Early Outcome of Bilateral versus Single Internal Mammary Artery Grafting in the Elderly

Running head: BIMA vs. SIMA grafting in the elderly

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Abstract

Background: Bilateral internal mammary artery (BIMA) grafting is increasingly used in the elderly without evidence of its risks or benefits compared to single internal mammary artery (SIMA) grafting.

Methods: 2899 patients aged 70 years or older (855 underwent BIMA grafting, 29.5%) operated on from January 2015 to December 2016 and included in the prospective multicenter E-CABG study were considered in this analysis.

Results: One-to-one propensity matching resulted in 804 pairs with similar preoperative risk profile. Propensity score matched analysis showed that BIMA grafting was associated with a non-statistically significant increased risk of in-hospital death (2.7% vs 1.6%, p=0.117). BIMA grafting cohort had a significantly increased risk of any sternal wound infection (7.7% vs. 5.1%, p=0.031) as well as higher risk of deep sternal wound infection/mediastinitis (4.0% vs. 2.2%, p=0.048). BIMA grafting cohort required more frequently extracorporeal membrane oxygenation (1.0% vs. 0.1%, p=0.02) and the intensive care unit stay (mean, 3.6 vs. 2.6 days, p<0.001) and in-hospital stay (mean, 11.3 vs. 10.0 days, p<0.001) were significantly longer compared with the SIMA grafting cohort. Test for interaction showed that urgent operation in patients undergoing BIMA grafting was associated with higher risk of in-hospital death (5.6% vs. 1.3%, p=0.009).

Conclusions: BIMA grafting in elderly seems to be associated with a worse early outcome compared with SIMA grafting, particularly in patients undergoing urgent operation. Until more conclusive results are gathered, BIMA grafting should be reserved only to elderly patients with stable coronary artery disease, without significant baseline comorbidities and long expectancy of life.

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Introduction

The use of bilateral internal mammary artery (BIMA) grafting has been shown to increase freedom from adverse events in the long-term follow-up after coronary artery bypass grafting (CABG) (1,2). On the other hand, the higher incidence of sternal wound infections (SWI) might overcome the late clinical benefits. Accordingly, BIMA grafts are still underutilized as its potential benefits in the elderly population are still debated (3,4). Only one randomized controlled trial has been designed to compare the outcomes of bilateral and single internal mammary artery (SIMA) grafting (5), whereas current knowledge stem from large retrospective studies and there is a lack of prospective studies specifically addressing the results of BIMA grafting in the elderly. This issue was investigated in this prospective multicenter registry.

Methods

Patient Population and Data Collection

The E-CABG registry is a prospective, multicenter study enrolling patients undergoing isolated CABG at 16 European centers of cardiac surgery (Besançon, France; Catanzaro, Italy; Genoa, Italy; Hamburg, Germany; Leicester, UK; Milan, Italy; Nuremberg, Germany; Naples, Italy; Oulu, Finland; Parma, Italy; Pedara, Italy; Rennes, France; Rome, Italy; Stockholm, Sweden; Trieste, Italy; Verona, Italy). The present study is registered in Clinicaltrials.gov (Identifier: NCT02319083) and its detailed protocol along with definition criteria are reported elsewhere (6). The Institutional Review Board of all the participating centers approved this study.

Out of 7352 consecutive patients operated on from January 2015 to December 2016 and enrolled in the E-CABG registry, 3139 patients (42.7%) were ≥70 years old. Patients operated on an emergency basis, undergoing reoperation or not receiving an internal mammary artery graft (240 patients) were excluded from the analysis. Therefore, 2899 patients were included in the present analysis. Among them, 855 patients (29.5%) underwent BIMA grafting.

Outcome End-points

The primary endpoints of this study were in-hospital death and SWI of any severity and deep wound infection/mediastinitis. Secondary end-points were prolonged inotropic support, intra-aortic balloon pump (IABP), extracorporeal membrane oxygenation (ECMO), acute kidney injury, stroke, chest tube output at 12 postoperative hours, the number of transfused red blood cell units, resternotomy for bleeding as well as intensive care unit stay and in-hospital length of stay.

