Cardiology Journal
2021, Vol. 28, No. 6, 816–824
DOI: 10.5603/CJ.a2021.0168
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ISSN 1897–5593
eISSN 1898–018X

VIA MEDICA

ORIGINAL ARTICLE

Impact of COVID-19 on in-hospital cardiac arrest outcomes: An updated meta-analysis

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Abstract

Background: *The main purposes of this meta-analysis are to update the information about the impact of coronavirus disease 2019 (COVID-19) pandemic on outcomes of in-hospital cardiac arrest (IHCA) and to investigate the impact of being infected by by severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) on IHCA outcomes.*

Methods: *The current meta-analysis is an update and follows the recommendations of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).*

Results: *In analyses, pre- and intra-COVID-19 periods were observed for: shockable rhythms in 17.6% vs. 16.2% (odds ratio [OR]: 1.11; 95% confidence interval [CI]: 0.71–1.72; $p = 0.65$), return of spontaneous circulation (ROSC) in 47.4% vs. 44.0% (OR: 1.36; 95% CI: 0.90–2.07; $p = 0.15$), 30-day mortality in 59.8% vs. 60.9% (OR: 0.95; 95% CI: 0.75–1.22; $p = 0.69$) and overall mortality 75.8% vs. 74.7% (OR: 0.80; 95% CI: 0.49–1.28; $p = 0.35$), respectively. In analyses, SARS-CoV-2 positive and negative patients were observed for: shockable rhythms in 9.6% vs. 19.8% (OR: 0.51; 95% CI: 0.35–0.73; $p < 0.001$), ROSC in 33.9% vs. 52.1% (OR: 0.47; 95% CI: 0.30–0.73; $p < 0.001$), 30-day mortality in 77.2% vs. 59.7% (OR: 2.08; 95% CI: 1.28–3.38; $p = 0.003$) and overall mortality in 94.9% vs. 76.7% (OR: 3.20; 95% CI: 0.98–10.49; $p = 0.05$), respectively.*

Conclusions: *Despite ROSC, 30-day and overall mortality rate were not statistically different in pre- vs. intra-COVID-19 periods, a lower incidence of ROSC and higher 20-day mortality rate were observed in SARS-CoV-2 (+) compared to SARS-CoV-2 (–) patients.* (Cardiol J 2021; 28, 6: 816–824)

Key words: coronavirus disease 2019, COVID-19, SARS-CoV-2, pandemic, in-hospital cardiac arrest, cardiopulmonary resuscitation, outcome, meta-analysis

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Received: 26.07.2020 Accepted: 2.08.2021 Early publication date: 17.12.2021

Introduction

The emergence of the world pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causing coronavirus disease 2019 (COVID-19) began in Wuhan, China in December 2019 [1–3]. In November 2021, respectively over 250 million confirmed cases and 5 million total deaths were reported globally [4].

The COVID-19 manifests itself as an asymptomatic or with a broad spectrum of features commonly regarding symptoms from the respiratory system, including even severe respiratory failure or death [5–7]. The most frequent symptoms involve: fever, cough, and dyspnea then myalgia or rhinorrhea [8–10]. In 14% of patients with pneumonia caused by SARS-CoV-2 hospitalization is required [5]. Subsequently in 15% of patients with initially severe outcomes of COVID-19 multi-organ failure or acute respiratory distress syndrome may occur [6, 11].

Nevertheless, the coexistence of chronic conditions from other systems such as: diabetes mellitus, hypertension, obstructive pulmonary disease, cardiovascular diseases or even obesity was related with worse predictions [8, 12–14].

To date a specific treatment has not been discovered [15]. However, the vaccinations may contribute to limiting the spread of SARS-CoV-2 [16, 17].

