Significant increase in the incidence of high-risk pulmonary embolism during the COVID-19 shutdown: the pandemic response causes serious collateral consequences

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Research

Keywords: COVID-19, high-risk pulmonary embolism, delay in hospital admission

Posted Date: July 27th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-46099/v1

Version of Record: A version of this preprint was published at European Journal of Internal Medicine on December 1st, 2020. See the published version at https://doi.org/10.1016/j.ejim.2020.10.007.

Abstract

Background

Strict stay-at-home rules, along with fear of coronavirus infection, have kept many patients from timely seeking medical attention during the novel coronavirus disease (COVID-19) pandemic. This situation may have led to an increase in the number of patients arriving at hospital in deteriorated clinical condition. In this regard, we aimed to investigate the incidence of pulmonary embolism (PE) patients defined as high-risk according to the European Society of Cardiology (ESC) presenting at our emergency department during the shutdown.

Methods

A retrospective data analysis explored the impact of the COVID-19 shutdown on the presentation of acute PE patients admitted to University Hospital Graz, Austria. We compared percentages of high-risk PE patients admitted during shutdown and during two control periods: the corresponding period in 2019 and an earlier period in 2020. By including data from the previous year, a general increase of high risk PE cases in 2020 compared to 2019 was ruled out. Risk assessment was carried out in accordance with current ESC guidelines for the diagnosis and management of acute PE.

Results

The percentage of patients with high-risk PE increased significantly during the COVID-19 shutdown period compared to the two control periods ($p = 0.003$; $p = 0.011$). Time from onset of symptoms to hospital admission was significantly longer in the study period compared to the control periods ($p = 0.046$ and $p = 0.044$, respectively).

Conclusion

The current findings indicate a significant increase in high-risk PE cases as well as delayed hospital admission of symptomatic PE patients during the COVID-19 shutdown period.

Background

When the novel coronavirus disease (COVID-19) started to spread globally in December 2019 and COVID-19 related deaths continued to increase rapidly, the World Health Organization (WHO) subsequently announced that this will be a crisis that will touch every aspect of our lives and the outbreak was declared a pandemic (1). As a reaction, country-wide shutdowns were initiated by governments around the world, including curfews and strict restrictions on social contact. After several weeks of ongoing shutdown in Austria, physicians observed a worrying trend: The strict measurements requiring people to stay at home

as well as the fear of contracting the virus obviously stopped patients from going to a hospital or consulting a general practitioner (2). As a result, patients presented very late or, if earlier, symptoms were frequently misjudged as “COVID-19-like”, which may thus in some cases have led to even more serious health conditions than those caused by a true infection with the novel coronavirus (3).

Pulmonary embolism (PE) is a leading cause of death worldwide. However, early diagnosis and subsequent initiation of anticoagulant treatment is of the utmost importance to reduce morbidity and mortality in these patients (4–9). Especially since the widespread use of direct oral anticoagulant medication (10, 11), treatment of PE is more feasible for both physicians and patients. The European Society of Cardiology (ESC) has established its treatment guidelines for PE and updated the guidelines in 2019 (12). In these guidelines, assessment of PE-related severity and risk of early death is based on clinical presentation and factors contributing to haemodynamic collapse in acute pulmonary embolism, reflecting acute right ventricular (RV) dysfunction. In addition, patients with pre-existing diseases such as cancer, chronic heart failure or pulmonary disease might also be at increased risk of early death (12, 13). In case of haemodynamic instability, patients are classified as high-risk indicating massive PE with severely reduced hemodynamic reserve. For these patients, a rapid systemic fibrinolytic therapy is recommended to reduce risk of cardiovascular collapse and early death (12, 14).

We aimed to investigate the incidence of PE patients defined as high-risk according to the European Society of Cardiology (ESC) at our emergency department in the period from March 16 to April 30, 2020 (forty-six days) during the countrywide shutdown that was initiated by the Austrian government to prevent further spread of the novel corona virus and to avoid collapse of the healthcare system.

