Supplemental Material to

"Predictors of short- and long-term outcome after open cardiac surgery in a high-volume referral tertiary hospital: the role of surgical team caseload."

Fabrizio Monaco, Gaia Barucco, Gabriele Valsecchi, Margherita Licheri, Elisa Nicelli, Elidodoro Cama, Marina Pieri, Giuseppe Dalessandro, Cristina Nakhnoukh, Carola Galbiati, Gabriele Sanchini, Camilla Biselli, Rosalba Lembo, Evgeny Fominskiy

Supplemental table 1. Strengthening the Reporting of Observational Studies in Epidemiology **(**STROBE) Statement—Checklist of items that should be included in reports of observational studies.

Supplemental table 2. Baseline clinical characteristics according the occurrence of major cardiovascular adverse event.

Supplemental table 3. Intraoperative characteristics according the occurrence of major cardiovascular adverse event.

Supplemental table 4. Post-operative course according the occurrence of major cardiovascular adverse event.

Supplemental table 5. Multivariable logistic regression model for major cardiovascular adverse event. The following pre-operative, intraoperative and postoperative variables were significant at the univariable analysis and included into the model: age, New York Heart Association class, chronic pulmonary disease, aortic stenosis, prior atrial fibrillation, platelets count, ejection fraction, creatinine, pre-operative intra-aortic balloon pump, surgery on ascending aortic, need of deep hypothermic arrest, ablation of atrial fibrillation, cardiopulmonary bypass time, inotropes/vasopressors for more than 4 hours, need of a mechanical circulatory support, length of mechanical ventilation, intensive care unit and hospital stay, chest drainage output, reintubation,

reoperation and hospital readmission. postoperative creatinine peak, hs-TnI before surgery, at the ICU admission, 4 hours later, and at day 1.

Supplemental Figure 1. Calibration plot of the frequencies of observed (y axis) and predicted (x axis) probabilities for 1-year mortality

Supplemental Figure 2. Calibration plot of the frequencies of observed (y axis) and predicted (x axis) probabilities for major cardiovascular event.

Supplemental Table 1. STROBE Statement—Checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3-4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-7
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	8

		(c) Consider use of a flow diagram	N/A
Descriptive data	14	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8 & Table 1-3
		(b) Indicate number of participants with missing data for each variable of interest	N/A
Outcome data	15	Report numbers of outcome events or summary measures	8-9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-9
		(*b*) Report category boundaries when continuous variables were categorized	Table 1-3
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

Supplemental Table 2. Baseline clinical characteristics.

