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Hospitalization, major complications and mortality in acute myocardial infarction patients during the COVID-19 era: A systematic review and meta-analysis

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ABSTRACT

Since the SARS-CoV-2 pandemic began, numerous studies have reported a concerning drop in the number of acute myocardial infarction (AMI) admissions. In the present systematic review and *meta*-analysis, we aimed to compare the rate of AMI admissions and major complication during the pandemic, in comparison with pre-pandemic periods. Three major databases (PubMed, Scopus, and Web of Science Core Collection) were searched. Out of 314 articles, 41 were entered into the study. Patients hospitalized for AMI were 35% less in the COVID-19 era compared with pre-pandemic periods, which was statistically significantly (OR = 0.65; 95% CI: 0.56–0.74; I^2 = 99%; $p < 0.001$; 28 studies). Patients hospitalized for STEMI and NSTEMI were 29% and 34% respectively less in the COVID-19 era compared with periods before COVID-19, which was statistically significantly (OR = 0.71; 95% CI: 0.65 –0.78; I^2 = 93%; $p < 0.001$; 22 studies, OR = 0.66; 95% CI: 0.58–0.73; I^2 = 95%; $p < 0.001$; 14 studies). The overall rate of in-hospital mortality in AMI patients increased by 26% in the COVID-19 era, which was not statistically significant (OR = 1.26; 95% CI: 1.0–1.59; I^2 = 22%; $p < 0.001$; six studies). The rate of in-hospital mortality in STEMI and NSTEMI patients increased by 15% and 26% respectively in the COVID-19 era, which was not statistically significant (OR = 1.15; 95% CI: 0.85–1.57; I^2 = 48%; $p = 0.035$; 11 studies, OR = 1.35; 95% CI: 0.64–2.86; I^2 = 45%; $p = 0.157$; 3 articles). These observations highlight the challenges in the adaptation of health-care systems with the impact of the COVID-19 pandemic.

1. Introduction

The "Coronavirus Disease 2019" (COVID-19) pandemic impressed an overwhelming pressure on the healthcare systems around the world, requiring reorganization and realignment of resources to cope with the demanding workload associated with COVID-19 surges [1,2]. During the COVID-19 era, a substantial excess mortality has been documented, not only attributable to SARS-COV-2 induced respiratory failure but also due

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to other non-COVID-19 diseases [3]. This raises concern about the public health consequences of the pandemic that are not directly related to COVID-19 infection or its delayed manifestations—the so-called collateral damage [3–5]. In this regard, the extreme public health adaptations, may have unfavorably disrupted the established diagnostic and therapeutic care pathways of non-communicable diseases.

COVID-19 is correlated to cardiovascular complication included ST elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI) [6]. Since the pandemic began, numerous studies have reported a concerning drop in the number of acute myocardial infarction (AMI) admissions [4,7,8], resulting in speculations about the underlying causes and implications of this observation. The decline in AMI admissions could either reflect a lower incidence of AMI at the time of the outbreak, or, more likely, a lower proportion of patients seeking medical care when they become symptomatic [9]. If the latter explanation is true, this can lead to catastrophic effects on patient prognosis, as early management of AMI is crucial and life-saving [10].

Because of the significant health implications of the change in AMI care during the ongoing COVID-19 pandemic, further clarification of this pattern is needed to properly inform measures aimed at improving AMI outcomes. The published studies are heterogeneous in methodology, and come from various regions and during different stages of the pandemic. In this context, pooling the available data can help understand the magnitude of the problem in different settings. In the present systematic review and *meta*-analysis, we aimed to evaluate the rate of AMI admissions, mortality, and major complication of patients admitted with AMI during the pandemic, in comparison with pre-pandemic periods.

2. Methods

2.1. Identification of studies

Three major scholarly databases (namely, PubMed/MEDLINE, Scopus, and Web of Science Core Collection) were searched from inception up to December 31, 2020, to identify studies examining the effect of COVID-19 on outcomes and variables in patients with myocardial infarction one year of the pandemic. A specific and appropriate search strategy was used for each database (Table 1). The search strategy includes a combination of keywords (COVID-19, and 'myocardial infarction') and medical subject headings (MeSH). The databases were searched without any language and publication status restrictions. All studies were entered into the Endnote software (version X7; Thomson Reuters).

Table 1
Search strategy and the results for each database.

# Records	Search Strategy	Database
177	(Hospitalization[MH] OR Hospitalization[TIAB] OR Hospitalizations[TIAB] OR mortality[MH] OR mortality[TIAB] OR Mortalities[TIAB] OR "Case Fatality Rate"[TIAB] OR "Case Fatality Rates"[TIAB] OR "Excess Mortalities"[TIAB] OR "Excess Mortality"[TIAB] OR "Age-Specific Death Rate"[TIAB] OR "Age-Specific Death Rates"[TIAB] OR "Death Rate"[TIAB] OR "Death Rates"[TIAB] OR "Differential Mortalities"[TIAB] OR "Differential Mortality"[TIAB] OR admission [TIAB]) AND ("myocardial infarction"[MH] OR "myocardial infarction"[TIAB] OR "Myocardial Infarctions"[TIAB] OR "Myocardial Infarct"[TIAB] OR "Myocardial Infarcts"[TIAB] OR "Heart Attack"[TIAB] OR "Heart Attacks"[TIAB] OR "Acute myocardial infarction"[TIAB]) AND (coronavirus[MH] OR Coronavirus[TIAB] OR "Covid-19"[TIAB] OR "SARS-CoV-2"[TIAB])	PubMed
235	TITLE-ABS-KEY(Hospitalization OR Hospitalizations OR mortality OR Mortalities OR "Case Fatality Rate" OR "Case Fatality Rates" OR "Excess Mortalities" OR "Excess Mortality" OR "Age-Specific Death Rate" OR "Age-Specific Death Rates" OR "Death Rate" OR "Death Rates" OR "Differential Mortalities" OR "Differential Mortality" OR admission) AND TITLE-ABS-KEY ("myocardial infarction" OR "Myocardial Infarctions" OR "Myocardial Infarct" OR "Myocardial Infarcts" OR "Heart Attack" OR "Heart Attacks" OR "Acute myocardial infarction") AND TITLE-ABS-KEY (Coronavirus OR "Covid-19" OR "SARS-CoV-2")	Scopus
121	TS=(Hospitalization OR Hospitalizations OR mortality OR Mortalities OR "Case Fatality Rate" OR "Case Fatality Rates" OR "Excess Mortalities" OR "Excess Mortality" OR "Age-Specific Death Rate" OR "Age-Specific Death Rates" OR "Death Rate" OR "Death Rates" OR "Differential Mortalities" OR "Differential Mortality" OR admission) AND TS=("myocardial infarction" OR "Myocardial Infarctions" OR "Myocardial Infarct" OR "Myocardial Infarcts" OR "Heart Attack" OR "Heart Attacks" OR "Acute myocardial infarction") AND TS=(Coronavirus OR "Covid-19" OR "SARS-CoV-2")	Web of Science core collection
533		Total
219		Duplicate
314		Total after remove duplicate

2.2. Selection of studies

After removing duplicates, titles and abstracts were screened and irrelevant articles were removed. The full text of the remaining articles was reviewed based on inclusion and exclusion criteria and reasons for their exclusion was recorded. Screening and selection steps were performed independently by two researchers. Disagreements were discussed to reach a final decision.

