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Outcomes of surgical treatment for active infective endocarditis under COVID-19 pandemic

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Abstract

Background: The coronavirus disease 2019 (COVID-19) pandemic has been and will continue to be a challenge to the healthcare system worldwide. In this context, we aimed to discuss the impact of the COVID-19 pandemic on the diagnosis, timing, and prognosis of surgical treatment for active infective endocarditis (IE) during the pandemic and share our coping strategy.

Methods: A total of 39 patients were admitted for active IE in the year 2020. The number of the same period last year was 50. Medical information of these two groups was extracted from our surgical database. Data were compared between the two groups and differences with or without statistical significance were discussed.

Results: In the pandemic year, we admitted fewer transferred patients (64.1% vs. 80%, $p = .094$). Timespan for diagnosis were prolonged (60 vs. 34.5 days, $p = .081$). More patients were admitted in emergency (41% vs. 20%, $p = .030$) More patients had heart failure (74.4% vs. 40%, $p = .001$), sepsis (69.2% vs. 42.0%, $p = .018$), or cardiogenic shock (25.6% vs. 8.0%, $p = .038$). Overall surgical risk (EuroSCORE II) was higher (4.15% vs. 3.24%, $p = .019$) and more commando surgery was performed (7.7% vs. 2.0%, $p = .441$). However, we did not see more postoperative complications, and early mortality was not worse either (0 vs. 4%, $p = .502$).

Conclusions: The negative impact of the COVID-19 pandemic on the clinical practice of surgical treatment for active IE was multifaceted. However, with the preservation of the effectiveness of multidisciplinary IE surgical team, the early outcomes were comparable with those in the normal years.

KEYWORDS
aortic valve, commando surgery, COVID-19, infective endocarditis, mitral valve

1 | INTRODUCTION

It has been a year since the outbreak of pneumonia caused by the 2019 novel coronavirus disease (COVID-19). As of January 31, 2021, there have been 102,083,344 confirmed cases of COVID-19, including 2,209,195 deaths reported globally, and a total of 10,877 confirmed cases and 4823 confirmed deaths across China.[1] In the past year, our healthcare system has stood the unprecedented test of the COVID-19 pandemic by centralizing most of the medical resources for the prevention and control of the pandemic. However,

Abbreviations: COVID-19, corona virus disease 2019; CT, computerized tomography; CTA, computerized tomography angiography; ECMO, extracorporeal membrane oxygenation; EuroSCORE, European System for Cardiac Operative Risk Evaluation; HACEK, including *Haemophilus*, *Actinobacillus*, *Cardiobacterium*, *Eikenella* and *Kingella*; HF, heart failure; IABP, intra-aortic balloon pump; IE, infective endocarditis.; PUMCH, Peking Union Medical College Hospital; qRT-PCR, quantitative real-time polymerase chain reaction; TTE, transthoracic echocardiography.

the issue of infective endocarditis (IE) should not be neglected under the COVID-19 pandemic. IE is associated with a mortality rate of more than 20%, and 50% when surgery is indicated and not performed.[2,3] An accurate diagnosis and timely surgical decision are extremely important for reducing the mortality of IE. Our study aims to discuss the impact of the COVID-19 pandemic on the diagnosis, surgical timing, and early prognosis of surgical treatment for active IE during the pandemic year and share our experience.

