



BMJ Open Type of hospitalisations and in-hospital outcomes in the Italian coronary care unit network at the time of COVID-19 pandemic: the BLITZ-COVID19 Registry

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ABSTRACT

Objective The aim of the study was to describe the epidemiology and outcome of patients hospitalised during the COVID-19 pandemic in intensive cardiac care units (ICCs).

Design Non-interventional, retrospective and prospective, nationwide study.

Setting 109 private or public ICCs in Italy.

Participants 6054 consecutive patients admitted to Italian ICCs during COVID-19 pandemic.

Primary and secondary outcome measures To obtain accurate and up-to-date information on epidemiology and outcome of patients admitted to ICCs during the COVID-19 pandemic, the impact that the COVID-19 infection may have determined on the organisational pathways and in-hospital management of the various clinical conditions being admitted to ICCs.

Results Acute coronary syndromes were the most frequent ICC discharge diagnoses followed by heart failure and hypokinetic arrhythmias. The prevalence of COVID-19 positivity was approximately 3%. Most patients with a COVID-19 diagnosis at discharge (52%) arrived to ICC from other wards, in particular 22% from non-cardiology ICCs. The overall mortality was 4.2% during ICC and 5.8% during hospital stay. The cause of in-hospital death was cardiac in 74.4% of the cases, non-cardiovascular in 13.5%, vascular in 5.8% and related to COVID-19 in 6.3% of the patients.

Conclusions This study provides a unique nationwide picture of current ICC care during COVID-19 pandemic.

Trial registration number NCT04744415.

INTRODUCTION

In the late February 2020, the first case of COVID-19 was reported in Italy, and, with its rapid spread, it created a major public health problem that has made necessary the reorganisation of hospital beds.^{1,2} Some intensive cardiac care units (ICCs) have been transformed, partially or completely, into intensive care for the treatment of respiratory failure

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Non-interventional, retrospective and prospective, nationwide study.
- ⇒ The first and largest nationwide survey evaluating epidemiology, use of resources and outcome of consecutive patients admitted to intensive cardiac cares during the COVID-19 pandemic.
- ⇒ Data limited to the hospitalisation period.

due to COVID-19. Other ICCs were identified as hub centres, where patients with acute cardiovascular disease were referred both directly from the community and from those structures temporarily dedicated to the management of COVID-19.^{1,2}

In this context, the rate and type of hospitalisations in ICCs in the national territory was unknown; in addition, there were no available data on a national scale relating to the levels of in-hospital mortality of the various pathologies admitted to the ICC and whether the coexistence of a COVID-19 infection might have changed in-hospital patients' outcomes.

The BLITZ-COVID19 study, promoted by the Heart Care Foundation of the National Association of Hospital Cardiologists (ANMCO), aimed to describe the epidemiology of hospitalisations in ICCs, the outcome of patients during hospitalisation, the impact that the COVID-19 infection may have determined on the organisational pathways and in-hospital management of the various clinical conditions being admitted to ICCs.

METHODS

The BLITZ-COVID19 (ClinicalTrials.gov Identifier: NCT04744415) was designed as

an observational, multicentre, nationwide study aimed to collect data on patients admitted to ICCs, using a web-based system. All consecutive patients, aged ≥ 18 years, hospitalised with any diagnosis in the participating ICCs in two scheduled enrolment periods (retrospective phase (phase 1) and prospective phase (phase 2)), have been enrolled. In each participant ICC, the enrolment period for each phase was 30 days. No specific, clinical exclusion criteria were foreseen. In phase 1, the enrolment took place between March and April 2020, while phase 2 was completed between November 2020 and February 2021. No follow-up period was foreseen. No specific protocols or recommendations for evaluation, management and/or treatment have been proposed during this observational study. The diagnostic procedures, pharmacological and non-pharmacological therapies, usually prescribed for cardiovascular diseases and those used for COVID-19 infection has been recorded in the database.

ANMCO invited all Italian ICCs located into public, academic or private hospitals to participate to the survey. The protocol was submitted to local ethical committees (ECs) according to current national regulations and the study started at each centre only on the receipt of approval by the EC and local authorities. Patients enrolled in the prospective phase were asked to sign an informed consent for the anonymous management of their individual data. Given the impossibility for organisational reasons of collecting informed consent for the retrospective phase, this data collection, according with ECs authorisation, was carried out in a totally anonymous form, so that there was no possibility of tracing the patient's identity. In fact, all ECs accepted to collect the informed consent only for the prospective phase of the study.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Statistical analysis

Categorical variables were reported as number and percentages, and compared by χ^2 test, while continuous variables were reported as median and IQR, and compared by Mann-Whitney U test. A $p < 0.05$ was considered statistically significant. All tests were two sided. Analyses were performed with SAS software, V.9.4.

