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Early respiratory outcomes following cardiac surgery in patients with COVID-19

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Abstract

Background: Both coronavirus disease (COVID-19) and cardiac surgery have a negative impact on pulmonary function. This study aimed to determine the postoperative respiratory outcomes of patients with COVID-19 who underwent cardiac surgery.

Methods: In this retrospective study, we reviewed and analyzed the patient characteristics and clinical data of 25 asymptomatic patients with COVID-19 who underwent urgent or emergency cardiac surgery at Tehran Heart Center Hospital, Iran, between 29 February and 10 April 2020.

Results: The mean age, EuroSCORE, and body mass index were 57.3 ± 15.1 years, 6.65 ± 1.29, and 25.7 ± 3.7 kg/m^2, respectively. Four patients underwent off-pump cardiac surgery and 21 underwent on-pump cardiac surgery with a median cardiopulmonary bypass time of 85 minutes (interquartile range (IQR, 50-147). The overall mortality rate and the length of stay in the intensive care unit (ICU) were higher compared to those of a propensity-matched group of patients who underwent cardiac surgery in the pre-COVID era. The median intubation time was 13 hours (IQR, 9.5-18), which was comparable to that of pre-COVID cardiac surgery patients. The readmission rate to the ICU was 16%. In this ICU readmitted group, the mean oxygen index, FiO_2, and mortality rate were higher and the PaO_2/FiO_2 ratio was lower than those of the nonreadmitted patients.

Conclusions: Although early respiratory outcomes of asymptomatic COVID-19 patients who underwent early cardiac surgery appeared to be satisfactory, compared to the propensity-scored matched non-COVID group, the postoperative outcomes were worse, especially in the ICU readmitted patients. We suggest postponing cardiac operations unless the patient requires emergency surgery.

KEYWORDS

cardiac surgery, COVID-19, outcomes, respiratory

1 | INTRODUCTION

On 11 March 2020, the World Health Organization (WHO) declared the coronavirus disease (COVID-19) as a pandemic. Unfortunately, Iran was one of the worst affected countries. COVID-19 mainly affects the lungs. Approximately 80% of symptomatic patients with COVID-19 develop the mild disease, while 15% develop severe disease with hypoxemia, dyspnea, and tachypnea, and 5% become critically ill with respiratory failure, septic shock and/or multiorgan dysfunction.[1] Abnormalities are visible on chest computed tomography (CT) in 85% of patients.[2] The majority of patients with the severe respiratory disease require invasive mechanical ventilation.[3] Inflammatory renal and lung diseases, such as acute respiratory distress syndrome (ARDS) and acute renal failure are serious complications of both COVID-19 and cardiopulmonary bypass (CPB).[3,4] There are few studies regarding the clinical outcomes of patients with COVID-19 in the intensive care unit (ICU). ICU mortality is between 22% and 66% in nonsurgical patients.[3,5] In a recent large case series in Italy, the mortality rate of patients admitted to ICU was about 26%.[3] There is little information available about the clinical outcomes of surgical COVID-19 patients. The surgery itself and mechanical ventilation have negative impacts on the lung. CPB aggravates these injuries even further in cardiac surgery patients.[6] In a retrospective cohort study of general surgical COVID-19 patients, all had lung CT abnormalities after surgery, and the mortality rate in ICU was 20.5%.[7] Studies about airway management during surgery in patients with COVID-19 are rare, and we based our strategies on the recommendations and suggestions of experts.[8] Experts recommend a lung protection strategy for intubated COVID-19 patients, similar to that in other ARDS patients[9,10]; we tried to apply these recommendations in the best possible way in the management of our patients. We were unable to find any study that focused on the postanesthesia respiratory outcomes of cardiac surgery patients. Our study aimed to explore the early postoperative respiratory outcomes of asymptomatic patients with COVID-19 who underwent urgent or emergency surgery at the discretion of the cardiac surgeons and cardiologists of our hospital. We hope that this study will provide useful information on the postoperative respiratory course of patients with COVID-19 who undergo cardiac surgery.