2 | PATIENTS AND METHODS

Peking Union Medical College Hospital (PUMCH) is located in Beijing. As the capital of China, the situation here has been grim for the prevention and control of COVID-19. During the past year, provinces like Hubei have been temporarily classified as high-risk districts. Transfer of patients from high-risk districts was either obstructed or delayed. Under these circumstances, our coping strategy for the practice of IE surgery is described in Figure 1. As a febrile illness, IE outpatients were screened for COVID-19 with quantitative real-time polymerase chain reaction (qRT-PCR), IgG/IgM antibodies, and chest computerized tomography (CT) before admission. For patients with high body temperature, the COVID-19 screening was done in specialized fever clinics where a rapid response team for COVID-19 consisted of specialists from infectious, respiratory, intensive care, and anesthesiology department and an extracorporeal life support team was ready for initiation. The patient would be quarantined, and the rapid response team would be initiated immediately if the diagnosis of COVID-19 infection was confirmed. Otherwise, if COVID-19 was excluded, patients were allowed to be admitted. After admission, the routine preoperative workup for IE like echocardiography, coronary computerized tomography angiography (CTA), or head CT was performed. Indication and timing for cardiac surgery were determined by a multidisciplinary team consisting of cardiac surgeons, cardiologists, infectious physicians, neurologists, nephrologists, intensive care specialists, and an extracorporeal life-supporting group with the principles of 2015 ESC guidelines for IE treatment.[3] Surgeries for patients with acute large cerebral infarction or intracranial hemorrhage were postponed till 2 weeks after onset. Inpatients with new-onset preoperative fever were screened once more for COVID-19 infection before surgery, unless in salvage cases.

This study was approved by the Institutional Review Board. Informed written consent was obtained from all patients. Between January 20, 2020, when COVID-19 was first declared an epidemic in China, and January 19, 2021, a total of 39 patients were admitted to our referral center due to active IE with surgical indication and underwent cardiac surgery. The total patient number of the same time period last year was 50. The medical information documented in our surgical database specially designed for IE patients was reviewed and the demographic characteristics, severity of symptoms, surgical risk and indications, surgery timing, and early prognosis of the two groups were compared.

Statistically, continuous variables were reported as median (interquartile range) since our data disobeys normal distribution. Categorical variables were reported as counts (percentages). For each descriptive variable, we tested if a statistically significant difference exists between the two groups; Mann–Whitney U test or χ^2 test was conducted for continuous or categorical variables, respectively.

