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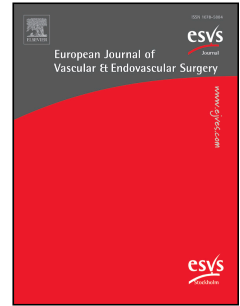

How does SARS-CoV-2 infection affect survival among patients with cardiovascular emergencies? A cohort study from a German insurance claims database

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1 # How does SARS-CoV-2 infection affect survival 2 among patients with cardiovascular emergencies? 3 A cohort study from a German insurance claims 4 database

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35 ## What this study adds

36 This large-scale analysis of nationwide and unselected health insurance claims data
37 covering 316,718 hospitalizations for cardiovascular and cerebrovascular
38 emergencies between January 2017 and October 2020 in Germany revealed an
39 association of the COVID-19 pandemic (for acute stroke) and confirmed SARS-CoV-
40 2 infection (for acute stroke, acute limb ischaemia, transient ischaemic attack) with
41 increased in-hospital mortality in patients admitted with cardiovascular and
42 cerebrovascular emergencies. These striking results add to the extremely limited
43 knowledge base concerning a possible relationship between COVID-19 and stroke.
44 Future studies are necessary to determine underlying causal factors.

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46 # Abstract (300 words)

47 **Objective:**

48 A previous study revealed a preliminary trend towards higher in-hospital mortality in
49 patients emergently admitted with acute stroke during the COVID-19 pandemic in
50 Germany. The current study aims to further examine the possible impact of a
51 confirmed SARS-CoV-2 infection on in-hospital mortality.

52 **Methods:**

53 This was a retrospective analysis of health insurance claims data from the second
54 largest insurance fund in Germany, BARMER. Patients hospitalized for ST-elevation
55 (STEMI) and non-ST-elevation (NSTEMI) myocardial infarction, acute limb ischaemia
56 (ALI), aortic rupture, acute stroke, or transient ischaemic attack (TIA) between
57 January 1, 2017, and October 31, 2020, were included. Admission rates per 10,000
58 insured and mortality were compared between March-June 2017-2019 (pre-COVID)
59 and March-June 2020 (COVID). Mortality rates were determined by the occurrence of
60 a confirmed SARS-CoV-2 infection.

61 **Results:**

62 A total of 316,718 hospitalizations were included (48.7% female, mean 72.5 years),
63 and 21,191 (6.7%, 95% CI 6.6-6.8%) deaths occurred. In-hospital mortality increased
64 during the COVID-19 pandemic when compared to the three previous years for
65 patients with acute stroke from 8.3% (95% CI 8.0-8.5) to 9.6% (95% CI 9.1-10.2)
66 while no significant changes were observed for STEMI, NSTEMI, ALI, aortic rupture,
67 and TIA. When comparing patients with confirmed SARS-CoV-2 infection (2.4%, 95%
68 CI 2.3-2.5) vs. non-infected patients, a higher in-hospital mortality was observed for
69 acute stroke (12.4% vs. 9.0%), ALI (14.3% vs. 5.0%), and TIA (2.7% vs. 0.3%) while

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no statistically significant differences were observed for STEMI, NSTEMI, and aortic rupture.

Conclusion:

This retrospective analysis of claims data provided hints for an association of COVID-19 pandemic with increased in-hospital mortality in patients with acute stroke. Furthermore, confirmed SARS-CoV-2 infection was associated with increased mortality in patients with stroke, TIA, and ALI. Future studies are urgently needed to better understand the underlying mechanism and relationship between the new coronavirus and acute stroke.

Keywords: COVID-19; Pandemics; Health Services Research; Myocardial Infarction; Stroke; Emergencies

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82
Introduction

83 The rapid spread of a new coronavirus (SARS-CoV-2) threw the global healthcare
84 system into turmoil.[1] Beginning with the implementation of infection control measures
85 during the first wave of the pandemic, the scientific community aimed to better
86 understand possible collateral damage in patients with emergent conditions.[2] In a
87 previous study using health insurance claims data, we observed declining admission
88 rates for cardiovascular and cerebrovascular emergencies in Germany.[3] These
89 findings confirmed the growing knowledge-base arising out of real-world data across
90 the globe.[4-8] Available outcome data in that previous study indicated a trend towards
91 increasing in-hospital mortality for acute stroke.[3] This observation was in line with
92 previous reports suggesting a particular impact of the pandemic on patients suffering
93 from neurovascular conditions.[4, 9-14]