Research of the literature presented on the mortality rate in intensive care units may be higher than 35% and according to this data, in-hospital cardiac arrest (IHCA) is described to be the main factor of this score [18, 19]. The IHCA prior to and throughout the COVID-19 pandemic was higher in number, but indistinguishable in outcomes [20]. The survival rate in intra-hospital cardiac arrest was much higher than in out-of-hospital cardiac arrest (OHCA) [20]. Moreover, as pointed out by Shao et al. [18] the survival of patients with non-shockable rhythms is below 0.8%. This is more disturbing, as cardiac arrests in COVID-19 patients occur much more often resulting from a respiratory failure mechanism than in patients with negative COVID-19 results [21, 22]. Because of the risk of SARS-CoV-2 infection, resuscitation of a patient with suspected or confirmed COVID-19 should be carried out using personal protective equipment (PPE) [23, 24]. However, as shown by many studies [25, 26], the use of PPE for aerosol generating procedures (AGPs) may adversely affect the quality of chest compression. In order to improve the quality of the conducted resuscitation, Malysz et al. [27] compared two techniques of manual chest compression — demonstrating that paramedics wearing PPE-AGP achieved better chest compression depth for over-the-head position compared to the standard chest position, however, over-the-head position resuscitation causes a lower full chest relaxation. It is therefore reasonable to use mechanical chest compression systems during resuscitation of a patient with COVID-19, both in pre-hospital and inpatient settings, which allow for standardization of chest compressions even during prolonged cardiopulmonary resuscitation [28].

The primary aim of this systematic review and meta-analysis is to assess the impact of the COVID-19 pandemic on outcomes due to IHCA. The secondary aim is to investigate the effect of SARS-CoV-2 infection of IHCA outcomes during the COVID-19 period.

Methods

The current systematic review and meta-analysis follows the recommendations of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for conducting and reporting its results [29]. A protocol of this meta-analysis has not been registered. Ethical approval and consent were waived because this study was a systematic review and meta-analysis of published literature. This meta-analysis is an update of the analysis previously published by the authors [20].

Methodology of systematic review and meta-analysis was described in a previous article [20]. The primary outcome was overall mortality. Secondary outcomes were return of spontaneous circulation (ROSC) as well as 30-day mortality.

The polled analysis was performed using RevMan 5.4 software (The Nordic Cochrane Center, Copenhagen, Denmark), using the odds ratio (OR) with 95% confidence interval (CI) for dichotomous outcomes, and the mean difference (MD) with 95% CI for continuous outcomes. When the continuous outcome was reported in a study as median, range, and interquartile range, means and standard deviations were estimated using the formula described by Hozo et al. [30]. A quantified heterogeneity in each analysis utilized the tau-squared and I-squared statistics. Heterogeneity was detected with the chi-squared test with n – 1 degree of freedom, which was expressed as I^2. Values of $I^2 > 50\%$ and $> 75\%$ were considered to indicate moderate and significant heterogeneity among studies, respectively. A random-effects model was used to pool study results independently of the p-value for heterogeneity or I^2 [31]. All p values were two-tailed and considered significant if < 0.05.