RESULTS

Among the 398 Italian ICCs, 109 (27.4%) participated in the registry (see online supplemental appendix 1) for a complete list of centres and investigators). The 109 ICCs were classified into 3 types according to their facilities: 21% had both cath lab and cardiac surgery on-site, 47% had cath lab only and the remaining 32% had neither interventional nor surgical facilities. The ICCs dedicated to the treatment of COVID-19 patients were 15 in the phase 1 and 10 in the phase 2.

During the phase 1, 2774 patients were enrolled, while in the phase 2, 3280 patients were prospectively included (a total of 6054 patients): 33.2% were females, 39.5% were ≥ 75 years old and 3.0% (184 patients) were COVID-19 positive (85 in phase 1 and 99 in phase 2).

ST and non-ST elevation myocardial infarction (STEMI and NSTEMI) were the most frequent discharge diagnoses (26.4% and 22.5%, respectively); 13.2% of the cases were diagnosed as heart failure and 7.1% as hypokinetic arrhythmia. A discharge diagnosis of COVID-19 was made for 50 patients (0.8%) (figure 1).

The prevalence of COVID-19 positivity was approximately 3% in all groups, except for the pulmonary embolism group, where it was found in 5.2% of cases (table 1). STEMI and COVID-19 patients were younger than patients with other main discharge diagnoses. Diabetes was the most frequent comorbidity in all patient groups, a previous acute myocardial infarction (AMI) ranged

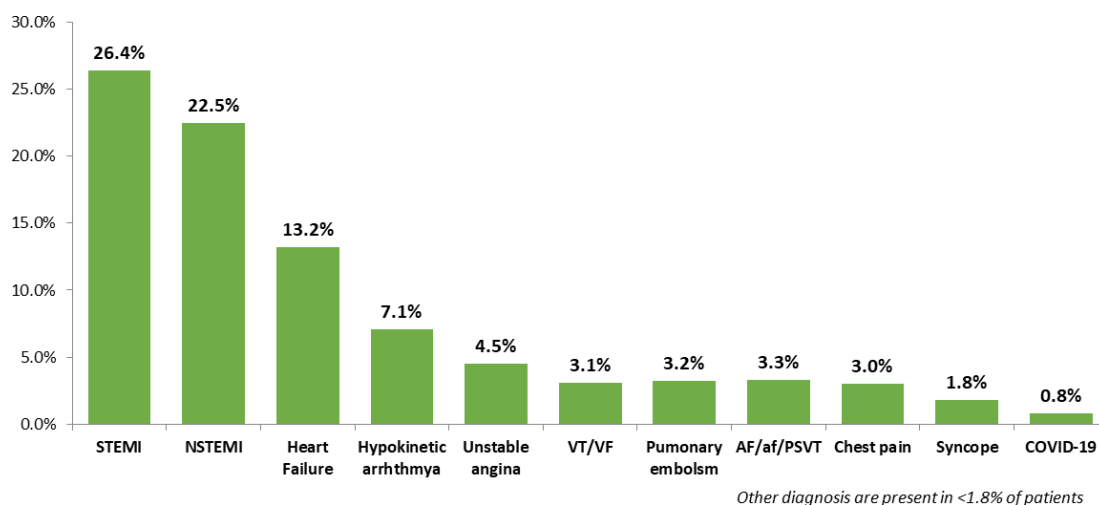


Figure 1 Main discharge diagnosis from ICC. AF, atrial fibrillation; af, atrial flutter; ICCs, intensive cardiac care; STEMI, ST-elevated myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; PSVT, paroxysmal supraventricular tachycardia; VF, ventricular fibrillation; VT, ventricular tachycardia.

