The impact of the COVID-19 pandemic on the care and management of patients with acute cardiovascular disease: a systematic review

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Abstract

Background: The COVID-19 pandemic has disrupted healthcare services around the world, which may have serious implications for the prognosis of patients with acute cardiovascular disease. We conducted a systematic review to assess the extent to which health services related to the care and management of acute cardiovascular events have been impacted during the COVID-19 pandemic.

Methods: PubMed, MedRxiv and Google Scholar were searched for observational studies published up to August 12, 2020 for studies that assessed the impact of the pandemic on the care and management of people with acute CVD.

Results: In total, 27 articles were included. Of these, 16 examined the impact on acute coronary syndromes (ACS), eight on strokes, one on ACS and strokes, and 2 on other types of CVD. When comparing the COVID-19 period to non-COVID-19 periods, eleven studies observed a decrease in ACS admissions ranging between 40 and 50% and five studies showed a decrease in stroke admissions of between 12 and 40%. Four studies showed a larger reduction in non-ST-segment elevation myocardial infarctions (NSTEMI) compared to ST-segment elevation myocardial infarctions (STEMI). A decrease in the number of reperfusion procedures, a shortening in the lengths of stay at the hospital, and longer symptom-to-door times were also observed.

Conclusions: The COVID-19 pandemic has led to a substantial decrease in the rate of admissions for acute CVD, reductions in the number of procedures, shortened lengths of stay at the hospital and longer delays between the onset of the symptoms and hospital treatment. The impact on patient’s prognosis needs to be quantified in future studies.

Introduction

First reported in December 2019 in Hubei province in China, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused the emergence of the disease COVID-19. COVID-19 was qualified as a pandemic by the World Health Organization (WHO) on March 11, 2020 [1]. As of September 13, 2020, the ongoing pandemic has infected more than 28 million people worldwide, with more than 920,000 deaths [2].

In addition to the direct impact of COVID-19 on morbidity and mortality, the pandemic has indirect consequences on health care for other diseases, the so-called collateral damage. Since the start of the pandemic, healthcare systems have adopted unprecedented measures to minimise disease transmission and prepare for the surge of COVID-19 patients. Consultations, routine diagnostic evaluations, and non-essential procedures were cancelled or deferred in order to prioritize the care of patients with COVID-19 and to limit the risk of contamination at the hospital. In addition, governments and health authorities worldwide recommended the deferral of elective procedures in order to preserve health staff and hospital resources, including cardiac services [3, 4].

Soon after the WHO declared COVID-19 a global pandemic, anecdotal evidence and surveys suggested a decrease in the number of patients presenting with cardiovascular diseases requiring emergency procedures [5, 6]. These observations have caused concern among doctors and public authorities around the prognosis of patients with acute cardiovascular disease (CVD), including acute coronary syndrome (ACS) and stroke. This is because the outcomes of these acute events depend largely on rapid diagnosis and prompt implementation of reperfusion therapies [7-9]. Understanding the indirect effects of the pandemic is important to inform recovery planning and to ensure that appropriate measures are in place to adopt the most effective response in this ongoing crisis and future public health crises.

The aim of this study was to systematically review the impact of the COVID-19 pandemic on the care and management of people with acute CVD.

Methods

Search terms

A systematic search in PubMed, MedRxiv and Google Scholar was performed for studies published during the COVID-19 pandemic and until August 12, 2020 using a combination of free-text terms related to the deferral of non-COVID-19 care during the pandemic. Details of the search terms are presented in *Supplementary material 1*. Additional relevant studies were identified by studying the reference lists of the included studies.

Study selection

Studies were eligible for inclusion if they were original studies, published in English and reported information on hospitalizations for acute CVD (e.g., ACS and stroke), treatment procedures provided, and/or management of patients with acute CVD, including length of stay and delays between symptom onset and diagnosis or start of treatment. The studies should compare a COVID-19 period to an earlier time before the pandemic (e.g., same weeks in 2019, previous months, previous years). Studies were excluded when no information on a pre/during-COVID-19 comparison was provided, when the articles were reviews, systematic reviews, comments, editorials, recommendations, guidelines, case reports or surveys and when no full-text of the studies was available. Pre-print articles were included.

Data extraction and analyses

Data extraction was performed using an extraction form that gathered information on the country, setting, study population, outcomes of interest, and comparison periods studied in the papers. The studies were further divided into groups according to the type of CVD studied (i.e., ACS, acute stroke, others). The definition of several medical terms can be found in *Supplementary material 2*. As the characteristics of the selected studies were heterogeneous in terms of subjects involved and outcomes studied, a meta-analysis was not performed.

