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Clinical and Cardiovascular Characteristics of Patients Suffering ST-Segment Elevation Myocardial Infarction After Covid-19: A Systematic Review and Meta-Analysis

Abdullah Gharibzadeh, MD[a], Farzad Shahsanaei, MD[b], and Nima Rahimi Petrudi, MD[c,*]

From the [a] Assistant Professor of Cardiology, Cardiovascular Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran, [b] Interventional Cardiologist, Hypertension Research center, Cardiovascular Research Institute, Isfahan University Of Medical Sciences, Isfahan, Iran and [c] Resident Of Cardiology, Cardiovascular Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.

Abstract: ST-segment elevation myocardial infarction (STEMI) is one of the fatal complications following Covid-19. We aimed to systematically assess the clinical sequels as well as cardiovascular findings in patients suffering STEMI following Covid-19.The manuscripts databases including PubMed, Web of knowledge (ISI), SCOPUS, Embase, and Google Scholar were deeply searched by the two reviewers using the relevant keywords related to the issue considered in the current review. Of 88 studies initially reviewed, 9 articles were included in final assessment. Nine articles including 447 patients with Covid-19 were included in the study. In terms of electrocardiographic findings, anterior lead involvement was reported in 12% - 61.6% of cases, inferior lead in 28.2% - 75% and lateral involvement in 7.7% - 100% of cases. The prevalence of LBBB was in the range of

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10.7% - 61.6% of cases. In terms of echocardiographic findings, a decrease in left ventricular ejection fraction was reported in 60% - 88% of patients. Wall motion abnormality was also observed in 60% - 82.1% of patients. In terms of angiographic findings, the multivessel disease was reported in 17.9% - 69% of cases. Also, 24% - 83% of cases needed to revascularization procedures. Cardiac arrest was also reported in 3.1% - 28.2% of cases. Based on the meta-analysis performed on the mortality of patients with STEMI in the field of Covid-19, the pooled prevalence of mortality was estimated at 25.2% (95%CI:17.5%-34.8%). Mortality and adverse consequences of STEMI in patients with Covid-19 are far higher than in the general population. Therefore, in-hospital cardiovascular tracking and monitoring of Covid-19 patients with potential cardiovascular disorders is necessary to achieve a more favorable outcome. (Curr Probl Cardiol 2021;00:101045.)

Introduction

Evidence for the short- and long-term effects of the current Covid-19 pandemic indicates that the path of preventive and curative management of the disease requires fundamental changes and improvements to maximize patient survival and reduce disability to the maximum possible level. According to the latest figures from the World Health Organization, more than 205 million cases of Covid-19 have been reported, leading to more than 4 million deaths.[1] In our country, Iran, according to the same report, the latest morbidity and mortality rates are estimated at 4.5 million cases and more than 100,000 cases, respectively.[1] Significant in mortality as well as post-infection disabilities are the potential complications of virus invasion to the extent that there is a possibility of involvement of various vital organs due to direct invasion of the virus or indirect consequences of the resulting virus.[2,3] In this regard, the occurrence of complications such as vascular thrombosis on the one hand and direct tissue invasion of the virus due to competition and high tendency to bind to tissue receptors (such as ACE II receptor) are the main factors in organic complications of the virus.[4,5] In this regard, the likelihood of coronary artery atherosclerosis, endothelial dysfunction, thrombotic microangiopathy and activation of coagulopathic cascades, and

ultimately increase the patient's susceptibility to ischemic heart attack and even ST-segment elevation myocardial infarction (STEMI) is expectable following severe Covid-19 disease. Several cases of STEMI have been observed following Covid-19, which in many cases, invasive therapeutic intervention such as PCI or CABG required.[6-8] However, due to the fear of hospitalization in a high epidemic situation and also the allocation of the majority of hospital wards to Covid-19 patients, in many cases the above treatment interventions are associated with significant delays and therefore morbidity and mortality due to delays in treatment should also be added to the above statistics.[9-11] Overall, summarizing the statistics presented on the clinical consequences and cardiovascular outcomes of the Covid-19 pandemic provides a clearer picture of the complications of the disease. What we will discuss in the present study will be a systematic review of the clinical features as well as cardiovascular features of patients with STEMI following Covid-19.

