ORIGINAL ARTICLE

Prognostic value of SARS-CoV-2 on patients undergoing cardiac surgery

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Abstract

Objective: To analyze Italian Cardiac Surgery experience during the pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) identifying risk factors for overall mortality according to coronavirus disease 2019 (COVID-19) status.

Methods: From February 20 to May 31, 2020, 1354 consecutive adult patients underwent cardiac surgery at 22 Italian Centers; 589 (43.5%), patients came from the red zone. Based on COVID-19 status, 1306 (96.5%) were negative to SARS-CoV-2 (COVID-N), and 48 (3.5%) were positive to SARS-CoV-2 (COVID-P); among the COVID-P 11 (22.9%) and 37 (77.1%) become positive, before and after surgery, respectively. Surgical procedures were as follows: 396 (29.2%) isolated coronary artery bypass grafting (CABG), 714 (52.7%) isolated non-CABG procedures, 207 (15.3%) two associate procedures, and three or more procedures in 37 (2.7%). Heart failure was significantly predominant in group COVID-N (10.4% vs. 2.5%, p = .01).

Results: Overall in-hospital mortality was 1.6% (22 cases), being significantly higher in COVID-P group (10 cases, 20.8% vs. 12, 0.9%, p < .001). Multivariable analysis identified COVID-P condition as a predictor of in-hospital mortality together with emergency status. In the COVID-P subgroup, the multivariable analysis identified increasing age and low oxygen saturation at admission as risk factors for in-hospital mortality.

Conclusion: As expected, SARS-CoV-2 infection, either before or soon after cardiac surgery significantly increases in-hospital mortality. Moreover, among COVID-19-positive patients, older age and poor oxygenation upon admission seem to be associated with worse outcomes.

KEYWORDS

cardiac surgical procedures, COVID-19, emergent cardiac surgery, SARS-CoV-2

1 | INTRODUCTION

On March 8, 2020 in response to the burden of coronavirus disease 2019 (COVID-19) on healthcare systems worldwide, elective surgical activities have been delayed owing to the redistribution of intensive care resources and the unquantifiable risk of being infected during hospitalization.[1] Noteworthy, many centers across the globe have witnessed a significant reduction (up to 60%–80%) in the treatment of several non-COVID clinical conditions especially in the areas of cancer and cardiovascular diseases. Indeed, several studies have shown that patients with established cardiovascular diseases may have a greater risk of increased COVID infection severity and prognosis.[2] However, the consequences of prolonged delay of appropriate treatment of acute and chronic cardiac disease (including cardiac surgery) can be detrimental.

Cardiac surgery (CS) patients represent a particularly vulnerable population due to the fact that perioperative concomitant COVID-19 infection is burdened by adverse outcomes.[3] Moreover, when COVID-pneumonia develops early after CS, several factors (surgery-related immunomodulation, extracorporeal-circulation (ECC)-related lung dysfunction, and high inflammatory response) can rapidly exacerbate adult respiratory distress syndrome (ARDS) with a very dismal prognosis.[4] Some limited experiences of CS in COVID patients reported high incidence of perioperative mortality (ranging 20%–30%) and morbidity, especially in terms of pulmonary complications.[5,6] Nowadays, very limited data are available concerning the risk profile of patients suffering from COVID, either pre- or postoperatively, undergoing cardiac surgery.[7]

Hence, the aim of the present multicenter study is to identify risk factors for in-hospital mortality in the overall and in the COVID-positive populations.

2 | MATERIAL AND METHODS

2.1 | Population

The Italian Society of Cardiac Surgery (SICCH) sponsored a multicenter study to understand how Italian CS departments performed in the early days of the March–April 2020 lockdown, and in the first month after this was lifted.[8] From February 20 to May 31, 2020, 1354 consecutive patients undergoing cardiac surgery at 22 Italian Centers were retrospectively enrolled. Preoperative and perioperative characteristics were anonymously inserted into a dedicated data set Tables 1 and 3, and statistical analysis was performed at the central core lab.