2 | MATERIALS AND METHODS

2.1 | Patients

In this retrospective study, the baseline characteristics and clinical data of patients with COVID-19 who underwent urgent or emergency cardiac surgery at Tehran Heart Center Hospital, Iran, between 29 February and 10 April 2020, and fulfilled our study criteria were reviewed and analyzed. Informed consent was obtained from all patients regarding using their medical information for research purposes. This study was approved by the research committee of the Tehran Heart Center for medical record review. The COVID-19 diagnosis was confirmed by a team comprising of a radiologist, an infectious disease specialist, and an intensivist, based on positive reverse transcription-polymerase chain reaction (RT-PCR) tests and/or chest CT according to the WHO interim guidance.[10] All of the patients were asymptomatic from their time of admission to the operating room and were receiving hydroxychloroquine and azithromycin. In addition, some were also prescribed antiviral drugs. General anesthesia was induced with routine anesthetic drugs. On-pump cardiac surgery was done in 21 (84%) patients, while four patients (16%) had off-pump surgery. The types of operations were diverse, and the majority of the patients had a coronary artery bypass graft (CABG) or combined CABG-valve surgeries with a mean graft number of 2.17 (Table 1). The patients received routine post-cardiac surgery care and monitoring in the cardiothoracic ICU. The ventilator parameters were adjusted by anesthesiologists and intensivists, according to the hemodynamic, respiratory, and arterial blood gas indices. A tidal volume of 6 to 8 mL/kg ideal body weight and different amounts of positive end-expiratory pressure (PEEP) were used. Depending on the clinical condition of the patient, our ICU early extubation protocol strategy was followed as much as possible. Fluid management was based on hemodynamic monitoring indices, urine output, and clinical judgment. A conservative volume strategy was applied as much as possible (Table 2). The baseline characteristics and clinical data of this cohort of patients were compared with 50 propensity-matched non-COVID-19 cardiac surgical patients that underwent emergency or urgent cardiac surgery from 1 November 2019 to 30 December 2019 at our hospital.

2.2 | Data collection

The patient characteristics and other relevant data were collected from the medical records. Furthermore, the ICU flow sheets and the data of the pre-COVID-19 cardiac surgery patients were retrieved from our surgery database. Data of patients that were 18-years old or younger had active respiratory disease, renal and hepatic failure, or a history of uncontrolled respiratory diseases were excluded. Hemodynamic and respiratory parameters, average fluid balance over 3 days, serum creatinine, postoperative bleeding, reopening of the chest due to surgical complications, amount of received packed red blood cells, and blood components were collated from the ICU flow sheets. EuroSCORE II was used for the risk stratification of the patients.[11]

2.3 | Outcomes

Our primary respiratory outcomes were extubation failure rate, intubation time, PaO_2/FiO_2 ratio, oxygen index, and the mean airway pressure (MAWP). Other outcomes included length of stay in ICU (ICU LOS), rate of readmission to ICU, acute kidney injury (AKI), and mortality within 30 days of surgery. The PaO_2/FiO_2 ratio and oxygenation index calculated from the computation of PaO_2, FiO_2, and MAWP variables were based on their specific formula. The severity of ARDS

TABLE 1 Baseline characteristics of cardiac surgery patients with COVID-19 disease

Variables	Total (n = 25)	Nonreadmitted (n = 21)	Readmitted (n = 4)	*P* value
Age, y	57.33 ± 15.13	56.87 ± 15.99	59.75 ± 10.87	.735
Sex				
Male	18 (72)	17 (81)	1 (25)	.053
Female	7 (28)	4 (19)	3 (75)	
BMI, kg/m^2	25.75 ± 3.72	25.7 ± 3.8	25.6 ± 3.5	
DM	10 (40)	8 (38.1)	2 (50)	.999
HTN	14 (56)	12 (57.1)	2 (50)	.999
Smoking	5 (20)	5 (23.8)	0	.549
Opioid	3 (12)	3 (4.3)	0	.999
EuroSCORE II	6.56 ± 1.29	6.38 ± 1.24	7.50 ± 1.29	.114
LVEF, %	43.12 ± 8.32	12.14 ± 8.00	50.00 ± 8.66	.128
History of respiratory disease	4 (16)	4 (19)	0	.999
Anesthesia time, h	4.70 ± 1.32	4.62 ± 1.38	5.13 ± 1.03	.195
CPB time, min	99.75 ± 63.06	101.69 + 62.78 (n = 16)	92.00 ± 73.50	.792
Types of operations				
CABG	15 (60)	13 (61.6)	2 (50)	.169
Valve	4 (16)	3 (14.3)	1 (25)	
CABG + valve	3 (12)	3 (14.3)	0	
Aortic aneurysm	2 (8)	1 (4.8)	1 (25)	
PFO + ASD, VSD	1 (4)	1 (4.8)	0	