Methods

We performed a retrospective data analysis from our medical records of the impact of COVID-19 shutdown on the diagnosis and treatment of acute PE at the emergency department of the University Hospital Graz, Austria. In accordance with the 2019 guidelines of the European Society of Cardiology (ESC) for the diagnosis and management of acute PE, risk assessment was carried out separating patients into four groups: low risk (LR), intermediate low risk (IML), intermediate high risk (IMH) and high risk (HR). The study period of interest was the time between the day when the Austrian government implemented aggressive containment efforts (March 16, 2020) and the day when containment efforts ended (April 30, 2020). We compared percentages of patients admitted with high risk PE between the shutdown period and two control periods when no pandemic was present: a corresponding period during the previous year (March 16 to April 30, 2019) and an earlier period during the same year (January 1 to February 15, 2020). In addition, to show that there is no general increase in 2020 compared to 2019 or seasonal effect, we included the corresponding period of the previous year (January 1 to February 15, 2019). As COVID-19 might be an additional risk factor for PE, the co-existence of a COVID-19 infection was excluded by reverse-transcriptase–polymerase-chain-reaction (PCR) assay obtained from nasal and pharyngeal swab specimens before admission. Furthermore, the time from onset of symptoms to

hospital admission was documented. The study protocol was approved by the Ethics Committee (EK 32–399 ex 19/20) of the Medical University of Graz.

Statistical Analysis

The primary outcome was incidence of high-risk PE in the defined time periods and the secondary outcome time from symptomatic PE to hospital admission. Data are presented as absolute and relative frequencies or as median and interquartile range (IQR, 1st to 3rd quartile). We assessed differences between the two time periods of the respective year (e.g. January 1 – February 15 (period 1) 2020 vs. March 16 – April 30 (period 2) 2020) as well as between the respective time periods in the two years (e.g. period 2 of 2019 vs. period 2 of 2020). We performed Fisher's exact test or Mann-Whitney U test. A p-value < 0.05 was considered statistically significant. The statistical analysis was conducted using R version 3.6.1 (https://www.r-project.org).

Results

We observed a slightly higher number of patients admitted to the hospital due to PE in 2020 (26 in period 1, 27 in period 2) compared to 2019 (19 in period 1, 22 in period 2) (Table 1). The main finding of our retrospective data analysis is a significant increase in the number of patients admitted to the hospital during the shut-down period (period 2 of 2020, 33.3%) due to life-threatening high-risk PE compared to the respective time period of 2019 (0%, $p = 0.003$) and period 1 of 2020 (3.8%, $p = 0.011$), whereas there were no significant differences between the two control time periods in 2019 (5.3% in period 1 vs. 0% in period 2, $p = 0.463$) or between the years 2019 and 2020 regarding period 1 (5.3% in 2019 vs. 3.8% in 2020, $p = 1.000$) (Table 1) (Fig. 1). A systemic fibrinolytic therapy was applied in six of the nine (66.7%) high-risk PE patients in period 2 of 2020. In three (33.3%) of the high-risk patients, fibrinolytic therapy was waived due to severe comorbidities, contraindications or an unfavourable prognosis. In period 1 of 2019 and 2020 there was one high risk PE necessitating fibrinolytic therapy each; no high-risk PE was observed in period 2 of 2019.

Table 1
Risk assessment, time between onset of symptoms to hospital admission and outcome during the four different time periods

	Period 1 2019 (N = 19)	Period 2 2019 (N = 22)	Period 1 2020 (N = 26)	Period 2 2020 (N = 27)	p[a]	p[b]	p[c]	p[d]
Risk[e]					0.011	0.003	0.463	1.000
HR	1 (5.3%)	0 (0.0%)	1 (3.8%)	9 (33.3%)				
IMH	3 (15.8%)	6 (27.3%)	4 (15.4%)	3 (11.1%)				
IML	8 (42.1%)	8 (36.4%)	11 (42.3%)	8 (29.6%)				
LR	7 (36.8%)	8 (36.4%)	10 (38.5%)	7 (25.9%)				
Symptoms (days)					0.044	0.046	0.096	0.068
Median (Q1, Q3)	1.0 (1.0, 2.5)	2.0 (1.0, 4.8)	2.0 (1.0, 4.8)	4.0 (2.5, 7.0)				
Outcome					1.000	0.495	-	1.000
alive	19 (100.0%)	22 (100.0%)	25 (96.2%)	25 (92.6%)				
death	0 (0.0%)	0 (0.0%)	1 (3.8%)	2 (7.4%)				

[a] Comparison of period 1 2020 and period 2 2020

[b] Comparison of period 2 2019 and period 2 2020

[c] Comparison of period 1 2019 and period 2 2019

[d] Comparison of period 1 2019 and period 1 2020

[e] p-values are for the comparison of HR vs. rest

The days from onset of symptoms to hospital admission were significantly higher in the shutdown period (median 4.0, IQR 2.5-7.0) compared to period 2 of 2019 (2.0, 1.0-4.8, p = 0.046) and period 1 of 2020 (2.0, 1.0-4.8, p = 0.044), respectively. There were no significant differences between the two periods of 2019 (1.0, 1.0-2.5 vs. 2.0, 1.0-4.8, p = 0.096) or periods 1 of 2019 and 2020 (1.0, 1.0-2.5 vs. 2.0, 1.0-4.8, p =

