

ST-segment elevation myocardial infarction and reperfusion therapy in the COVID-19 pandemic

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Introduction

The coronavirus disease 2019 (COVID-19) pandemic has been placing enormous pressure on global healthcare systems. Considerable resource allocation to the treatment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, although fully inevitable, originated remarkable constraints in the access of patients with other diseases – in fact, elective admissions and nonurgent procedures or interventions were mostly canceled or deferred worldwide.

Another point of concern was the ability of overwhelmed health systems to continue providing proper care to patients with non-COVID related urgent medical conditions, including those presenting with acute myocardial infarction (AMI) [1]. Notwithstanding most care programs for the management of ST-segment elevation myocardial infarction (STEMI) in Europe and United States of America (US) remained fully operational during the pandemic peak, there was a general belief of a significant reduction in the number of admitted patients. Many reports confirmed significant delays and reduction in hospital admissions for AMI worldwide, with noticeable consequences on outcomes.

Admissions for Myocardial Infarction

During the COVID-19 pandemic outbreak, a consistent decline in the number of admissions for AMI and cardiac catheterization laboratory activations was observed, decreasing by up to 49% and 38%, respectively [2-5]. The relative number of patients referred for primary percutaneous coronary intervention (PPCI) that ultimately received a diagnosis other than STEMI remained constant or was even mildly decreased, validating a true decline in STEMI presentations [6,7]. Furthermore, Fabris et al. reported a marked reduction in STEMI incidence in Italy, in a U-shaped curve phenomenon with the lower admissions rate corresponding to the early phase of lockdown [8]. Patients' fear of getting infected while in hospital, amplified by numerous campaigns emphasizing the need for social distancing and for staying at home, might have contributed.

Reperfusion Therapy in STEMI

Longer delays to reperfusion therapy were observed, although with significant regional differences (Table 1). Wilson et al. reported more than a 3-fold increase in the number of STEMI patients presenting late (>12 hours after the onset of symptoms) during the pandemic outbreak [6]. In Spain, longer ischemic duration was mainly driven by a significant increase in time from symptoms to first medical contact (71 vs. 105 minutes, $p < 0.001$) [7]. In other countries, namely Portugal and Belgium, door-to-balloon time was predominantly increased, perhaps related to logistical constraints [9,10]. These results are worrisome as total ischemic time is a major determinant of infarct size in STEMI and prompt revascularization is the most effective intervention in reducing its morbidity and mortality [11].

In addition, the specific patterns of reperfusion varied widely. Chinese authorities issued an experts' statement on the approach to STEMI patients, in which thrombolytic therapy became recommended as the preferred reperfusion strategy in those with unconfirmed COVID-19 status [12]. Accordingly, significant reduction in PPCI and higher risk for adverse in-hospital outcomes and

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Table 1: Treatment delays and reperfusion therapy strategies in patients admitted with STEMI during COVID-19 outbreak (compared to equivalent periods of previous years). * Statistical significance at p-value of < 0.05.

Study	Country	n	Age	Male sex	Symptoms to first medical contact (minutes)	Door-to-balloon (minutes)	Primary PCI	Fibrinolysis
Freitas et al. [9]	Portugal	49	62±12 vs. 65±14	85% vs. 78%	240 (120-570) vs. 360 (120-600)	49 (30-110) vs. 140 (90-180)*	-	4% vs. 14%
Claeys et al. [10]	Belgium	116	63±15 vs. 63±12	74% vs. 80%	114 (50-240) vs. 138 (67-331)	39 (22-69) vs. 45 (30-83)*	95% vs. 96%	2% vs. 2%
Scholz et al. [21]	Germany	387	64 vs. 65	72% vs. 72%	163±8 vs. 150±14	51±1 vs. 53±2	91% vs. 91%	0.8% vs. 0.8%
Rodríguez-Leor et al. [7]	Spain	1009	64±13 vs. 63±13	78% vs. 78%	71 (30-180) vs. 105 (45-222)*	-	-	-
De Rosa et al. [2]	Italy	197	65±10 vs. 67±10	75% vs. 80%*	-	Increased by 32%*	95% vs. 95%	-
Wilson et al. [6]	United Kingdom	388	65 vs. 63	78 vs. 68%	Late presentation: 10 vs. 34%*	-	-	-
Fardman et al. [18]	Israel	424	61 (54-70) vs. 62 (55-71)	83% vs. 81%	130 (75-243) vs. 186 (97-732)*	49 (27-75) vs. 56 (30-118)*	-	-
Xiang et al. [12]	China, non-Hubei province	10296	63±13 vs. 63±13	75% vs. 76%	Timely reperfusion: 65% vs. 60%*		OR 0.76 (95% CI 0.71-0.81)*	OR 1.66 (95% CI 1.50-1.74)*