2.3. Eligibility criteria

We included original studies that assessed the effect of COVID-19 on at least one or more of the following outcomes such as AMI admissions (STEMI or NSTEMI), AMI mortality rate (including in-hospital mortality), and major complications in patients with myocardial infarction and compared with equivalent period in pre pandemic. Major complications were defined as cardiogenic shock, life-threatening arrhythmias, cardiac free wall/ventricular septal rupture, major bleeding, renal failure/dialysis, mechanical ventilation, thrombosis, stroke, heart failure, or severe functional mitral regurgitation.

Only full-text studies in English language were included. We excluded review articles, conference abstracts, posters, case reports; studies without reported quantitative values for AMI admissions, mortality and major complications; and duplicate studies whose results have been published in several articles, in which case the highest quality study was included after quality assessment.

2.4. Quality assessment of the studies

The Newcastle-Ottawa Scale was used to assess study quality [11]. The quality assessment was performed independently by two authors and the disagreements were resolved by discussion (Table 2).

2.5. Data extraction and analysis

Data extraction was performed independently by two investigators and was checked by a third investigator. A standardized data collection sheath was used to extract the data from the included studies. This form included information on characteristics and the demographic and pre-hospital data together with patient's outcome.

Table 2
Quality assessment tool the Newcastle-Ottawa Scale (NOS).

Study	Criteria						
	Representativeness of the sample	Sample size	Non-respondents	Ascertainment of the exposure	Comparability of subjects in different outcome groups	Assessment of outcome	Statistical test
Daoulah	Y	Y	Y	Y	Y	Y	Y
Dreger	Y	Y	Y	Y	Y	NA	Y
Fileti	Y	Y	Y	Y	Y	Y	Y
Wu	Y	Y	Y	Y	Y	Y	Y
Mafham	Y	Y	Y	Y	Y	Y	Y
Oikonomou	Y	Y	Y	Y	Y	Y	Y
Rashid	Y	Y	Y	Y	Y	Y	Y
Reinstadler	Y	Y	Y	Y	Y	Y	Y
Rodriguez-Leor	Y	Y	Y	Y	Y	Y	Y
Tan	Y	Y	Y	Y	Y	Y	Y
Tomasoni	Y	Y	Y	Y	Y	Y	Y
De Rosa	Y	Y	Y	Y	Y	Y	Y
Braiteh	Y	Y	Y	Y	Y	Y	Y
Lauridsen	Y	Y	Y	Y	Y	Y	Y
Gluckman	Y	Y	Y	Y	Y	Y	Y
Papafaklis	Y	Y	Y	Y	Y	Y	Y
Vacanti	Y	Y	NA	Y	Y	NA	Y
Schwarz	Y	Y	Y	Y	Y	Y	Y
Scholz	Y	Y	Y	Y	Y	Y	Y
Seiffert	Y	Y	Y	Y	Y	Y	Y
Hauguel-Moreau	Y	Y	Y	Y	Y	Y	Y
Solomon	Y	Y	Y	Y	Y	Y	Y
Kundi	Y	Y	NA	Y	NA	NA	Y
Bugger	Y	Y	Y	Y	Y	Y	Y
Alessandra Di Liberto	Y	Y	Y	Y	Y	NA	Y
Folino Franco	Y	Y	Y	Y	Y	NA	Y
Daniel Kiblboeck	Y	Y	Y	Y	Y	Y	Y
Abdelaziz	Y	Y	NA	NA	NA	NA	Y
Gioel Gabrio Secco	Y	Y	Y	Y	Y	Y	Y
Hautz	Y	Y	Y	Y	Y	Y	Y
Zaleski	Y	Y	Y	Y	Y	NA	Y
Wilson	Y	Y	Y	Y	Y	Y	Y
Claeys	Y	Y	Y	Y	Y	Y	Y
Gramegna	Y	Y	Y	Y	Y	Y	Y
Kwok	Y	Y	Y	Y	Y	Y	Y
Choudhary	Y	Y	Y	Y	Y	Y	Y
Félix-Oliveira	Y	Y	Y	Y	NA	NA	Y
Cammalleri	Y	Y	Y	Y	Y	Y	Y
Rangé	Y	Y	Y	Y	Y	Y	Y
Khot	Y	Y	Y	Y	Y	Y	Y
Lantelme	Y	Y	Y	Y	Y	Y	Y

Meta-analysis was used to synthesize the findings. The random-effect method was used to cumulate the estimates form all included studies for each outcome, and the cumulated effect sizes were obtained with a 95% confidence interval (CI). We used the Mantel-Haenszel method and reported the value including its 95 %CI as effect size measure. I^2 was used to investigate heterogeneity among studies, and the p-value of a χ^2 test with a significance level <0.05 suggests heterogeneity. Egger's test was used to assess the risk of publication bias. Meta-analyses were performed using the Meta package in the statistical software R V.3.5.1. This study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [12].

3. Results

After the removal of duplicate records, we screened 314 articles title and abstract, 85 full texts were reviewed, quality assessment of included articles was performed using the Newcastle-Ottawa Scale (NOS), which grades each article on the cohort selection, as well as the adequacy of outcomes measured, the analysis was then carried out on 41 articles (Fig. 1). The included studies came from Italy [13–20], United States [21–26], United Kingdom [7,27–31], Germany [32–36], Austria [37–39], France [8,40,41], Greece [42,43], Spain [44], Denmark [45], Switzerland [46], Belgium [47], Portugal [48], Turkey [49], India [50], and Saudi Arabia [51].

The demographic, pre-hospital information, type of treatment, and quality assessment with Newcastle-Ottawa Scale adapted for cross-sectional studies are presented in Supplementary Table S2. Studies show that there was no significant difference in patients' risk factors such as diabetes, hypertension, family history of CVD, hypercholesterolemia and smoking in the COVID-19 and the previous period. The main characteristics of the studies are shown in Supplementary Table S3. All of the studies have examined at least one of the studied outcomes (admissions, mortality, or major complications).