Quality assessment

The quality of all included studies was assessed using a modified Newcastle-Ottawa Scale for cohort studies [10]. The 5-point scale assesses the quality of Participant Selection (three items), Comparability (one item) and Outcome (one item). Good quality was defined as having a total of 5 stars for all items combined, fair quality was defined as a total of 3 or 4 stars and poor quality was defined as a total of 1 or 2 stars. The results of the poor-quality studies were not described in the main text but can be found in the tables.

Results

Search and study characteristics

Of the 1,548 records identified through the systematic search, 76 were eligible for full text screening. Of these, 21 studies were included and 6 additional articles were added through reference checking (**Figure 1**). The characteristics of the 27 included studies are displayed in **Table 1**. In total, 13 studies were conducted in Europe, eight in North America, three in Asia, and one each in Africa, Australia, and South America. Nineteen studies had a good quality score, four had a fair quality score, and four had a poor quality score (*Supplementary material 3*).

The studies differed in terms of study population and the sample size ranged between 64 and 1,113,075 patients, with a median of 740 participants (interquartile range (IQR): 162-1,635). Most studies compared the pandemic period with the same weeks in 2019 [11-25] and/or with earlier years [13, 14, 18, 19, 26]. Some studies used an earlier period in 2020 [11, 13, 27-34], and two studies analysed the weekly changes in admissions and procedures over several months [35-37]. The main results of each study are shown in **Table 2**.

Acute coronary syndrome

Seventeen studies addressed the impact of COVID-19 on hospital admissions for ACS (n=12), outcome severity (n=6), treatment procedures (n=3), length of hospital stay (n=3) and delays to diagnosis or treatment (n=6).

ACS admissions: Eleven studies observed a reduction in ACS admissions during the pandemic compared to a pre-pandemic period,[11-13, 17, 27, 29, 32, 33, 35-37] with a percentage decrease between 40 and 50%. Two studies, from the UK and USA, reported a decrease in hospitalisations for myocardial infarction (MI) between mid-February and the end of March, but observed a partial reversal of this decline during April-May 2020 [27, 35]. A French study reported that the incidence of out-of-hospital cardiac arrests was higher during the pandemic than before [14].

Four studies showed that the decrease in admissions for non-ST-segment elevation myocardial infarctions (NSTEMI) was greater than for ST-segment elevation myocardial infarctions (STEMI) [12, 13, 35, 37], whereas one study showed no difference between MI subtypes [17]. For example, a UK study observed a decrease of 42% for NSTEMI admissions and of 23% for STEMI admissions [35]. An Italian study showed that the reduction in admissions for STEMI during the pandemic was higher among women (41.2%; P=0.011) compared with men (17.8%; P=0.191) [12].

A study in Iran showed that the proportion of men, compared with women, treated for STEMI was greater during than before the COVID-19 outbreak (72.6% before the pandemic vs. 85.7% during the pandemic) [15]. However, seven studies observed no difference between the sexes in the numbers of ACS admissions, treatments or delays [11, 13, 18, 26, 28, 35, 36].

ACS severity: A French study showed that the odds of in-hospital survival after an out-of-hospital cardiac arrest was 64% lower during than before the pandemic [14]. Four studies observed a higher in-hospital mortality during the outbreak [12, 26, 27, 29], ranging between an increase of 4.1 and 9.6%.

Treatment and length of stay: A study in the UK showed a 21% decrease in the number of percutaneous coronary interventions (PCI) procedures for STEMI patients and a 37% decrease in PCI procedures for NSTEMI patients [35]. A study in Australia found no difference in the case volume for ACS patients undergoing PCI before versus during the pandemic [18]. Three studies observed a shorter length of stay during the pandemic, with a shortening ranging from 6h to 1.2 days [11, 27, 35].

Delays: Two studies, from China and Australia, observed longer symptom-to-door-times.[18, 29] A study from France identified longer symptom-to-balloon times [26] whereas a study from Iran observed a shorter door-to-balloon time [15]. Two studies, from the USA and Austria, did not observe any difference in door-to-balloon times pre- versus during-COVID-19 [28, 36].

<u>Acute strokes</u>

Nine studies reported on the impact of COVID-19 on stroke, including eight on hospitalizations, two on outcome severity, five on access to care, and five on delays to diagnosis or treatment.

Stroke admissions: Five studies showed a reduction in hospitalisations for strokes during the outbreak compared to a non-COVID period [19, 20, 25, 30, 33], with the percentage reduction ranging between 12 and 40%. For example, a study in Brazil observed a 36% reduction in total stroke admissions and this reduction was mainly seen in transient, mild and moderate strokes [20]. Two studies, from Canada and France, reported no difference before versus during COVID-19 [22, 23] whereas a study from Ghana observed an increase in stroke admissions [24].