The diagnosis and severity of SWI was defined and graded according to the Centers for Disease Control and Prevention classification of the surgical site infections (7). Severity of postoperative renal dysfunction was defined according to the KDIGO criteria (8). Definition criteria of the other end-points are reported in detail elsewhere (6).

Statistical Analysis

Statistical analysis was performed using the SAS statistical package, version 9.2 (SAS Institute Inc, Cary, NC), the SPSS v. 24.0 statistical software (IBM Corporation, New York, USA) and the Stata statistical software (StataCorp LLC, Texas, USA). No attempt to replace missing values was made. Mann-Whitney U-test, Fisher's exact test, Chi-square test, and Kruskal-Wallis tests were used for univariate analysis in the unmatched population. A propensity score matching was employed to select two groups of patients undergoing SIMA or BIMA grafting, respectively, with similar baseline characteristics. The propensity score was estimated using a non-parsimonious logistic regression model including the following covariates: age, gender, body mass index, hemoglobin, estimated glomerular filtration rate, chronic dialysis, functioning kidney transplant, pulmonary disease, stroke, poor mobility, extracardiac arteriopathy, diabetes, left ventricular ejection fraction, EuroSCORE II, previous percutaneous coronary intervention, urgent operation, critical preoperative status, ventricular arrhythmias, out-of-hospital cardiac arrest, preoperative IABP, left main coronary artery stenosis, number of diseased vessels and revascularization technique. The proportion of missing data of this

regression model was 3.3%. One-to-one propensity score matching was performed employing the nearest neighbour method and a caliper of 0.2 of the standard deviation of the logit of the propensity score. To evaluate the balance between the matched groups, the t-test for paired samples for continuous variables, the McNemar test for dichotomous variables and the analysis of the standardized differences after matching have been used. Standardized differences lower than 0.10 were considered an acceptable imbalance between the treatment groups. These tests were used to evaluate any difference in the adverse events of propensity score matched pairs. Tests for interaction for in-hospital mortality and deep sternal wound infection/mediastinitis were performed in subgroups with relevant baseline characteristics among propensity score matched pairs. In case of discordant classification of patients within a pair, due to residual variation in baseline variables, we gave precedence to the characteristics of the patients undergoing BIMA grafting.

Multilevel mixed-effects linear, ordered and logistic regression were used for institutional-volume adjusted analysis of the impact of BIMA grafting on the outcomes. In these regression models, the institutional volumes of BIMA grafting were included as a covariate along with other baseline and operative covariates as listed above. All tests were two-sided and $p<0.05$ was set for statistical significance.

Results

Outcomes in the Overall Series

The prevalence of BIMA grafting at the participating centers varied from 0% to 91%. Four centers reported the use of BIMA grafting in >50% of patients, and nine centers in <10% of patients. In the overall cohort, the study groups differed in a number of baseline covariates which translated in to a significantly higher EuroSCORE II in the SIMA grafting cohort (mean, 3.5±3.7% vs. 3.0±3.4%, p=0.002) (Table 1). When operative details were considered, more distal anastomoses were performed in the BIMA grafting group, accounting for longer cardiopulmonary bypass duration and length of the

operation (Table 2).

In-hospital mortality was similar between groups (Table 3). The incidence of SWI was significantly higher among patients undergoing BIMA grafting. BIMA grafting was associated with a lower risk of prolonged inotropic support and need of IABP. Chest tube output at 12 hours postoperatively was higher after BIMA grafting, but these patients received less red blood cell transfusions. The length of stay in the intensive care unit and in-hospital stay were longer in BIMA grafting cohort (Table 3).

The analysis of the cohort of patients who underwent BIMA grafting showed that centers with high proportion of BIMA grafting (>50% of treated patients) had significantly higher rates of any SWI (8.9% vs. 5.0%, p=0.045), prolonged use of inotropes (35.7% vs. 13.7%, p<0.0001), of postoperative use of IABP or ECMO (excluding preoperative IABP: 3.3% vs. 0.4%, p=0.007) as well as longer intensive care unit stay (4.4±4.7 vs. 2.5±3.2, p<0.0001) and in-hospital stay (12.0±9.5 vs. 9.9±4.8 days, p=0.001) compared to centers with low proportion of BIMA grafting (<50% of treated patients). Centers with high proportion of BIMA grafting tended also to have higher in-hospital mortality (3.2% vs. 1.1%, p=0.08) compared to centers with low proportion of BIMA grafting.