0.068). (Table 1) (Fig. 2) We observed three deaths in total, two in period 2 of 2020 and one in period 1 of 2020. (Table 1)

Discussion

Since December 2019, when the first case of COVID-19 was reported in China, it spread rapidly, taking on pandemic proportions and affecting the whole world (15–18). Considering the fear of the virus and the horrifying reports from many countries, on March 16, 2020 the Austrian government implemented aggressive containment efforts such as social distancing, self-isolation and quarantining to relieve the healthcare system and to curb the spread of the virus. Overwhelmed by the anticipated impact of COVID-19, all medical resources have been directed towards the COVID-19 pandemic, while depriving other patients of important medical procedures or therapies (3, 18). So far, many people are concerned about the economic collateral damage, however, little is known about health-related collateral consequences caused by the social shutdown (18). Metzler et al. recently reported a decline in acute coronary syndrome admissions in Austria since the outbreak of COVID-19 (2), which might be a perilous response to the pandemic. In our daily clinical practice, we have noticed a worrying number of non-COVID-19 patients being seriously affected by the current pandemic. We observed a significant increase in high-risk PE admissions to our hospital. Several factors might explain this important observation. These include patients´ misinterpretation of PE-related symptoms such as sudden shortness of breath, coughing, dyspnea or sharp chest pain as being related to an acute respiratory infection. Given the strict containment efforts as well as the fear of a nosocomial infection, people with such symptoms have potentially stayed at home longer, thus cases of low-risk PE possibly progressed to a potential life-threatening high-risk PE-situation. PE is a leading cause of death worldwide, but especially since the widespread use of direct oral anticoagulant medication (10, 11), it seems to be a preventable cause of death among hospitalized patients (9). Early diagnosis and immediate initiation of treatment, as demonstrated in several clinical trials (6–12), are mandatory in reducing the associated risk of serious life-threatening problems or even death in PE patients. Fortunately, the majority of our patients survived after administration of fibrinolytic therapy. However, this kind of treatment is precluded for selected patients meeting high-risk PE criteria as defined by ESC guidelines for the clinical management of PE due to its high bleeding risk (13).

In 2003, when the outbreak of severe acute respiratory syndrome (SARS) took the world by surprise, researchers also made similar observations (19, 20). In efforts to prevent further disease transmission, extraordinary infection control measures limited access to hospitals and medical doctors (20, 21). While the emergency decisions were successful in controlling the outbreak, they also created collateral consequences that may not have been considered when SARS outbreak focused strategies were initially developed (20). Planned surgeries were cancelled, resulting in a significant increase in numbers of patients awaiting cardiac surgery (21), cancer treatments were interrupted (22) and poor advanced planning led to a haphazard selection of patients requiring medical care (23). Although there is no long-term data on the impact of such measures on population health available, researchers in 2003 already warned that this could be a serious problem in future pandemics (24).

Regarding our data, it is conceivable that such delays could have had a large impact on individual outcomes. In the selected control periods in early 2020 and 2019, only one high risk PE each occurred, but the numbers of intermediate risk patients were similar, indicating that delay in treatment leads to an increase in PE severity, thus also leading to an increase in PE mortality. Furthermore, we observed a slightly higher number of patients admitted to the hospital due to PE in the shutdown period than in the control periods. The percentage of low-risk patients was lower in the shutdown period, possibly indicating that in the control periods low-risk patients had been able to be treated on an outpatient basis as they had milder disease progressions because they consulted a general practitioner sooner. This observation also underlines our assumption that delays in seeking medical attention might lead to disease progressions.

In the current situation of a rapidly and widespread disease outbreak, healthcare decision-makers understandably focus on immediate actions to prevent further disease transmission. This is not meant to be a criticism of the decisions made, since decisions in such exceptional times are extremely challenging and require great courage and responsibility, but we have to emphasize that other critically ill patients should not be undertreated.

Although currently only limited data is available, first observations suggest a decline or a delay in the admission of critically ill patients to the hospital during the shutdown period. As there is no comparable previous experience, the actual long-term consequences after the COVID-19 crisis cannot be estimated. The fact that the current situation prevents patients, even those with life-threatening conditions, from hospital admission might lead to an increase in mortality caused by non-COVID-19 reasons. In a recent publication, Italian researchers made similar observations to Metzler et al. in Austria, and in addition emphasized a significant increase in mortality during the shutdown period that was not fully explained by COVID-19 cases alone (25).