94 Only a few months later, the world faces a second pandemic wave, and numerous
95 questions remain unanswered in front of this upcoming challenge.[15, 16] Due to the
96 complex multimorbidity of patients with cardiovascular and cerebrovascular
97 emergencies, these patients are known to be at particular risk for a SARS-CoV-2
98 infection and unfavourable outcomes.[17]

99 For the current study, we used large, updated health insurance claims data and
100 additional information on confirmed SARS-CoV-2 infection status to further illuminate
101 the impact of COVID-19 on in-hospital mortality. The research hypothesis was that
102 patients with cardiovascular and cerebrovascular emergencies experience worse
103 direct and indirect mortality during the COVID-19 pandemic.

104

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Methods

Study design

This was a retrospective analysis of routinely collected health insurance claims data. The details of the current analysis were published before.[3] In short, based on their primary diagnosis, we included all patients with inpatient treatment between January 1, 2017, and October 30, 2020, for cardiovascular and cerebrovascular emergencies. These included 1A) ST-segment elevation myocardial infarction (STEMI), 1B) non-ST-segment elevation myocardial infarction (NSTEMI), 2) acute limb ischaemia (ALI)[18], 3) acute aortic rupture, 4A) acute stroke and 4B) transient ischaemic attack (TIA) (for detailed coding see **Supplemental eTable 1**).

The available study data was compared between the three previous years (January 1, 2017, until December 31, 2019) and the time after the first disease outbreak news from the World Health Organization (WHO) had been issued (January 1, 2020, until October 30, 2020). To address seasonal effects in terms of in-hospital mortality, data collected during the heyday of the pandemic (COVID: March through June 2020) were additionally compared to a control period in the previous three years (pre-COVID: March through June 2017-2019). For the comparison of in-hospital mortality by SARS-CoV-2 infection status, corresponding data concerning confirmed infection status from March 1, 2020, and October 30, 2020 was available. The primary study endpoint was the in-hospital mortality among the patients admitted with cardiovascular and cerebrovascular emergencies by study period and confirmed SARS-CoV-2 infection status.

Sample and database

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128 The longitudinal data of Germany's second-largest insurance fund, BARMER,
129 includes the outpatient and inpatient medical care provided to up to 9 million (from
130 2008 to 2020) German citizens (10.8% of Germany's population) involving more than
131 24 million hospitalizations between January 1, 2008, and June 30, 2020. Details
132 concerning the database have been described in various previous studies.[3, 19-21]

133 **Study variables**

134 The diagnoses and comorbidities routinely collected in health insurance claims data
135 follow the commonly accepted international standard for reporting diseases and
136 health conditions using World Health Organization (WHO) International Classification
137 of Diseases in its 10th revision of the German Modification (ICD-10-GM) and
138 Operations and Procedures Codes (OPS) as a German adaptation of the
139 International Classification of Procedures in Medicine (ICPM) by WHO. The code
140 U07.1 was used to identify patients with confirmed (laboratory test, e.g. with
141 polymerase chain reaction or similar test) SARS-CoV-2 infection as per request of
142 the WHO since March 2020.

143 **Ethical considerations**

144 Our study complies with the Helsinki Declaration of 2013. Several review boards and
145 consensus guidelines determined that using anonymized data from claims or national
146 statistics retrospectively is not human subject research because de-identified
147 datasets were used.[22, 23]

148 **Statistical analysis**

149 We summarized baseline characteristics of the patients with means and standard
150 deviation for age and with percentages for discrete variables. A comparison of 95%
151 confidence interval (CI) and two-proportion z-test was used to test for differences.

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152 Rates per 10,000 insured were calculated on a monthly base. As sensitivity analysis,
153 we used both complete data from 2020 and data concerning only the four months
154 March to June 2017-2019 vs. 2020.

155 In-hospital mortality was calculated as proportion of deceased patients among all
156 patients with in-hospital stay during the study period in percent. The admission rate
157 was calculated as number of admissions per 10,000 insured patients in the same
158 time period.