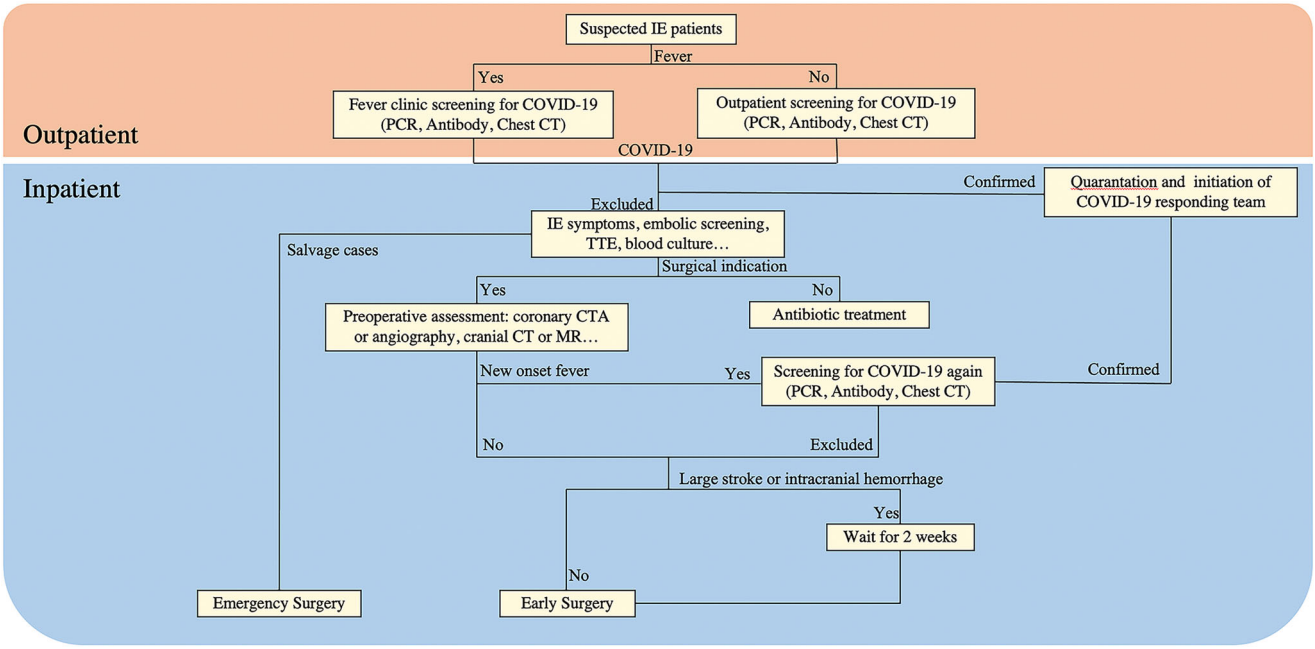

FIGURE 1 Flowchart of the preoperative management of suspected infective endocarditis (IE) patients during the COVID-19 pandemic. CT, computerized tomography; COVID-19, coronavirus disease 2019; CTA, computerized tomography angiography; MR, magnetic resonance; PCR, polymerase chain reaction; TTE, transthoracic echocardiography

Statistics were performed using the SPSS software, version 25 (PSSFW, SPSS, IBM). $p < .05$ was considered statistically significant.

3 | RESULTS

The pandemic of COVID-19 broke out in the winter of 2019, and the severity of the epidemic in China peaked in February 2020. The nationwide social distancing policy and traffic restriction policy for high-risk districts managed to subdue the increasing spread of the total number of confirmed COVID-19 cases. However, the number of newly admitted IE patients per month was stable despite the changing situation of the pandemic nationwide (Figure 2).

Thanks to the strict prevention and control measures, no COVID-19 infection was confirmed among our IE surgical patients (Table 1). However, the practice of diagnosis and surgical treatment for active IE was impacted in multiple aspects. Diagnosis efficiency seemed to be impacted by the COVID-19 pandemic. The interval between the first symptom onset and the definite diagnosis of IE was longer in the 2020 group (60 vs. 34.5 days), though the difference was not significant ($p = .081$). Patients' admission was also impacted, the absolute number of IE patients who underwent cardiac surgery in the COVID-19 pandemic year was 39, less than 80% of that of the year 2019, which was 50. This year we admitted more native patients than the year 2019, while fewer referral patients were transferred from provinces outside Beijing (64.1% vs. 80%, $p = .094$). Moreover, the rate of emergency admission this year was statistically higher than that of the last year (41% vs. 20%, $p = .030$). Detailed patients' characteristics are listed in Table 1. Proportion of males (76.9% vs. 76.0%, $p = .919$) and mean age (47.5 vs. 47.1, $p = .905$) were similar between the two groups. Prosthetic valve IE were not more frequently seen in the pandemic year (10.3% vs. 6.0%, $p = .730$). The spectra of infected valves were not significantly different between the two groups. Aortic and mitral valves were involved most frequently. Aortic valve infection was seen in 51.3% of the 2020 group and 52.6% of the 2019 group, respectively. Mitral valve infection was seen in 66.7% of the 2020 group and 51.1% of the 2019 group. No differences were found in the percentage of multivalve infection between the two groups (28.2% vs. 27.7%, $p = .955$). The proportion of healthcare-associated IE was also similar (79.5% vs. 84.0%, $p = .582$). Etiology of IE infections in the year 2020 was not different from that in 2019, with oral streptococci being the most common pathogen (43.6% vs. 50%, $p = .548$). *Staphylococcus aureus* infection was seen in 12.8% of the 2020 group, while 10.0% in the 2019 group. Difference was not significant ($p = .936$).