Table 1 Baseline characteristics, comorbidities and use of resources

	STEMI 1595 pts	NSTE-ACS 1635 pts	Heart Failure 801 pts	Arrhythmias 816 pts	PE 194 pts	COVID 50 pts	Other 963 pts	Total 6054 pts
Females, n (%)	403 (25.3)	472 (28.9)	315 (39.3)	319 (39.1)	103 (53.1)	11 (22.0)	386 (40.1)	2009 (33.2)
Age (years), median (IQR)	66 (57–75)	71 (61–80)	76 (67–83)	76 (67–83)	69 (57–78)	68 (60–77)	72 (60–81)	71 (61–80)
Age ≥75 years, n (%)	425 (26.7)	613 (37.5)	420 (52.4)	457 (56.0)	62 (32.0)	16 (32.0)	401 (41.6)	2394 (39.5)
Positive for COVID, n (%)	38 (2.4)	36 (2.2)	11 (1.4)	20 (2.5)	10 (5.2)	50 (100)	19 (2.0)	184 (3.0)
Diabetes, n (%)	320 (20.1)	524 (32.1)	272 (34.0)	199 (24.4)	34 (17.5)	14 (28.0)	217 (22.5)	1580 (26.1)
Previous AMI, n (%)	235 (14.7)	431 (26.4)	245 (30.6)	151 (18.5)	12 (6.2)	4 (8.0)	185 (19.2)	1263 (20.9)
Previous CABG/PCI, n (%)	204 (12.8)	444 (27.2)	206 (25.7)	138 (16.9)	9 (4.6)	4 (8.0)	210 (21.8)	1215 (20.1)
Neoplasm, n (%)	62 (3.9)	67 (4.1)	50 (6.2)	60 (7.4)	28 (14.4)	3 (6.0)	64 (6.7)	334 (5.5)
TTE, n (%)	1466 (91.9)	1499 (91.7)	732 (91.4)	669 (82.0)	180 (92.8)	34 (68.0)	817 (84.8)	5397 (89.2)
Coronary angiography, n (%)	1441 (90.3)	1312 (80.2)	230 (28.7)	116 (14.2)	7 (3.6)	3 (6.0)	331 (34.4)	3440 (56.8)
PCI, n (%)	1390 (87.2)	947 (57.9)	47 (5.9)	23 (2.8)	0 (0.0)	1 (2.0)	98 (10.1)	2506 (41.4)
Chest TC scan, n (%)	95 (6.0)	143 (8.8)	138 (17.2)	71 (8.7)	96 (49.5)	13 (26.0)	173 (18.0)	729 (12.0)
B/CPAP, n (%)	68 (4.3)	72 (4.4)	174 (21.7)	10 (1.2)	12 (6.2)	29 (58.0)	59 (6.1)	424 (7.0)
Invasive ventilation, n (%)	36 (2.3)	13 (0.8)	15 (1.9)	3 (0.4)	3 (1.6)	9 (18.0)	37 (3.8)	116 (1.9)
Definitive pacemaker, n (%)	14 (0.9)	17 (1.0)	12 (1.5)	386 (47.3)	2 (1.0)	0 (0.0)	97 (10.1)	528 (8.7)

ACS, acute coronary syndrome; AMI, acute myocardial infarction; B/CPAP, Bilevel/Continuous Positive Airway Pressure; CABG, coronary artery bypass graft; NSTE, non-ST-segment elevation; PCI, percutaneous coronary intervention; PE, pulmonary embolism; STEMI, ST-elevated myocardial infarction; TTE, transthoracic echocardiogram.

from 6.2% in pulmonary embolism to 30.6% in heart failure and a previous coronary revascularisation in 4.6% of patients with pulmonary embolism and 27.2% in non-ST-segment elevation (NSTEMI)-acute coronary syndrome (ACS) patients (table 1).

Patients admitted to ICC were most often triaged by emergency room, 25.2% of patients with STEMI diagnosis at discharge were transported directly to ICC by the emergency medical service while most patients with a COVID-19 diagnosis at discharge (52%) arrived to ICC from other wards, in particular 22% from non-cardiology intensive care units.

A transthoracic echocardiogram was performed in 89.2% of patients and a coronary angiography in 56.8% of cases. A definitive pacemaker insertion, Bilevel/Continuous Positive Airway Pressure (B/CPAP) and invasive ventilation were used in 8.7%, 7.0% and 1.9% of the patients, respectively (table 1).

As expected, coronary angiography and PCI were mainly performed in patients with a diagnosis of STEMI or NSTEMI-ACS (90.3% and 80.2% for the former, 87.2% and 57.9% for the latest, respectively), while CT scan was performed to a greater extent in patients with COVID-19 and pulmonary embolism (26.0% and 49.5%, respectively).