Overall cohort was further divided in two groups depending on the SARS-CoV-2 infective status, COVID-P (48 cases positive [3.6%] to SARS-CoV-2 nasal swab and/or with chest computed tomography [CT] scan positive for interstitial pneumonia) and COVID-N (1306 cases negative to SARS-CoV-2). Patients who underwent elective surgery, urgent surgery (patients who have not been electively admitted for operation but who require intervention or surgery on the current admission for medical reasons. These patients cannot be sent home without a definitive procedure), and emergent surgery (operation before the beginning of the next working day after the decision to operate; emergency included also salvage that are patients requiring cardiopulmonary resuscitation (external cardiac massage) on route to the operating theater or before induction of anesthesia).

Under official endorsement by the SICCH task force on COVID-19, the Central Ethical Committee (EC number 1232/4/20), followed by each single-center institutional review board approved the study and waived the need for informed consent.

2.2 | Patient and public involvement

Given the retrospective nature of the study, patients were not initially involved in it during hospitalization. Nevertheless, they were contacted either through phone calls or through visits in the in-patients clinics to perform the follow-up.

2.3 | Definition of terms and end-points

All the variables collected in the data set were defined according to Euroscore II.[9] SARS-CoV-2 swab assays were performed according to the World Health Organization and based on the detection of unique viral genome sequences by real-time reverse transcription-polymerase chain reaction (RT-PCR).[10]

According with law decrees issued by Italian Prime Minister, Italy was divided in three rescue zone with different level of containment measures, in descending order: red zone, high level of infection, max limitation; yellow zone intermediate level of infection, intermediate containment measures; green zone, low index, and few limitation.[11,12]

2.4 | The primary end-point was in-hospital mortality statistics

Normal distribution of continuous variables was assessed by Kolmogorov–Smirnov test. Normally and non-normally distributed variables were reported as mean ± standard deviation and median (Interquartile range) respectively. Pairwise comparison was performed with T-test or Mann–Whitney U-test in case of continuous variables and χ^2 with Fisher exact test in case of categorical variables.

A univariate analysis was initially run and then only those variables which meet a preset cutoff (<0.10) for significance were included in the multivariable model.

A parsimonious logistic regression model was built to identify the best predictors for in-hospital mortality, both in overall population and in COVID-19 positive patients. Results are reported as odds ratio (OR), 95% confidence limits (95 CLs), and p-value. The final model was internally validated using bootstrapping. The receiver operating characteristic (ROC) curve was used to estimate the discrimination power and to identify cutoffs. All the analyses were performed with SPSS (IBM Corp. IBM SPSS Version 24.0), Med-Calc (MedCalc Software bv), and R-project (Core Team 2013. R Foundation for Statistical Computing), $p < .05$ was considered as the threshold for statistical significance.

3 | RESULTS

3.1 | Overall cohort

The general preoperative characteristics of patients are listed in Table 1. Each patient had a mandatory screening for SARS-CoV-2, which always included a chest CT scan, nasal swab, corporal temperature monitoring, and blood tests. The vast majority of the