As for symptoms of IE, more patients complained of symptomatic heart failure (HF) at admission in the pandemic year (74.4% in 2020 vs. 40% in 2019, $p = .001$). More patients had sepsis (69.2% vs. 42.0%, $p = .018$) and cardiogenic shock (25.6% vs. 8.0%, $p = .038$) before surgery. The percentage of IE with only echocardiography

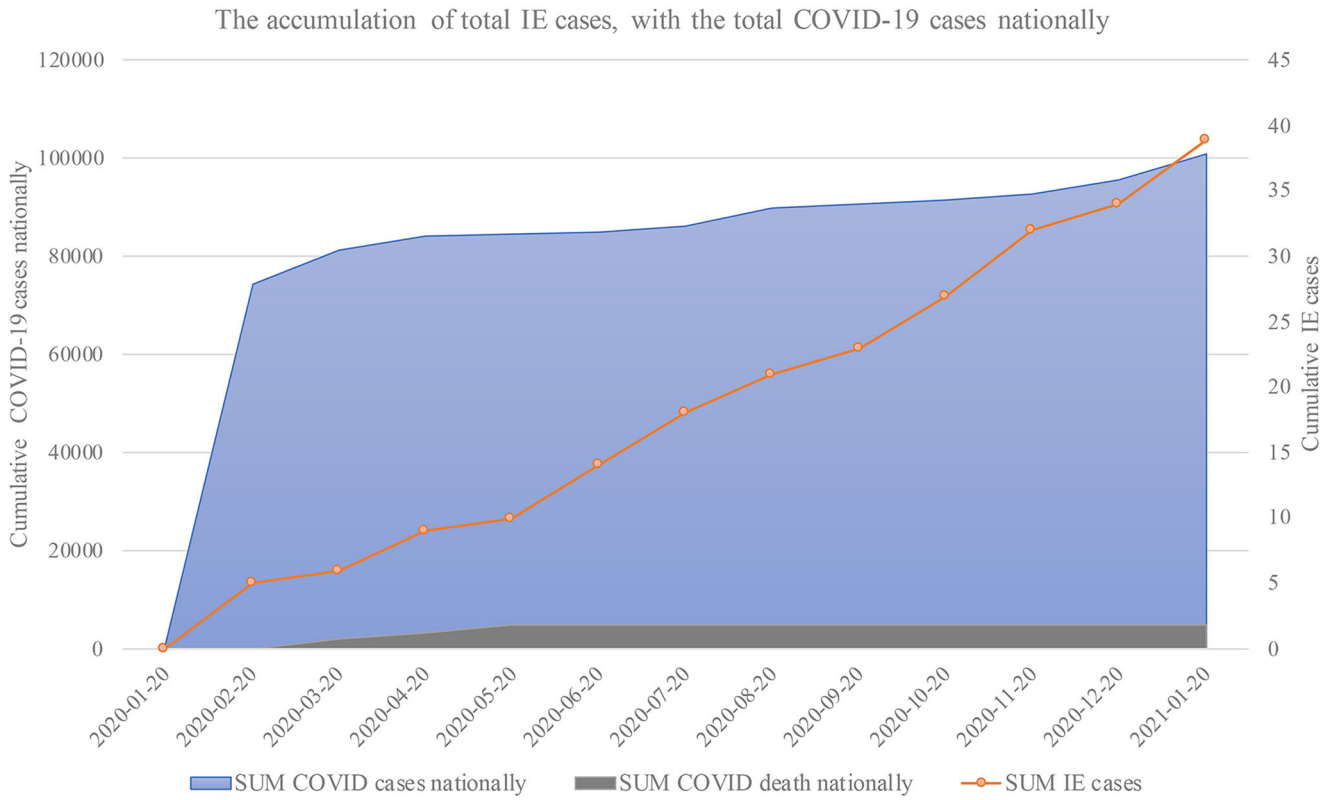

FIGURE 2 Graphical representation of the accumulative number of patients who underwent surgeries for active IE, with the accumulation of total COVID-19 cases and COVID-19-related deaths nationally. The pandemic was most serious around February, while the monthly increase of IE surgical cases was steady. COVID-19, coronavirus disease 2019; IE, infective endocarditis