	Population (N=1000)	Uneventful course (N=631)	MACE 30-days (N=369)	p-value
Demographic data				
Age, years (IQR)	65 (55-72)	63 (52-71)	68 (59-74)	0.001
Female sex, n (%)	372 (37.2)	246 (39.0)	126 (34.1)	0.126
Body Surface Area, m^2 (IQR)	1.84 (1.7-1.97)	1.83 (1.70-1.98)	1.84 (1.72-1.96)	0.785
NYHA class				0.027
----------1, n (%)	287 (28.7)	189 (30.0)	98 (26.6)	
----------2, n (%)	577 (57.7)	365 (57.9)	212 (57.5)	
----------3, n (%)	122 (12.2)	73 (7.3)	49 (13.3)	
----------4, n (%)	11 (1.1)	3 (0.5)	8 (2.2)	
CCS score				0.226
CCS score 0, n (%)	863 (86.3)	537 (85.1)	326 (88.3)	
CCS score 1, n (%)	78 (7.8)	55 (8.7)	23 (6.2)	
CCS score 2, n (%)	44 (4.4)	28 (4.4)	16 (4.3)	
CCS score 3, n (%)	15 (1.5)	11 (1.7)	4 (1.1)	
Ejection fraction, % (IQR)	60 (55-65)	61 (56-66)	60 (53-65)	0.03
Comorbidities				
Prior myocardial infarction, n (%)	61 (6.1)	35 (5.5)	26 (7.0)	0.343
Prior Cardiac Arrest, n (%)	7 (0.7)	2 (0.3)	5 (0.5)	0.108
Previous Stroke, n (%)	31 (3.1)	23 (3.6)	8 (2.2)	0.182
Previous TIA, n (%)	28 (2.8)	11 (1.7)	11 (3.0)	0.792
Prior Deep Vein Thrombosis, n (%)	3 (0.3)	2 (0.3)	1 (0.3)	0.692
Prior Pulmonary embolism, n (%)	2 (0.2)	0 (0.0)	2 (0.5)	0.136
Peripheral venous disease, n (%)	27 (2.7)	15 (2.4)	12 (3.3)	0.424
Hypertension, n (%)	442 (44.2)	272 (43.1)	170 (46.1)	0.363
Prior Pulmonary hypertension, n (%)	28 (2.8)	19 (3)	9 (2.4)	0.593
Prior Atrial fibrillation, n (%)	201 (20.1)	145 (23)	60 (16.2)	0.003
COPD, n (%)	42 (4.2)	18 (2.9)	24 (6.5)	0.007
Diabetes, n (%)	110 (11)	72 (11.4)	38 (10.3)	0.297
End stage renal disease, n (%)	7 (0.7)	2 (0.3)	5 (1.4)	0.108
Dialysis, n (%)	2 (0.2)	1 (0.1)	1 (0.3)	0.602
Cancer, n (%)	12 (1.2)	6 (1.0)	6 (1.6)	0.255
Smoke, n (%)	527 (52.7)	325 (51.5)	167 (54.7)	0.322
Chronic Heart failure, n (%)	2.0(0.2)	0 (0.0)	2 (0.5)	0.136
Aortic stenosis, n (%)	232 (23.2)	133 (21.1)	99 (26.8)	0.039
REDO, n (%)	115 (11.5)	63 (10)	52 (14.1)	0.052
Medications				
ACE inhibitors, n (%)	259 (26)	157 (24.9)	102 (27.9)	0.203
ARB, n (%)	70 (7.0)	47 (7.4)	23 (6.3)	0.296
Beta blockers, n (%)	540 (54.3)	332 (52.6)	208 (57.1)	0.167
Alpha Blockers, n (%)	2 (0.2)	1 (0.2)	1 (0.3)	0.598

Calcium channel blockers, n (%)	12 (1.2)	9 (1.4)	3 (0.8)	0.304
Dihydropyridine, n (%)	86 (8.6)	57 (9.0)	29 (8.0)	0.326
Potassium-sparing diuretic, n (%)	67 (6.7)	38 (6.0)	29 (8.0)	0.243
Digoxine, n (%)	48 (4.8)	26 (4.1)	22 (6)	0.178
Long lasting nitrate, n (%)	2 (0.2)	2 (0.3)	0 (0.0)	0.402
Statins, n (%)	322 (32.4)	202 (32.0)	120 (33.0)	0.757
Sulfonylureas, n (%)	4 (0.4)	2 (0.3)	2 (0.5)	0.465
ASA, n (%)	52 (5.2)	29 (4.6)	23 (6.3)	0.245
Clopidogrel, n (%)	13 (1.3)	8 (1.3)	5 (1.4)	0.548
Ticagrelor, n (%)	8 (0.8)	3 (0.5)	5 (1.4)	0.124
Prasugrel, n (%)	1 (0.1)	1 (0.2)	0 (0.0)	0.634
Glycoprotein iib/iiia inhibitors, n (%)	7 (0.7)	4 (0.6)	3 (0.8)	0.504
Warfarin, n (%)	22 (2.2)	13 (2.1)	9 (2.5)	0.672
Dabigatran, n (%)	3 (0.3)	2 (0.3)	1 (0.3)	0.693
Surgeon's experience				0.262
Expert, n (%)	373 (37.3)	241 (38.2)	132 (35.8)	
Intermediate, n (%)	358 (35.8)	214 (33.9)	144 (39.0)	
Junior < 50, n (%)	269 (26.9)	176 (27.9)	93 (25.2)	
Anesthesiologist's experience				0.414
Expert, n (%)	100 (10)	57(9)	43 (11.7)	
Intermediate, n (%)	760(76)	484 (76.7)	276 (74.8)	
Junior, n (%)	140 (14)	90 (14.3)	50 (13.6)	
Laboratory tests				
Hb, mg/dl (IQR)	13.9 (12.8-14.9)	14 (12.8-15)	13.8 (12.6-14.8)	0.092
White Blood Cell, 10^9/L (IQR)	6.6 (5.6-7.7)	6.6 (5.6-7.7)	6.5 (5.5-7.9)	0.781
Platelets, 10^9/L (IQR)	207 (176-243)	209 (180-249)	200 (170-235)	0.006
APTT, s (IQR)	29 (28-31)	30 (28-31)	29 (28-31)	0.099
INR, n (IQR)	1 (1-1.1)	1 (1-1.1)	1 (1-1.1)	0.366
Glucose, mg/dL (IQR)	94 (86-105)	94 (85-105)	95 (88-107)	0.056
Creatinine, mg/dL (IQR)	0.94 (0.81-1.09)	0.93 (0.8-1.06)	0.96 (0.82-1.13)	0.001