159 Data processing was performed with software SAS version 9.04 (SAS Institute, North
160 Carolina, USA) and SPSS version 25 (IBM Corporation, New York, United States),
161 visualization was performed with software Adobe Illustrator version 24.1.2 (Adobe,
162 California, United States).

163

164 **Results**

165 We identified 316,718 hospitalizations (mean age 72.5 years, 48.7% females, 95% CI
166 48.6% to 48.9%) for cardiovascular or cerebrovascular emergencies between
167 January 1, 2017 and October 30, 2020 (monthly mean: 6,885 patients). Among all
168 hospitalizations, a total of 21,191 (6.7%, 95% CI 6.6% to 6.8%) deaths occurred.
169 84,106 hospitalizations were registered between March and June 2017-2019 and
170 25,024 hospitalizations were registered between March and June 2020.

171 Using data concerning the entire study period, the monthly hospital admission rate for
172 cardiovascular or cerebrovascular emergencies was 1.25 per 10,000 in mean and
173 decreased from 1.27 per 10,000 before 2020 to 1.15 per 10,000 in 2020.

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174 **Monthly hospital admissions for cardiovascular and cerebrovascular**
175 **emergencies between 2017-2019 and 2020**

176 When comparing the time period between 2017-2019 (pre-COVID-19) and 2020
177 (COVID-19), the hospital admission rates per 10,000 insured were for STEMI (0.72-
178 0.66/10,000; -9%), NSTEMI (1.59-1.48/10,000; -8%), ALI (0.49-0.45/10,000; -9%),
179 aortic rupture (0.05-0.04/10,000; -17%), acute stroke (3.46-3.24/10,000; -5%), and
180 transient ischaemic attack (1.32-1.18/10,000; -13%) (**Table 1 and 2**).

181 **Comparison of in-hospital mortality in patients admitted with cardiovascular**
182 **and cerebrovascular emergencies between 2017 and 2020**

183 When comparing the pooled four months (March to June) between 2017 and 2020,
184 the in-hospital mortality of patients admitted with acute stroke increased during the
185 COVID-19 pandemic when compared to the last three years from 8.3% (95% CI 8.0%
186 to 8.5%) to 9.6% (95% CI 9.1% to 10.2%). No statistically significant differences were
187 observed in patients admitted with STEMI, NSTEMI, ALI, aortic rupture, and TIA.
188 (**Table 3**). In-hospital mortality of patients admitted with acute stroke was negatively
189 associated with hospital admission rate. In patients admitted with STEMI, NSTEMI,
190 ALI, aortic rupture, and TIA, no association of in-hospital mortality with hospital
191 admission rate was observed.

192 **Comparison of in-hospital mortality in patients admitted with cardiovascular**
193 **and cerebrovascular emergencies by confirmed SARS-CoV-2 infection status**

194 Since the submission of a positive SARS-CoV-2 test result was requested by the
195 WHO and German authorities in March 2020, a total of 1,243 patients (2.4%, 95% CI
196 2.3% to 2.5%) were treated with confirmed infection among the cohort. The infection

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197 rate varied between 1.8% (95% CI 1.5% to 2.1%) in patients admitted with TIA and
198 3.0% (95% CI 2.7% to 3.3%) in patients admitted with NSTEMI (**Table 1 and 2**).

199 The in-hospital mortality of SARS-CoV-2 positive patients admitted with
200 cardiovascular and cerebrovascular emergencies was significantly higher when
201 compared to non-infected patients for acute stroke (12.4% vs. 9.0%), ALI (14.1% vs.
202 4.9%), and TIA (2.7% vs. 0.3%). No significant differences were observed in mortality
203 for patients admitted with STEMI, NSTEMI, and aortic rupture (**Figure 1**).