3.1. *Reduction of hospitalizations for AMI in the COVID-19 era*

3.1.1. *Hospitalizations for AMI*

As depicted in Fig. 2, the number of admissions for AMI was reported in 28 studies. The results of our *meta*-analysis indicated that the number of patients hospitalized for AMI were 35% less in the COVID-19 era compared with pre-pandemic periods (OR = 0.65; 95% CI: 0.56 to 0.74; I^2 = 99%; $p < 0.001$). It was shown that admissions for AMI was significantly different between the pre-COVID-19 and the COVID-19 era.

3.1.2. *Hospitalizations for STEMI*

Fig. 3 shows that 22 articles from the included studies reported the number of STEMI admissions. The results of our *meta*-analysis indicate that the patients hospitalized for STEMI were 29% fewer in the COVID-

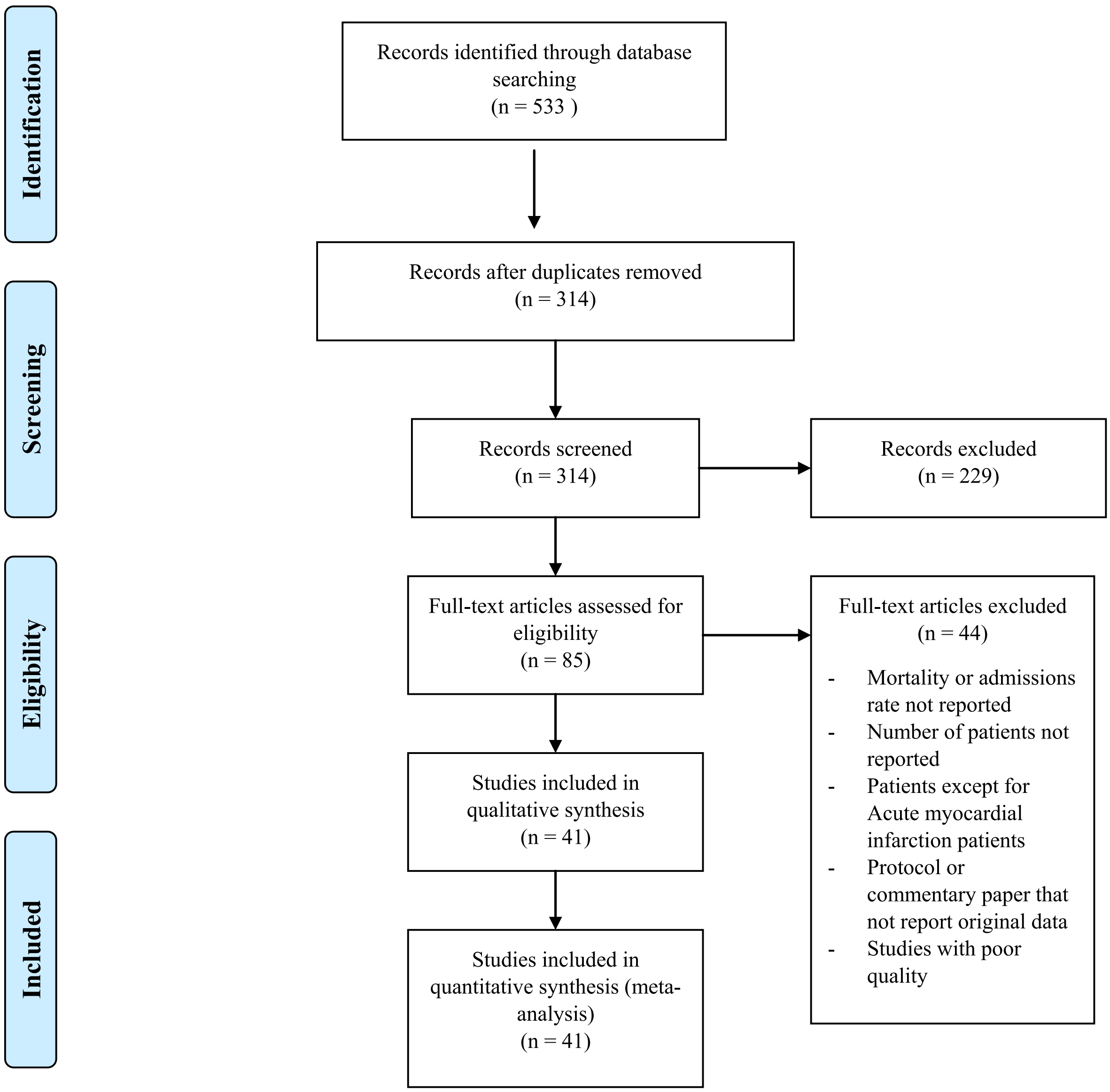

Fig. 1. The figure illustrates the PRISMA diagram for the identification and selection of studies.

19 era compared with the periods before, which was statistically significantly (OR = 0.71; 95% CI: 0.65–0.78; I^2 = 93%; $p < 0.001$).

3.1.3. Hospitalizations for NSTEMI

Fig. 4 shows that 14 articles from the included studies reported the number of NSTEMI patients admitted. The results of our *meta*-analysis indicated that the patients hospitalized for NSTEMI were 34% significantly decreased in the COVID-19 era compared with before the COVID-19 pandemic (OR = 0.66; 95% CI: 0.58–0.73; I^2 = 95%; $p < 0.001$).

3.2. Mortality

3.2.1. Mortality for AMI

As demonstrated in Fig. 5, six articles from the included studies reported the rate of AMI patients in-hospital mortality. The results of our *meta*-analysis show that the rate of in-hospital mortality in AMI patients increased by 26% in the COVID-19 era which was not statistically significant (OR = 1.26; 95% CI: 1.0–1.59; I^2 = 22%; $p = 0.262$).

3.2.2. Mortality for STEMI

Fig. 6 shows that 11 articles from the included studies reported the rate of in-hospital mortality in STEMI patients. The results of our *meta*-analysis show that the rate of in-hospital mortality in STEMI patients increased by 15% in the COVID-19 era was not statistically significant (OR = 1.15; 95% CI: 0.85–1.57; I^2 = 48%; $p = 0.035$).

3.2.3. Mortality for NSTEMI

Fig. 7 shows that three articles reported the rate of in-hospital mortality in NSTEMI patients. The results of our *meta*-analysis show that the rate of in-hospital mortality in NSTEMI patients increased by 35% in the COVID-19 era which was not statistically significant (OR = 1.35; 95% CI: 0.64–2.86; I^2 = 45%; $p = 0.157$).

3.3. Major complications in AMI

Fig. 8 shows that 11 articles reported the rate of major complications in AMI patients. Comparing the results of the two time periods for major complications in AMI patients shows that the rate of major complications for AMI patients during the COVID-19 era increased by 39% which was not statistically significant (OR = 1.39; 95% CI: 0.95–2.04; I^2 = 94%; $p < 0.001$).