TABLE 1 General preoperative clinical features of the study population

Preoperative data	Overall (n = 1354)	COVID-P (n = 48)	COVID-N (n = 1306)	p value
Age, years	66.9 ± 11.6	65.9 ± 10.6	66.9 ± 11.7	.55
Male gender	932 (68.8%)	31 (64.6%)	901 (69.0%)	.53
COVID zones				
"Red"	589 (43.5%)	25 (52.1%)	564 (43.8%)	.42
"Yellow"	391 (28.9%)	12 (25.0%)	379 (299%)	
"Green"	374 (27.6%)	11 (22.9%)	363 (27.8%)	
Hypertension	900 (66.5%)	30 (62.5%)	870 (66.6%)	.54
Dyslipidemia	458 (33.8%)	13 (27.1%)	445 (34,1%)	.35
Obesity	170 (12.6%)	6 (12.5%)	164 (12.4%)	1.00
Previous heart surgery	67 (4.9%)	2 (4.2%)	65 (5.0%)	1.00
COPD	107 (7.9%)	6 (12.5%)	101 (7.7%)	.27
Smoke				
No	818 (60.4%)	25 (56.8%)	793 (62.3%)	.40
Former	217 (16.0%)	6 (13.6%)	211 (16.6%)	
Active	282 (20.8%)	13 (29.5%)	269 (21.1%)	
Diabetes				
No	1042 (77%)	40 (83.3%)	1002 (77.7%)	.53
NIDD	218 (16.1%)	5 (10.4%)	213 (16.5%)	
IDD	77 (5.7%)	3 (6.3%)	74 (5.7%)	
Diabetes (any)	295 (21.8%)	8 (16.7%)	287 (22.3%)	.48
Preoperative EF (%)	55.2 ± 10.4	56.4 ± 9.4	55.1 ± 10.4	.43
Preoperative EF (categorical)				
EF < 30%	46 (3.4%)	0 (0%)	46 (3.8%)	.38
30% <EF < 50%	302 (22.3%)	10 (22.2%)	292 (24.0%)	
EF > 50%	915 (67.6%)	35 (77.8%)	880 (72.2%)	
Serum creatinine (mg/dL)	1.09 ± 0.9	0.92 ± 0.28	1.10 ± 0.91	.37
Weight, kg	76.3 ± 14.6	75.5 ± 19.6	76.3 ± 14.4	.71
Height, cm	169.7 ± 9.0	170.2 ± 9.3	169.7 ± 9.0	.71
BSA	1.88 ± 0.22	1.88 ± 0.28	1.89 ± 0.22	.75
BMI	26.4 ± 4.3	25.8 ± 5.0	26.4 ± 4.3	.30
Previous MI	111 (8.2%)	2 (4.2%)	109 (8.3%)	.42
Coronary artery disease	172 (12.7%)	7 (14.6%)	165 (12.6%)	.66
Previous PCI	88 (6.5%)	2 (4.2%)	86 (6.6%)	.76
Composite CAD (at least 1 of previous 3)	258 (19.1%)	7 (14.6%)	251 (19.2%)	.57
Chronic renal failure	135 (10.0%)	7 (14.6%)	128 (9.8%)	.32
Dialysis	5 (0.4%)	0 (0%)	5 (0.4%)	1.0
History of HF	38 (2.8%)	5 (10.4%)	33 (2.5%)	.01[a]
Cerebrovascular Accident	80 (5.9%)	3 (6.5%)	77 (5.9%)	.76
Emergency Operation	33 (2.4%)	3 (6.3%)	30 (2.3%)	.11

TABLE 1 (Continued)

Preoperative data	Overall (n = 1354)	COVID-P (n = 48)	COVID-N (n = 1306)	p value
Operations				.34
Isolated CABG	396 (29.2%)	387 (29.6%)	9 (18.8%)	
Isolated non-CABG	714 (53%)	683 (52.3%)	31 (64.6%)	
Two procedures	207 (15.3%)	200 (15.3%)	7 (14.6%)	
Three or more procedures	37 (2.7%)	36 (2.8%)	1 (2.1%)	

Abbreviation: BMI, body mass index; BSA, body surface area; CABG, coronary artery bypass grafting; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; EF, ejection fraction; HF, heart failure; IDD, insulin-dependent diabetes; MI, myocardial infarction; NIDD, non-insulin-dependent diabetes; PCI, percutaneous intervention.
*Classification of the operations was done according to the Euroscore II.[8]

patients came from the red zone (589, 43.5%) and urgent and emergent operations were performed in 1288 (95%) and in 66 (5%) patients respectively. Isolated coronary artery bypass grafting (CABG) was performed in 396 cases (29.2%), isolated non-CABG procedure in 714 (52.7%) cases, two procedures in 207 (15.3%) patients, and three or more procedures in 37 (2.7%) patients.

Postoperative outcomes are summarized in Table 2. Overall in-hospital mortality was 1.6% (22 cases), resulting significantly higher in COVID-P group (20.8% vs. 0.9%, p < .001). The variables initially included in the multivariable analysis, after univariate analysis, were COVID positivity, emergency operation, dialysis, and COPD.

Multivariable logistic regression analysis confirmed that COVID positivity (OR = 28.6 [CI: 11–74], p < .001), along with emergency operation (OR = 13.9 [CI: 4–48], p < .001), resulted independent predictors of in-hospital mortality. No thromboembolic events were recorded. Median length of stay was 7 days (4–12), similar in both subgroups.

3.2 | COVID subgroup

Perioperative variables of COVID-P patients are summarized in Table 3. Eleven out of 48 (23%) patients underwent surgery despite positive SARS-CoV-2 swab due to urgent (10 cases) or emergent (1 cases) conditions. While the remaining 37 (77%) cases resulted positive at postoperative swab.