Materials and Methods

The main issues focused in our systematic review and meta-analysis was to describe the clinical as well as electrocardiographic, echocardiographic, and angiographic features of STEMI in patients suffering Covid-19. The current systematic review followed the principles of the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" guideline.[12] First, all manuscripts related to the pointed issue were deeply searched by the two reviewers using the related keywords including "ST-segment elevation myocardial infarction", "Covid-19", "electrocardiography", "echocardiography" and "angiography" in the international manuscript databases such as PubMed, Web of knowledge (ISI), SCOPUS, Embase, and Google Scholar. Any disagreement across our reviewers was rechecked by the third reviewer as the final arbitrator. The details of eligibility and the reasons for excluding the papers were shown schematically (Fig 1). In the inclusion criteria for selecting the articles were (1) English language papers, (2) The articles with complete structure and contents, and (3) Access to the full text of the article. Thus, the manuscripts with only abstract availability or with incomplete information were not included in to our review. The retrieved articles were placed in Endnote software and then duplicate and shared articles were removed in the foreword databases. Finally, the obtained information was categorized and analyzed by descriptive statistics and content analysis. The study quality was evaluated based on the following criteria: (1) the systematic review and meta-analysis based on the questions primarily

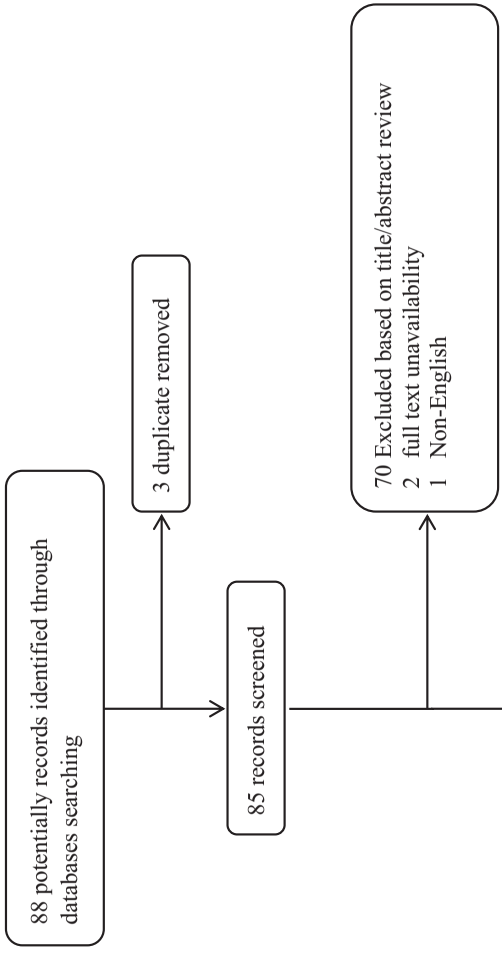

FIG 1. The flowchart of screening the eligible studies.

described and formulated; (2) predefined criteria for including and excluding the assessed studies as eligibility criteria; (3) searching the literature performed on a systematic and comprehensive approach; (4) to minimize the bias, the full texts of the article were dually reviewed; (5) the quality of included studies were rated independently by the reviewers for appraising internal validity; (6) studies' characteristics and findings were comprehensively listed; (7) the publication and risk of bias were listed; and (8) heterogeneity was also assessed. The risk of bias for each study was assessed using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions and also according to QUADAS-2 tool. Of the 27 articles available, a total of 12 full-text articles were retrieved and placed at Endnote. After considering the inclusion and exclusion criteria and eliminating duplicate and common articles in the foreword databases, 9 articles were obtained and finally assessed. At this stage, all obtained articles were studied separately and the type of article and the main axis of the article were reviewed and extracted. For statistical analysis, the Comprehensive Meta-Analysis Software (CMA, version 3.0) was employed. We presented dichotomous data related to pooled prevalence of STEMI-related death following Covid-19 as prevalence rate and its 95% Confidence Interval (CI). Data were assessed by both fixed effects and random effect models, however the random effect analyses were reported if the heterogeneity was significant evaluated by the I2 statistic.

Results

In the present study, 88 studies were initially evaluated. With the removal of 3 duplicated articles, 85 articles were reviewed in the next stage, of which 70 were excluded from the study based on the titles of the articles and a review of their abstracts, 2 articles due to lack of access to the full text of the article and 1 article due to the non-English language, and a total of 12 studies were included in the content evaluation in the next stage. At this stage, 3 articles were excluded from the study due to insufficient information and variables required to perform the project, and finally 9 articles were included in the final review and analysis (Fig 1).[13-21] According to the criteria of QUADAS-2 scoring system in which articles are examined based on features such as patient selection, study index test, evaluation of outcome and validity of results and findings, and writing of article texts, none of the articles was classified at a low level and therefore all 9 articles were included in the systematic review (Fig 2).