Multilevel mixed-effects regression methods were performed for institutional-volume adjusted analyses of the impact of BIMA grafting on the outcomes (Tab. 3). These regression models showed that BIMA grafting was associated with a significantly higher risk of SWI, which was particularly marked for deep SWI/mediastinits, of increased blood loss at 12 hours and prolonged stay in the intensive care unit.

Propensity Score Matched Analysis

One-to-one propensity matching provided 804 pairs with similar baseline characteristics as confirmed by standardized differences being all lower than 0.10 (Tables 1,2).

Among these propensity score matched pairs, BIMA grafting cohort had a significantly increased risk of any SWI (7.7% vs. 5.5%, p=0.031) as well as deep SWI/mediastinitis (4.0% vs. 2.2%, p=0.048), whereas its increased risk of in-hospital death (2.7% vs 1.6%, p=0.117) was not statistically significant

(Table 3).

Tests for interaction showed that urgent operation in patients undergoing BIMA grafting was associated with higher risk of in-hospital death (5.6% vs. 1.3%, p=0.009) (Table 4).

Among propensity score matched pairs, BIMA grafting was associated with an increased risk of ECMO (1.0% vs. 0.1%, P=0.020), increased postoperative blood loss (at 12 hours mean, 495 mL vs. 435 mL, p<0.001) as well as longer stay in the intensive care unit (mean, 3.6 vs. 2.6 days, p<0.001) and in-hospital stay (mean, 11.3 vs. 10.0 days, p<0.001) compared to SIMA grafting. No differences in other outcomes were observed (Table 3).

Discussion

This study demonstrated that BIMA grafting was associated with an increased risk of SWI among elderly patients undergoing elective or urgent CABG. Propensity score matched analysis showed that patients undergoing BIMA grafting also had a significantly higher risk to require ECMO along with prolonged intensive care unit and in-hospital stay. A trend towards increased in-hospital mortality was observed in these matched pairs. Test for interaction demonstrated that the risk for in-hospital mortality was significantly higher in patients undergoing urgent operation using BIMA grafting. A trend toward increased risk of early mortality was observed also among octogenarians undergoing BIMA grafting (5.0% vs. 0.8%, 121 patients in each cohorts). Although this difference did not reach statistical significance, this finding suggests that BIMA grafting may not be justified in the very elderly because of a possible increased risk of adverse early events as well as their short life expectancy.

BIMA grafting may confer a survival advantage as well as increases the freedom from repeated revascularizations late after CABG. However, several reports suggest the loss of survival benefit of BIMA in elderly patients. Benedetto et al. (4) demonstrated that BIMA grafting did not add survival advantage in patients older than 69 years. However, the limited number of patients aged 70 years or more (121 patients, 16% of the BIMA grafts cohort) prevented conclusive results. Similarly,

Mohammadi et al. showed that BIMA was not associated with superior late survival for patients aged 66 years and older (9). Kieser et al. (10) observed a survival advantage with the use of BIMA grafting only in patients <70 years old. The results of this study suggested that the use of BIMA grafts could be even detrimental in the elderly (10). Gatti et al. (11) recently failed to confirm any advantage of BIMA grafting in octogenarians. On the other hand, Kurlansky et al. demonstrated improved long-term survival advantage of BIMA grafting at 12 years for patients aged 65 and older (12). Similarly, Pettinari et al reported increased 10-year survival for BIMA patients aged 70 years and older (13). Such conflicting results may be due to differences in the study populations and a possible bias in preoperative patient selection. In this context it is worth noting that Taggart et al. (14) demonstrated no advantage with the use of BIMA grafts in terms of survival and freedom from MACCE at 5-year in the ART Trial. These findings suggest that the routine use of BIMA grafting may not offer any significant benefit either to septuagenarians with significant comorbidities with short expectancy of life or to octogenarians due to the natural limits of the lifespan. Still, BIMA grafting may be considered a valid means of myocardial revascularization in elderly patients with diseased ascending aorta or without available vein grafts.