TABLE 1 Patients' characteristics

	2020 (*N* = 39)	2019 (*N* = 50)	*p* value
Demographics			
Male	30 (76.9%)	38 (76.0%)	.919
Age	47.5 ± 14.4	47.1 ± 16.9	.905
Source of patients (Transferred)[a]	25 (64.1%)	40 (80%)	.094
Admission pathway (Emergency)[b]	16 (41%)	10 (20%)	.030
Type of IE			
Native valve IE	35 (89.7%)	46 (88%)	1.000
Native nonvalve IE	0	3 (6.0%)	.335
Prosthetic valve IE	4 (10.3%)	3 (6.0%)	.730
Valve (some patients had more >1 infected valve)			
A	20 (51.3%)	30 (52.6%)	.897
M	26 (66.7%)	24 (51.1%)	.144
T	9 (23.1%)	5 (10.6%)	.120
P	2 (5.1%)	1 (2.1%)	.869
More than one	11 (28.2%)	13 (27.7%)	.955
Acquisition of IE			
Healthcare-associated IE	31 (79.5%)	42 (84.0%)	.582
Etiology			
Oral streptococci	17 (43.6%)	25 (50%)	.548
Streptococcus gallolyticus (S. bovis)	1 (2.6%)	2 (4.0%)	1.000
Staphylococcus aureus	5 (12.8%)	5 (10.0)	.936
Coagulase-negative staphylococci	2 (5.1%)	4 (8.0%)	.912
Enterococci	1 (2.6%)	1 (2.0%)	1.000
HACEK group	0	1 (2.0%)	1.000
Fungi	1 (2.6%)	1 (2.0%)	1.000
Others	2 (5.1%)	4 (8.0%)	.912
Unknown	8 (20.5%)	9 (18.0%)	.765
Symptoms (some patients had >1 symptoms)			
Asymptomatic valve disorder[b]	9 (23.1%)	29 (28.0%)	.001
Symptomatic HF[b]	29 (74.4%)	20 (40.0%)	.001
Renal Failure	6 (15.4%)	10 (20.0%)	.782
Shock	10 (25.6%)	4 (8.0%)	.038
Sepsis	27 (69.2%)	21 (42.0%)	.018
Local cardiac complication	8 (20.5%)	10 (20%)	.952
Embolic complication	16 (41.0%)	20 (40.0%)	.922
COVID-19 infection			

Abbreviations: HACEK, including *Haemophilus*, *Actinobacillus*, *Cardiobacterium*, *Eikenella* and *Kingella*.

[a]Difference between the two groups was not statistically significant but was considered potentially meaningful and was also discussed.

[b]Difference between the two groups was statistically significant.

features of valve malfunction other than symptomatic HF was significantly lower in 2020 (23.1% vs. 58.0%, $p = .001$). The percentage of local cardiac and embolic complications did not show significant differences between the two groups.

Although symptoms were more severe for the 2020 group, the surgical decision and timing were similar between the two groups. Information about surgery is listed in Table 2. The commonest indication for cardiac surgery was valve malfunction with or without HF, seen in 87.2% of patients in 2020 and 90% in 2019. More patients underwent surgery due to persistent infection in the pandemic year than in 2019 (28.2% vs. 12.0%, $p = .054$). We assessed the surgical risk preoperatively using the European System for Cardiac Operative Risk Evaluation II (EuroSCORE II) and Carlson Comorbidity Index. The EuroSCORE II of 2020 patients were significantly higher than that of 2019 patients (4.15% vs. 3.24%, $p = .019$) (Figure 3). Perivalve abscess was found in 20.5% patients in the 2020 group and 12.0% in the 2019 group ($p = .380$). Commando surgery was done in 7.7% of 2020 patients and 2.0% of 2019 patients, respectively. The difference was not significant ($p = .441$). Median CBP time was 123 min for the 2020 group and 133 min for the 2019 group, without significant difference ($p = .625$). Postoperatively, 7.7% patients had cardiac vasoplegic syndrome (CVS) in the 2020 group and 12.0% had CVS in the 2019 group ($p = .726$). Delayed extubation happened in 23.1% of the 2020 group and 26.0% of the 2019 group; the difference was not significant. One patient of the 2019 group used IABP and ECMO because of the postoperative acute coronary syndrome and did not survive. There was no in-hospital mortality in the 2020 group, while the in-hospital mortality of the 2019 group was 4.0%. The difference was not statistically significant ($p = .502$). Length of postoperative hospital stay was not significantly different between the two groups (10 vs. 11 days, $p = .469$). One patient of the 2020 group underwent a redo surgery in the second month of follow-up due to a malfunction of the repaired valve and one patient of the 2019 group underwent a redo surgery at 6 months because of prosthesis reinfection.