In COVID-P cohort, the variables initially included in the multivariable analysis for in-hospital mortality, after univariate analysis, were age (both as continuous or as dummy variables, and oxygen saturation that was confirmed also at multivariable analysis Table 2. Using ROC curve (Figure 1) analysis, cut-offs were also identified: age ≥ 75 years (AUC 0.80 [95 CI = 0.65–0.93]; sensitivity 71%, specificity 90%) and oxygen saturation at admission ≤ 80% (AUC 0.80 [95 CI = 0.68–0.92]; sensitivity 61%, specificity 100%) (Figures 1–2). In Table 4, a model with cut-offs was also reported. The leading cause

TABLE 2 Postoperative outcomes stratified by COVID-19 status

Postoperative outcome	COVID-P (n = 48)	COVID-N (n = 1306)	p value
In-hospital mortality	10 (20.8%)	12 (0.9%)	<.001
ICU stay, mean and range, days	10 (0–46)	3 (0–21)	<.001
LOS, median and quartiles, days	8 (1–12)	7 (4–12)	.71
Maximum Serum creatinine, mg/dL	1.28 ± 0.57	1.40 ± 1.1	.54
Lowest glomerular filtrate rate, mg/dL	67.1 ± 26.8	72.1 ± 32.2	.31
AKI	9 (19%)	150 (11%)	.13
Maximum reactive C-protein, median and quartile, mg/dl	25 (15–142)	22 (14–128)	.52
Maximum count WBC, ×10^9/L	14.35 ± 6.4	14.6 ± 6.3	.83
Therapy on discharge			.87
None	14 (29.2%)	414 (35%)	
Heparin	17 (35.4%)	239 (20%)	
Anticoagulant	16 (33%)	477 (40%)	
Heparin + anticoagulant	1 (2.1%)	48 (4.1%)	

Abbreviations: AKI, acute kidney injury; COVID-19, coronavirus disease 2019; ICU, intensive care unit; LOS. length of stay; SO$_2$, oxygen saturation; WBC, white blood cell.

of death in this subgroup was a respiratory failure (70% vs. 30% for other causes, p < .001).

Interestingly, we recorded a trend towards higher mortality rates in patients who had a positive swab upon admission (4/11, 36%) with respect to patients who became COVID-19 positive in the postoperative period (6/37 16%), although no statistical significance was found, due to the small sample size (p = .126).

TABLE 3 Clinical features of COVID-19 patients population

Variable	N = 48
Preoperative SARS-CoV positive swab	11 (22.9%)
Postoperative SARS-CoV positive swab	37 (77.1%)
Interval time to symptoms, days	5 (3–13)
No symptoms	3 (6.3%)
Fever	35 (72.9%)
Dyspnea	22 (45.8%)
Cough	13 (27.1%)
Other symptoms	3 (6.3%)
Pneumonia	31 (64.5%)
Double lung involvement	16 (33.3%)
PO_2, mmHg, at admission	71 (60–85)
PCO_2, mmHg, at admission	38 (35–46)
SO_2, %, at admission	92 (88–97)
Maximum D-Dimer, µg/L	827 (3–2780)
Maximum fibrinogen, mg/dL	552 (202–724)
Maximum IL-6, pg/L	36 (21–98)
Maximum reactive C-protein, mg/dL	25 (15–142)
Maximum pro-calcitonin, mg/dL	0.3 (0.08–2.42)
Maximum LDH, mg/dL	515 (381–666)
Maximum count WBC, $×10^9$/L	14.35 ± 6.4
Postoperative respiratory failure	19 (39.6%)
Postoperative renal failure	9 (18.8%)
Postoperative transfused patients	27 (56.3%)
Chloroquine	29 (60.4%)
Lopinavir + Ritonavir	14 (29.2%)
Tocilizumab	7 (14.6%)
Antibiotics	31 (64.6%)
Pronation therapy	4 (8.3%)
ECLS	3 (6.3%)

Abbreviations: COVID-19, coronavirus disease 2019; ECLS, extracorporeal life support; IL-6, interleukin 6; LDH, lactate dehydrogenase; PCO_2, partial pressure of carbon dioxide; PO_2, partial pressure of oxygen; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SO_2, oxygen saturation; WBC, white blood cell.