204 Discussion

205 In this large-scale retrospective analysis of health insurance claims from Germany,
206 the results suggested an ecological association between the COVID-19 pandemic
207 and increased in-hospital mortality in patients emergently admitted with acute stroke.
208 This association was apparent when comparing those treated during the pandemic
209 vs. previous years, while mortality rates were not statistically different during the
210 pandemic in all other included emergent conditions. Thereby, increasing mortality
211 rates in acute stroke patients were associated with a declining hospital admission
212 rate. At the patient level, confirmed SARS-CoV-2 infection status was associated with
213 higher in-hospital mortality in acute stroke as well as in ALI and TIA. These striking
214 results confirm previous international reports using real-world data from imaging
215 systems or registries.[4, 9-12]

216 **Kansagra et al.** used preliminary data from imaging software to analyse 231,753
217 patients treated at 856 hospitals in the United States from July through April 2020.
218 The authors observed a distinct decrease in the numbers of patients who underwent
219 acute stroke imaging by 39% during the COVID-19 pandemic.[4] While our previous
220 study on emergency admissions in Germany confirmed these declining presentations

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221 of patients with acute stroke, both studies unfortunately did not provide reliable
222 outcome data to further illuminate a possible relationship between COVID-19 and
223 short-term mortality. The current study provided complementary data on mortality by
224 SARS-CoV-2 infection status.

225 Interestingly, **Mao et al.** reported a case series of 214 patients with new coronavirus
226 disease treated in a known COVID-19 hotspot in Wuhan, China.[24] Neurologic
227 manifestations were common among infected patients, what suggests an association
228 between COVID-19 and acute stroke symptoms.[24] There is growing evidence for a
229 neuroinvasive potential of SARS-CoV-2, but it remains challenging to interpret the
230 direction of the interaction between acute stroke and SARS-CoV-2 infection using
231 data from clinical and administrative registries.[13, 25, 26] There is also evidence for an
232 increased rate of cryptogenic strokes possibly related to an acquired
233 hypercoagulability and mortality, what emphasizes the complex confounding in
234 available studies.[10] Having said this, future studies should further illuminate the
235 possible neurological impact of a confirmed SARS-CoV-2 infection.

236 To answer that question, **Ntaios et al.** recently initiated a global COVID-19 stroke
237 registry. The authors used data on patients with acute ischaemic stroke in 28 sites in
238 16 countries to perform a propensity score-matched comparison of COVID-19
239 positive vs. negative patients (n=336). An association between COVID-19 and severe
240 stroke was observed, further emphasizing the need for studies to uncover the
241 underlying relationship between both factors.[12] Notably, in another registry analysis
242 using data on almost 800 endovascular thrombectomies in Germany, the authors
243 found no changes in workflow time intervals, efficacy, and functional outcomes during
244 the COVID-19 pandemic when compared to 2019. However, only data from
245 experienced stroke centres were included while the nationwide reality also includes

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246 patients admitted to low-volume hospitals, what was also discussed in a survey
247 among stroke units in Germany.[27] Emphasizing a potential difference between both
248 cohorts, **Tiedt et al.** included fewer female patients with slightly higher age when
249 compared to the current study. Furthermore, the previous study was limited to
250 endovascular thrombectomies while this study included all-comers independently
251 from their treatment modality.[28] Another recent cross-sectional study of patients from
252 a large New York healthcare registry found that patients diagnosed with COVID-19
253 were at only 25% the odds of stroke compared to other patients, but these stroke
254 patients had a 9-fold increase in mortality.[29] Again, the current study could confirm
255 these findings.

256 In light of these previous studies, the current study findings suggest that the COVID-
257 19 pandemic has a negative impact on short-term outcomes in acute stroke patients
258 in Germany, although there are various confounders and a selection bias likely
259 interfering with the COVID-19-mortality relationship. It has been discussed that
260 patients with severe neurological symptoms will still be hospitalised while less
261 affected patients avoid emergency services.

262 Another interesting finding of the current study was related to the admission and
263 treatment of patients suffering from ALI.[18] In contrast to previous reports suggesting
264 an increasing rate of this emergency during the COVID-19 pandemic, the current
265 study observed rather stable admission rates.[30-32] However, the pronounced
266 association between confirmed SARS-CoV-2 infection and in-hospital mortality in
267 ALI-patients confirms that there is an underlying relation between both conditions.
268 From this study, it must be highlighted that the German healthcare system with its
269 distinct peculiarities in terms of hospital beds and intensive care infrastructure was
270 less affected than severely affected healthcare systems such as in Italy or Spain.