IQR: interquartile ranges; NYHA: New York Heart Association; CCS: Canadian Cardiovascular Society; TIA: transient ischemic attack; COPD: Chronic obstructive pulmonary disease; OSAS: Obstructive Sleep Apnea Syndrome; ACE: Angiotensin converting enzyme; ARB: Angiotensin II Receptor Blockers; PPI: proton pump inhibitor; ASA: acetylsalicylic acid; aPTT: activated partial thromboplastin time; INR: international normalized ratio.

Supplemental Table 3. Operating Theatre

	Population (N=1000)	Uneventful course (N=631)	MACE 30 days (N=369)	p-value
Preoperative Inotropes/vasopressors, n (%)	997 (99.7)	630 (99.8)	367 (36.8)	0.308
Preoperative IAPB, n (%)	5 (0.5)	0 (0.0)	5 (1.4)	0.007
Urgency rating				
Elective, n (%)	996 (99.6)	630 (99.8)	366 (99.2)	0.126
Urgent, n (%)	2 (0.2)	1 (0.2)	1 (0.3)	
Emergent, n (%)	2 (0.2)	0 (0.0)	2 (0.5)	
Endocarditis, n (%)	15 (1.5)	6 (1.0)	9 (2.4)	0.068
CAD, n (%)	4 (0.4)	1 (0.2)	3 (0.8)	0.145
AMI, n (%)	4 (0.4)	1 (0.2)	3 (0.8)	0.145
Dissection, n (%)	2 (0.2)	0 (0.0)	2 (0.5)	0.136
Cardiogenic shock, n (%)	4 (0.4)	1 (0.2)	3 (0.8)	0.145
Pulmonary Edema, n (%)	4 (0.4)	1 (0.2)	3 (0.8)	0.145
On pump surgery, n (%)	983 (98.3)	618 (97.9)	4 (98.9)	0.233
Aortic cross clamp, n (%)	968 (96.8)	607 (96.2)	361 (97.8)	0.145
Cardioplegia type				0.178
None, n (%)	32 (3.2)	24 (3.8)	8 (2.2)	
Buckberg, n (%)	7 (0.7)	6 (1.0)	1 (0.3)	
Custudiol, n (%)	960 (96)	600 (95.1)	360 (97.6)	
Surgical Approach				0.294
Sternotomy, n (%)	956 (95.6)	600 (95.1)	356 (96.5)	
Minimal Invasive, n (%)	44 (4.4)	31 (4.9)	13 (3.5)	
Cardioplegia delivery				0.233
None, n (%)	32 (3.2)	24 (3.8)	8 (2.2)	
Anterograde, n (%)	893 (89.3)	557 (88.3)	336 (37.6)	
Retrograde, n (%)	5 (0.5)	2 (0.3)	3 (0.8)	
Combined, n (%)	70 (7)	48 (7.6)	22 (6.0)	
Aortic valve surgery, n (%)	339 (33.9)	206 (32.6)	133 (36.0)	0.274
Mitral valve surgery, n (%)	481 (48.1)	304 (48.2)	177 (48.0)	0.949
Tricuspid valve surgery, n (%)	112 (11.2)	66 (10.5)	46 (12.5)	0.335
Coronary bypass grafting, n (%)	186 (18.6)	113 (17.9)	73 (19.8)	0.464
Graft number				
1, n (%)	70 (37.6)	41 (36.3)	29 (39.7)	0.694
2, n (%)	64 (34.4)	37 (32.7)	27 (37.0)	
3, n (%)	48 (25.8)	32 (28.3)	16 (21.9)	
4, n (%)	4 (2.2)	3 (2.7)	1 (1.4)	
Ascending Aorta surgery, n (%)	137 (13.7)	75 (11.9)	62 (16.8)	0.031
Bentall, n (%)	27 (2.7)	11 (1.7)	16 (4.3)	0.024
Ascending Aorta Enlargement, n (%)	6 (0.6)	2 (0.3)	4 (1.1)	0.138
Aortic Arch Surgery, n (%)	9 (0.9)	3 (0.5)	6 (1.6)	0.068