Note: Data are presented as mean ± SD or n (%).
Abbreviations: ASD, atrial septal defect; BMI, body mass index; CABG, coronary artery bypass graft; CPB, cardiopulmonary bypass; DM, diabetes mellitus; HTN, hypertension; LVEF, left ventricular ejection fraction; PFO, patent foramen ovale; VSD, ventricular septal defect.

was determined using the PaO_2/FiO_2 ratios based on the Berlin definition.[12] AKI was defined based on changes in serum creatinine according to the KDIGO guidelines for postoperative patients.[13]

2.4 | Statistical analysis

Continuous variables are presented as the mean ± SD (standard deviation) or median (interquartile range; IQR). Categorical variables are expressed as frequencies and percentages. Quantitative variables were compared using the Student *t* test or the Mann-Whitney *U* test, as appropriate, while categorical variables were compared using the χ^2 or the Fisher exact test as required. The statistical analysis was performed with SPSS software, version 21 (SPSS Inc. Chicago, IL) and SAS version 9.2 (SAS Institute, Inc). All *P* values were two-tailed and a $P \leq .05$ was considered to be statistically significant.

3 | RESULTS

A total of 25 patients who had COVID-19 and underwent cardiac surgery were enrolled in the study. Twenty-one patients had positive RT-PCR tests, and four had positive chest CT showing pneumonia. The baseline characteristics of patients are shown in Table 1. The mean age was 57.3 ± 15 years, and the mean EuroSCORE was 6.56 ± 1.29. The median body mass index was 26.3 kg/m^2 (IQR, 22.5-28.6). Sixty-eight percent of the patients had one or more comorbidities. Hypertension (56%) was the most common, followed by diabetes type 2 (40%). Twenty percent of the patients were cigarette smokers. Four patients (16%) had a history of respiratory diseases, one patient had asthma, and three patients had chronic obstructive pulmonary disease. However, all of their conditions were under control. The mean time from admission to surgery was 2.12 ± 0.93 days. The mean left ventricular ejection fraction (LVEF) was 43.12 ± 8.32%. Off-pump cardiac surgery was done on four patients, and on-pump cardiac surgery was done on 21 (84%) patients, with a median CPB time of 85 minutes (IQR, 50-147). The operations were diverse and included CABG (15), valve (4), combined CABG-valve (3), patent foramen ovale + atrial septal defect + ventricular septal defect closure (PFO + ASD + VSD; 1), and thoracic aortic aneurysm type A (2). The median anesthesia time was 4.5 hours (IQR, 4.5-5). The mean PaO_2, FiO_2, PaO_2/FiO_2 ratio, MAWP, and oxygen index during the first 6 hours after surgery were 146 ± 27.99mm Hg, 0.63 ± 0.48, 232.82 ± 49.23, 10.5 cm H_2O ± 1.50 and 4.47 ± 1.13, respectively. The median PEEP was 5.5 (5.25-6). On the basis of the Berlin definition of ARDS, on admission to the ICU, one patient had severe ARDS, 12 (44.4%)