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271 **This study has limitations**. The retrospective observational design of the current
272 study does only allow to derive associations and to generate hypotheses valid for
273 Germany that should be addressed by prospective randomized studies in the future.
274 There are likely various confounders with possible impact on the relationship
275 between COVID-19 and in-hospital mortality in the affected target population.
276 Besides a direct impact of a SARS-CoV-2 infection on mortality, it appears also
277 possible that a changed staffing or infrastructure led to worse accessibility of care. It
278 remains unknown if a patient first got infected with SARS-CoV-2 and then developed
279 stroke, or the other way around. Moreover, the severity of the disease for the
280 admitted patients was not available. False positives in reverse transcription PCR
281 testing might additionally interfere with the results of the current study. Unfortunately,
282 the nature of the data and timeliness of the research question made adjusted
283 analyses impossible. Having said that, a significant selection with impact on central
284 conclusions cannot be ruled out. However, the striking observations made in the
285 current study and the circumstances during the ongoing health crisis emphasize the
286 importance to search for hypotheses in available data. Furthermore, due to the
287 topicality of the current study data, it may be possible that missing outcome data
288 introduces a possible selection bias. As sensitivity analysis, we used both complete
289 data from 2020 and data concerning only the four months March to June, where an
290 appropriate completeness was secured. Due to the ecological study design, we
291 cannot quantify to which extent the declining hospital admission rate potentially
292 explain higher acute stroke mortality. Yet, the fact that mean age and sex ratio were
293 largely stable over time in this patient group provides little evidence for this
294 hypothesis. Further, in-hospital mortality and COVID-19 time period were unrelated in
295 all other conditions included in this study. And finally, the direct impact of SARS-CoV-
296 2 infection on acute stroke mortality was visible at the patient level. Furthermore, a

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297 significant selection bias in the current study cannot be ruled out as only inpatients
298 admitted to legally endorsed hospitals were included. It appears possible that there is
299 a subgroup not covered because they decided not to use the emergency system.

300 The cardiovascular community should further support ongoing efforts to collect data
301 to protect our patients from evitable collateral damage.[33] With growing evidence for
302 an impact of COVID-19 on patients with acute stroke derived from real-world data,
303 we should pay particular attention to this vulnerable group. Increased awareness and
304 public recommendations to use emergency services may be reasonable.

305

306 **Conclusions**

307 This retrospective analysis of claims data provided hints for an association of COVID-
308 19 pandemic with increased in-hospital mortality in patients with acute stroke.
309 Furthermore, confirmed SARS-CoV-2 infection was associated with increased
310 mortality in patients with stroke, TIA, and ALI. Future studies are urgently needed to
311 better understand the underlying mechanism and relationship between the new
312 coronavirus and acute stroke.

313

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325 Peters (Research Group GermanVasc, University Medical Center Hamburg-
326 Eppendorf, Hamburg, Germany) for his scientific and biostatistical support.

327

328 Conflicts of Interest

329 The authors declare no conflicts of interest relevant for the current investigation.

330

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332 This work was not funded.

333

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334 ## Figure legends

335 Figure 1: In-hospital mortality as % and 95% confidence interval of patients treated
336 with cardiovascular (ST-elevation myocardial infarction [STEMI] or non-ST-elevation
337 myocardial infarction [NSTEMI]) and cerebrovascular (acute stroke or transient
338 ischaemic attack [TIA]) emergencies between March and October 2020 by the
339 occurrence of SARS-CoV-2 infection of no submitted infection (blue) or confirmed
340 SARS-CoV-2 positive infection (red). ALI = acute limb ischaemia. *p <.001 fortwo-
341 proportion z-test.

342

343 Supplementary material (title to be presented in html – do not edit the actual table in
344 the supplementary material file):

345 *Table S1: Coding criteria used for this retrospective observational study of health insurance claims.*
346
347
348

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Copy editors: please note that only the critical style editing has been made to these tables. Full copy editing is still needed. I have used green background color to highlight the edits that should be repeated in the following columns in the same row (or, in Table 3, in the following rows of the same column).

Tables

Table 1: Baseline characteristics of the cohort admitted to a legally endorsed German hospital between January 2017 and October 2020 for peripheral vascular emergencies.

