR: odds ratio, CKD: chronic kidney disease, E/e': early mitral inflow velocity/mitral annular early diastolic velocity, SvO_2: mixed venous oxygen saturation, LAD: left anterior descending artery, LCX: left circumflex artery, RCA: right coronary artery. *P < 0.05.

factor without changes in the statistical significance of the other risk factors mentioned above (OR: 0.94, 95% CI [0.92, 0.96], P < 0.001; Supplementary Table 3). The nadir SvO_2 of other grafting periods or cardiac index was not associated with adverse outcomes, and the ROC curve analysis revealed an optimal cut-off value for SvO_2 at LCX grafting of 70.5%, with a sensitivity of 58.1% and a specificity of 63.5% (area under the ROC: 0.66, 95% CI [0.62, 0.69], P < 0.001).

Comparisons of post-operative outcomes between the $SvO_2 \geq 60\%$ group and $SvO_2 < 60\%$ group are displayed in Table 4. Patients with $SvO_2 < 60\%$ at LCX grafting were associated with significantly longer lengths of ICU and hospital stays and higher in-

cidences of AKI and 30-day or in-hospital mortality.

In the multivariable analysis to identify risk factors of nadir SvO_2 < 60% during LCX grafting among selected variables, only pre-operative anemia remained as an independent risk factor (OR: 2.09, 95% CI [1.33, 3.29], P = 0.001; Table 5).

Discussion

In this retrospective study, transient decline of SvO_2 below 60% induced by mechanical cardiac displacement for LCX grafting was significantly associated with the composite of morbidity endpoints after OPCAB, along with previously well-known risk factors such as advanced age, CKD, E/e', and EuroSCORE II. In addition, among the known risk factors that may influence the myocardial performance governing the global oxygen supply-demand balance, only the presence of pre-operative anemia was identified as an independent risk factor for SvO_2 < 60% during LCX grafting.

SvO_2 is perceived as a suitable index for monitoring hemodynamic alterations, reflecting acute changes in the balance between oxygen delivery and consumption [16–18]. In general, the oxygen extraction ratio of major organs (except the myocardium) usually resides within the vicinity of 20% [19] and oxygen extraction ratio over 50% has been suggested as a critical value indicating a shock state reaching the maximum oxygen extraction ratio beyond compensation [20]. Thus, an SvO_2 between 50% and 60% is typically considered marginal and requires close follow-up [21]. Accordingly, the hemodynamic management goal of SvO_2 ≥ 60%

Table 4. Post-operative Data of Patients Classified by Nadir SvO_2 during Grafting of LCX

Variable	SvO_2 ≥ 60% (n = 978)	SvO_2 < 60% (n = 93)	P value
ICU days	3 (2, 3)	3 (2, 4)*	0.015
Hospital days	13 (10, 15)	14 (11, 20)*	0.003
30-day or in-hospital mortality	13 (1.3)	6 (6.5)*	< 0.001
Post-operative MI	4 (0.4)	0 (0)	0.537
Prolonged mechanical ventilation > 24 h	71 (7.3)	10 (10.8)	0.223
Post-operative CVA	21 (2.1)	2 (2.2)	0.998
AKI	192 (19.6)	41 (44.1)*	< 0.001

Values are presented as median (Q1, Q3) or number of patients (%). SvO_2: mixed venous oxygen saturation, LCX: left circumflex artery, SvO_2 ≥ 60% group: patients whose nadir SvO_2 during LCX grafting was more than or equal to 60%, SvO_2 < 60% group: patients whose nadir SvO_2 during LCX grafting was less than 60%, ICU: intensive care unit, MI: myocardial infarction, CVA: cerebrovascular accident, AKI: acute kidney injury. *P < 0.05 compared with the SvO_2 ≥ 60% group.