4 | COMMENT

As a major referral center for infective endocarditis in north China, Peking Union Medical College Hospital usually admits patients from all over the country. The outbreak of the COVID-19 pandemic compelled redistribution of medical resources. Therefore, the diagnosis, admission, workup, and surgical treatment for active IE patients were impacted in many aspects. First, the nationwide social distancing policy and traffic restriction policy targeted to high-risk districts constituted a barrier to patients seeking medical care and inter-hospital transport. Patients with high body temperature had to undergo COVID screenings repeatedly during their referral process before they got the definite diagnosis of IE. As a result, the start of intravenous antibiotics treatment and the diagnosis of IE could be delayed, and the general condition of patients could be worse at admission. Second, as a febrile disease, the differential diagnosis from COVID-19 was necessary whenever patients present new onset of fever during the treatment after the diagnosis of IE, which means

TABLE 2 Surgical information

Timing			
Symptom to diagnosis (days)	60 (28, 113)	34.5 (16.5, 65.25)	0.081
Indication to Surgery (days)	6 (3, 12,5)	6 (4, 7)	0.656
Indications (some patients had >1 indication)			
Valve malfunction with or without heart failure	34 (87.2%)	45 (90.0%)	0.936
Uncontrolled infection	11 (28.2%)	6 (12.0%)	0.054
Prevention of embolism	27 (69.2%)	32 (64.0%)	0.604
Others (Prosthesis, devices, or other cardiac malformation)	12 (30.8%)	12 (24.0%)	0.475
Surgical Risk Model			
EuroSCORE II (%)[a]	4.15 (2.73, 8.37)	3.24 (1.83, 5.04)	0.019
Charlson comorbidity index	2 (1, 3)	2 (0, 3.25)	0.629
Surgery			
CBP time (min)	123 (103, 175)	133 (98, 194)	0.625
Multivalve surgery	12 (30.8%)	16 (32.0%)	1.000
Perivalve abscess	8 (20.5%)	6 (12.0%)	0.380
Commando surgery	3 (7.7%)	1 (2.0%)	0.441
Postoperative complications			
Vesoplegic syndrome	3 (7.7%)	6 (12.0%)	0.726
Mechanical ventilation > 72 h	9 (23.1%)	13 (26.0%)	0.808
Dialysis	6 (15.4%)	5 (10.0%)	0.525
ECMO	0	1 (2.0%)	1.000
In-hospital mortality	0	2 (4.0%)	0.502
Length of stay (days)	10 (7, 14)	11 (7.25, 15.5)	0.469
Redo during follow-up	1 (2.6%)	1 (2.0%)	1.000

Abbreviation: EuroSCORE, European System for Cardiac Operative Risk Evaluation II.

[a]Difference between the two groups was statistically significant.

another round of screening. Thirdly, routine preoperative examinations were more time-consuming for patients presenting with a fever as the equipment and examination room had to be sterilized repeatedly. These factors made it challenging for cardiac surgeons to practice surgical treatment for active IE patients and may partly explain why more patients had sepsis and cardiogenic shock before surgery during the COVID pandemic.