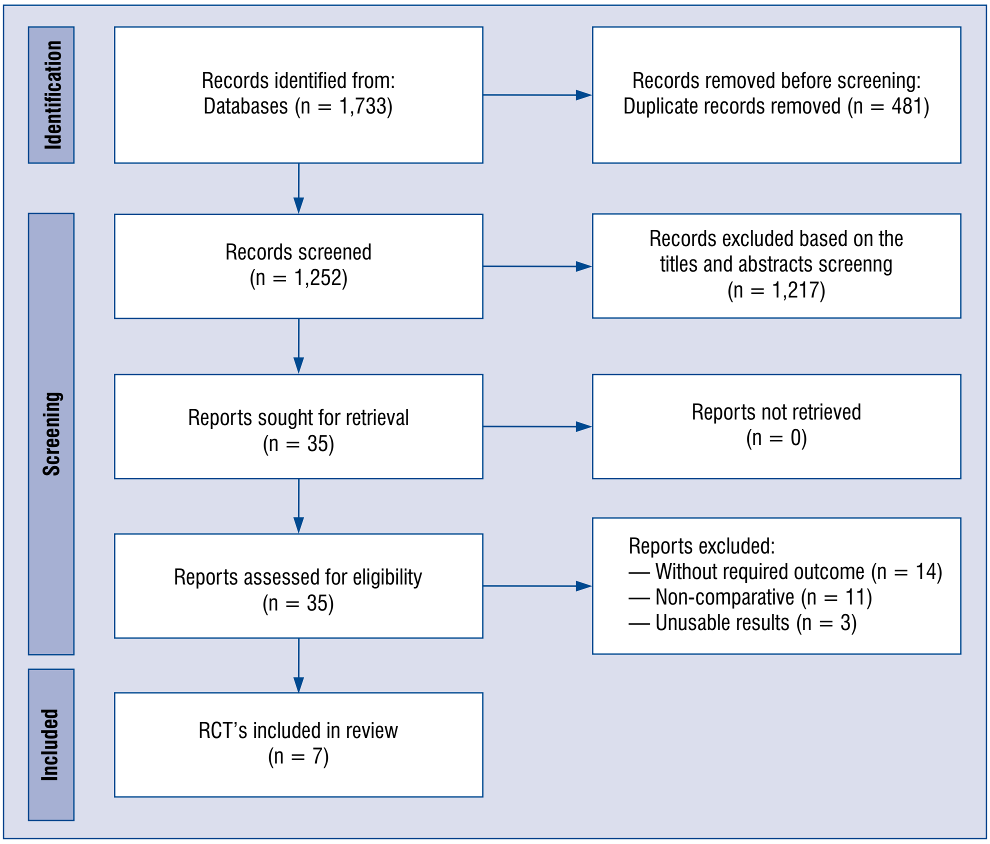

Figure 1. Flow diagram showing stages of the database search and study selection as per Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines; RCT — randomized controlled trials.

Results

Characteristics of studies included in the meta-analysis

A total of 1,733 articles were identified from the Medline (PubMed), Embase, Cochrane library, and a manual search as described above. After excluding duplicates, 1,252 articles remained. In the next step (screening the titles and abstracts of all retrieved articles), 1,217 articles were excluded. Thereafter, the full text was reviewed, and 28 studies were excluded because they contained pediatrics, which does not present a comparative group, report unusable results or were reviews or meta-analyses. Finally, 7 studies published from 2020 to 2021 including 3,049 IHCA patients were included in this meta-analysis (Fig. 1) [32–38]. Detailed characteristics of the studies included in the meta-analysis are presented in Table 1.

Five studies reported IHCA outcomes in pre- vs. intra-COVID-19 periods [32, 34–37] and 3 in COVID-19 period, dividing participants as SARS-CoV-2 positive vs. negative patients [33, 36, 38]. Each study was then screened for risk of bias and methodological quality using the Cochrane Collaboration tool for assessing the risk of bias (Figs. 2, 3).

Analyses in pre- vs. intra-COVID-19 periods

Patient age in the pre- vs. intra-COVID-19 periods varied and amounted to 71.6 ± 13.3 vs. 69.9 ± 14.4 years, respectively (MD: 0.62; 95% CI: –0.71 to 1.95; p = 0.36). Characteristics of patients with IHCA in pre vs. intra-COVID-19 periods and resuscitation process are presented in Table 2.

Shockable rhythms were observed in 17.6% of cases in the pre-COVID-19 period compared to 16.2% for the in COVID-19 period (OR: 1.11; 95% CI: 0.71–1.72; p = 0.65).

Five studies reported ROSC in pre- vs. intra-COVID-19 periods. Polled analysis of ROSC varied and amounted to 47.4% vs. 44.0%, respectively (OR: 1.36; 95% CI: 0.90–2.07; p = 0.15).

Thirty-day mortality was observed in 1 study and was 59.8% for pre-COVID-19 period compared to 60.9% for COVID-19 period (OR: 0.95; 95% CI: 0.75–1.22; p = 0.69). In turn, overall mortality was indicated in 5 studies, and was occurring 75.8%

Table 1. Participant characteristics in included trials.