Drug therapy in ICC

Among the 6054 patients, 1832 (30.3%) were treated with low molecular weight heparins (LMWHs), almost exclusively with enoxaparin, 1112 (18.4%) with oral anticoagulants, 765 (12.6%) with unfractionated heparin and 732 (12.1%) with fondaparinux.

Aspirin was given to 71.3% and a dual antiplatelet therapy was prescribed in 53.7% of the patients. An inhibitor of the RAAS was used in 61.2% of cases, a beta-blocker in 68.5% and a statin in 65.6%. Inotropic support was necessary for 7.2% of patients and 7.3% were treated with intravenous nitrates.

Outcomes in ICCs and in hospital

The median length of ICC and hospital stay was 4 days IQR (2–5) and 7 (5–11), respectively (3 IQR (2–5) and 6 (4–10) days in phase 1, and 4 (2–5) and 7 (5–11) days in phase 2, respectively). Among patients discharged alive, 73.2% were transferred from the ICC to another ward, 19.1% were discharged at home, 6.4% were transferred to another hospital and only 1.3% to a rehabilitation service.

The overall mortality was 4.2% during ICC and 5.8% during hospital stay (figure 2 shows the mortality by phase). In-hospital mortality in patients with STEMI was 5.6% and in NSTEMI-ACS patients 2.8%. The cause of in-hospital death was cardiac in 74.4% of the cases, non-cardiovascular in 13.5%, vascular in 5.8% and related to COVID-19 in 6.3% of the patients.

COVID-19 patients

There were 184 COVID-19 patients, 85 enrolled in phase 1 and 99 in phase 2; the median age of these patients

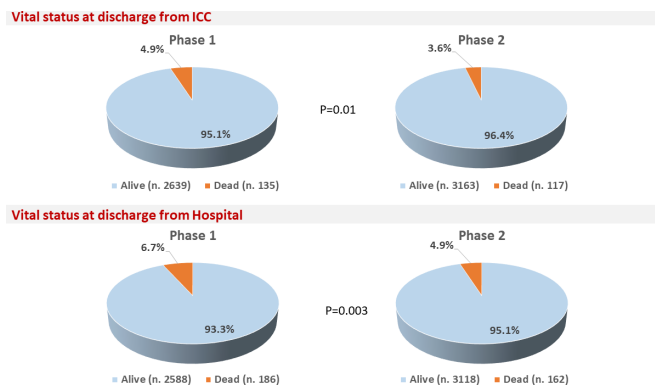


Figure 2 Vital status at discharge by phase (ICC and Hospital). ICC, intensive cardiological unit.

was 69 (59–79) years, 25.5% were female and 65.2% had symptoms of COVID-19; symptomatic patients were much more frequent in the first phase (88.2% vs 45.5%, $p < 0.0001$) (table 2). Differences were found between the two phases also in the need of assisted ventilation, used in 78.8% in phase 1 and in 43.4% in phase 2, $p < 0.0001$. The median length of ICC stay was similar to the total population (median 4 days) while the length of in-hospital stay was longer (median 9 days in COVID-19 vs 7 days in not COVID-19). The length of in-hospital stay of COVID-19 patients was longer in phase 1 than in phase 2 (median 12 vs 7 days, $p < 0.0001$, respectively) (table 2).

Among the 184 COVID-19 patients, 50 (27.2%) were discharged from ICC with a main diagnosis of COVID-19, 20.7% had a STEMI, 15.2% an NSTEMI and 6.0% had a heart failure diagnosis.

Among COVID-19 patients, the mortality was 8.2% in ICC and 16.9% during the hospitalisation; a higher ICC and in-hospital mortality was observed in phase 1 with respect to phase 2, even though statistically significant only for the latter ($p = 0.002$) (figure 3). The in-hospital cause of death was related to the COVID-19 infection in 61.3%, cardiac in 32.3% and vascular in 6.4% of the cases.

The most frequent comorbidity in COVID-19 patients was diabetes (32.6%), followed by coronary artery disease (25.5% of the patients with previous AMI and 20.7% with prior coronary revascularisation). Transthoracic echocardiography was performed in 76.1%, coronary angiography in 41.3% and a chest CT scan in 22.3% of COVID-19 patients (chest CT scan in not COVID-19 was 11.6%).