Table 5. Predictive Power of Selected Variables for Nadir SvO_2 < 60% during Grafting of LCX

Variable	Univariable analysis		Multivariable analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Age	1.03 (1.00, 1.05)*	0.041	1.01 (0.99, 1.04)	0.250
HTN	0.98 (0.61, 1.57)	0.935		
DM	1.20 (0.78, 1.84)	0.414		
COPD	0.24 (0.32, 1.74)	0.236		
CKD	1.86 (1.06, 3.27)*	0.031	1.25 (0.68, 2.30)	0.206
Old CVA	0.85 (0.44, 1.63)	0.614		
MI within one month	1.20 (0.75, 1.90)	0.451		
CHF	1.37 (0.73, 2.54)	0.325		
Pre-operative anemia	2.35 (1.51, 3.64)*	< 0.001	2.09 (1.33, 3.29)*	0.001
Ejection fraction	1.00 (0.98, 1.02)	0.953		
E/e'	1.02 (0.98, 1.05)	0.338		
LVEDD	1.01 (0.98, 1.04)	0.645		

SvO_2: mixed venous oxygen saturation, LCX: left circumflex artery, OR: odds ratio, HTN: hypertension, DM: diabetes mellitus, COPD: chronic obstructive pulmonary disease, CKD: chronic kidney disease, CVA: cerebrovascular accident, MI: myocardial infarction, CHF: chronic heart failure, E/e': early mitral inflow velocity/mitral annular early diastolic velocity, LVEDD: left ventricular end-diastolic diameter. *P < 0.05.

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has been advocated for cardiothoracic and vascular surgeries [10–12]. Likewise, maintaining SvO_2 above 60% has been advocated for OPCAB as well, without relevant evidence specific to this procedure [4]. We, therefore, selected the reference value of SvO_2 as 60% for an early and safe warning of tissue O_2 debt and prediction of inadequate tissue oxygenation.

In the current study, SvO_2 < 60% during LAD, LCX, and RCA was associated with an increased risk of composite of morbidity in the univariable analysis. However, when accounting for confounders in the multivariable analysis, only the prognostic importance of SvO_2 < 60% during LCX grafting was pronounced, whereas the significance of SvO_2 < 60% during LAD and RCA grafting disappeared. We presume that the extremely low incidence of isolated SvO_2 < 60% during LAD or RCA grafting (while most of the patients exhibiting SvO_2 < 60% during LAD or RCA grafting also exhibited SvO_2 < 60% during LCX grafting) contributed to diminishing the prognostic significance of SvO_2 during these periods. In addition, our results confirmed that hemodynamic deterioration during lateral wall exposure (LCX grafting) was the most severe, as was previously known [4]. Similar results were observed when SvO_2 at each time point were analyzed as a continuous variable; only SvO_2 during LCX grafting retained its close association with poor prognosis, with an OR indicating that every 1% decrease in SvO_2 during LCX grafting was responsible for a 6.3% increased risk of adverse outcomes. Additionally, the optimal cut-off value of SvO_2 to predict outcome was 70.5%, which corresponds to an approximately 10% decrease from baseline. However, the area under the ROC curve as well as sensitivity and specificity of SvO_2 as continuous variables were low, possibly because of the overlap of SvO_2 ranges among patients. Nonetheless, the OR of SvO_2 < 60% as a dichotomous variable on outcome was 2.72, which was even higher than that of CKD and showed the prognostic importance of SvO_2 considering that the composite of morbidity was mostly driven by AKI. While the clinical consequences of transient hemodynamic deterioration related to cardiac displacement have not yet been comprehensively investigated, and the advocacy of maintaining SvO_2 above 60% in OPCAB was without pertinent evidence [4], the current study provides primary evidence in that regard.

Interestingly, no difference was observed in the serially assessed cardiac index between the morbidity and non-morbidity groups (Supplementary Table 2). Although the trend of cardiac index was similar to that of SvO_2, cardiac index during LCX grafting (or at any other grafting period) showed no association with the outcome in the logistic regression analysis. Likewise, serially assessed MAP, CVP, and mPAP were all similar between the morbidity and non-morbidity groups, which may be attributable to our standardized anesthetic protocol to stabilize hemodynamic parameters during the period of cardiac displacement. Nonetheless, SvO_2 significantly differed between the two groups; this underlines the prognostic importance of SvO_2 reflecting net circulatory menace, which could not be detected by other commonly targeted major hemodynamic variables. Among the other revealed risk factors, high E/e', reflecting increased left ventricular filling pressure, also showed a close association with poor outcome, which corroborates our previous finding in a similar subset of patients implicating the prognostic significance of diastolic dysfunction [22].