Study	Country	Pre-COVID-19 period			COVID-19 period								
					Total			COVID-19 positive patients			COVID-19 negative patients		
		No.	Age	Sex, female	No.	Age	Sex, female	No.	Age	Sex, female	No.	Age	Sex, female
Aldabagh et al. 2021	USA	–	–	–	–	–	–	450	66.4 (13.1%)	179 (39.8%)	334	66.8 (15.5%)	148 (44.3%)
Lyu et al. 2021	Singapore	10	NS	NS	17	NS	NS	–	–	–	–	–	–
Miles et al. 2020	USA	117	66.3 (3.5%)	50 (42.7%)	125	66.8 (3.2%)	43 (34.4%)	–	–	–	–	–	–
Roedl et al. 2021	Germany	84	69.8 (3.5%)	24 (28.6%)	93	67.8 (3.5%)	33 (35.5%)	–	–	–	–	–	–
Sultanian et al. 2021	Sweden	532	70.1 (18.2%)	205 (38.5%)	548	67.8 (18.9%)	197 (35.9%)	72	67.8 (13.0%)	23 (31.9%)	285	67.0 (20.8%)	93 (32.6%)
Tong et al. 2021	China	362	75.8 (3.2%)	122	267	76.3 (3.2%)	113	–	–	–	–	–	–
Yuriditsky et al. 2020	USA	–	–	–	110		29 (26.4%)	55	69.8 (3.8%)	7 (12.7%)	55	68.9 (5.9%)	22 (40.0%)

NS — not specified

for pre-COVID-19 period compared to 74.7% for COVID-19 period (OR: 0.80; 95% CI: 0.49–1.28; p = 0.35).

Analyses in SARS-CoV-2 positive vs. negative patients

Mean age among IHCA patients with SARS-CoV-2 positive and negative amounted to 66.9 ± ± 12.5 vs. 67.1 ± 17.5 years respectively (MD: 0.37; 95% CI: –0.93 to 1.67; p = 0.57). Shockable rhythms in the group of patients with confirmed SARS-CoV-2 were observed in 9.6% of cases and it was statistically significantly lower than in the group of patients with negative results of the SARS-CoV-2 test (19.8%; OR: 0.51; 95% CI: 0.35–0.73; p < 0.001). Detailed characteristics of the patients and the resuscitation process are presented in Table 3.

The ROSC in the SARS-CoV-2 positive patients was observed in 33.9% of IHCA cases which was statistically significantly less than with SARS-CoV-2 negative patients — 52.1% (OR: 0.47; 95% CI: 0.30–0.73; p < 0.001). 30-day mortality in the case of SARS-CoV-2 positive vs. negative patients varied and amounted to 77.2% vs. 59.7% (OR: 2.08; 95% CI: 1.28–3.38; p = 0.003). A similar trend was observed for overall mortality, but it was not statistically significant (94.9% vs. 76.7%, respectively; OR: 3.20; 95% CI: 0.98–10.49; p = 0.05).

Discussion

In this meta-analysis outcomes were compared of IHCA during the COVID-19 pandemic to outcomes of IHCA that happened before the SARS-CoV-2 outbreak. Depending on the study, primary outcomes were defined differently. Some considered actual survival to that predicted by the GO-FAR score which is a validated prediction model for determining survival following IHCA [33, 36, 38]. Other studies considered ROSC, which was defined as sustained ROSC or palpable pulse that lasted over 20 min and did not require cardiopulmonary resuscitation to be performed [38].

Contradictory to the results of our previous meta-analysis which showed no significant impact of COVID-19 pandemic to survivability ratio, most studies that we analyzed now show that the rate of survival is lower during the COVID-19 pandemic than in the pre-pandemic period. It was observed in a cohort study performed by Lyu et al. [32] that IHCA was more commonly observed during the ongoing pandemic and, what is more important, the survivability ratio in patients that underwent

Study	Risk of bias domains							
	D1	D2	D3	D4	D5	D6	D7	Overall
Abdabagh 2021	+	+	+	–	?	+	+	+
Lyu 2021	–	+	+	–	?	+	+	+
Miles 2020	+	+	–	–	?	–	–	–
Roedl 2021	–	–	–	–	?	–	–	–
Sultanian 2021	+	+	–	–	?	+	+	+
Tong 2021	+	+	–	–	?	+	+	+
Yuriditsky 2020	–	X	–	–	?	–	X	–

Figure 2. A summary table of review authors' judgements for each risk of bias item for each study. Domains: D1 — bias due to confounding; D2 — bias due to selection of participants; D3 — bias in classification of interventions; D4 — bias due to deviations from intended interventions; D5 — bias due to missing data; D6 — bias in measurement of outcomes; D7 — bias in selection of the reported result; Judgement: X Serious; – Moderate; + Low; ? No information.