Treatment: Four studies showed a reduction in cases of reperfusion therapies, such as mechanical thrombectomy (MT) or intravenous thrombolysis (IVT), during the COVID-19 pandemic, ranging from 18 to 33% [21-23, 30]. For example, a study from France showed that IVT procedures reduced by 41% and that MT procedures reduced by 28% [23]. One study from USA showed no difference in the number of patients undergoing endovascular therapy (EVT) between the pandemic and pre-COVID-19 periods [19].

Delays: Three studies have shown longer symptom-to-door times [22, 25, 30] and one study showed extended door-to-needle times during the pandemic [22]. Two studies did not find any significant symptom-to-door delays [20, 23] or door-to-needle delays [23] compared to pre-COVID-19.

<u>Other outcomes</u>

The CVD-COVID-UK consortium assessed the impact of COVID-19 on the broader group of CVD and observed a drop in hospitalizations numbers during the lockdown as well as a reduction in the number of procedures for cardiac, cerebrovascular and other vascular conditions [31]. However, a small recovery towards usual levels was observed from mid-April 2020. A study from Italy assessed the changes in hospital admissions for patients with congenital heart diseases during the pandemic compared to the same period in 2019. Although the overall number of urgent hospitalizations remained stable during the outbreak, the patients admitted during the outbreak showed an increased level of complexity of the underlying congenital heart defects [16].

Discussion

The present systematic review of 27 studies worldwide evaluated the impact of the pandemic COVID-19 on the care for patients with acute cardiovascular disease. Our results show that the total number of admissions to the hospital decreased during the pandemic by 40-50% for ACS emergencies and 12-40% for stroke emergencies. The reduction in ACS admissions was greater for NSTEMI than for STEMI patients. The number of reperfusion therapies for strokes decreased by 18-33%. For ACS, the length of stay at the hospital was shorter compared to non-COVID periods. Also, there were greater time delays between the onset of the symptoms and the treatment procedures inside the hospital for both ACS and strokes.

The results from the present study are in agreement with the burden on the healthcare system and care for individuals with acute CVD seen during previous pandemics. For example, during the Middle East respiratory syndrome (MERS) outbreak, a 33% reduction was seen in admissions to emergency services, with a 14% decrease in admissions for MI and a 17% reduction for ischemic stroke [38]. The reasons underlying this reduction are uncertain, but several hypotheses exist.

One hypothesis to explain the decrease in hospitalizations could be that patients might be reluctant to seek hospital care for fear of infection or contagion. This feeling might have been magnified by the stay-at-home orders and the alerting news from the media, potentially leading patients to delay or defer urgent care [39, 40]. Surveys in the UK showed that fear of being exposed to COVID-19 is the most frequent reason reported for the decrease in ACS admissions, followed by worries of putting pressure on an already overburdened healthcare system [41]. The increase in out-of-hospital cardiac arrests observed in France [14] may be explained by this behaviour of medical-care avoidance. The study from France suggests that the occurrence of ACS during the lockdown was probably similar to non-COVID-19 periods, despite the suggestion of a decrease in CVD in the beginning of the pandemic, due to changes in lifestyle and environmental factors such as traffic reduction and increases in exercise [42]. The reluctance in seeking emergency care seems to be more prevalent in less severe cases, for example, patients with mild stroke and TIA [43]. This hypothesis is supported by the findings of a study included in this review, which reported a reduction in admissions only in transient, mild and moderate strokes [20].

Second, the observed reduction in admissions could be explained by the adaptation of the healthcare system to the pandemic. Higher thresholds for referral to the hospital or emergency department, less intensive care capacity, declines in ambulatory cardiovascular visits, or deferrals of less urgent cases could all lead to an overall reduction in admissions. Furthermore, the deferral of less urgent cases could justify the difference, observed in some studies, between the reduction in hospitalizations for STEMI and NSTEMI, as STEMI is usually associated with more severe symptoms. On the other hand, previous evidence suggests an increased severity of COVID-19 related symptoms in patients with CVD [44]. This is supported by the findings of a Chinese study, where COVID-19 patients who required Intensive Care Unit (ICU) admissions were more likely to suffer from CVD than non-ICU patients [45]. As consequence, this could increase the risk that, for example, stroke signs in patients admitted for COVID-19 symptoms could be undiagnosed due to the medical focus on COVID-19 and the protective measures adopted by the hospitals (e.g., separate registration for patients with COVID-19 symptoms, triage, instalment of isolation areas), thus leading to a decrease in acute stroke admissions.