Notably, nearly 50% did not receive any specific therapy for COVID-19 infection, especially in the second phase (figure 4). LMWHs were used in 49.5% of COVID-19 patients, 12.5% were treated with unfractionated heparin and 9.8% with fondaparinux. Oral anticoagulants, particularly direct anticoagulants, were used in 10.9% of patients. Aspirin was prescribed in 62.0% and a dual antiplatelet therapy in 45.7% of the COVID-19 cases. Among other therapies, beta blockers were prescribed to 52.2%, statins to 47.3%, diuretics to 45.7% and a renin angiotensin system inhibitor to 40.8% of patients; 12.5% of COVID-19 patients required intravenous inotropic support compared with 7.2% of the overall population.

Table 2 COVID-19 patients: baseline characteristics, type of symptoms and length of stay

	Phase 1 (n=85)	Phase 2 (n=99)	Total (n=184)	P value
Females, n (%)	20 (23.5)	27 (27.3)	47 (25.5)	0.56
Age, median (IQR)	68 (59–77)	71 (60–80)	69 (59–79)	0.31
Age ≥75 years, n (%)	25 (29.4)	38 (38.4)	63 (34.2)	0.20
With symptoms, n (%)	75 (88.2)	45 (45.5)	120 (65.2)	<0.0001
pneumonia	67 (89.3)	33 (73.3)	100 (83.3)	0.02
fever	48 (64.0)	24 (53.3)	72 (60.0)	0.25
Assisted ventilation, n (%)	67 (78.8)	43 (43.4)	110 (59.8)	<0.0001
O ₂ Therapy, n (%)	43 (64.2)	40 (93.0)	83 (75.5)	0.0006
CPAP, n (%)	29 (43.3)	10 (23.3)	39 (35.5)	0.03
Intubation, n (%)	11.9	4.7	9.1	0.31
Length of in ICC stay Median (IQR)	4 (3–6)	4 (2–6)	4 (3–6)	0.55
Length of in-hospital stay Median, (IQR)	12 (7–22)	7 (4–12)	9 (6–15)	<0.0001

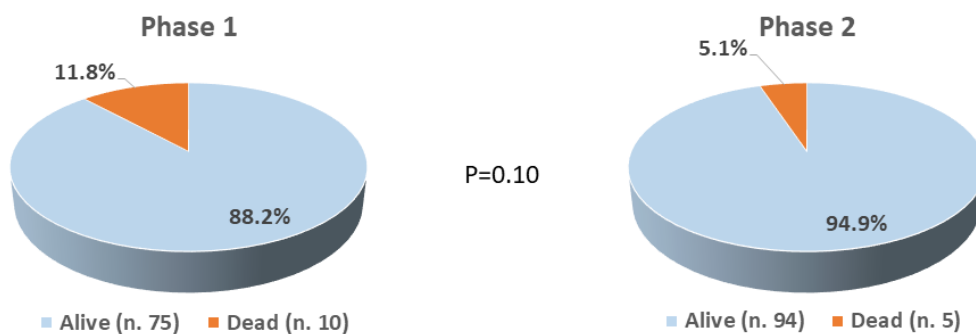
Phase 1 (enrolment between March and April 2020): 30 days for the retrospective phase.
Phase 2 (enrolment between November 2020 and February 2021): 30 days for the prospective phase.
ICC, intensive cardiac care.

DISCUSSION

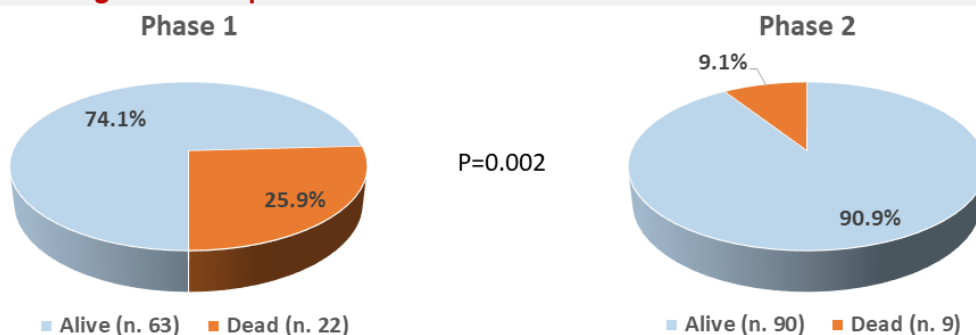
This is the first nationwide survey assessing type of hospitalisation, use of resources and in-hospital outcome of consecutive patients admitted to ICCs during the COVID-19 pandemic. Data were collected both retrospectively and prospectively in two distinct phases of the pandemic. Our data show that, during the pandemic period, Italian ICCs only partially changed the type of hospitalisation, as evidenced by the low percentage

of COVID-19 patients. The reduced percentage of COVID-19 patients observed in our registry may be due to the fact that during the pandemic period, several beds in non-cardiology intensive care units were dedicated to the treatment of more complex COVID-19 patients who deserved ventilatory or circulatory support, preserving the acute cardiovascular care. Nonetheless, ICCs have played an important role in the management of COVID-19 patients, as about a quarter of patients with