IE is a complicated disease that can present with a large variety of nonspecific symptoms, making it challenging to be diagnosed timely. The interval between the onset of the first symptom and definite diagnosis can be long. Although this interval was reported to be shorter in literature (2–15 days),[4] our data were quite different. The diagnosis of IE seems to be more time-consuming in China. Most of our patients were first visited community clinics complaining fever and received short courses of suppressive, other than curative antimicrobials. Most patients do not seek comprehensive medical evaluation until severe complications or HF occur. This could be the reason for delayed diagnosis in IE. Nevertheless, we found the diagnosis was even more delayed under the COVID-19 pandemic. Traffic restriction policy in high-risk districts could be a barrier to patient transfer and referral process. In the early phase of the pandemic, patients from other provinces have to be quarantined for 14 days before admission. Moreover, outpatients with fever had to be tested by qRT-PCR and chest CT to exclude the diagnosis of COVID-19 first;[5,6] the average timespan for receiving the test results was longer than 24 h. These factors could explain why the diagnosis of IE was more delayed this year than in the year 2019.

Our data showed the absolute number of patients were less than last year. Less transferred patients from other provinces were admitted. Moreover, the proportion of emergency admission raised significantly. Early studies focusing on IE diagnosis under the pandemic also found a reduction in the absolute number of IE episodes and the percentage of transferred patients.[7,8] These changes indicated that the diagnosis and referral process of IE patients were