4 | DISCUSSION

From a nationwide perspective, the present multicenter series probably represents the most comprehensive effort to address the impact of the pandemic on CS attempted so far. The main findings of our study are the following: (1) Over a 2-month period, every cardiac department in the present report operated on 50 patients on average (1354/27, 6 patients per week), clearly showing how CS activity was
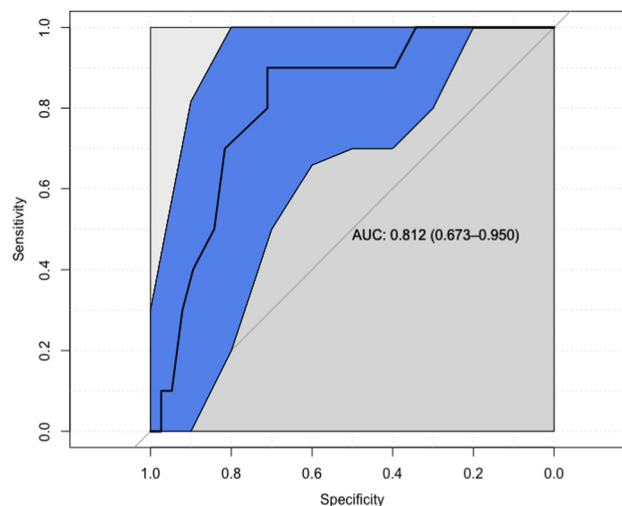
FIGURE 1 ROC curve: predictivity of age for higher in-hospital mortality; AUC, area under curve; confidence limits are plotted (blue area); ROC, receiver operating characteristic

significantly impacted by the pandemic outbreak. (2) Despite this limited activity, the incidence of COVID positivity in our hospitalized patients' population was 10-fold greater than the general population, raising many concerns on the level of patients screening, healthcare protection, and the role of hospitals as incubators and virus spreaders. (3) In COVID-P patients submitted to CS, in-hospital mortality was 20-fold greater than in COVID-N patients (20% vs. 0.9%), with lung dysfunction and ARDS as the main cause of mortality. (4) Among COVID-P patients, advanced age and low oxygen saturation at admission were independent predictors of in-hospital mortality. Furthermore, none of the clinical or procedural factors seemed to play a role in outcome prediction.

Despite the very limited sample of COVID-P group, in this series we can confirm how advanced age (>75 years) and low O_2 saturation levels at admission (<88%) were an independent risk factors for in-hospital mortality in the COVID-P population. Age indeed, in multiple large epidemiological analyses, has proven as the single independent risk factor for mortality in COVID-19 patients.[13] Low oxygen saturation at the admission could be a poor indicator of lung function mainly due to pneumonia extension and can anticipate a rapid escalation to ARDS in a subgroup of patients in which CS maneuver (sternotomy, mechanical ventilation, and ECC) can further contribute to lung damage. At the beginning of March 2020, Italian northern regions were the first western area to absorb the strike of the first pandemic wave. The uncontrolled virus spreading with the related abrupt need for ventilators and ICU beds, lead the Italian government to institute total lockdown, reorganize the health system, and to postpone many elective activities, including most of the CS services.[14] Indeed, due to the initial severe gap of knowledge (unknown level of virus penetration, scarcity of swab test and PPE, unclear healthcare protection protocols) therapeutic approach for cardiac urgencies was less than empirical, with uncertain organization and dismal outcomes. At nearly one year from COVID outbreak, few data
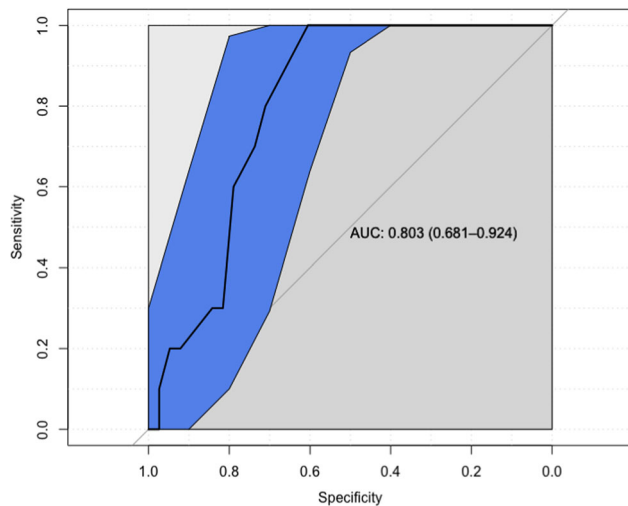
FIGURE 2 ROC curve: predictivity of oxygen saturation for higher in-hospital mortality. AUC, area under curve; confidence limits are plotted (blue area); ROC, receiver operating characteristic