The most relevant finding of our study is that the use of BIMA grafting exposed elderly patients to a significantly higher risk of any SWI as well as of deep SWI/mediastinitis. The observed rates of SWIs were consistent with current literature. Saito et al. (15) reported a rate of deep SWI of 2.3% after BIMA grafting compared to 1.3% after SIMA grafting in a large multicenter study. Similarly, Taggart et al. (14) reported a 1.87 relative risk of sternal wound complications after BIMA grafting (3.5% vs 1.9%, p=0.005).

The observed numerically increased mortality was not negligible in patients undergoing BIMA grafting (2.7% vs. 1.6%, p=0.117). Although such a difference did not reach statistical significance, these results are of clinical importance particularly when considering the significantly higher risk of requiring ECMO in the BIMA graft cohort. Furthermore, patients undergoing BIMA grafting had significantly longer intensive care unit and in-hospital stay, an observation that further suggests the

possible harms with this revascularization technique when employed in the elderly. These findings should, however, be viewed in the light of a possible selection bias persisting even after propensity score matching. In fact, elderly undergoing BIMA grafting had a significantly lower operative risk than those undergoing SIMA grafting. This may be explained by a reluctance to use BIMA grafts in elderly with significant comorbidities. Furthermore, despite the fact that only 6% of patients who underwent BIMA grafting were excluded from the comparative analysis using propensity score matching, the results of BIMA grafting might not be replicated in those patients with poorer risk profile who underwent SIMA grafting.

Other studies did not demonstrate any difference in operative mortality between SIMA and BIMA grafting. Dorman and coworkers reported comparable operative mortality (SIMA 2.4% vs BIMA 3.1%, p=0.279) in a retrospective propensity-matched analysis of 1107 patients undergoing CABG, as well as comparable incidence of postoperative complications (1). Similarly, Itoh et al showed no difference in early mortality in a cohort of elderly patients undergoing CABG, but found a 10-fold increased risk of deep SWI in the BIMA group (16). Analogously, Taggart et al. showed similar 30-day mortality in the ART Trial (1.2% in both groups, relative risk=1.06, 95%CI 056-2.02) (5). One possible explanation for such differences may reside in a different risk profile of these study populations. In fact, in the present series more than one third of patients underwent an urgent procedure, whereas in the other series about 15% patients underwent a non-elective procedure (16). Similarly, the prevalence of recent myocardial infarction is much higher than reported in previous studies (13). Other studies excluded patients undergoing urgent operation for evolving myocardial infarction (5). The present findings suggests that BIMA grafting should probably not be contraindicated based only on advanced age. In fact, interaction tests showed that BIMA grafting could be safely performed in the elective setting. However, further studies are needed to get more conclusive results on the benefits and harms of BIMA grafting in the elderly with stable coronary artery disease.

Limitations

This study has several limitations which deserve to be acknowledged. First, this is not a randomized controlled trial, which guarantees uniformity in patient selection. However, surgical registries report the aggregate of different clinical experiences and are more reflective of the effectiveness of a surgical technique in the real world, compared to randomized controlled trials. Second, this study lacks of details on the harvesting technique, which is a risk factor for sternal wound complications. Third, the lack of data on late outcome prevents more conclusive results on the harms and benefits related with this revascularization technique in these patients. The enrolment of patients in the E-CABG prospective registry started in January 2015 and we planned the first analyses on intermediate outcome at 3 years. Fourth, the observed differences might reflect the different patient selection and treatment strategies at each institution. In this regard, a possible impact of institutional experience with BIMA grafting on the outcome cannot be excluded and deserves further analysis, although we employed a multilevel mixed-effects regression methods to adjust for institutional-volume differences. Fifth, we lack details on the quality check of grafts (e.g. transit-time flowmetry or epicardial ultrasound). On the other hand, the E-CABG registry is a prospective multicenter registry, with clear definition criteria which guarantee the uniformity of collected data.

Conclusions

The results of this study do not support the routine use of BIMA grafting in the elderly because of an increased risk of SWI and a significantly increased risk of early mortality in patients undergoing urgent procedure. Until more conclusive results are gathered, BIMA grafting should be reserved only to elderly patients with stable coronary artery disease, without significant baseline comorbidities and long expectancy of life.

Conflict of interest

None.

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Table 1. Baseline characteristics.