Vital status at discharge from ICC



Vital status at discharge from Hospital


Figure 3 Vital status at discharge by phase (from ICC and Hospital) in COVID-19 patients. ICC, intensive cardiac care.

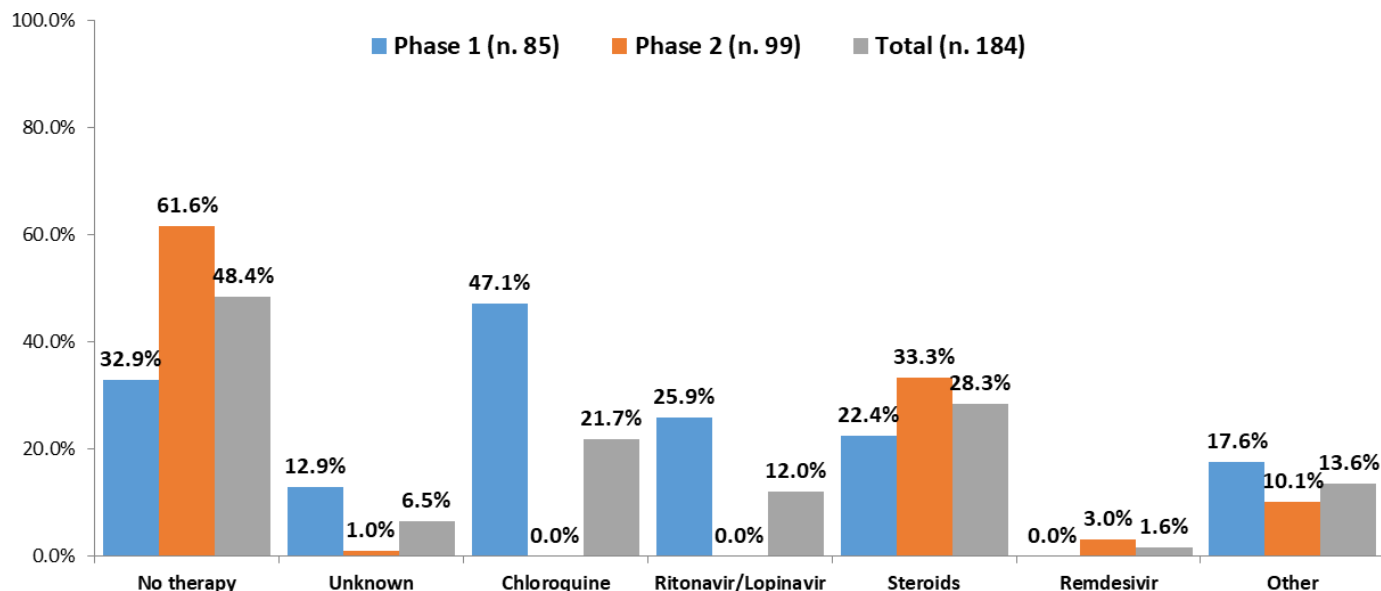


Figure 4 Specific therapy for COVID-19 infection.

a diagnosis of COVID-19 at discharge arrived in ICC from non-cardiology intensive care units.