TABLE 4 Multivariable logistic regression model for In-hospital mortality in COVID-19 patients' population

Model A[a]	OR (95% CI)	*p* value
Age, years	1.17 (1.03–1.35)	.033
O$_2$ saturation at admission, %	0.79 (0.65–0.98)	.027
Model B[b]		
Age ≥ 75 years	5.99 (1.12–31.9)	.036
O$_2$ saturation ≤ 88%	8.02 (1.51–42.7)	.015

Abbreviations: COVID-19, coronavirus disease 2019; LCI, confidence limits; OR, odds ratio.
[a]c-index 0.80 (0.78–0.98).
[b]c-index 0.80 (0.63–0.98).

(almost only case/centers experience) have been published so far on the impact of COVID-19 on surgically treated patients.[15,16] However, the impact of health system rearrangement, human and physical resources allocation, and viremia-related thromboembolic and respiratory burden on complex surgical outcomes is mandatory for safe surgical activity restart.

If we look back to the beginning of the COVID outbreak, which came largely unpredicted and for almost 3 weeks completely unrecognized in Northern Italy, it is easy to understand how multiple patients with initial/asymptomatic phases might have undergone normal surgical activity without adequate screening. Furthermore, in these initial rearrangement times, hospitals and health workers themselves might have functioned as disease spreaders. Indeed, in the present experience, the incidence of SARS-CoV-2 positivity in patients submitted to CS resulted in 3.6%. This number is impressive if we consider that only 0.38% of the overall population was found positive on the day the survey was closed. Thus, it has to be considered that infection incidence at the worst of the first wave was 10-

fold higher in-hospital admitted patients compared with the general population. Several explanations can justify this observation, including the following: the overall penetration of the SARS-CoV-2 in the Italian population was much higher than officially reported; the saturation screening that occurred for surgery patients uncovered real-life data, or hospitals and healthcare facilities have worked as incubators and disease spreader.

Indeed it is evident how the medical community was found unprepared, and this was especially harsh in the setting where the aerial diffusion of the virus is facilitated by invasive procedure on the airways (intubation, bronchial aspiration, transesophageal echocardiography, and respiratory therapy); in this setting, the accurate management of aerosol and air-spraying is mandatory for this very contagious disease.[17] Furthermore, considering that a molecular swab was performed in every patient before surgery, and only 11 over 48 patients were operated on with a pre-operative positive sample, we assume that most patients developed symptoms and positive swab in the postoperative period. A positivization of previously negative SAR-CoV-2 patient might occur either when the patient is operated in the 48–72 h of SARS-CoV-2 incubation time, or more likely when the patient acquires the infection within the hospital premises. This is an important message that should be delivered: appropriate and complete separation of COVID positive and negative pathways is mandatory to protect both patients and healthcare workers. Furthermore, the fear of being infected during hospitalization for elective diagnostic or interventional procedures, prevents many patients, even with acute symptoms, to access the local or tertiary centers. This fact is reflected by a dramatic reduction worldwide of planned surgical activities (as evident also in the present report) but, unfortunately, determined a steep increase in mortality for acute pathology due to under-referral and treatment.[18]

The overall pattern of surgical procedures performed within the monitored period is within the regular activities generally performed. Indeed, none of the cardiac pathologies appeared to prevail over the others. Furthermore, the preoperative clinical profile of the present study population appeared not significantly different from the average profile of the CS population and none of the standard risk factors recorded prevailed above the others.

Another fundamental issue emerging from the present report is the high mortality of patients with COVID pneumonia submitted to CS. In the COVID population, in-hospital mortality peaked to 20% (10/48 patients) compared with 0.9% mortality rate (12/1306 patients) in the COVID-N population, meaning that COVID-19 infection increased the risk of death by 20-fold. Despite some evidence reported how normal seasonal flu is able to affect the outcome of cardiac surgery, facilitating postoperative respiratory failure and ARDS, the Covid infection impacts this population on a greater extent compared with regular flu.[19]

It is immediately recognizable how the occurrence of the COVID-19 affects the survival by two-fold times than the emergency status (OR COVID 28.3 vs. OR Emergency 13.9). In this viewpoint, multiple different risk factors, including cardiac disease, surgical procedure, or preoperative risk factors were tested to identify independent predictors of in-hospital mortality in COVID positive patients submitted to CS. Indeed, it is

reasonable to suppose that pulmonary function could be more impaired in valvular disease than in CABG or aortic patients with preserved EF. Anyway, none of the cardiac conditions or the type of surgical procedures seemed to play a prognostic role.