TABLE 2 Clinical data and outcomes of cardiac surgery patients with COVID-19

Variables	Total (n = 25)	Nonadmitted (n = 21)	Readmitted (n = 4)	*P* value
Systolic BP, mm Hg	112.26 ± 14.92	114.80 ± 13.47	98.89 ± 16.97	.048
Diastolic BP, mm Hg	63.93 ± 6.86	63.62 ± 7.44	65.53 ± 1.93	.328
CVP, cm H_2O	13.36 ± 2.81	13.45 ± 3.01	12.86 ± 1.58	.706
Norepinephrine, μg/kg/min	0.02 ± 0.03	0.01 ± 0.02	0.03 ± 0.03	.430
Dopamine, μg/kg/min	0.20 ± 0.11	0.24 ± 1.10	0 ± 0	.672
Dobutamine, μg/kg/min	1.48 ± 2.84	1.19 ± 2.69	3.01 ± 3.56	.252
Epinephrine, μg/kg/min	0.01 ± 0.02	0.01 ± 0.02	0.01 ± 0.03	.796
Lymphocyte, $\times 10^9$/L	1092.24 ± 527.70	1162.019 ± 545.70	725.01 ± 170.78	.132
Hb, mg/dL	10. 31 ± 1.39	10.37 ± 1037	8.88 ± 0.91	.048
CRP, mg/dL	10.07 ± 7.13	9.01 ± 3.16	10.2 ± 7.69	.752
FiO_2, %	0.63 ± 0.48	0.63 ± 0.05	0.701 ± 0.15	.261
PEEP, cm H_2O	6.59 ± 2.61	5.63 ± 0.56	11.63 ± 3.50	.041
PaO_2, mm Hg	146.34 ± 27.99	149.4 ± 28.30	75.01 ± 23.86	<.001
MAWP, cm H_2O	10.28 ± 1.25	10.19 ± 1.32	12.25 ± 1.50	.010
Oxygen index	4.47 ± 1.13	4.50 ± 1.20	13.88 ± 4.40	.023
PaO_2/FiO_2 ratio	238.82 ± 49.23	237.13 ± 50.41	98.50 ± 39.82	<.001
ICU LOS, d	3 (2-4)	3 (2-6)	6.5 (5.25-2.35)	.011
Fluid balance, mL				
Postoperative day 1	−50 (−300 to 252)	−50 (−300 to 400)	850 (−415 to 925)	.597
Postoperative day 2	150 (−850 to 300)	115 (−200 to 450)	500 (250 to 800)	
Postoperative day 3	0 (−850 to 300)	−100 (−900 to 10)	800 (600 to 875)	
Postoperative drainage, mL				
Postoperative day 1	300 (200-900)	400 (200-900)	450 (300-60)	.234
Postoperative day 2	200 (100-375)	100 (75-400)	100 (50-500)	
AKI	10 (40)	7 (33.7)	3 (75)	.267
Mortality	4 (16.0)	1 (4.8%)	3 (75)	.007

Note: Data are presented as mean ± SD or median (interquartile range) or n (%).
Abbreviations: AKI, acute kidney injury; CRP, C-reactive protein; CVP, central vein pressure; FiO_2, fraction of inspiratory of oxygen; Hb, hemoglobin; ICU LOS, length of stay in intensive care unit; MAWP, mean airway pressure for intubated patients; PaO_2, pressure of inspiratory oxygen; PEEP, positive expiratory pressure.

moderate, and 10 (37%) mild ARDS. After 8 hours, no patient had severe ARDS, 6 (24%) patients had moderate, and 17 (48%) patients had mild ARDS. Forty percent of the patients had AKI on postoperative day 3. Three (12%) patients had another operation due to bleeding. A packed red blood cell transfusion was done in 14 (56%) patients. The mean hemodynamic parameters of the patients in the early postoperative hours are shown in (Table 2). Fourteen patients received the usual doses of inotropes, and four patients received high doses with the maximum dose of norepinephrine 0.08 μ/kg/min, dobutamine 10 μ/kg/min, and epinephrine 0.05 μg/kg/min. One patient needed an intra-aortic balloon pump (IABP). The majority of patients had a normal sinus rhythm (84%), 18% sinus tachycardia, 12% atrial fibrillation, and one had persistent ventricular tachycardia that required defibrillation. These percentages do not include the patients readmitted to the ICU. Unfortunately, out of four (16%) of the patients readmitted to ICU, three (75%) of them died. There was no statistical difference between the patients that were readmitted to ICU and those that were not in terms of the baseline characteristics. Compared to the nonadmitted group, the FiO_2, oxygen index, and PEEP were higher, and the PaO_2/FiO_2 ratio was lower (Table 2). The median time from discharge to readmission to ICU was 4.5 days (3-6.5). The overall mortality rate of 16% was higher compared to non-COVID-19 cardiac surgery patients (2%) with similar baseline characteristics (Table 3). The median intubation time was 13 hours (9.5-18), which was comparable to non-COVID-19 patients ($P = .723$). However, this time did not include the second intubation time of the readmitted group. The median first ICU LOS was 3 days (2-4) in patients with COVID-19, which was longer compared to the non-COVID-19 cardiac surgery patients (1.8 [0.9-3] days).