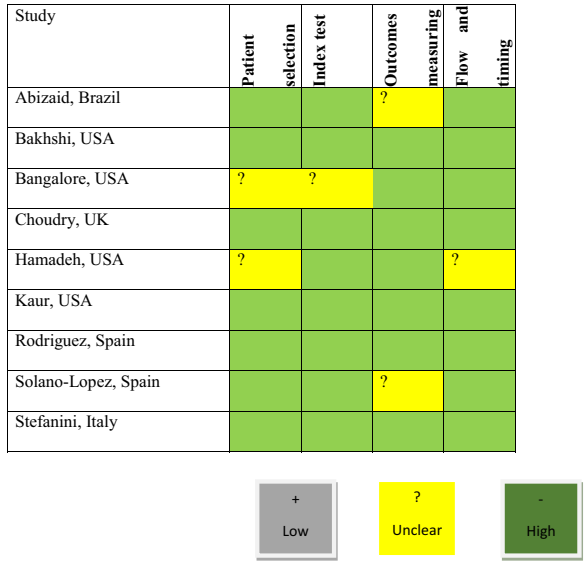

FIG 2. Methodological quality of the included studies. (Color version of figure is available online.)

As summarized in Table 1, in total, 9 articles including 447 patients with Covid-19 were included in the study. Of these, 336 were male and 111 were female. The age of patients ranged from 56 to 68 years. With the exception of one study that reported the results of its one-month follow-up, the results of other studies focused on in-hospital findings. Also, 3 of the 9 studies were conducted in a multi-center manner. In terms of cardiovascular characteristics and findings in the studied patients, the following results were obtained (Table 2): (1) In terms of electrocardiographic findings, anterior lead involvement was reported in 12% – 61.6% of cases, inferior lead in 28.2 to 75% and lateral involvement in 7.7% - 100% of cases. The prevalence of LBBB was in the range of 10.7% - 61.6% of cases. Another finding on the ECG included left axis deviation, which was visible in 50% of patients. (2) In terms of echocardiographic findings, firstly, a decrease in left ventricular ejection fraction or LVEF (to less than 35%) was reported in 60% - 88% of patients. Wall motion abnormality was also observed in 60% - 82.1% of patients. (3) In terms of angiographic findings, first, the occurrence of multi-vessel disease was reported in 17.9% - 69% of cases. Also, 24% - 83% of cases needed to revascularization procedures. Cardiac arrest was also reported in 3.1% - 28.2% of cases. (4) In terms of other clinical outcomes, cardiogenic shock was reported in 18.5% of cases, need for intubation in 12.8%

TABLE 1. The details of studies

Author, country	Study type	Covid-19 Population (n)	Male/Female	Mean age	Follow-up time	Rate of STEMI
Abizaid, Brazil[13]	Multicenter prospective	152	103/49	64.0	In-hospital	83 (54.6%)
Bakhshi, USA[14]	Retrospective cohort	5	5/0	56.8	1 month	3 (60.0%)
Bangalore, USA[15]	Retrospective cohort	18	15/3	64.0	In-hospital	8 (44.4%)
Choudry, UK[16]	Retrospective cohort	39	33/6	61.7	In-hospital	24 (61.5%)
Hamadeh, USA[17]	Multicenter retrospective	78	49/29	65.0	In-hospital	78 (100%)
Kaur, USA[18]	Retrospective cohort	4	4/0	60.2	In-hospital	4 (100%)
Rodriguez, Spain[19]	Retrospective cohort	1010	78/13	60.0	In-hospital	91 (9.0%)
Solano-Lopez, Spain[20]	Multicenter prospective	32	29/3	66.0	In-hospital	32 (100%)
Stefanini, Italy[21]	Retrospective cohort	28	20/8	68.0	In-hospital	25 (89.3%)