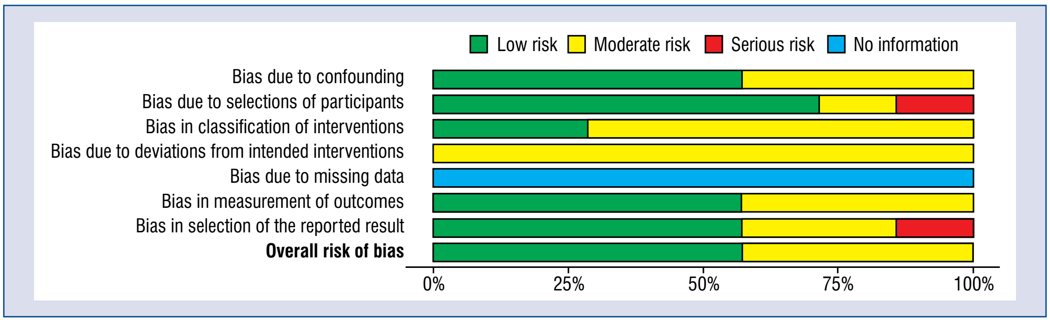

Figure 3. A plot of the distribution of review authors' judgements across randomized studies for each risk of bias item.

IHCA had decreased. This corresponds to a study performed by Miles et al. [34] in which there is statistically significant difference of survival rate of patients who suffered from IHCA during the COVID-19 pandemic and before the COVID-19 pandemic (3% vs. 13%; p = 0.007). Studies that consider both OHCA and IHCA reveal that during the pandemic phase, no less than 10% of all OHCAs and 16% of IHCAs were caused by SARS-CoV-2 infection. In these cases, mortality was higher, accordingly 3.4-fold in OHCA cases, and 2.3-fold in IHCA cases.

Sometimes results were ambiguous, as in the case of Yuriditsky et al. [38] where SARS-CoV-2 infection status did not bear any significance while considering ROSC as well as 30-day survivability rate. In comparison to some earlier publications, ROSC and 30-day survival was greater in IHCA that happened in COVID-19.

In some instances, such as in an analysis performed by Roedl et al. [35] even though the pandemic caused a decrease in number of hospital admissions, the incidence of IHCA was amplified and was occurring frequently in patients with COVID-19. Interestingly, contrary to other studies that are presented in the present meta-analysis, while compared to patients with non-COVID-19-related respiratory failure, the outcome was improved.

An interesting result comes from Tong et al. [37], which states that even after regulating for decreased comorbidity and elevated time to resuscitation team arrival, under the pandemic circumstances, ROSC in IHCA was hugely affected and its rate was considerably lower. It is worth

Table 2. Polled analysis of in-hospital cardiac arrest (IHCA) characteristics among pre- vs. intra-coronavirus disease 2019 (COVID-19) periods.