DHA, n (%)	18 (1.8)	7 (1.1)	11 (3)	0.036
Ascending Aorta replacement, n (%)	97 (9.7)	59 (9.4)	38 (10.3)	0.626
Left ventricle aneurysmectomy, n (%)	4 (0.4)	3 (0.5)	1 (0.3)	0.529
Septal defect closure, n (%)	22 (2.2)	12 (1.2)	10 (1.0)	0.406
Septal defect type				
Atrial, n (%)	21 (2.1)	12 (1.9)	9 (2.4)	0.313
Ventricular, n (%)	1 (0.1)	0 (0.0)	1 (0.3)	
Atrial Fibrillation Ablation, n (%)	56 (5.6)	46 (7.3)	10 (2.7)	0.001
CPB time, min (IQR)	83 (66-113)	80 (65-108)	87 (68-120)	0.002
Aortic cross clamp time, min (IQR)	63 (49-87)	61 (49-84)	68 (50-90)	0.017
Hemofiltration on CPB, n (%)	234 (23.4)	137 (21.7)	97 (26.3)	0.101
Lowest temperature CPB, °C (IQR)	30.1 (28.5-31.6)	30.2 (28.5-31.5)	30 (28.5-31.5)	0.440
Lowest Ht CPB, % (IQR)	25 (22-28)	25 (23-28)	25 (22-27)	0.170
Lowest glucose surgery, mg/dL (IQR)	92 (84-103)	92 (84-103)	92 (84-103)	0.878

MACE: Major cardiovascular event; IQR: interquartile ranges; IABP: intra-aortic balloon pump; CAD: Coronary artery disease; AMI: acute myocardial infarction; DHA: Deep Hypothermic Arrest; RBC: Red blood cell; CPB: Cardiopulmonary bypass; Ht: hematocrit.

Supplemental Table 4. Postoperative course

	Population (N=1000)	Uneventful course (N=631)	MACE at 30 days (N=369)	p-value
Inotropes/Vasopressors > 4h, n (%)	724 (72.5)	423 (68.6)	291 (79.1)	0.001
Mechanical circulatory support, n (%)	116 (11.6)	51 (8.0)	65 (17.6)	0.001
IABP, n (%)	99 (0.1)	47 (7.4)	52 (14.1)	
VA-ECMO, n (%)	6 (0.6)	0 (0.0)	6 (1.6)	
Other, n (%)	11 (0.2)	4(0.6)	7 (1.9)	
ICU stay, days (IQR)	1 (1-2)	1 (1-1)	1 (1-3)	0.001
Orotracheal Intubation time, hours (IQR)	12 (10-17)	12 (9-14)	14 (11-18)	0.001
Reintubation, n (%)	13 (1.3)	0 (0.0)	13 (3.5)	0.001
Chest drainage, ml (IQR)	400 (300-540)	400 (290-510)	420 (320-600)	0.001
Creatinine peak, mg/dL (IQR)	0.79 (0.65-0.96)	0.94 (0.8-1.17)	1.01 (0.83-1.25)	0.006
Troponin pre-operative, ng/L (IQR)	7 (4-15)	6 (4-14)	9 (5-19)	0.001
Troponin 3-12 hours after surgery, ng/L (IQR)	3624 (2117-2363)	3576 (2026-6284)	3766 (2412-7294)	0.044
Troponin day 1, ng/L (IQR)	4126 (2363-6907)	4094 (2228-6646)	4412 (2636-8061)	0.004
Troponin day 2, ng/L (IQR)	2104 (1207-3717)	2052 (1166-3342)	2210 (1264-4462)	0.009
Troponin day 3, ng/L (IQR)	1201 (696-2032)	1188 (696-1982)	1978 (622-9623)	0.081
Troponin Peak, ng/L (IQR)	4711 (2744-7817)	4563 (2570-7394)	5204 (2935-9013)	0.008
Reoperation, n (%)	69 (6.9)	19 (3.0)	50 (13.6)	0.001
Hospital stay, days (IQR)	5 (4-7)	5 (4-6)	6 (5-9)	0.001
Hospital readmission, n (%)	48 (4.9)	8 (1.3)	40 (11.2)	0.001
Transfusion, n (%)	328 (32.8)	193 (30.6)	135 (36.6)	0.052