Third, the social restrictions imposed during the lockdown caused individuals to be alone more often, potentially leading to mild stroke signs or deficits such as dysarthria, aphasia or mild paresis going unnoticed. People living alone are more likely to have more severe complaints and increased risk of early mortality [46, 47]. Moreover, several negative emotional side-effects of the shutdown have been reported, such as loneliness, household stress, anxiety regarding the immediate and long-term future, fear of unemployment and depression [48]. Some of those effects have been identified as risk factors for CVD, particularly in the elderly [49]. Also, the fact that the number in admissions for ACS in the UK declined before the lockdown [5] suggests that the consequences of the shutdown (e.g., social isolation, stress) might contribute less to the observed reduction in admissions, compared to the medical-care avoidance and the healthcare system restructuration.

In comparison to the others studies included in this review, a study in Ghana found an increase in stroke admissions of 7.5% between January and June 2020 compared to the same period in 2019 [24]. This observation could be explained in part by the rapidly rising burden of stroke in sub-Saharan Africa [50].

Twelve studies investigated the sex differences in the impact of COVID-19 on the care and management of ACS (n=9), acute strokes (n=2) and other CVD (n=1) [11-13, 15, 16, 18, 22, 25, 26, 28, 35, 36]. Ten observed no difference between the sexes whereas two studies reported a higher reduction in STEMI-related admissions among women compared with men [12, 15]. Previous studies have shown that sex differences in the treatment of acute MI may contribute to a further increase in CVD mortality among women [51]. No significant difference across ethnic groups was reported in the studies [11, 27, 28, 35] and potential differences across social classes was not investigated in the studies.

Regarding the number of procedures for ACS treatments, Mafham *et al.* reported and quantified a drop in the numbers of PCI of 21% for STEMI patients and 37% for NSTEMI patients. The last percentage is comparable to the numbers observed in a study in Spain (percentage reduction of 40%) that did not fulfil all inclusion criteria in order to be included in this review [52]. Furthermore, the shortened length of stay observed in some studies [11, 27, 35] could be explained by a combination of factors such as a higher pressure for both patients and doctors for early discharges and reduced wait times for necessary procedures.

Several studies discussed in this review reported longer symptom-to-door times [18, 22, 25, 29, 30] during the pandemic compared to pre-pandemic periods. The results regarding the door-to-balloon times and door-to-needle times are more ambiguous as two studies observed longer delays [22, 26] and three found no difference in time delay [23, 28, 36] or observed shorter delays during the pandemic [15]. This absence of consistency may be due to the difference in care management across the hospitals whose data were retrieved by the studies included in the review. In addition, patients that present later in their acute illness may have more complex outcomes [29]. Previous work suggests that minutes of delay for a PCI intervention are enough to impact the 1-year mortality of patients with STEMI [53]. Therefore, rapid and efficient care services are important as patients with symptoms indicative of acute myocardial ischemia benefit from rapid in-hospital assessment, with the gain being greatest among those with STEMI [7]. Those patients are prone to out-of-hospital cardiac arrests [54] and their incorrect management results in avoidable deaths and complications, such as fatal arrhythmias [55].

This study systematically reviewed the impact of the COVID-19 pandemic on acute care for CVD. We conducted a comprehensive review in multiple sources and assessed the quality of the included studies. The results of this study have immediate relevance for cardiovascular health authorities and clinicians. There are some limitations to this review. First, there was substantial heterogeneity between studies in study outcomes, population, and design, which hampered the comparability across studies and precluded formal meta-analyses. Some study outcomes were either not reported for all studies or described differently across studies, making the comparison between studies difficult. Several studies were also conducted in small study populations and the results from these studies should be interpreted with caution. Second, it is possible that some less prominent results found in the studies were not reported in this review. Third, although this review included studies from each continent, studies from countries with very high infection rates, such as India, were not represented [2]. Fourth, we only assessed short-term consequences of the pandemic on the care for people with acute ACS and were not able to assess the long-term outcomes. It is very likely that the healthcare systems will adapt with time, when more knowledge on COVID-19 will be available and when people will gain more experience with the management of the crisis. This hypothesis is supported by the observation made in some papers [27, 31, 35] of a recovery towards usual levels of admissions in mid-April and May. However, fear is a natural protection mechanism, therefore, it seems probable that the same reduction in admissions will be seen again in the future, in the context of a second wave or a possible next pandemic. Consequently, clear and precise messages from the public health authorities will be essential in order to advise and best protect the population.

In conclusion, this systematic review summarizes all available literature on impact of the COVID-19 on the care and management of patients with acute CVD. The results showed a substantial decrease in the rate of admissions for acute CVD, shortened lengths of stay at the hospital, reductions in the number of procedures, and longer delays between the onset of the symptoms and the treatment at the hospital. The impact on patient's prognosis needs to be quantified in future studies, so as to ensure that appropriate measures are in place to adopt more effective response in this ongoing global health crisis.

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Table 1. Characteristics of the included studies.