Our study has several limitations since it is based on a retrospective data analysis and was based on a single centre. However, our results should encourage other researchers to address this important research question in further studies.

In conclusion, a significant increase in high-risk PE patients together with delayed hospital admission of symptomatic patients was observed during the COVID-19 shutdown period.

Ethical Approval and Consent to participate

The study protocol was approved by the Ethics Committee (EK 32–399 ex 19/20) of the Medical University of Graz.

Declarations

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Consent for publication

The Authors grant the Publisher the sole and exclusive license of the full copyright in the Contribution, which license the Publisher hereby accepts.

Availability of supporting data

Not applicable

Competing interests

The authors declare that there is no conflict of interest regarding the publication of this article

Funding

This research article received no funding

Author Contributions

All authors have contributed significantly to the paper, they understand and endorse it. They have read and approved the version being submitted for publication.

Acknowledgements

Not applicable

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Figures

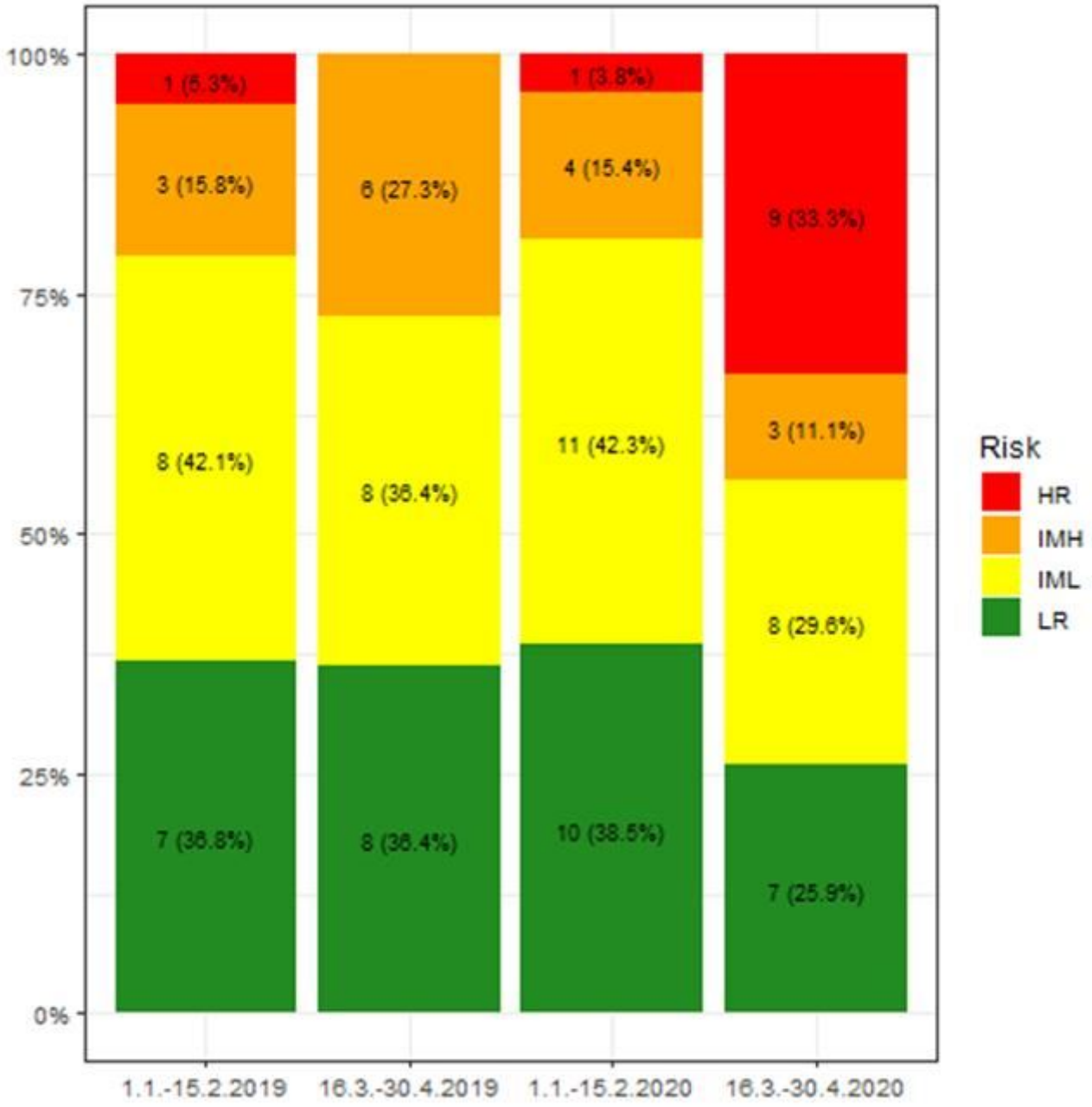

Figure 1

Distribution of risk groups within the four time periods.