	ALI		Aortic rupture		Acute stroke		TIA	
	2017 to 2019 n = 16 312	Jan-Oct 2020 n = 4 070	2017 to 2019 n = 1 662	Jan-Oct 2020 n = 397	2017 to 2019 n = 114 831	Jan-Oct 2020 n = 28 996	2017 to 2019 n = 43 758	Jan-Oct 2020 n = 10 537
Mean no. of hospital cases per month	453	407	46	40	3,190	2,900	1,216	1,054
Females	8 726 (53.5)	2,193, 53.9	609, 36.7	151, 38.2	63,501, 55.3	16,092, 55.5	26,079, 59.6	6,248, 59.3
Age -	72.6 ± 0.6	72.4 (0.7)	74.3 (1.6)	72.8 (2.9)	74.8 (0.5)	74.9 (0.7)	72.9 (0.7)	73.5 (0.6)
In-hospital mortality	969 (5.9) [5.6-6.3]	209, 5.1 (4.5-5.9)	711, 42.8 (40.4-45.2)	154, 38.8 (34.0-43.8)	9,738, 8.5 (8.3-8.6)	2,665, 9.6 * (9.1-10.2)	148, 0.3 (0.3-0.4)	42, 0.4 (0.3-0.5)
Monthly mean admission rate per 10 000 insured	0.49	0.45	0.05	0.04	3.46	3.24	1.32	1.18
Hospital cases with SARS-CoV-2 test	N/A	3,323	N/A	314	N/A	23,997	N/A	8,515
Thereof confirmed SARS-CoV-2 infection	N/A	63 (1.9) [1.5-2.4]	N/A	7, 2.2 (0.9-4.5)	N/A	588, 2.5 (2.3-2.7)	N/A	150, 1.8 (1.5-2.1)

Data are presented as n (%) [95% confidence interval] or mean ± standard deviation, unless stated otherwise. TIA: Transient ischaemic attack. ALI: Acute limb ischaemia; N/A = not available..

*p < .001 for comparison of 95% confidence interval and two-proportion z-test)

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Table 2: Baseline characteristics of the cohort admitted to a legally endorsed German hospital between January 2017 and October 2020 for cardiac emergencies..

	STEMI		NSTEMI	
	2017 to 2019 n = 24 078	Jan-Oct 2020 n = 5 931	2017 to 2019 n = 52 910	Jan-Oct 2020 n = 13 236
Mean no. of hospital cases per month	669	593	1,470	1,324
Females	8 957(37.2)	2,212, 37.3	21,957, 41.5	5,598, 42.3
Age - y	67.8 ± 0.6	67.8 (0.8)	73.1 (0.6)	72.9 (0.6)
In-hospital mortality	2,996 (12.4) [12.0-12.9]	723, 12.1 (11.4-13.1)	3,195, 6.0 (5.8-6.2)	728, 5.5 (5.1-5.9)
Monthly mean admission rate per 10,000 insured	0.72	0.66	1.59	1.48
Hospital cases with SARS-CoV-2 test - n	N/A	4 882	N/A	10,712
Thereof confirmed SARS-CoV-2 infection	N/A	117 (2.4) [2.0-2.9]	N/A	318, 3.0 (2.7-3.3)

Data are presented as n (%) [95% confidence interval] or mean ± standard deviation, unless stated otherwise. STEMI: ST-elevation myocardial infarction. NSTEMI: Non-ST-elevation myocardial infarction; N/A = not available

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Table 3: In-hospital mortality for patients admitted for cardiovascular and cerebrovascular emergencies in March, April, May, and June before (2017-2019) vs. during (2020) the COVID pandemic.

	Pre-COVID March to June 2017-2019	During COVID March to June 2020	Change - %
STEMI	11.8 (11.1-12.6)	11.6 (10.3-12.9)	-0.2
NSTEMI, % (95% CI)	5.7 (5.4-6.1)	5.4 (4.8-6.0)	-0.3
ALI, % (95% CI)	5.9 (5.3-6.6)	5.5 (4.4-6.7)	-0.4
Aortic rupture, % (95% CI)	43.0 (38.9-47.1)	38.1 (30.4-46.2)	-4.9
Acute stroke, % (95% CI)	8.3 (8.0-8.5)	9.6 (9.1-10.2)	+1.3 *
TIA, % (95% CI)	0.3 (0.2-0.4)	0.3 (0.2-0.5)	+/-0

Data are presented as % [95% confidence interval].STEMI: ST-elevation myocardial infarction. NSTEMI: Non-ST-elevation myocardial infarction. ALI: Acute limb ischaemia. TIA: Transient ischaemic attack.