	Overall series				Propensity score matched pairs			
	SIMA grafting 2044 pts	BIMA grafting 855 pts	p-value	Standardized difference	SIMA grafting 804 pts	BIMA grafting 804 pts	p-value	Standardized difference
Age (years)	76.1±3.8	75.6±4.0	0.016	0.130	75.7±3.7	75.6±4.0	0.740	0.016
Female	464 (22.7)	155 (18.1)	0.006	0.114	149 (18.5)	149 (18.5)	1.000	0.000
Body mass index (kg/ m^2)	27.2±3.9	26.8±3.8	0.014	0.100	26.9±3.7	26.8±3.8	0.548	0.029
Hemoglobin (g/L)	133±34	135±17	0.057	0.067	135±17	135±17	0.471	0.031
eGFR (mL/min/1.73 m^2)	67.7±18.3	68.2±17.4	0.429	0.032	68.2±18.1	68.3±17.3	0.893	0.007
Dialysis	24 (1.2)	6 (0.7)	0.252	0.049	9 (1.1)	6 (0.7)	0.439	0.039
Functioning kidney transplant	5 (0.2)	4 (0.5)	0.325	0.037	3 (0.4)	3 (0.4)	1.000	0.000
Type of diabetes			<0.0001	0.180			1.000	0.007
Non-insulin dependent	400 (19.8)	172 (20.5)			158 (19.6)	160 (19.9)		
Insulin dependent	302 (15.0)	77 (9.2)			76 (9.4)	75 (9.3)		
Poor mobility	57 (2.8)	29 (3.4)	0.383	0.035	28 (3.5)	26 (3.2)	0.777	0.014
Stroke	107 (5.2)	31 (3.6)	0.064	0.078	32 (4.0)	27 (3.4)	0.484	0.033
Pulmonary disease	265 (13.0)	64 (7.5)	<0.001	0.182	61 (7.6)	63 (7.8)	0.845	0.009
Extracardiac arteriopathy	574 (28.1)	208 (24.4)	0.040	0.084	204 (25.4)	198 (24.6)	0.729	0.017
Myocardial infarction	648 (32.0)	197 (23.3)	<0.001	0.197	171 (21.3)	183 (22.8)	0.450	0.036
Prior percutaneous coronary intervention	385 (18.8)	154 (18.0)	0.603	0.021	142 (17.7)	147 (18.3)	0.746	0.016
Left ventricular ejection fraction			0.046	0.119			1.000	0.054
30-50%	537 (26.4)	188 (22.0)			185 (23)	178 (22.1)		
21-30%	63 (3.1)	31 (3.6)			25 (3.1)	26 (3.2)		
<21%	8 (0.4)	1 (0.1)			1 (0.1)	2 (0.2)		
Left main stenosis	1155 (56.6)	504 (59.1)	0.226	0.049	471 (58.6)	469 (58.3)	0.918	0.005
No. of diseased vessels	2.7±0.5	2.8±0.5	<0.001	0.142	2.8±0.5	2.8±0.5	0.752	0.016
Urgent procedure	947 (46.3)	320 (37.4)	<0.001	0.181	294 (36.6)	304 (37.8)	0.595	0.026
Indication for coronary surgery			<0.001	0.248			0.800	0.050
Unstable angina	371 (18.3)	130 (15.4)			122 (15.2)	127 (15.8)		
NSTEMI	560 (27.7)	163 (19.3)			139 (17.3)	152 (18.9)		
STEMI	88 (4.4)	34 (4.0)			32 (4.0)	31 (3.9)		
Critical preoperative state	94 (4.6)	44 (5.1)	0.530	0.025	44 (5.5)	36 (4.5)	0.339	0.046
Out-of-hospital cardiac arrest	8 (0.4)	4 (0.5)	0.770	0.012	2 (0.2)	4 (0.5)	0.414	0.041
Preoperative inotropes	19 (0.9)	20 (2.3)	0.003	0.111	12 (1.5)	12 (1.5)	1.000	0.000
Preoperative IABP	57 (2.8)	26 (3.0)	0.710	0.015	25 (3.1)	20 (2.5)	0.435	0.038
Ventricular arrhythmias	26 (1.3)	8 (0.9)	0.588	0.032	11 (1.4)	8 (1.0)	0.467	0.035
EuroSCORE II	3.5±3.7	3.0±3.4	0.002	0.128	3.0±4.1	2.9±3.0	0.471	0.035

Continuous variables are reported as means and standard deviation and nominal variables as counts and percentages. Clinical variables are according to the EuroSCORE II definition criteria. eGFR: glomerular filtration estimated according to the CKD-EPI equation; NSTEMI: non ST-elevation myocardial infarction; STEMI: ST-elevation myocardial infarction; IABP: intra-aortic balloon pump.