Parameter	No. of studies	Events		Events		Heterogeneity between trials		P-value for differences across groups
		Pre-COVID-19 period	COVID-19 period	OR	95% CI	P-value	I^2 statistic	
Female sex	4	36.6%	37.4%	0.95	0.68–1.32	0.04	63%	0.76
IHCA location:								
ICU	3	24.7%	17.5%	1.93	1.05–3.56	0.01	77%	0.03
ED	2	12.2%	17.1%	0.73	0.42–1.27	0.12	60%	0.27
Ward	3	39.0%	40.6%	0.58	0.58–2.49	< 0.001	95%	0.46
Comorbidities:								
Hypertension	1	58.3%	74.2%	0.49	0.26–0.92	NA	NA	0.03
CAD	2	25.3%	11.1%	2.69	2.00–3.63	0.38	0%	< 0.001
Diabetes	3	25.6%	16.4%	1.51	0.79–2.88	0.008	79%	0.21
Cancer	3	15.7%	10.8%	1.44	0.65–3.22	0.004	82%	0.37
Previous MI	2	13.3%	5.5%	2.84	1.18–6.80	0.28	13%	0.02
CKD	2	28.4%	27.5%	1.01	0.60–1.70	0.25	24%	0.96
Etiology:								
RI	2	9.7%	19.5%	0.31	0.03–3.51	< 0.001	98%	0.34
Acute MI	2	17.6%	6.4%	3.14	2.16–4.56	0.55	0%	< 0.001
Acute HF	1	3.4%	2.4%	1.44	0.32–6.57	NA	NA	0.64
Stroke	2	0.2%	0.6%	0.35	0.05–2.20	0.99	0%	0.26
Sepsis	2	10.8%	4.6%	3.34	2.04–5.48	0.77	0%	< 0.001
Witnessed arrest	2	76.0%	75.1%	1.13	0.90–1.42	0.83	0%	0.28
Shockable rhythm	5	17.6%	16.2%	1.11	0.71–1.72	0.10	48%	0.65
ALS treatment:								
Defibrillation	2	32.1%	28.9%	0.83	0.29–2.35	0.004	88%	0.72
Intubation	2	48.8%	41.2%	1.37	1.10–1.70	0.74	0%	0.005
MV	3	61.0%	49.1%	1.42	0.82–2.45	0.01	77%	0.22
Adrenaline	2	67.3%	67.9%	0.97	0.74–1.29	0.31	3%	0.86
Antiarrhythmics	2	13.9%	10.8%	1.32	0.95–1.84	0.88	0%	0.10
MCC	2	12.8%	10.8%	1.27	0.80–2.01	0.27	19%	0.31
TTM	2	7.1%	5.3%	1.82	0.54–6.07	0.04	76%	0.33
ECPR	1	6.0%	4.3%	1.41	0.37–5.43	NA	NA	0.33
Outcomes								
Cardiac re-arrest	2	25.4%	17.9%	1.61	0.89–2.89	0.23	32%	0.11
ROSC	5	47.4%	44.0%	1.36	0.90–2.07	0.007	71%	0.15
30-day mortality	1	59.8%	60.9%	0.95	0.75–1.22	NA	NA	0.69
Overall mortality	5	75.8%	74.7%	0.80	0.49–1.28	0.06	55%	0.69

ALS — advanced life support; CAD — coronary artery disease; CKD — chronic kidney disease; CI — confidence interval; ECPR — extracorporeal cardiopulmonary resuscitation; ED — emergency department; HF — heart failure; ICU — intensive care unit; MCC — mechanical chest compression; MI — myocardial infarction; MV — mechanical ventilation; NA — not applicable; OR — odds ratio; RI — respiratory failure; ROSC — return of spontaneous circulation; TTM — targeted temperature management

mentioning is that even patients who were not directly suffering from SARS-CoV-2 infection were also affected by the new resuscitation practice that was implemented in IHCA cases.

According to Aldabagh et al. [33] people suffering from COVID-19 are more prone to be more seriously affected by IHCA. Even the GO-FAR score underestimates the seriousness of SARS-CoV-2 in-

Table 3. Polled analysis of in-hospital cardiac arrest (IHCA) characteristics among severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) positive vs. negative groups.