*p <.001 for two proportion z-test.

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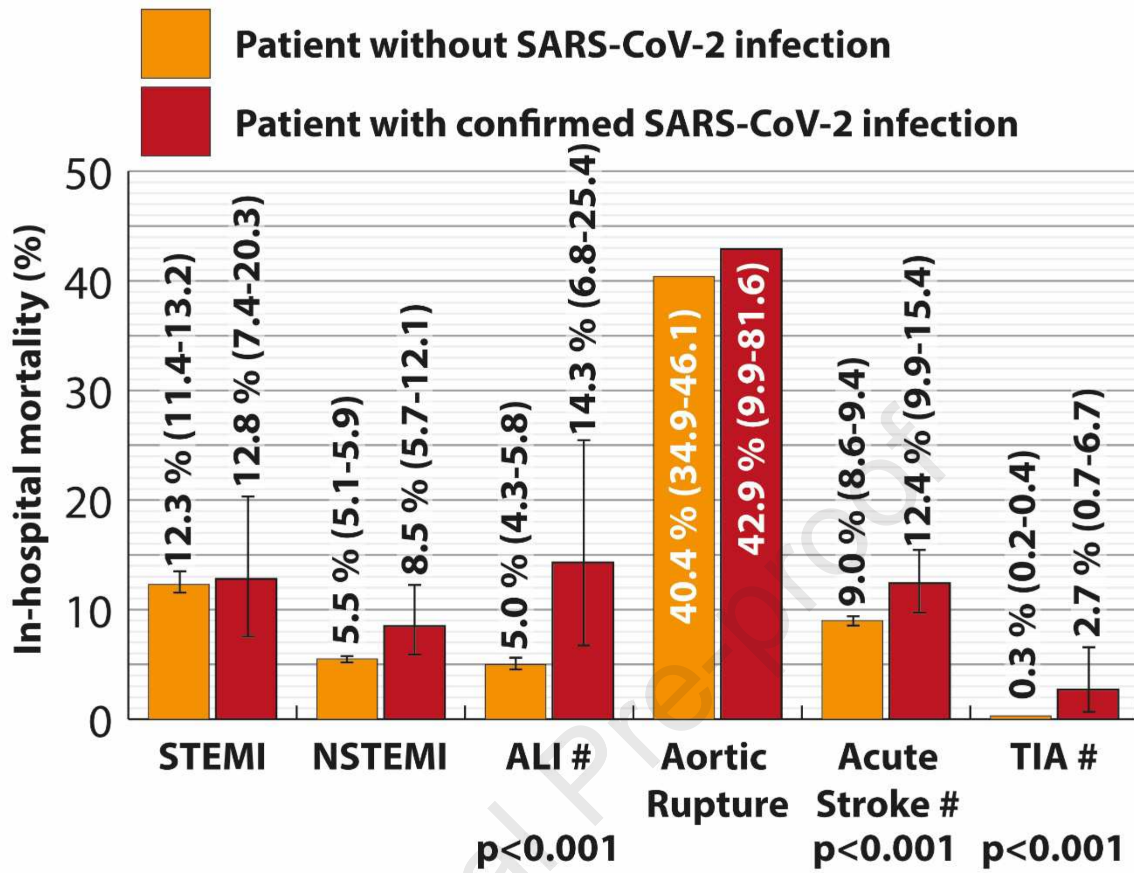
Figures



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-Please check that the supplementary table 1 will be entitled analogously in the main text and in the supplementary material (e.g. Supplementary Table S1).