TABLE 2. The details of cardiac involvement in COVID-19 patients

Author, country	Covid-19-related MI	Findings	Mortality
Abizaid, Brazil	83	Syntax score of 16, multi-vessel disease = 69%, complex lesion = 73%, thrombus containing lesion = 51.3%	23.7% 19
Bakhshi, USA	3	Low LVEF (<35%) = 60.0%, Wall motion abnormality = 60.0%,	40.0% 2
Bangalore, USA	8	Anterior ST elevation = 12%, inferior ST elevation = 50%, Lateral change = 100%, Low ejection fraction = 88%, wall-motion abnormality = 75%, coronary artery disease = 100%, Percutaneous coronary intervention = 83%	50.0% 4
Choudry, UK	39	Anterior/LBBB = 61.6%, Inferior = 28.2%, Lateral = 7.7%, Cardiac arrest = 28.2%, Cardiogenic shock = 18.5%, Intubation = 12.8%, Coronary intervention = 97.4%, Multivessel thrombosis = 17.9%	17.9% 7
Hamadeh, USA	78	Coronary intervention = 24%, cardiac resuscitation=17%, Intubation = 42%, mechanical ventilation = 18%, re-infarction = 21%, ischemic stroke=16%	12.0% 9
Kaur, USA	4	Normal sinus rhythm = 100%, Left axis deviation = 50%, inferolateral = 75%, anterolateral = 25%,	75.0% 3
Rodriguez, Spain	91	Heart failure = 31.9%, mechanical thrombectomy=44%,	23.1% 21
Solano-Lopez, Spain	32	Cardiac arrest = 3.1%, ST-depression = 21.9%, ST-elevation = 62.5%, Multi-vessel coronary vessel = 51.6%,	15.6% 5
Stefanini, Italy	28	wall-motion abnormality = 82.1%, diffuse hypokinesia = 10.7%, reduced LVEF = 60%, culprit lesion requiring revascularization = 60.7%, coronary artery disease=39.3%, ST-depression = 21.9%, ST-elevation = 89.3%, LBBB = 10.7%, Reduced LVEF = 25%, wall-motion abnormality = 92.8%	39.3% 11

- 42% of cases, recurrent myocardial infarction in 21% of cases, cerebral ischemia in 16% of cases and need for mechanical ventilation in 18%.

Based on the meta-analysis performed on the mortality of patients with STEMI in the field of Covid-19, the pooled prevalence of mortality was estimated at 25.2% (95%confidence interval of 17.5% - 34.8%) (Table 3).

TABLE 3. The details of calculating mortality related to STEMI following COVID-19

Author, country	Death rate	95% Confidence Interval for death		*P* value
		Lower limit	Upper limit	
Abizaid, Brazil	22.9	15.1	33.1	0.001
Bakhshi, USA	66.7	15.4	95.7	0.571
Bangalore, USA	50.0	20.0	80.0	1.000
Choudry, UK	17.9	8.8	33.1	0.001
Hamadeh, USA	11.5	6.1	20.7	0.001
Kaur, USA	75.0	23.8	96.6	0.341
Rodriguez, Spain	23.1	15.6	32.8	0.001
Solano-Lopez, Spain	15.6	6.7	32.5	0.001
Stefanini, Italy	39.3	23.2	58.0	0.261

However, in terms of mortality reporting, the articles had significant heterogeneity (I^2 index = 60.592, $P = 0.009$) (Fig 3). However, publication bias was not significant for the studied studies (*P* value was 0.531) (Fig 4).

Discussion

Cardiovascular complications are among the most important and potentially fatal complications in patients with severe Covid-19. In general, regarding the effect of Covid-19 disease and coronavirus-related disease on the cardiovascular system, various mechanisms have been described, including the following: (1) Direct effect on myocardial tissue following direct invasion of virus, (2) Transmission of the virus through specific ACEII receptors located on myocardial tissue, (3) Increased

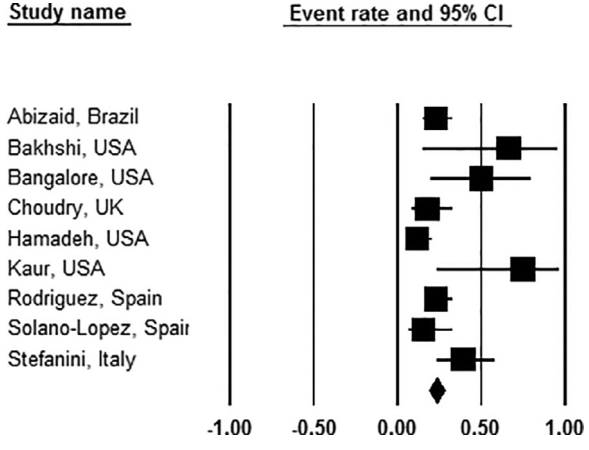

FIG 3. Pooled death rate related to STEMI following COVID-19 (death rate = 25.2%, 95% CI: 17.5% - 34.8%)