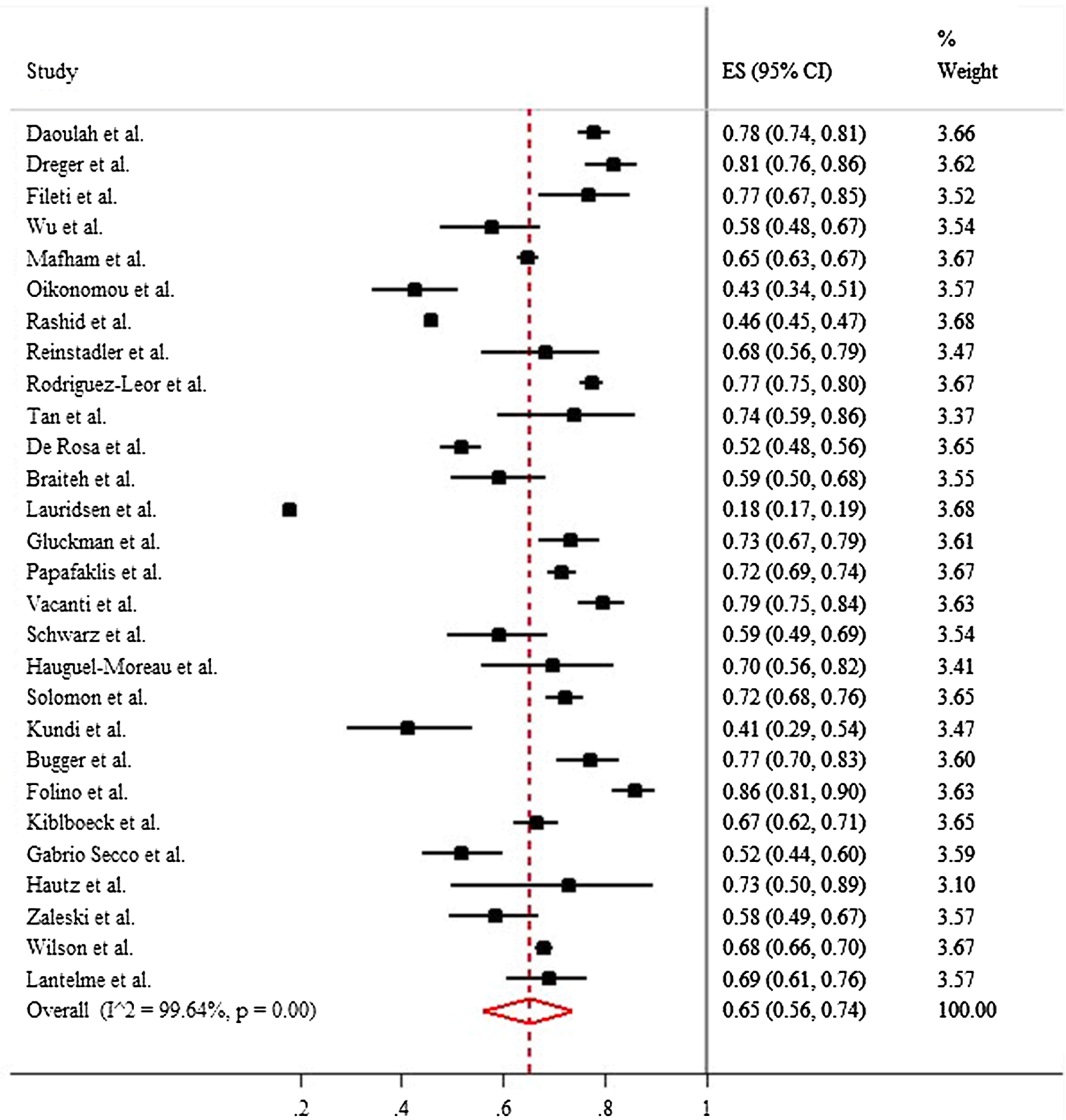

Fig. 2. The image presents the admission Rate Forest Plot in AMI patients.

4. Discussion

In this systematic review and *meta*-analysis, the final key points were significant reductions in the number of AMI admissions—either ST-segment elevation (STEMI) or non-STEMI (NSTEMI)—during the COVID-19 pandemic compared to pre-pandemic periods. Importantly, the in-hospital mortality rate was increased, without statistically significance, among patients admitted with AMI during the COVID-19 pandemic; however, accumulation of data from studies focusing on STEMI and NSTEMI did not show a statistically significance increase in mortality rates, also the rate of major complications of AMI was not significantly different during the pandemic, but demonstrated an increasing trend.

4.1. Understanding the decline in AMI admissions

Early in the pandemic, when the first studies reporting a decline in AMI cases came out, speculation started about the potential mechanisms of this concerning observation [8,19,24]. Despite several subsequent investigations, the full scale of the reasons behind such decline is not yet clear. One possibility is a variation in the incidence of AMI in the early days of the pandemic. Studies have hypothesized that a reduction in air pollution, physical activity level, and a lower amount of acute work-related stress during lock-downs [47,52] may have contributed to a lower incidence of AMI. On the other hand, there are other putative mechanisms that could have led to an increase in the number of incident AMI cases. Apart from the emotional stress associated with the pandemic[53], COVID-19 infection itself can result in ischemia and plaque rupture through inflammation, coagulation disturbances, and alterations in myocardial supply and demand [54,55].

Notably, previous studies have demonstrated that natural disasters, and societal or economic crises are associated with increased rates of cardiovascular disease related hospitalizations [56,57]. As an example, after the 9/11 terrorist attacks, the occurrence of life-threatening arrhythmic events increased by more than two-fold in the following month, and the diagnosis of cardiovascular disease increased by 53% during the next three years [58,59]. Nonetheless, the COVID-19 pandemic seems different in this regard. The early pandemic response involved national lock-downs, and recommendations for social distancing and staying at home. These measures could have led to a