-Short title: Cohort Study: SARS- CoV-2 Infection and Survival with Cardiovascular Emergencies

-Fig 1, produce in ¾ page width. Remove background lines. Change label for y-axis: “In-hospital mortality - %”. In x-axis, write “rupture” and “stroke” with lower case first letters. Delete p<0.001 from x-axis. Change # to * in x-axis. Move colour labels below the graph area, use smaller and non-bold font. Change yellow to blue. Keep red in journal’s red. Keep numbers for bars, but write them in smaller font and non-bold, and remove %-symbols (e.g. the first number for STEMI should read “12.3 (11.4 – 13.2)”.

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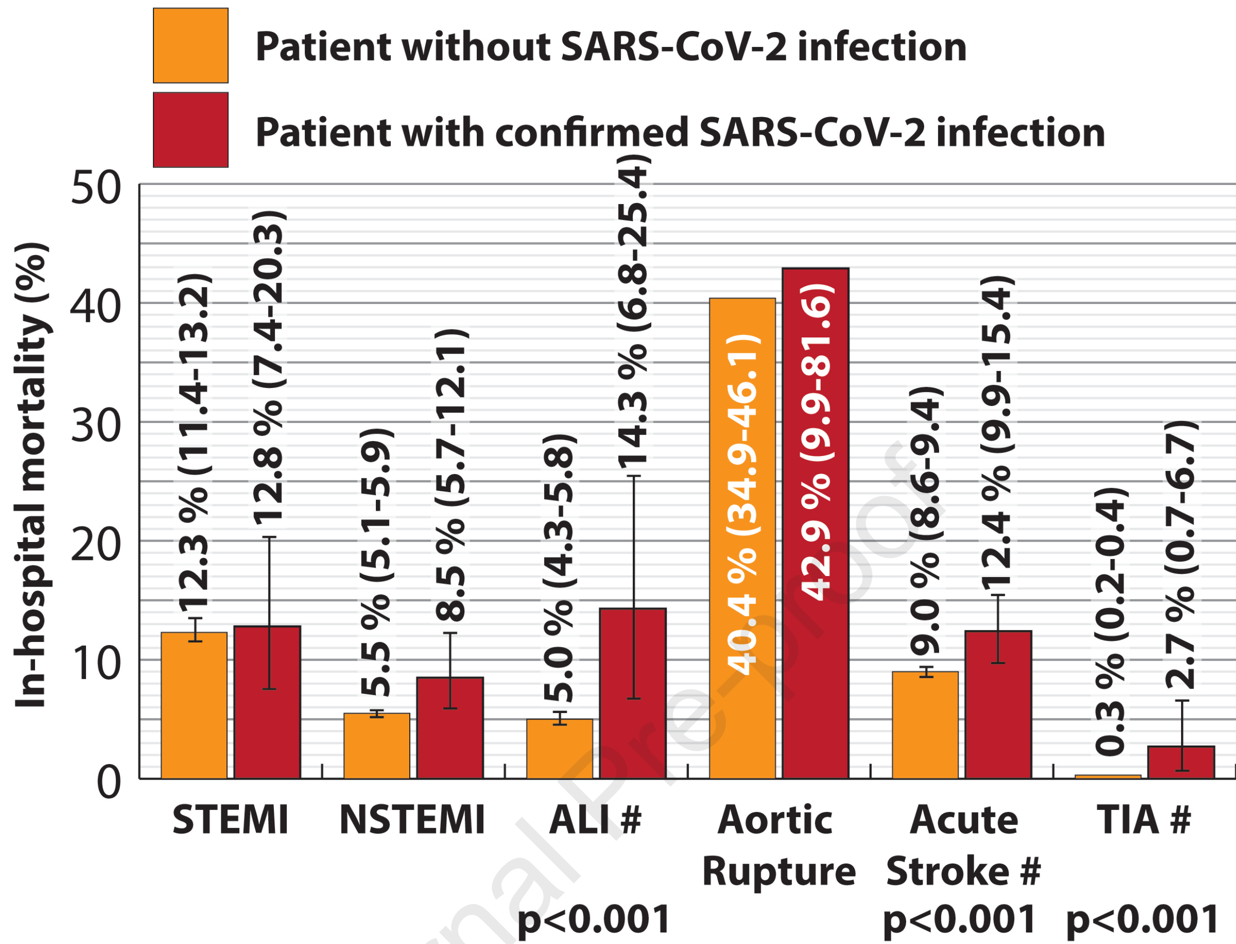

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