First author	Publication date	Country	Setting	Study population	Outcome	Comparison period	Quality of Study
ACS							
Bhatt *et al.* [11]	July, 2020	USA	Tertiary care centre	6,083 patients with CVD	CVD hospitalizations, length of stay, severity	1/3/2020-31/3/2020 vs 1/1/2019-29/2/2020 and 1/3/2019-31/3/2019	Good
De Filippo *et al.* [32]	April, 2020	Italy	Multicentre tertiary care	2,202 ACS patients	ACS hospitalizations	20/2/2020-31/3/2020 vs 20/2/2019-31/3/2020 and 1/1/2020-19/2/2020	Poor
De Rosa *et al.* [12]	April, 2020	Italy	Multicentre tertiary care	937 MI patients	MI hospitalizations, severity	12/3/2020-19/3/2020 vs 12/3/2019-19/3/2019	Good
Dhruv *et al.* [33]	May, 2020	USA	Tertiary care centre	776 MI and stroke patients	MI and stroke hospitalizations	1/3/2020-30/4/2020 vs 1/1/2020-29/2/2020	Poor
Garcia *et al.* [34]	June, 2020	USA	Multicentre tertiary care	STEMI patients*	PPCI procedures	1/3/2020-31/3/2020 vs 1/1/2019-29/2/2020	Poor
Gitt *et al.* [13]	July, 2020	Germany	Tertiary care centre	382 ACS patients	ACS hospitalizations	1/3/2020-21/4/2020 vs idem 2017-2019 and 1/1/2020-29/2/2020	Fair
Gluckman *et al.* [27]	August, 2020	USA	Multicentre tertiary care	14,724 MI patients	MI hospitalizations, length of stay, severity	29/3/2020-16/5/2020 vs 23/2/2020-28/3/2020 and 30/12/18-22/2/2020	Good
Hammad *et al.* [28]	May, 2020	USA	Multicentre tertiary care	143 STEMI patients	STEMI door-to-balloon times	23/3/2020-15/4/2020 vs 1/1/2020-22/3/2020	Good
Mafham *et al.* [35]	July, 2020	UK	Multicentre tertiary care	> 67,776* ACS patients	ACS hospitalizations, length of stay, PPCI	1/1/2019-24/5/2020	Good
Marijon *et al.* [14]	May, 2020	France	Multicentre tertiary care	30,768 patients with OHCA	Incidence of OHCA, outcome severity	16/3/2020-26/4/2020 (i.e., weeks 12-17)	Good

						vs Weeks 12-17, 2012-2019 and 2011-2020 excl. weeks 12-17	
Metzler *et al.* [37]	April, 2020	Austria	Multicentre tertiary care	725 ACS patients	ACS hospitalizations	2/3/2020-29/3/2020	Poor
Popovic *et al.* [26]	June, 2020	France	Tertiary care centre	1,635 STEMI patients	STEMI door-to-balloon times, severity	26/2/2020-10/5/2020 vs idem 2008-2017	Good
Reinstadler *et al.* [36]	July, 2020	Austria	Multicentre tertiary care	163 STEMI patients	STEMI hospitalizations, door-to-balloons times	24/2/2020-5/4/2020	Good
Salarifar *et al.* [15]	May, 2020	Iran	Tertiary care centre	139 STEMI patients	STEMI door-to-balloon times	29/2/2020-29/3/2020 vs 1/3/2019-30/3/2019	Good
Solomon *et al.* [17]	May, 2020	USA	Multicentre tertiary care	43,017,810 person-weeks MI patients	MI hospitalizations	1/1/2020-14/4/2020 vs 1/1/2019-15/4/2019	Good
Tam *et al.* [29]	April, 2020	China	Tertiary care centre	149 MI patients	MI hospitalizations, symptom-to-door-times, severity	25/1/2020-31/3/2020 vs 1/11/2019-24/1/2020	Good
Toner *et al.* [18]	July, 2020	Australia	Tertiary care centre	122 ACS patients	PCI procedures, symptom-to-door-times	16/3/2020-15/4/2020 vs idem 2014-2019	Good
Stroke							
Desai *et al.* [19]	May, 2020	USA	Tertiary care centre	740 stroke patients	Stroke hospitalizations, treatments	1/3/2020-31/3/2020 vs idem 2017-2019	Fair
Diegoli *et al.* [20]	August, 2020	Brazil	Multicentre tertiary care	1,169 stroke patients	Stroke hospitalizations, severity, onset-to-door times	16/2/2020-15/4/2020 vs 15/2/2019-15/4/2019	Good
Kerleroux *et al.* [21]	July, 2020	France	Multicentre tertiary care	1,513 patients with acute ischemic stroke	Treatment MT	15/2/2020-30/3/2020 vs 15/2/2019-30/3/2019	Good
Montaner *et al.* [30]	August, 2020	Spain	Multicentre tertiary care	102 stroke patients	TIA hospitalizations, onset-to-door times, reperfusion therapy	15/3/2020-31/3/2020 vs 15/1/2020-14/3/2020	Fair