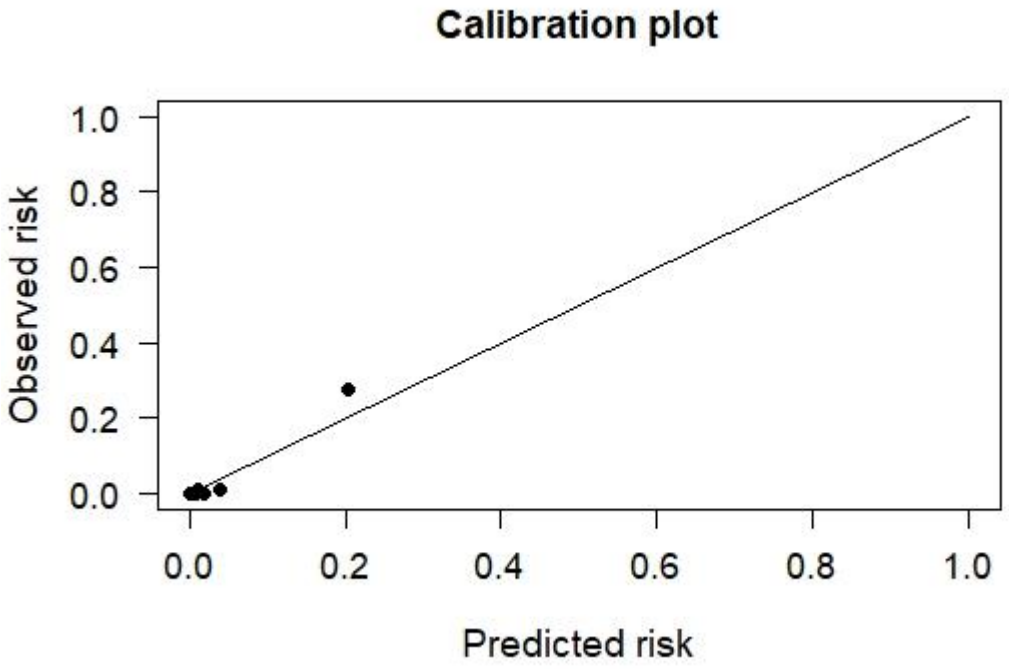
MACE: major cardiovascular event; IABP: Intra-aortic balloon pump; VA-ECMO: venous-arterial external membrane oxygenator; ICU: intensive care unit; IQR: interquartile ranges.

Supplemental Table 5. Multivariable logistic regression model for MACE

Variable	Odd Ratio	Adjusted Odd ratio	95% C I	p value
Age	1.04	1.03	1.02-1.05	<0.0001
Reoperation	2.95	2.50	1.66-5.33	0.0004
Mechanical circulatory support				
IABP	1.81	1.55	1.18-2.93	0.023
VA-ECMO	4.64	1.36	0.04-8.69	0.97
Other	2.82	1.66	0.79-10.06	0.10

MACE: major cardiovascular event; Adjusted OR: OR corrected for overoptimism after internal validation ; CI: confidence intervals; IABP: intra-aortic balloon pump; VA-ECMO: venous-arterial extracorporeal membrane oxygenator.

Supplemental Figure 1.



Supplemental Figure 2.