Table 2. Operative data.

	Overall series				Propensity score matched pairs			
	SIMA grafting 2044 pts	BIMA grafting 855 pts	p-value	Standardized difference	SIMA grafting 804 pts	BIMA grafting 804 pts	p-value	Standardized difference
Operative technique			0.034	0.105			0.934	0.019
On-pump	1590 (77.8)	631 (73.8)			606 (75.3)	601 (74.7)		
Off-pump	431 (21.1)	217 (25.4)			192 (23.9)	196 (24.3)		
Beating heart on-pump	23 (1.1)	7 (0.8)			6 (0.7)	7 (0.9)		
Vein graft	3905 (83.6)	832 (31.4)	<0.001	1.243	686 (85.3)	201 (25.0)	<0.001	1.525
Radial artery graft	100 (2.1)	21 (0.8)	<0.001	0.109	11 (1.4)	4 (0.5)	0.071	0.084
No. of distal anastomoses	2.6±1.0	3.0±0.9	<0.001	0.455	2.6±0.9	3.0±0.8	<0.001	0.473
No. of proximal anastomoses	1.3±0.8	0.4±0.6	<0.001	1.262	1.2±0.9	0.3±0.5	<0.001	1.267
Cross-clamping time (min)	53±24	65±26	<0.001	0.450	53±22	64±26	<0.001	0.456
Cardiopulmonary bypass time (min)	84±34	87±36	<0.001	0.030	82±31	83±34	0.959	0.031
Length of the operation (min)	222±69	271±73	<0.001	0.892	217±66	279±76	<0.001	0.873

Continuous variables are reported as mean and standard deviation. Categorical variables are reported as absolute number and percentages (in parentheses). SIMA: single internal mammary artery; BIMA: bilateral internal mammary artery.

Table 3. Outcomes.

	SIMA grafting 2044 pts	BIMA grafting 855 pts	p-value	Multilevel mixed-effects regression estimates*	SIMA grafting 804 pts	BIMA grafting 804 pts	p-value
In-hospital death	90 (1.6)	42 (1.6)	0.280	1.14, 0.49-2.70	13 (1.6)	22 (2.7)	0.117
Intensive care unit stay (days)	2.8±4.9	3.1±3.6	<0.001	**0.55, 0.09-0.99**	2.6±4.1	3.6±4.4	**<0.0001**
In-hospital stay (days)	9.8±7.7	10.2±6.8	<0.001	**0.80, 0.00-1.60**	10.0±6.8	11.3±8.5	**<0.0001**
Prolonged inotropic support	1373 (29.4)	654 (24.6)	<0.001	1.30, 0.93-1.83	229 (28.5)	236 (29.4)	0.695
Intra-aortic balloon pump	247 (5.3)	79 (3.0)	<0.001	1.26, 0.56-3.05	29 (3.6)	25 (3.1)	0.586
Postoperative ECMO	25 (0.5)	22 (0.8)	0.133	9.32, 0.63-138.8	1 (0.1)	8 (1.0)	**0.020**
Percutaneous coronary intervention	56 (1.2)	44 (1.7)	0.107	1.20, 0.42-3.38	9 (1.1)	12 (1.5)	0.513
Stroke	69 (1.5)	26 (1.0)	0.069	0.41, 0.14-1.18	15 (1.9)	8 (1.0)	0.144
Sternal wound infection - overall	232 (5.0)	182 (6.8)	0.001	**2.08, 1.25-3.44**	41 (5.1)	62 (7.7)	**0.031**
Deep sternal wound infection/mediastinitis	91 (1.9)	84 (3.2)	0.001	**4.15, 2.07-8.33**	18 (2.2)	32 (4.0)	**0.048**
Acute kidney injury			0.152	1.27, 0.98-1.64			0.419
Stage 1	793 (17.4)	487 (18.6)			148 (18.9)	175 (22.3)	
Stage 2	121 (2.6)	55 (2.1)			22 (2.8)	20 (2.6)	
Stage 3	133 (2.9)	62 (2.4)			24 (3.1)	24 (3.1)	
Chest tube output at 12 hours (mL)	441±303	497±314	<0.001	**55.36, 25.28-85.43**	435±268	495±335	**<0.0001**
Transfused RBC units	1.4±2.8	0.9±1.7	<0.001	0.13, -0.06-0.34	1.2±2.0	1.0±1.8	0.406
Resternotomy for bleeding	128 (2.7)	73 (2.7)	0.996	1.61, 0.79-3.29	19 (2.4)	19 (2.4)	1.000