As we recall the only prognostic marker we could recognize is age and saturation upon admission. Accordingly, we should consider very carefully undergoing cardiac surgery with a 75-year or older patient in case of clinical evident COVID pneumonia or even a simple positive swab and try to delay the procedure as long as possible through medical or palliative approaches. Furthermore is important to recover the most efficient pulmonary function, reaching a near-normal saturation to mostly minimize procedure-related risk.

In this viewpoint, is useful to recall how infections are one of the most dreadful complications after surgical procedures. In cardiac surgery, despite surgical site infection occurring with higher incidence, pneumonia accounts for serious complications and related mortality. In a revision of the STS database with more than 365,686 records, Likosky et al.[20] found that pneumonia accounted for 75% of overall postoperative infections, largely more than surgical site infections that accounted for 16% of the overall infections recorded. In a subsequent different series Ailawadi et al.[21] found how postoperative pneumonia highly impacted in-hospital mortality (hazard ratio 8.89; 95% CI 5.02–15.75), and increased hospital length of stay(bootstrap 95% CI 10.31–16.58).

A positive remark can be finally derived: despite the high level of hospital rearrangement and the probable delayed patient presentation, the mortality in the COVID-N population (0.9%) resulted significantly lower than the benchmark mortality set by national survey of the ministry of health.[22]

As this mortality was achieved in a group of nondeferrable, somehow urgent, procedures, we believe that, despite all the limitations ascribable to the initial pandemic outbreak, the hub-and-spoke healthcare reorganization model was able to guarantee a successful safety net for acute cardiac and oncological pathology to offer the best patient care ever.

5 | STUDY LIMITATION

The main limitation of this report is, despite involving a nationwide database, the limited amount of surgical cases that were performed during this 3-months period: an average of less than 50 cases per center were performed during the 84 days span of monitoring. Consequently, it is very hard to perform any reliable statistical evaluation; furthermore, noticeable events were sporadic and conclusions on case-related effects can only be anecdotal. Moreover, some information regarding preoperative and postoperative data, such as type of previous surgery, renal clearance, and re-intubation rate are missing.

The two groups are too much different in terms of size and this makes a possible matching unreliable, even if data reported in Table 1 show as they are statistically similar for all the variables but the history of heart failure. Finally, we failed, very likely due to the small sample size to identify other technic predictors for early mortality.

6 | CONCLUSIONS

The SARS-CoV-2 pandemic highly affected cardiac surgery service in Italy. In this Italian Society of Cardiac Surgery sponsored database were collected data from 1354 surgical cases performed during the first wave: roughly 3.5% of patients ($n = 48$ pts)) were affected by COVID-19, 22% (11 pts) of these presenting with the infection before surgery, but the remaining 78% became COVID-19 positive during the hospital stay, showing how important is to identify and isolate hospital-based hotspots. In cardiac surgery, COVID-19 claimed almost 20% mortality, comparable with other surgery, especially in elderly (>75 years) patients.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Giorgia Bonalumi, Alberto Pilozzi Casado, Andrea Garatti, and Alessandro Barbone: Conception and design of the work, writing of the original draft. Michele Di Mauro, Fabio Barili, Gino Gerosa, and Alessandro Parolari: Revision for intellectual content, visualization, approval of the final draft. All other authors contributed to the revision of the final graft, data recollection, and curation

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REFERENCES

1. Mohamed Abdel Shafi A, Hewage S, Harky A. The impact of COVID-19 on the provision of cardiac surgical services. *J Card Surg*. 2020;35(6):1295-1297.
2. Li B, Yang J, Zhao F, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. *Clin Res in Cardiol*. 2020;109:(5):531–538. doi:10.1007/s00392-020-01626-9
3. Archer JE, Odeh A, Ereidge S, et al. Mortality and pulmonary complications in patients undergoing surgery with perioperative

SARS-CoV-2 infection: an international cohort study. *The Lancet*. 2020;396(10243):27–38. doi:10.1016/s0140-6736(20)31182-x

4. Auld SC, Caridi-Scheible M, Blum JM, et al. ICU and ventilator mortality among critically ill adults with coronavirus disease 2019. *Crit Care Med*. 2020;48(9):e799-e804.