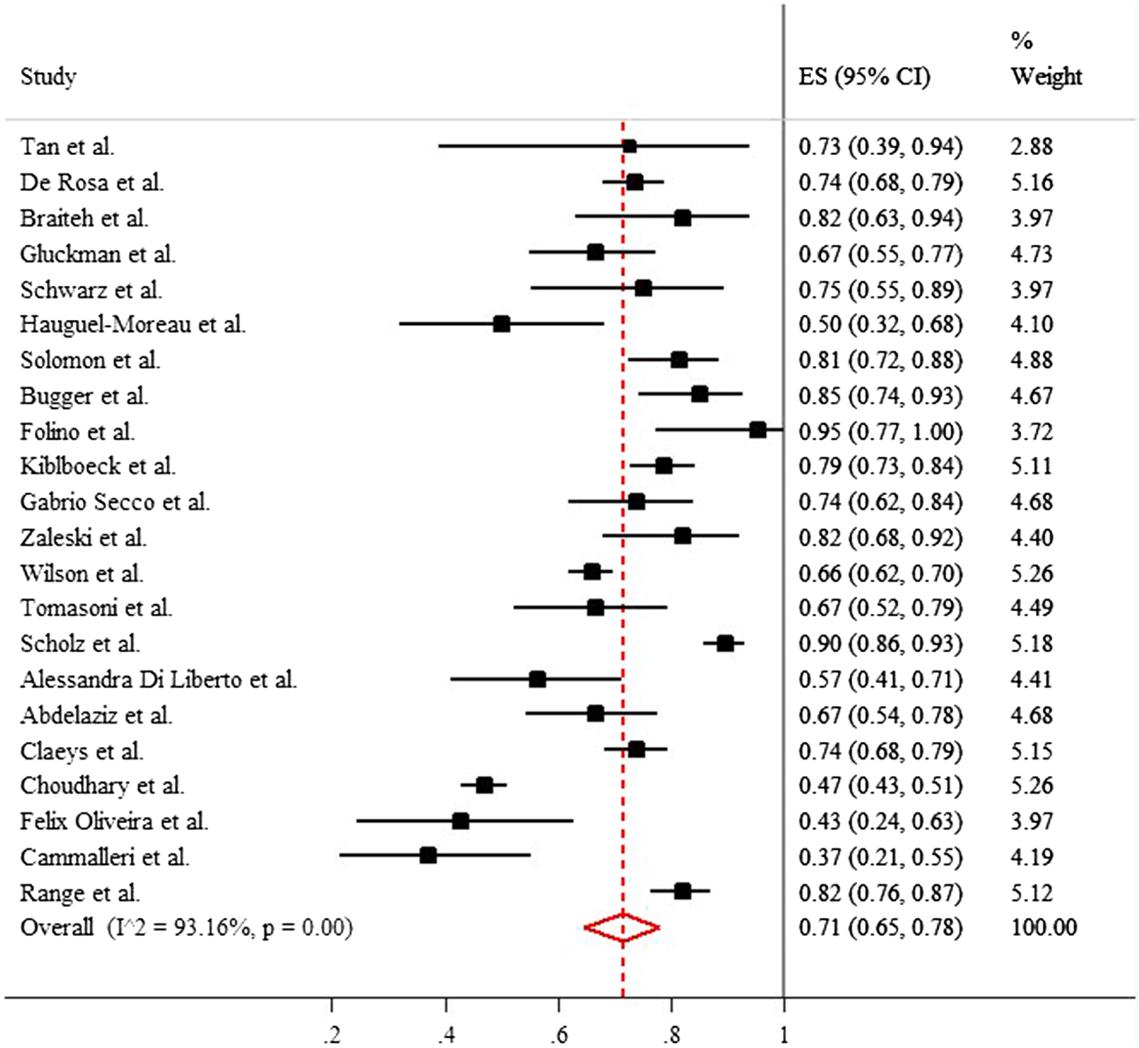

Fig. 3. The image presents the admission Rate Forest Plot in STEMI patients.

reluctance for hospitalization among patients—even those who suffered an acute illness. The observed decline in admissions is not limited to AMI patients, as stroke presentations have similarly decreased during the pandemic [60,61]. Hammad et al. showed that after the COVID-19 outbreak, patients with STEMI tried to avoid hospitals due to fear of contracting COVID-19, believing symptoms were related to COVID-19, or not wanting to overburden the already strained health-care systems [9]. Such misled adverse health-seeking behavior prompted national campaigns that aimed to raise awareness of cardiovascular diseases during the pandemic, and encourage patients to seek emergency care if they experience symptoms [7,62,63].

4.2. Should we expect a rebound?

In contrast to the overall results of this *meta*-analysis, a few studies report an increase in the number of patients admitted with AMI. Gramegna et al. report an early decrease in STEMI admissions in Italy after identification of the first COVID-19 case and the subsequent lock-down, followed by a rebound increase in cases that was larger than the rate of STEMI admissions during similar periods in 2018 and 2019 [19]. Studies by Gluckman et al. from the United States and Wu et al. from the United Kingdom reported a significant decrease in AMI cases early in the pandemic; however, in the later stages, hospitalizations for AMI started to slowly rise [23,27]. Notably, studies included in this *meta*-analysis report AMI hospitalization data for periods between the start of the outbreak until July 2020 at the latest [33,42]. As a result, data regarding variations in AMI admission rates for later stages of the COVID-19 pandemic are currently not available. Considering that COVID-19 is mainly a regional challenge with episodic surges, these numbers may turn out differently as the pandemic continues. In fact, one study has reported an inverse correlation between the number of newly diagnosed COVID-19 cases and the trend in AMI admissions, raising concern of potential post-COVID-19 rebound phenomenon for hospitalizations [64]. At least hypothetically, the lock-down period may have only delayed the occurrence of AMIs, which means these delayed events are bound to present at a later time—a catch-up in AMI incidence rates [52]. It is notable that in the case of the 9/11 terrorist attacks, an increase in cardiovascular disease occurrence was observed for up to three years after the crisis [59].

4.3. Features of AMI admissions during the pandemic

If patients are avoiding admissions by delaying their presentation to the hospital, it can be expected for more severely affected patients to be admitted, while milder cases may opt to stay at home. According to our results, the decline in the number of NSTEMI admissions was more pronounced compared to STEMI. This observation can be expected as STEMI usually manifests with more severe and non-remitting symptoms provoking emergency department visits, whereas NSTEMI patients may neglect their symptoms and delay medical attention [7,52]. Notably, we