Over the years, the function of the ICCs has undergone significant changes.³ From units for the treatment of severe arrhythmias in patients hospitalised for AMI they have become intensive therapies for the treatment of a number of severe cardiac conditions.³ These radical functional and structural changes have been well documented by several epidemiological studies published over the last years.⁴⁻⁵ However, compared with surveys conducted in our country about 10 years ago, the type of ICC admissions has not significantly changed during the COVID-19 pandemic.⁴ As difference from previous registries⁴⁻⁶ where patients with NSTEMI-ACS were more represented compared with STEMI, in BLITZ-COVID19 there was a comparable admission number of NSTEMI-ACS and STEMI patients. This finding is likely consistent with the higher reduction of NSTEMI-ACS admissions compared with STEMI during the COVID-19 pandemic, as observed also in other Italian studies.⁷⁻⁹

During the COVID-19 pandemic period, which particularly affected Italy with a significant number of deaths and hospitalisations in intensive care units,¹⁰⁻¹¹ the overall mortality of patients admitted to ICC, especially in the phase 1 of our survey, was substantially higher compared with nationwide surveys previously conducted in our country. These data are also confirmed by the higher in-hospital mortality of patients with ACS even if in both these categories of patients coronary angiography and PCI were performed in a percentage of patients similar to that of other studies.⁴⁻⁶ This is consistent with evidence, much derived from Italian experiences, which has suggested that mortality rate of patients with cardiovascular disease increased during the pandemic.^{7-9 12-17} For instance, in-hospital mortality after ACS increased by 3–4 times compared with the prepandemic period.^{8 14} The reasons for this high mortality rate for ACS are multifactorial and

not completely understood. In a retrospective registry conducted in European high-volume PCI centres, the total ischaemia time and door-to-balloon time in patients with STEMI treated with PCI during COVID-19 pandemic was significantly increased compared with the prior year, suggesting that the system of care was suboptimal and clinical presentations were more aspecific during the COVID-19 pandemic, especially during the lockdown for COVID-19.¹⁸ In this regard, a possible explanation for the difference in in-hospital mortality observed in our registry between the first and second phase may be related to the fact that the second phase includes, for some centres, even months of recruitment in the absence of national lockdown for COVID-19. This could have impacted on the process of care and related outcomes, although we observed a greater use of revascularisation procedures in ACS compared with previous Italian or European registries.^{4 5 19 20} Indeed, a retrospective analysis on patients admitted to the emergency departments for AMI in nine Italian centres, documented an increase in the number of admissions for AMI after the removal of the national lockdown for COVID-19 in Italy, especially in the first weeks following the lockdown removal.²¹

Although in previous studies of hospitalised patients with COVID-19 the concomitant presence of chronic cardiac disease was significantly associated with mortality, in a recent multinational patient registry specifically established to determine the role of cardiovascular diseases in the COVID-19 pandemic, only those with heart failure were at greatest risk of in-hospital death.^{22 23} Since in our study the main diagnosis of heart failure was present in a minority of our COVID-19 patients (6%), it could explain the relative impact of COVID-19 on the overall mortality observed in our series.

In our study, COVID-19 patients had longer hospitalisation, greater use of CT scans and higher in-hospital mortality rates than non-COVID patients admitted to ICC.

Notably, the overall prevalence of pulmonary embolism in our study is lower than in previous studies evaluating COVID-19 patients hospitalised in the first months of the pandemic.^{8 14} This difference may be ascribed to the implemented use of antithrombotic prophylactic strategies in patients admitted with COVID-19, as documented by the fact that heparin therapies were used in over half of the COVID-19 patients enrolled in our registry.

Study limitations

The study suffers several limitations. First, our study must be evaluated in the light of the known limitations of observational studies. Second, patients were enrolled in ICC centres and the population, therefore, does not include patients who died before ICC admission or those admitted to non-ICC cardiology wards. Nonetheless, the BLITZ-COVID19 study is the largest survey on patients admitted to ICC during the COVID-19 pandemic. In addition, on-site auditing was not performed, and our analysis is based on the diagnosis made by the attending physicians. However, because patient management was based on the working diagnosis made by the attending physician, our analysis is suitable for evaluation of patient management. Finally, because our survey did not provide data on long-term outcomes, the relationship between different patterns of care and major clinical events in COVID-19 patients managed by cardiologists in ICCs cannot be evaluated.

CONCLUSION

In conclusion, the BLITZ-COVID-19 registry is the largest survey to date on patients admitted to ICCs during COVID-19 pandemic and provides a nationwide picture of current ICC care during this particular time frame. The overall rate of admission diagnoses is comparable to previous surveys conducted in our country a decade ago, with ACS remaining the most frequent primary admission diagnosis of patients admitted to Italian ICCs. Notably, COVID-19 was only present in approximately 3% of cases. Nevertheless, mortality during ICC stay seems to be higher than in previous nationwide surveys, especially during the national lockdown period for COVID-19, suggesting that the management of patients admitted to ICC was somehow impacted by the pandemic.

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