Neves Briard *et al.* [22]	July, 2020	Canada	Tertiary care centre	294 stroke patients	Stroke hospitalizations, symptom-to-door times, door-to-needle times, treatments	30/3/2020-31/5/2020 vs 30/3/2019-31/5/2019	Good
Pop *et al.* [23]	May, 2020	France	Multicentre tertiary care	319 stroke patients	Stroke hospitalizations, delays, treatments, severity	1/3/2020-31/3/2020 vs 1/3/2019-31/3/2019	Good
Sarfo *et al.* [24]	July, 2020	Ghana	Tertiary care centre	832 stroke patients	Stroke hospitalizations	1/1/2020-31/6/2020 vs 1/1/2019-31/6/2019	Good
Teo *et al.* [25]	July, 2020	China	Tertiary care centre	162 patients with stroke and transient ischemic attack	Stroke hospitalizations, onset-to-door	23/1/2020-24/3/2020 vs 23/1/2019-24/3/2019	Good
Other							
CVD-COVID-UK consortium [31]	July, 2020	UK	Multicentre tertiary care	1,113,075 patients with CVD	Hospitalizations for CVD, medical procedures	23/3/2020-10/5/2020 vs 3/2/2020-22/3/2020 and 28/10/2019-2/2/2020	Fair
Scognamiglio *et al.* [16]	June, 2020	Italy	Tertiary care centre	64 patients with congenital heart diseases	Hospitalizations, severity	1/3/2020-30/4/2020 vs 1/3/2019-30/4/2019	Good

Note: TIA, transient ischemic attack. Dates are displayed in the following format: DD/MM/YY. * The exact number for the study population was not mentioned in the paper.

Table 2. Main results of the included papers.

First author	Publication date	Results
ACS		
Bhatt *et al.* [11]	July, 2020	- Reduction in daily hospitalizations of 43.4% ((95% CI, 27.4-56.0); P<0.001). - Shorter length of stay (4.8 days vs. 6.0 days; P=0.003). - No difference observed in in-hospital mortality (6.2% vs. 4.4%; P=0.30).
De Filippo *et al.* [32]	April, 2020	- Reduced mean admission rate of 13.3 admissions per day compared to earlier period in the same year (18.0 admissions per day; incidence rate ratio, 0.74 (95% CI, 0.66-0.82); P<0.001). Rate during the previous year (18.9 admissions per day; incidence rate ratio, 0.70 (95% CI, 0.63-0.78); P<0.001).
De Rosa *et al.* [12]	April, 2020	- 48.4% reduction in admissions (P<0.001) with a bigger reduction for NSTEMI: (65.1% (95% CI, 60.3–70.3); P<0.001) than STEMI; (26.5% (95% CI, 21.7–32.3); P=0.009). - Among STEMIs, the reduction was higher for women (41.2%; P=0.011) than men (17.8%; P=0.191). - Increase in complications (RR = 1.8 (95% CI, 1.1–2.8); P=0.009). - Increase in STEMI case fatality rate (13.7% vs 4.1% in 2019) (RR = 3.3 (95% CI, 1.7-6.6); P<0.001).
Dhruv *et al.* [33]	May, 2020	- Reduction in hospitalizations for MI (difference-in-differences estimate, 0.67 (95% CI, 0.46-0.96); P=0.04) and stroke (difference-in-differences estimate, 0.42 (95% CI, 0.28-0.65); P<0.001).
Garcia *et al.* [34]	June, 2020	- Decrease in PPCI procedures of 38% ((95% CI, 26-49); P<0.001).
Gitt *et al.* [13]	July, 2020	- Unchanged numbers for STEMI admissions, but a significant 50% reduction in NSTEMI admissions.
Gluckman *et al.* [27]	August, 2020	- Decrease in MI-associated hospitalizations at a rate of –19.0 (95% CI, –29.0 to –9.0) cases per week. - Shorter median length of stay in the early COVID-19 period by 7 hours and in the later COVID-19 period by 6 hours compared with the before period (56, IQR: (41-115) hours and 57, (41- 116) hours vs. 63, (43-122) hours, respectively; P<0.001). - Greater risk of mortality during the later COVID-19 period (OR = 1.52 (95% CI, 1.02-2.26)).
Hammad *et al.* [28]	May, 2020	- No difference observed in door-to-balloon times.
Mafham *et al.* [35]	July, 2020	- Reduction of 40% in the hospital admissions for ACS with a larger reduction for NSTEMI (percentage reduction in admissions 42% (95% CI, 38–46)) compared to STEMI (percentage reduction in admissions 23% (16–30)). - Reductions in the number of PCI procedures for STEMI (percent reduction 21% (95% CI, 12–29)) and NSTEMI (37% (29–45)). - Length of stay fell from 4 days in 2019 to 3 days by the end of March 2020.
Marijon *et al.* [14]	May, 2020	- Increase in the maximum weekly incidence of OHCA during the lockdown from 13.42 (95% CI, 12.77–14.07) to 26.64 (25.72–27.53) per million inhabitants (P<0.0001). - Significant lower survival rate at hospital admission (OR = 0.36 (95% CI, 0.24–0.52); P<0.0001).
Metzler *et al.* [37]	April, 2020	- The weekly number of STEMI hospital admissions in March was 94, 101, 89, and 70 and the number of NSTEMI declined from 132 to 110, to 62, and to 67.
Popovic *et al.* [26]	June, 2020	- Delayed seek to care (mean delay first symptom-balloon 3.8 ± 3 vs. 7.4 ± 7.7, P<0.001) resulting in a two-fold higher in-hospital mortality (non COVID-19 4.3% vs. COVID-19 8.4%; P=0.07).