Continuous variables are reported as mean and standard deviation. Categorical variables are reported as counts and percentages (in parentheses). SIMA: single internal mammary artery; BIMA: bilateral internal mammary artery; ECMO: extracorporeal membrane oxygenation; RBC: red blood cell; *: estimates are odds ratio or coefficients with 95% confidence interval. In bold are statistical significances.

Table 4. Analysis of the in-hospital mortality and sternal wound infection/mediastinitis in different subgroups of patients with testing for interaction. SIMA: single internal mammary artery; BIMA: bilateral internal mammary artery; OR: odds ratio; CI: confidence interval; LVEF: left ventricular ejection fraction.

In-hospital death	SIMA grafting (%)	BIMA grafting (%)	OR	95%CI		Interaction	
						Chi-square	p-value
Overall			1.72	0.85	3.44		
Male gender	1.7	2.4	1.47	0.68	3.18	0.66	0.416
Female gender	1.3	4.0	3.08	0.61	15.54		
Age <80 years	1.8	2.3	1.34	0.63	2.86	1.78	0.182
Age ≥80 years	0.8	5.0	6.26	0.74	52.81		
No extracardiac arteriopathy	1.8	2.5	1.37	0.63	3.01	1.14	0.287
Extracardiac arteriopathy	1.0	3.5	3.59	0.74	17.50		
No diabetes	1.8	2.5	1.41	0.62	3.20	0.68	0.411
Diabetes	1.3	3.4	2.73	0.71	10.40		
LVEF >50%	1.8	2.5	1.37	0.63	3.01	1.13	0.287
LVEF ≤50%	0.8	3.5	3.59	0.74	17.47		
No myocardial infarction	1.8	2.1	1.19	0.53	2.67	2.38	0.123
Myocardial infarction	1.1	4.9	4.68	1.00	21.97		
Elective operation	1.8	1.0	0.55	0.18	1.66	6.91	0.009
Urgent operation	1.3	5.6	4.44	1.48	13.36		

Deep sternal wound infection/mediastinitis			OR	95%CI		Interaction	
						Chi-square	p-value
Overall			1.82	1.01	3.23		
Male gender	2.3	3.4	1.48	0.76	2.88	1.31	0.252
Female gender	2.0	6.7	3.50	0.94	12.99		
Age <80 years	2.5	4.1	1.67	0.91	3.09	0.59	0.443
Age ≥80 years	0.8	3.3	4.10	0.45	37.25		
No extracardiac arteriopathy	2.2	2.3	1.80	0.90	3.59	0.00	0.975
Extracardiac arteriopathy	2.5	2.1	1.84	0.60	5.59		
No diabetes	2.3	3.5	1.56	0.77	3.16	0.51	0.476
Diabetes	2.1	5.1	2.48	0.86	7.14		
LVEF >50%	2.2	4.0	1.88	0.95	3.73	0.05	0.828
LVEF ≤50%	2.4	3.9	1.62	0.52	5.05		
No myocardial infarction	2.4	3.4	1.41	0.72	2.77	1.80	0.179
Myocardial infarction	1.6	6.0	3.84	1.05	13.99		
Elective operation	2.2	3.4	1.56	0.73	3.38	0.32	0.574
Urgent operation	2.3	4.9	2.20	0.89	5.48		

SIMA: single internal mammary artery; BIMA: bilateral internal mammary artery; OR: odds ratio; CI: confidence interval; LVEF: left ventricular ejection fraction.