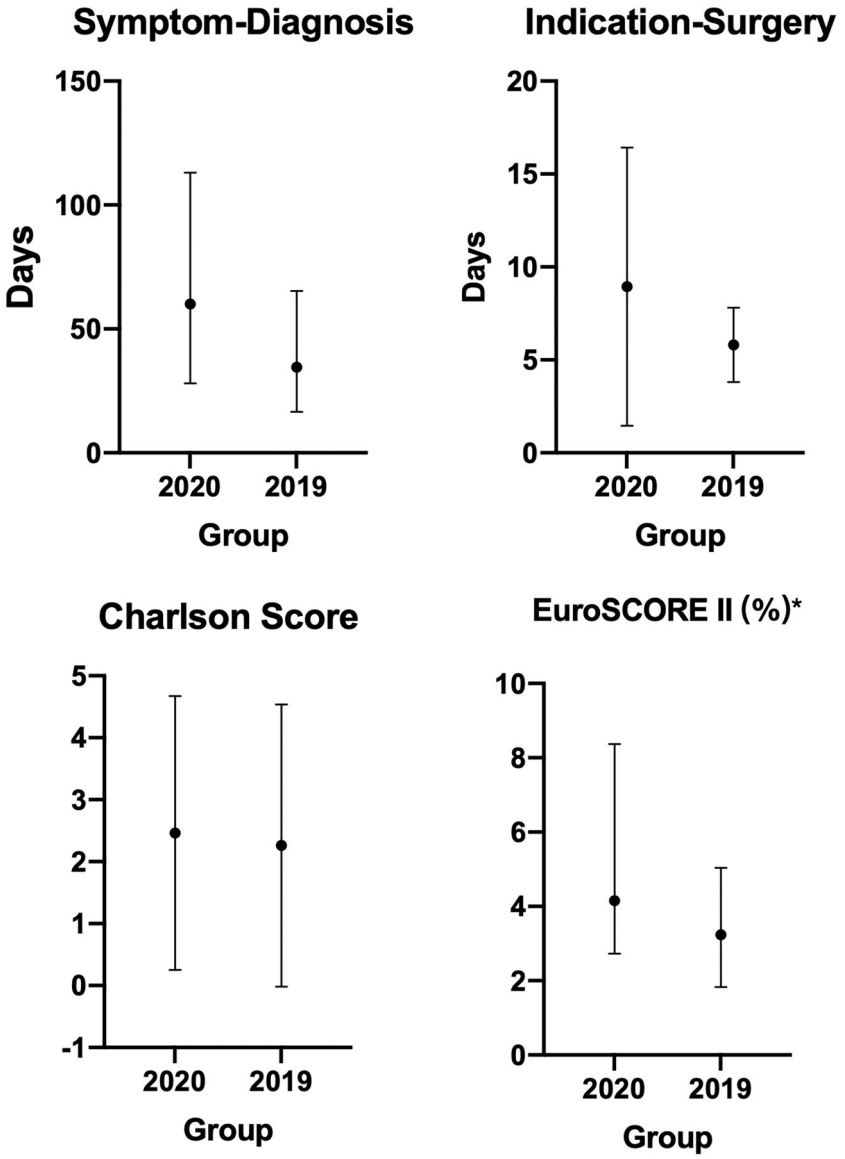

FIGURE 3 Mann–Whitney *U* test was conducted for continuous variables, indicating that the timespan for diagnosis was prolonged (60 vs. 34.5 days, $p = .081$). Surgical timing was not impacted (6 vs. 6 days, $p = .656$), while surgical risk (EuroSCORE II) raised significantly (4.15% vs. 3.24%, $p = .019$). Charlson comorbidity score was similar between the two groups

disturbed and delayed by the pandemic. In the case of IE, delayed diagnosis and referral process can cause sudden deterioration.[9] More patients deteriorated and ended up visiting the emergency room, which may explain the rise of emergency admission.

Our data referring to IE symptoms and surgical risks corroborated the hypothesis that the COVID-19 pandemic contributed to the delay and deterioration of IE patients. More patients had symptomatic HF, sepsis, or cardiogenic shock at admission during the pandemic. EuroSCORE II of 2020 IE patients also raised significantly compared to that of 2019. The percentage of multivalve infections did not increase. However, we performed commando surgery for three patients in 2020 and one patient in 2019. Although the difference was not statistically significant, which is attributed partly to sample size limitation, this may indicate that the local infection aggravated because of the delay due to the pandemic. Data from surgical indication also supported the point, as more patients underwent surgeries because of persistent infection. Since inpatients had been screened for COVID-19 by qRT-PCR, antibody, and chest CT before admission, they did not need to be screened again unless in cases of new onset of unexplainable fever. Moreover, the nasopharyngeal swab collection for afebrile inpatients can be performed bedside with personal protective equipment for the relevant medical staff. In that case, the interval between indication and surgery was not prolonged during the pandemic year.

We have organized a multidisciplinary IE surgical team since 2012, including cardiac surgeons, cardiologists, infectious physicians, neurologists, nephrologists, intensive care specialists, and an extracorporeal life-supporting group. During the COVID-19 pandemic, weekly video meetings were held every Saturday morning to discuss details about surgical indication, timing, and perioperative management for active IE patients due to the social distancing policy. Efforts were made to adhere to the principle of early surgery for active IE patients. In that case, we did not find more postoperative complications or in-hospital mortality in the pandemic year than in the prepandemic era. Early outcomes of our IE surgical patients of the pandemic year was not worse than that of the year 2019.

5 | STUDY STRENGTHS AND LIMITATIONS

This retrospective study summarized and analyzed the impact of the COVID-19 pandemic on the diagnosis, indication, timing, risk, and early prognosis of surgical treatment for active IE during the past year and proposed our coping strategy. However, the study is limited by its retrospective nature. As a single-centered retrospective study, all our patients were diagnosed, operated on, and cared perioperatively by our multidisciplinary team in PUMCH. Moreover, we must be aware of the uncertainty around this evolving pandemic and the regional variability around the world. All these factors may reduce the credibility and impact the extrapolation of our conclusions.

6 | CONCLUSIONS

The negative impact of the COVID-19 pandemic on the clinical practice of surgical treatment for active IE was multifaceted. The diagnosis, early treatment, and referral for IE patients were delayed by the pandemic. Patients admitted to referral centers were in more critical condition. Overall surgical risk raised significantly and more high-risk surgeries like the commando surgery were performed. However, with the preservation of the effectiveness of multidisciplinary IE surgical team through online meetings, and by adhering to the principle of early surgery for active IE, the early outcomes were comparable with those in the normal years.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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