Reinstadler *et al.* [36]	July, 2020	- Decrease in STEMI admissions (calendar week 9/10 (n = 69, 42% out of the total STEMI admissions N = 163); calendar week 11/12 (n = 51, 31%); calendar week 13/14 (n = 43, 26%)). - No difference observed in door-to-balloon times (P=0.60).
Salarifar *et al.* [15]	May, 2020	- Shorter door-to-device time (47.0 vs. 60.0 min, P=0.00).
Solomon *et al.* [17]	May, 2020	- Decrease in the weekly rates of hospitalization for MI by up to 48% (incidence rate ratio = 0.52 (95% CI, 0.40-0.68); P<0.001). - Similar decrease in NSTEMI (incidence rate ratio = 0.51 (95% CI, 0.38-0.68)) and STEMI patients (incidence rate ratio = 0.60 (0.33-1.08)).
Tam *et al.* [29]	April, 2020	- Reduction in daily MI emergency attendance (85 vs 64). - Longer symptom-to-first medical contact time. - Worse in-hospital outcomes (e.g., deaths, cardiogenic shock) (14.1 vs. 29.7%, P=0.02) and increase in mortality (5.9% vs 12.5%, P=0.24).
Toner *et al.* [18]	July, 2020	- No difference observed in the case volume for PCI procedures (20 vs. historical mean 18 cases/month; P=0.20). - Higher median symptom-to-door time (11.1, IQR: (5.0-102) vs. 2.4 (1.3-6.2) hours, P<0.001).
Stroke		
Desai *et al.* [19]	May, 2020	- Decreased number of strokes admissions (40%, P=0.001). - No difference observed in the number of patients undergoing EVT (P=0.430).
Diegoli *et al.* [20]	August, 2020	- Decrease of 36.4% in total stroke admissions (12.9/100,000 per month vs to 8.3/100,000 (P=0.0029)). - Decrease observed only in cases with transient, mild, or moderate stroke presentations. - No difference observed in onset-to-door times.
Kerleroux *et al.* [21]	July, 2020	- 21% decrease (0.79 (95% CI, 0.76–0.82); P<0.001) in MT case volumes.
Montaner *et al.* [30]	August, 2020	- 25% reduction in admitted cases (mean number of 58 cases every 15 days in previous months to 44 cases in the 15 days after the outbreak, P<0.001). - Delayed onset-to-door time (89 minutes pre-COVID-19 vs. 127 minutes post-COVID-19, P<0.001). - Reduction in reperfusion therapies and thrombolytic therapy (average of 28 versus 23, P<0.001).
Neves Briard *et al.* [22]	July, 2020	- No difference observed in the number of admissions. - Longer delays to hospital presentation (197, IQR: (64- 501) vs. 116 (60-212) minutes, P=0.03). - Longer door-to-needle (34, IQR: (25-41) vs. 22 (21-30) minutes, P<0.01). - Reduction in patients treated with thrombolysis or thrombectomy (36% treated during COVID-19 vs. 54% pre-COVID-19, P=0.01).
Pop *et al.* [23]	May, 2020	- No difference observed in the number of admissions (-0.6%). - 33.3% fewer acute revascularization treatments (34 vs. 51 in 2019; 40.9% fewer IVT and 27.6% fewer MT). - No significant difference in pre-hospital and intra-hospital time delays or severity of clinical symptoms.
Sarfo *et al.* [24]	July, 2020	- Increase of +7.5% in stroke admissions (95% CI, 5.1–10.5).
Teo *et al.* [25]	July, 2020	- Significantly fewer patients admitted with TIA (4.1% vs. 15.7%, P=0.016). - Longer median stroke onset-to-door time (154 vs. 95 minutes, P=0.12).
Other		