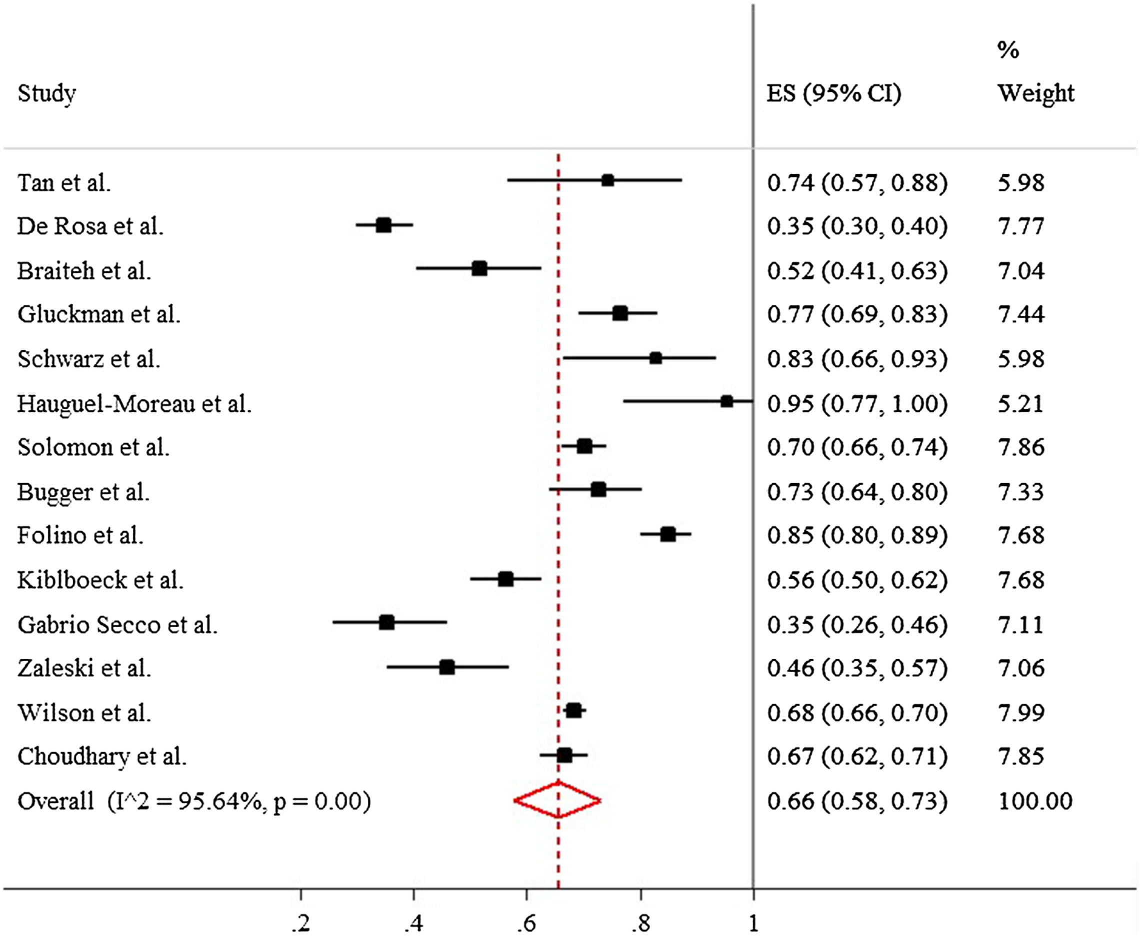

Fig. 4. The image presents the admission Rate Forest Plot in NSTEMI patients.

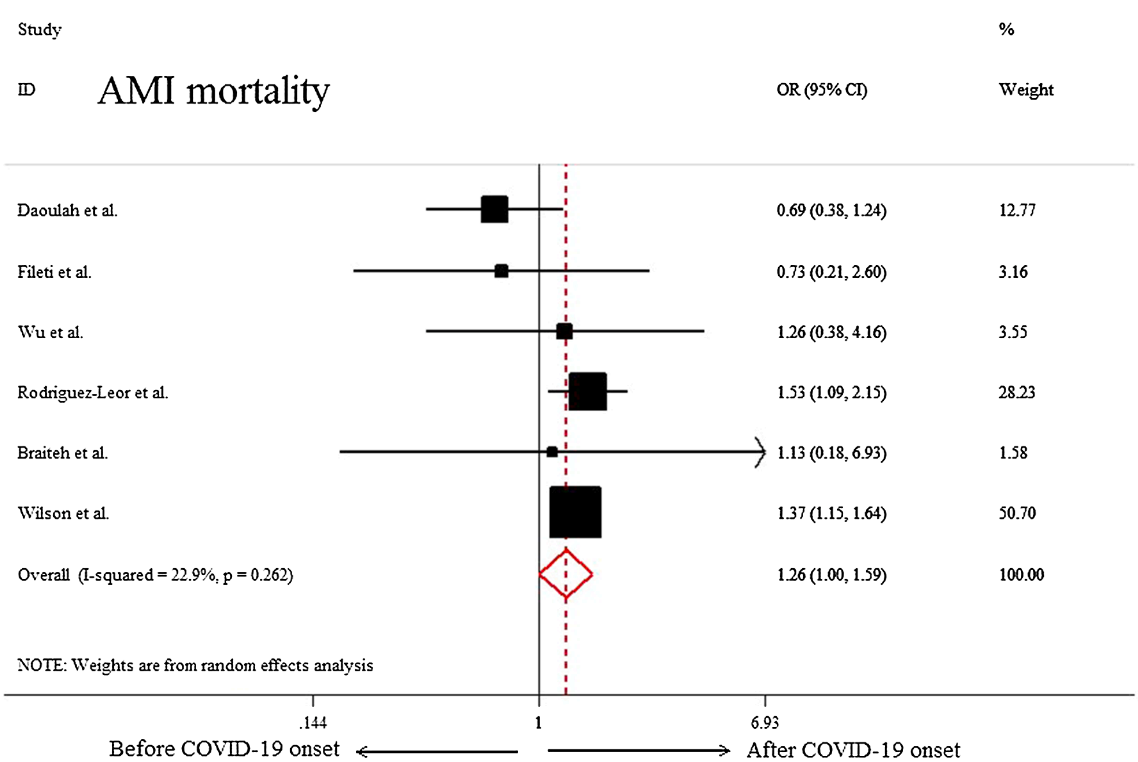

Fig. 5. The image presents the in-hospital mortality Rate Forest Plot in AMI patients.