Parameter	No. of studies	Events		Events		Heterogeneity between trials		P-value for differences across groups
		SARS-CoV-2 positive	SARS-CoV-2 negative	OR	95% CI	P-value	I^2 statistic	
Female sex	3	36.2%	39.0%	0.65	0.35–1.21	0.02	73%	0.17
IHCA location:								
ICU	3	36.4%	27.4%	1.69	0.62–4.56	< 0.001	86%	0.30
ED	3	13.0%	10.3%	1.55	1.05–2.27	0.36	2%	0.03
Ward	3	47.5%	46.3%	0.76	0.44–1.33	0.04	70%	0.34
Comorbidities:								
Hypertension	2	75.0%	69.2%	1.33	0.99–1.79	0.76	0%	0.06
CAD	3	19.2%	27.7%	0.34	0.14–0.84	0.008	79%	0.02
Diabetes	3	49.9%	26.6%	1.40	0.67–2.90	0.01	78%	0.37
Cancer	2	4.7%	7.4%	0.40	0.03–5.50	0.02	80%	0.50
Previous MI	1	1.4%	7.0%	0.58	0.17–1.99	NA	NA	0.38
CKD	1	9.1%	30.9%	0.22	0.08–0.66	NA	NA	0.007
Etiology:								
RI	1	12.5%	5.3%	2.57	1.08–6.14	NA	NA	0.03
Acute MI	2	1.4%	8.2%	0.16	0.04–0.65	0.97	0%	0.01
Stroke	1	1.4%	0.8%	1.99	0.18–22.29	NA	NA	0.58
Sepsis	1	0.0%	1.4%	0.43	0.02–8.10	NA	NA	0.57
Witnessed arrest	1	76.4%	82.8%	0.67	0.36–1.25	NA	NA	0.21
Shockable rhythm	3	9.6%	19.8%	0.51	0.35–0.73	0.62	0%	< 0.001
ALS treatment:								
Defibrillation	1	20.8%	30.2%	0.61	0.33–1.13	NA	NA	0.12
Intubation	1	48.6%	39.6%	1.44	0.86–2.42	NA	NA	0.17
MV	1	27.8%	49.1%	0.40	0.23–0.70	NA	NA	0.001
Adrenaline	1	68.1%	61.8%	1.32	0.76–2.29	NA	NA	0.32
Antiarrhythmics	1	8.3%	11.9%	0.67	0.27–1.67	NA	NA	0.39
MCC	1	8.3%	11.6%	0.69	0.28–1.73	NA	NA	0.43
TTM	1	0.0%	1.1%	0.56	0.03–10.90	NA	NA	0.70
Outcomes								
ROSC	2	33.9%	52.1%	0.47	0.30–0.73	0.32	1%	< 0.001
30-day mortality	2	77.2%	59.7%	2.08	1.28–3.38	0.85	0%	0.003
Overall mortality	3	94.9%	76.7%	3.20	0.98–10.49	0.02	73%	0.05

ALS — advanced life support; CAD — coronary artery disease; CKD — chronic kidney disease; CI — confidence interval; ED — emergency department; ICU — Intensive Care Unit; MCC — mechanical chest compression; MI — myocardial infarction; MV — mechanical ventilation; NA — not applicable; OR — odds ratio; RI — respiratory failure; ROSC — return of spontaneous circulation; TTM — targeted temperature management

fection and the rate of survival to hospital discharge is remarkably lower than in non-COVID-19 patients. In the current article, it is suggested that all these findings might be reasonably helpful in educating patients as well as healthcare professionals about risk factors that coincide with SARS-CoV-2 infection and may be useful in establishing new standards of treatment and the setting of code status designation.

Limitations of the study

There are several limitations to this review. Firstly, there is the small number of studies included in the meta-analysis, however, compared to the author's previous study, the number of patients included in the analysis was increased from 1,609 to 3,049 IHCA patients. The second limitation is the fact that in 4 studies, the authors truthfully point to IHCA data during the COVID-19 period, but do not classify these patients as SARS-CoV-2 positive and negative patients [32, 34, 35, 37].

Conclusions

In conclusion, in pre- vs. intra-COVID-19 periods no statistical difference was observed in ROSC, 30-day or overall mortality rate. However, during the COVID-19 pandemic, a positive SARS-CoV-2 result was associated with a lower incidence of ROSC and a higher 30-day mortality rate compared to SARS-CoV-2 negative patients.

Acknowledgments

The study was supported by the ERC Research Net and by the Polish Society of Disaster Medicine.

Conflict of interest: None declared

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