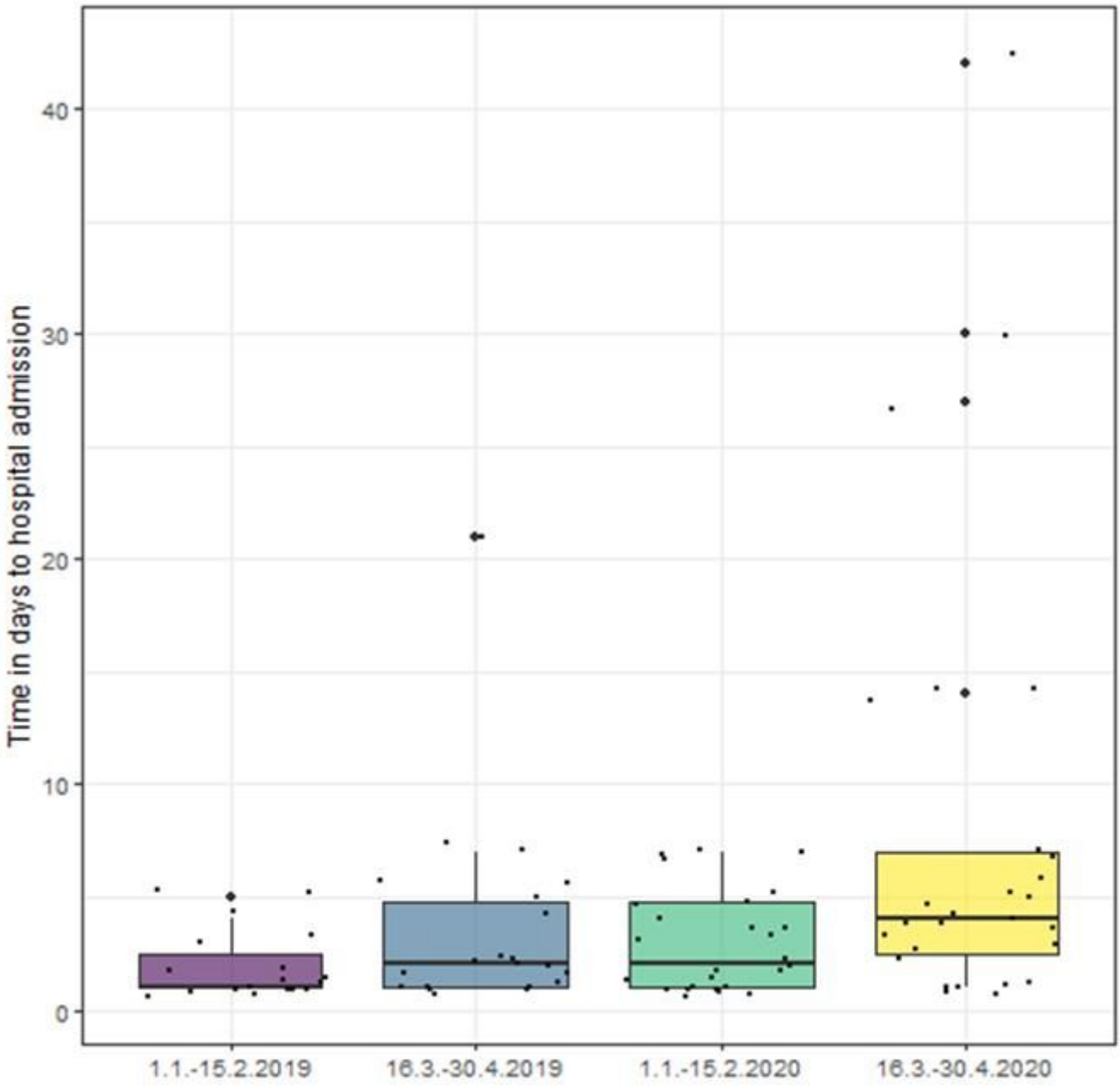

Figure 2

Boxplots showing the time lag between the onset of symptoms and hospital admission for the four time periods.