5. Garatti A, Castelvecchio S, Daprati A, et al. Clinical course of COVID-19 infection in patients urgently operated of cardiac surgical procedures. *Ann Surg*. 2020;272(4):e275-e279.

6. Bonalumi G, Giambuzzi I, Barbone A, et al. A call to action becomes practice: cardiac and vascular surgery during the COVID-19 pandemic based on the Lombardy emergency guidelines. *Eur J Cardiothorac Surg*. 2020;58(2):319-327.

7. Bakaeen FG, Gillinov AM, Roselli EE, et al. Cardiac surgery and the coronavirus disease 2019 pandemic: What we know, what we do not know, and what we need to do. *J Thorac Cardiovasc Surg*. 2020; 160(3):722-726.

8. Parolari A, di Mauro M, Bonalumi G, et al. Safety for all: coronavirus disease 2019 pandemic and cardiac surgery: a roadmap to "phase" 2. *Eur J Cardiothorac Surg*. 2020;58(2):213-216.

9. Chalmers J, Pullan M, Fabri B, et al. Validation of EuroSCORE II in a modern cohort of patients undergoing cardiac surgery. *Eur J Cardiothorac Surg*. 2013;43(4):688-694.

10. Boodman C, Lagacé-Wiens P, Bullard J. Diagnostic testing for SARS-CoV-2. *CMAJ*. 2020;192(26):E713.

11. DECRETO-LEGGE. Misure urgenti in materia di contenimento e gestione dell'emergenza epidemiologica da COVID-19 (20G00020) (GU Serie Generale n. 45 del 23-02-2020), Febraury 23, 2020. Last accessed June, 27, 2021. https://www.gazzettaufficiale.it/eli/id/2020/02/23/20G00020/sg

12. Decreto del presidente del consiglio dei ministri 1 marzo 2020. Ulteriori disposizioni attuative del decreto-legge (6). 2020. Last accessed June 27, 2021. https://www.comune.calcio.bg.it/sites/default/files/dpcm_-_1_marzo_2020_.pdf

13. Omori R, Matsuyama R, Nakata Y. The age distribution of mortality from novel coronavirus disease (COVID-19) suggests no large difference of susceptibility by age. *Sci Rep*. 2020;10(1): 16642.

14. Bonalumi G, di Mauro M, Garatti A, et al. The COVID-19 outbreak and its impact on hospitals in Italy: the model of cardiac surgery. *Eur J Cardiothorac Surg*. 2020;57(6):1025-1028.

15. Farr A, Foessleitner P. Faculty Opinions recommendation of Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study. *Faculty Opinions – Post-Publication Peer Review of the Biomedical Literature*. Published online, 2020. doi:10.3410/f.738039537.793578769

16. Keizman E, Ram E, Kachel E, Sternik L, Raanani E. The impact of COVID-19 pandemic on cardiac surgery in Israel. *J Cardiothorac Surg*. 2020;15(1):294.

17. Forrester JD, Nassar AK, Maggio PM, Hawn MT. Precautions for operating room team members during the COVID-19 pandemic. *J Am Coll Surg*. 2020;230(6):1098-1101.

18. De Filippo O, D'Ascenzo F, Angelini F. Reduced rate of hospital admissions for ACS during COVID-19 outbreak in Northern Italy. *N Engl J Med*. 2020;383(1):88-89.

19. Groeneveld GH, van Paassen J, van Dissel JT, Arbous MS. Influenza season and ARDS after cardiac surgery. *N Engl J Med*. 2018;378(8): 772-773.

20. Likosky DS, Wallace AS, Prager RL. Sources of variation in hospital-level infection rates after coronary artery bypass grafting: an analysis of the society of thoracic surgeons adult heart surgery database. *Ann Thorac Surg*. 2015100(5):1570-1575.

21. Ailawadi G, Chang HL, O'gara PT, et al. Pneumonia after cardiac surgery: experience of the National Institutes of Health/Canadian Institutes of Health Research Cardiothoracic Surgical Trials Network. *J Thorac Cardiovasc Surg*. 2017;153(6):1384-1391.