Additionally, we investigated the risk factors for SvO_2 < 60% during mechanical cardiac displacement, including variables that affect cardiac function and oxygen delivery. No significant association was observed between SvO_2 and parameters derived from pre-operative transthoracic echocardiography, such as LVEF, E/e', and LVEDD, while pre-operative anemia was identified as the only predictor yielding a 2.1-fold increased risk of developing SvO_2 < 60%. This result seems logical because the influence of anemia would be critical in providing adequate oxygen-carrying capacity, especially during periods of hemodynamic instability, and adds background rationale to the importance of pre-operative anemia correction to improve patient outcomes [23].

Efforts to increase the cardiac index may be considered to attenuate the decrease in SvO_2 during mechanical cardiac displacement. However, increasing cardiac index inevitably accompanies increased myocardial oxygen consumption, which may incur ischemia and add technical burden to surgeons due to increased HR. Moreover, our results indicated that a decrease in cardiac index during grafting was not associated with detrimental outcomes. On the other hand, previous evidence has indicated that hyperoxia enhances oxygen supply by redistributing blood flow to relatively hypoperfused renal tissues and reduces systemic oxygen consumption without a significant effect on cardiac index [24,25]. Despite the potential drawbacks of hyperoxia [26], it remains to be proven whether a transient increase in the inspired oxygen fraction during grafting may actually yield improved outcomes by attenuating the decrease in SvO_2 without jeopardizing the coronary reserve.

This study has inherent limitations owing to its retrospective nature allowing for temporal bias over a 10-year period. In addition, the duration of the SvO_2 decline would also be as important as the magnitude of the drop, but this could not be clearly addressed in the current study. However, the median duration of LCX grafting in cases with SvO_2 < 60% was 11 (8–15) min, while the SvO_2 did not remain consistently below 60% during that period. Despite being a retrospective study, hemodynamic data including SvO_2 were serially gathered at the predefined five time

points with additional recordings of the lowest cardiac index and SvO_2 between the time points, as well as the exact duration of each grafting. Thus, we can assure that the duration of SvO_2 < 60% was only limited to the period of grafting. Lastly, an analysis incorporating SvO_2 values during the immediate post-operative period would have been more comprehensive.

In conclusion, transient hemodynamic deterioration induced by mechanical cardiac displacement during LCX grafting, when severe enough as reflected by SvO_2 < 60%, was associated with a 2.7-fold increased risk of adverse outcomes in patients undergoing OPCAB. Among the pre-operative risk factors including echocardiography, anemia alone was associated with the occurrence of SvO_2 < 60% during LCX grafting. The results of the current study should arouse awareness on the importance of transient hemodynamic deterioration during cardiac displacement and SvO_2 as a reliable prognostic factor in this context.

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Conflicts of Interest

Young-Lan Kwak has been an editor in chief for the Korean Journal of Anesthesiology since 2016. However, she was not involved in any process of review for this article, including peer reviewer selection, evaluation, or decision-making. There were no other potential conflicts of interest relevant to this article.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

Kyuho Lee (Data curation; Investigation; Writing – original draft)
Kwang-Sub Kim (Investigation; Methodology; Visualization)
Jong-Kwang Park (Conceptualization; Validation; Visualization)
Jun Hyug Choi (Data curation; Investigation)
Young-Lan Kwak (Conceptualization; Project administration; Validation; Writing – review & editing)
Jae-Kwang Shim (Conceptualization; Investigation; Methodology; Validation; Writing – review & editing)

Supplementary Materials

Supplementary Table 1. Incidence of morbidity endpoints.
Supplementary Table 2. Intraoperative hemodynamic data of patients classified by the composite of morbidity endpoints.
Supplementary Table 3. Predictive power of selected variables for composite morbidity according to logistic regression analysis.

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