CVD-COVID-UK consortium [31]	July, 2020	- Decrease in total admissions and emergency department attendance by 57.9% (95% CI, 57.1-58.6) and 52.9% (52.2-53.5) respectively compared with the previous year. - Medical procedures for cardiac and cerebrovascular conditions decreased by 31-88%.
Scognamiglio *et al.* [16]	June, 2020	- Reduction in the number of admissions by 55% (20 versus 44). - Increase in the level of complexity of the underlying congenital heart disease (simple versus moderate/complex defect P=0.001).

Note: RR, risk ratio; SD, standard deviation.

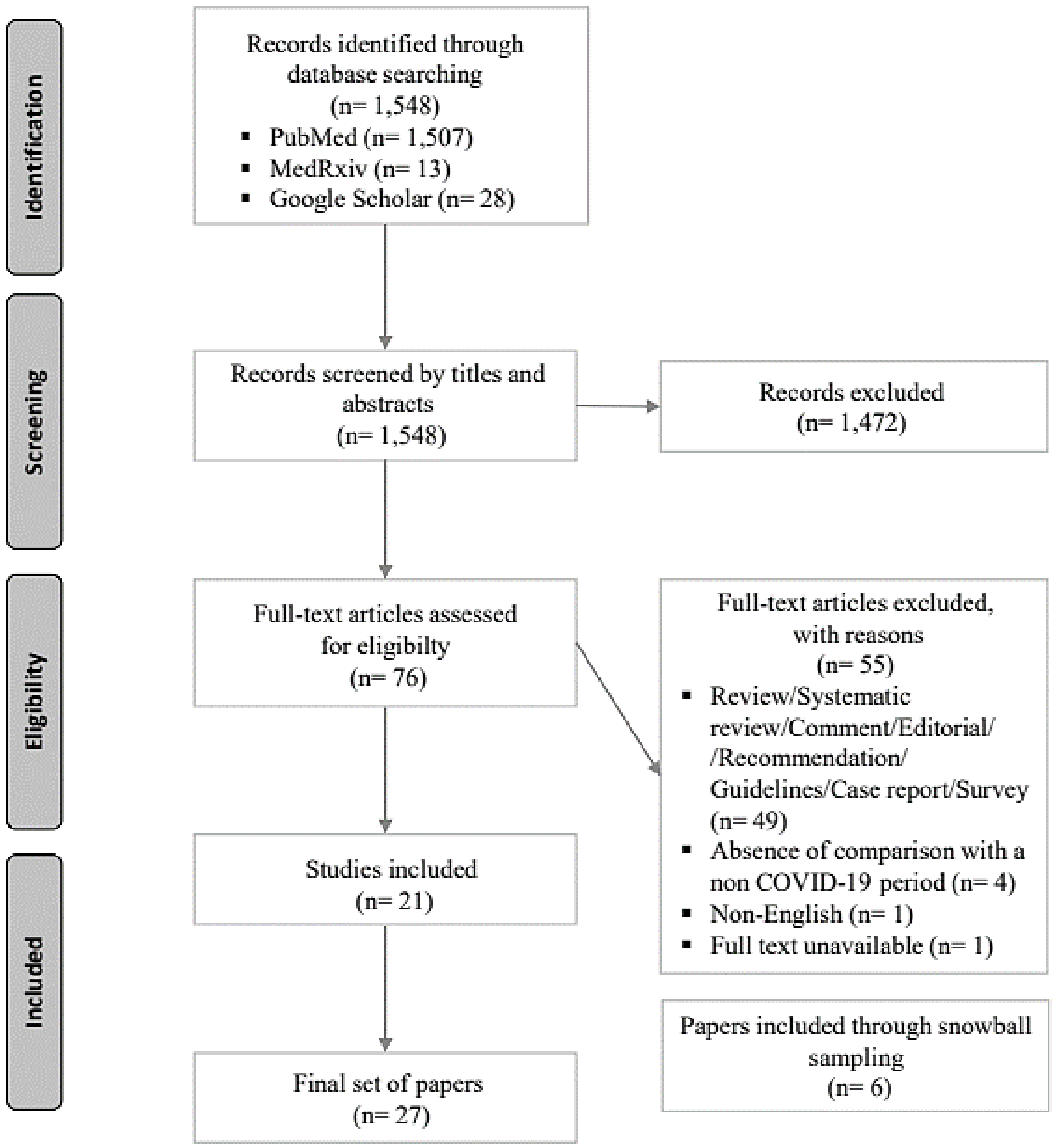

Figure 1. Flowchart of study selection.