Table 2: Outcomes in patients admitted for STEMI during the COVID-19 outbreak (compared to equivalent periods). * Statistical significance at p-value of < 0.05.

Study	Country	Killip class IV at presentation	Cardiac arrest at admission	Left ventricular ejection fraction	Mechanical complications	In-hospital death
Freitas et al. [9]	Portugal	6% vs. 18%*	9% vs. 13%	48±11 vs. 44±14	-	4% vs. 14%
Claeys et al. [10]	Belgium	-	12% vs. 13%	-	-	7% vs. 6%
Scholz et al. [21]	Germany	13% vs. 13%	10% vs. 11%	-	-	9% vs. 9%
Rodríguez-Leor et al. [7]	Spain	7% vs. 7%	8% vs. 7%	-	0.4% vs. 0.9%	5% vs. 7%*
De Rosa et al. [2]	Italy	-	-	-	-	4% vs. 14%*
Wilson et al. [6]	United Kingdom	-	-	44 (42-56) vs. 47 (35-52) *	-	11% vs. 15%
Fardman et al. [18]	Israel	4% vs. 7%*	-	45 (40-50) vs. 45 (38-51)	1% vs. 4%*	3% vs. 4%
Xiang et al. [12]	China, non-Hubei province	-	-	-	-	4 vs. 5%*

mortality were noted in that country [12-14]. On the other hand, no major changes in reperfusion strategy were observed across Europe and the US, as PPCI remained the default treatment [3,15,16].

STEMI Outcomes during COVID-19 Pandemic

Several studies reported an increase in adverse events in patients admitted for STEMI during the pandemic outbreak, including excess of mortality (Table 2) [6,17]. There was a significant trend towards increased STEMI severity at admission [9,18]. A great number of patients presented in Killip-Kimball classes III and IV during the lockdown, in relation to delays in reperfusion and longer ischemic time duration, as mentioned above [9]. In fact, Cammalleri et al. showed that patients arriving in March 2020 had higher cardiac biomarkers at hospital admission, when comparing to similar 2019 cohort [19]. Furthermore, Fardman et al. reported a significant increase of the incidence of STEMI mechanical complications (OR 4.09 [95% CI: 1.42-14.8], p=0.02) [18]. Accordingly, more patients

were discharged with severe left ventricular dysfunction and there was a trend towards higher in-hospital mortality, even if data are highly inconsistent between studies [6,9,17].

SARS-CoV-2 infection alone might help explain these findings, as these patients had significantly higher mortality when compared to other STEMI patients admitted during the same period [2,20]. In fact, differences in mortality between 2019 and 2020 became attenuated when adjusting for confirmed COVID-19 diagnosis [7]. However, in one study, STEMI fatality rate in 2020 remained significantly higher even after excluding SARS-CoV-2 positive patients [2]. A recent metaanalysis including 50,123 patients suggests that, on a more global scale, STEMI mortality during the pandemic was not significantly increased [17]. Nonetheless, it remains possible that the observation period was too short to detect significant differences, and further studies with longer follow-up periods are necessary to draw solid conclusions.

These results underscore the enormous impact of time to reperfusion on clinical outcomes. All efforts should be employed to reduce total ischemic duration, even during a pandemic.

Conclusion

The COVID-19 pandemic poses significant challenges to healthcare systems worldwide. Nevertheless, diagnosis and treatment of heart diseases cannot be postponed, as they are closely linked to morbidity and mortality. Patients must be informed in order to early recognize AMI symptoms and seek medical assistance and healthcare system must provide safe access to timely PPCI.

The impact of COVID-19 on STEMI management and outcomes demands careful attention by scientific communities. These results are the basis for the establishment of evidence-based strategies in an event of a future pandemic outbreak.

Conflicts of Interest

No conflicts of interest to declare.

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