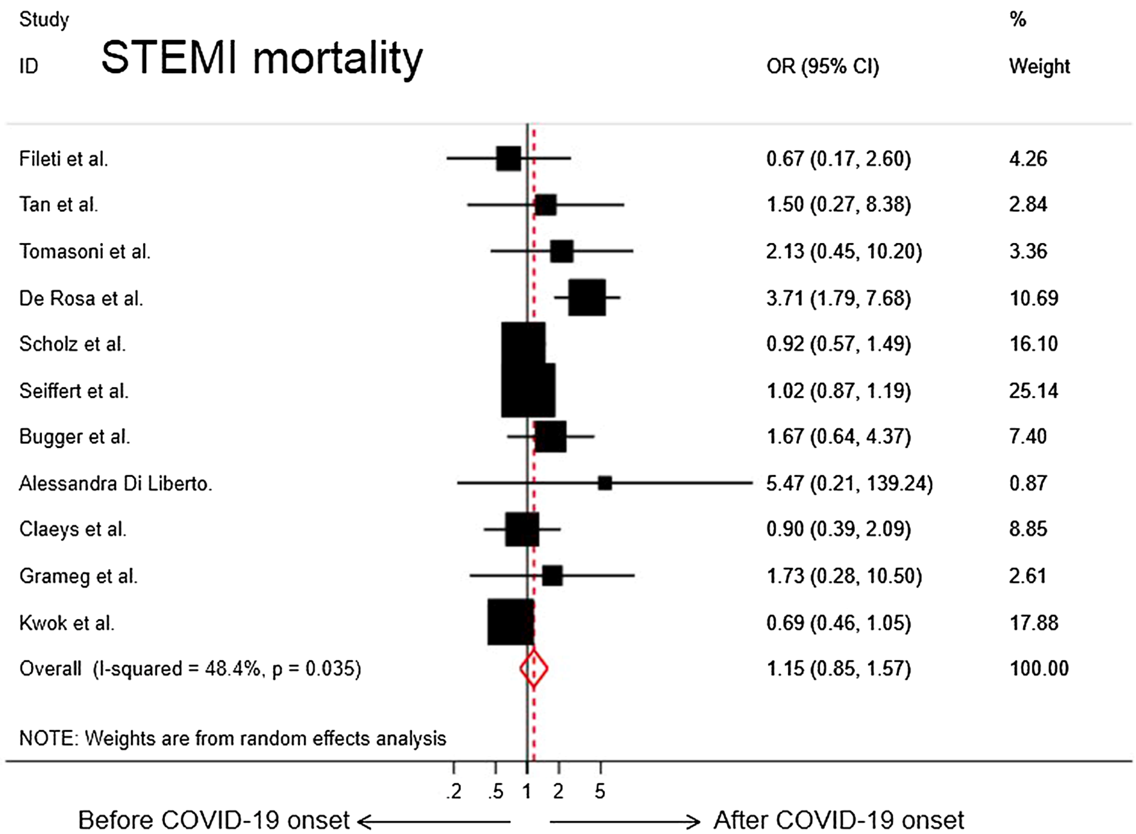

Fig. 6. The image presents the in-hospital mortality Rate Forest Plot in STEMI patients.

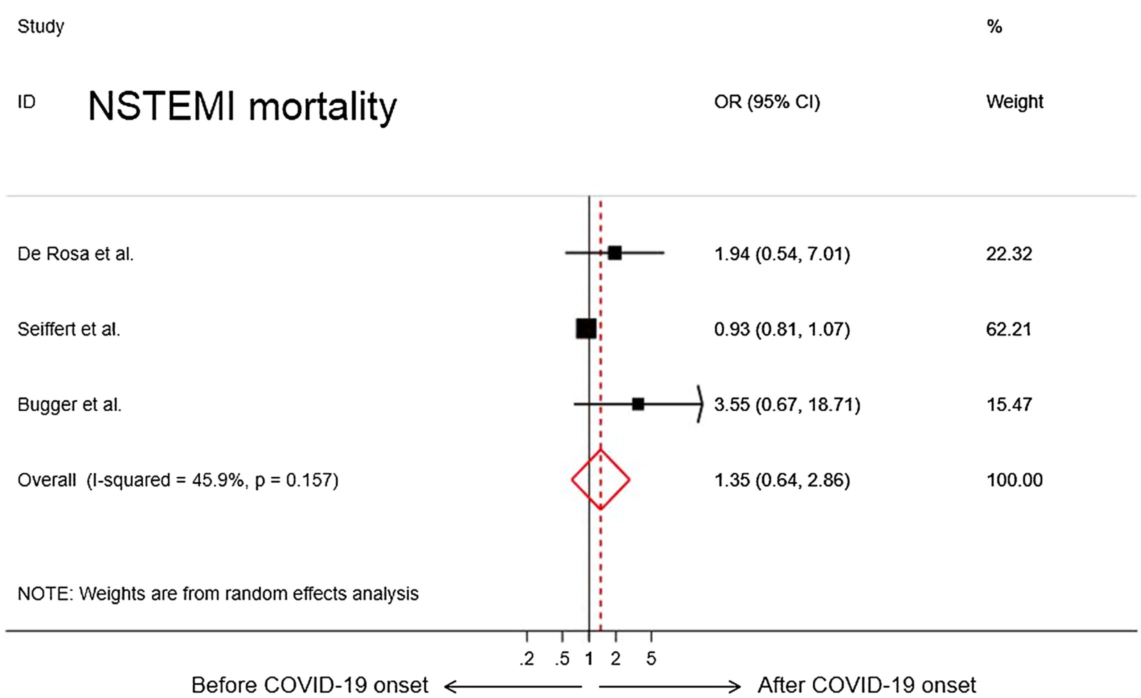

Fig. 7. The image presents the in-hospital mortality Rate Forest Plot in NSTEMI patients.

found no significant differences regarding age, sex, and the presence of conventional cardiovascular risk factors between AMI patients who were admitted before or after the COVID-19 outbreak.

In the study by Scholz et al. from Germany, there was an overall decline in STEMI hospitalizations; however, STEMI admission rates differed based on patients transport routes. After the onset of the COVID-19 pandemic, the number of STEMI cases who were brought in by emergency medical services (EMS) increased. On the other hand, STEMI cases admitted via self-referral or inter-facility transport, and the occurrence of intra-hospital AMI decreased [35]. This observation