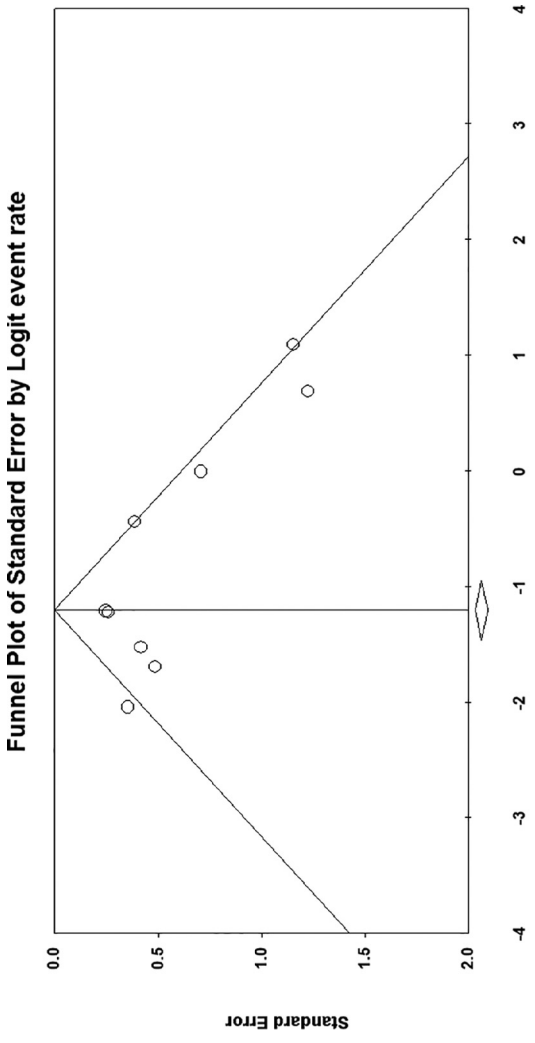

FIG 4. Insignificant publication bias as evidenced by funnel plot asymmetry ($P = 0.5311$).

susceptibility to vascular thrombosis, especially in coronary arteries, and increased risk of Cardiac ischemic disease, (4) Activation of inflammatory processes and thus production and secretion of inflammatory cytokines. The activation of the above processes will lead to a variety of cardiovascular disorders such as coronary heart disease, a variety of cardiac arrhythmias, acute heart failure, cardiomyopathies and eventually death due to the progression and exacerbation of heart disorders. One of the most important of these complications is acute myocardial infarction, especially STEMI due to Covid-19, which is considered as one of the fatal complications of this disease. What we focused on in the present systematic review was the assessment of the occurrence of STEMI in patients with Covid-19 as well as the associated cardiovascular findings. In this study, a total of 9 studies evaluating the occurrence of STEMI following Covid-19 were systematically reviewed and meta-analyzed. Thus, our primary target population was patients with coronary artery disease without evidence of cardiovascular involvement who had experienced STEMI during hospitalization or within 30 days of discharge.

What was considered an initial and important conclusion was that the clinical consequences of ischemic heart disease following Covid-19 disease appear to be far worse and the extent of the involvement far more severe than in cases without Covid-19. However, no comparative study has been conducted in this regard. In other words, a review of our findings shows that, first, the occurrence of STEMI in the context of Covid-19 is associated with a significant mortality of about 25.2%, and in fact about a quarter of patients with STEMI following Covid-19 seems to be non-survived. However, even in the case of one-year mortality of patients with MI in the general non-Covid-19 population, this number is lower than the rate reported in patients with Covid-19.[22,23] In fact, Covid-19 infection appears to be an independent factor associated with an increased mortality rate in patients with STEMI. This is due to the fact that the cardiovascular involvement caused by Covid-19 will be much more severe than the general population with STEMI.

What we showed was the high prevalence of heart involvement in these patients based on electrocardiographic, echocardiographic, and angiographic findings. In this regard, it was shown that a significant reduction in LVEF was observed in 60% - 88% and wall motion abnormality in 60% - 82.1% of patients. Also, the occurrence of multi-vessel disease was reported in 17.9% - 69% of cases that 24% - 83% needed to schedule for coronary revascularization. Cases leading to cardiac arrest were also reported to be 3.1% - 28.2%. Also, re-infarction was reported in 21% of patients, all of which are significant. Accordingly, it should be

acknowledged that given the far worse consequences of STEMI in patients with Covid-19, it would be crucial to consider some precautions as soon as coronary heart disease is diagnosed, especially in patients with risk factors for heart disease: First, in the presence of cardiovascular risk factors, the program to control these risk factors should be a priority. Second, a comprehensive cardiovascular evaluation and monitoring of these patients during hospitalization is strongly recommended.

Conclusion

In conclusion, the severity and extent of STEMI following Covid-19 will be far greater than the general population without Covid-19. In this way, the rate of in-hospital mortality due to STEMI is also significant in these patients and according to the literature review, about a quarter of patients die within hospitalization. Therefore, control of cardiovascular risk factors as soon as possible in patients with Covid-19 will be critical as soon as they are admitted to the hospital with continuous monitoring.

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