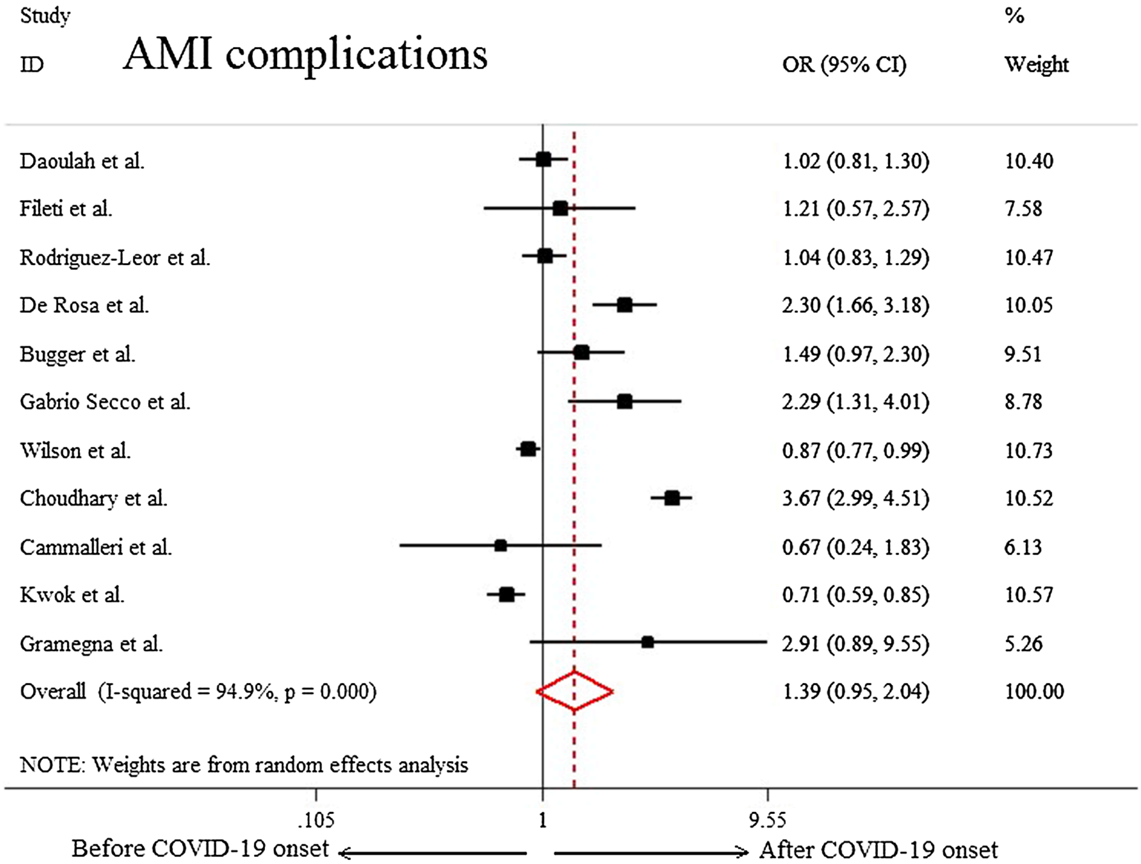

Fig. 8. The image presents the Rate of Major complication in AMI patients.

supports the hypothesis that milder cases did not activate EMS and preferred to stay at home; however, this may not hold true in all countries.

Furthermore, the studies included in this *meta*-analysis were conducted in 15 different countries from North America, Europe, and Asia. While this diversity is important in understanding the global impact of COVID-19, it should be noticed that low- to middle-income countries are under-represented among the published studies.

4.4. Mortality and major complications

Our results indicate non-significant increases in the rates of in-hospital mortality in total AMI and NSTEMI patients, and no significant increased rate of in-hospital mortality in STEMI patients. Also, there is not a statistical difference in major complications associated with AMI during the COVID-19 pandemic. Our findings confirm an earlier *meta*-analysis by Rattka et al., which found no differences in STEMI mortality rates before and after COVID-19. The mentioned study included records that were published prior to August 2020 [4], whereas our study benefits from a more recent review. On the other hand, a later *meta*-analysis by Chew et al. found a significant increase in STEMI mortality rates [65]. Despite the above-mentioned *meta*-analyses, we have focused on both STEMI and NSTEMI. This discrepancy in results is in part due to the ever-changing global status of the pandemic and differences in methodologies.

Unfavorable in-hospital outcomes may be the result of delays in presentation, and admission with more severe disease. Delays in presentation can be patient-driven, for instance by prolongation of the time interval between symptom onset and first medical contact during the pandemic [65]. At the same time, intra-hospital delays and alterations in AMI management have played an important role contributing to the reduced AMI survival during the COVID-19 era. Studies have found a considerable post-COVID-19 increase in door-to-balloon times for STEMI cases [4,65]. Moreover, after the COVID-19 outbreak, the overall number of catheterization laboratory activations for STEMI were reduced [66], and patients with AMI, with or without concurrent COVID-19 infection, were less likely to receive coronary angiography and revascularization [65,67]. Adapting to the new situation has been challenging and the in-hospital management of AMI was affected, perhaps due to overwhelming COVID-19 admissions, stringent infectious control measures, strategies to minimize the risk posed to hospital staff, limited availability of personal protective equipment, and uncertainty about the overlap of patients' symptoms with COVID-19 infection [8,54,65]. Services that support AMI care, such as respiratory therapy, could also have been overwhelmed during COVID-19 surges. In addition, complications of AMI such as presentation with out of hospital cardiac arrest or cardiogenic shock were observed in a greater proportion of patients during the pandemic [65,68], contributing to higher morbidity and mortality of post-COVID-19 outbreak AMI patients. It should also be noted that the true mortality impact of the COVID-19 pandemic is crucial for public health and decision-makers. A study published in the Lancet shows that 18·2 million people died globally because of the COVID-19 pandemic (as measured by excess mortality) between the beginning of the pandemic (Jan 1, 2020) and the end of Dec 2021, which is 3-times higher than the reported number of COVID-19-related deaths. Also, a study analyzing US mortality in March-July 2020 reported a 20% increase in excess mortality, only partly explained by COVID-19. Estimates of COVID-19 excess mortality suggest the mortality impact of the COVID-19 pandemic has been more devastating than the situation documented by official statistics. The full impact of the pandemic has been much greater than what is indicated by reported deaths due to COVID-19 alone[3,69].

4.5. Strengths and limitations

This *meta*-analysis included a large number of studies from several countries around the world, presenting a more accurate picture of the post-pandemic AMI care. Moreover, we did not limit our search to STEMI patients, and instead focused on all AMI admissions to achieve more inclusive results. In this sense, this *meta*-analysis provides important information about the impact of COVID-19 on AMI care, and helps in determining strategies to counteract unfavorable effects of future outbreaks. Nevertheless, this study is subject to several limitations. As mentioned earlier, the available data largely corresponds to the early pandemic and first lock-down periods, and we found no published data about the state of AMI admissions in later stages of the pandemic. Future studies should address this issue. Second, data from many regions and countries, such as low- to middle-income countries, was scarce. Third, while the differences in admissions between pre- and post-COVID-19 periods are statistically significant, the included studies used varying methodologies to report outcomes; hence, caution is advised in interpretation of the findings.

5. Conclusion

The number of AMI admissions significantly decreased during the COVID-19 pandemic. Compared to pre-pandemic periods, the rates of in-hospital mortality and major complications did not differ significantly between the post-COVID- 19 and the pre-COVID-19 group. These observations highlight the challenges in the adaptation of health-care systems with the impact of the COVID-19 pandemic. Improved strategies should be in place to prevent collateral damage in AMI patients during the ongoing pandemic, as well as in future outbreaks. Additional large-scale studies at multiple centers are also needed to accurately determine the relationship of clinical outcomes of patients with AMI and its each subgroup during COVID-19 era.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Authors' Contribution

SA, HP and MT had the idea for and designed the study and had full access to all the data. SA, HT, SS and ZA collected the data. MB and SR performed the statistical analysis. SA, HT and HP mainly wrote the manuscript. NO, NLB and SA had Critical revision of the manuscript. SA, MT, and SMG had overall coordination. All authors provided critical feedback and contributed to the final manuscript.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2022.101058.

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