TABLE 3 Baseline characteristics and clinical data of non-COVID and COVID-19 patients

Variables	Total (n = 75)	Non-COVID (n = 50)	COVID-19 (n = 25)	*P* valve
Sex				
Male	50 (66.7)	32 (64)	18 (72)	.488
Female	25 (33.3)	18 (36)	7 (28)	
Age, y	60.35 ± 11.23	61.86 ± 8.45	507.33 ± 15.13	.174
DM	52 (42.7)	52 (44)	10 (40)	.741
HTN	42 (56)	28 (56)	14 (56)	1.000
Smoking	13 (17.3)	8 (16)	5 (20)	.750
Types of operation				
CABG	52 (69.3)	37 (74%)	15 (60%)	.467
VALVE	9 (12)	5 (10%)	4 (16%)	
CABG + VALVE	5 (6.7)	2 (4%)	3 (12%)	
Others	9 (12)	6 (12)	3 (12)	
History of respiratory disease	6 (8.1)	2 (4.1)	4 (16)	.171
Number of grafts	22.93 ± 99 (n = 58)	3.28 ± 0.93 (n = 40)	2.17 ± 0.62 (n = 18)	<.001
Off-pump/on-pump				
Off-pump	11 (14.7)	7 (14)	4 (16)	.999
On-pump	64 (85.3)	413 (86)	21 (84)	
CPB time, min	97.17 ± 53.77 (n = 63)	95.98 ± 49.64 (n = 43)	99.75 ± 63.6 (n = 20)	.798
LVEF, %	44.73 ± 8.96	45.30 ± 9.23	43.60 ± 8.31	.192
ICU LOS, d	2 (99-303)	1.88 (0.92-3.04)	3 (2-4)	.002
Intubation time, h	14 (10-18)	14 (10-18)	13 (9.5-18)	.723
Readmission to ICU	4 (5.3)	0	4 (16)	
Hb, mg/dL	12.69 ± 2.25	13.88 ± 1.55	10.32 ± 1.39	<.001
Reoperation	4 (5.3)	1 (2)	3 (12)	.105
Mortality	5 (6.7)	1 (2)	4 (16)	.040

Note: Data are presented as mean ± SD or median (interquartile range) or n (%).
Abbreviations: CABG, coronary artery bypass graft; CPB, cardiopulmonary bypass; CABG, coronary artery bypass graft; DM, diabetes mellitus; HTN, hypertension; ICU, intensive care unit; LVEF, left ventricular ejection fraction.

4 | DISCUSSION

To the best of our knowledge, the literature contains no investigation on the respiratory outcomes of postcardiac surgery patients with COVID-19. In this retrospective study, we reviewed and analyzed the baseline characteristics and clinical data of 25 patients that underwent emergency or urgent cardiac surgeries at the discretion of the cardiac surgeons and cardiologists of our hospital. This study aimed to evaluate patients' respiratory outcomes after cardiac surgery. To understand the impact of COVID-19 on the main postoperative outcomes, we selected 50 cardiac surgery patients from our surgery database using propensity matching, who had urgent or emergency operations over 3 months before COVID-19 began spreading in Iran (from 1 November 2019 to 30 December 2019). The only statistical difference between the baseline characteristics was the larger number of grafts in the CABG patients compared to the non-COVID-19 group, which is not likely to be clinically significant. However, the rate of ICU readmission in the COVID-19 cardiac surgery patients (16%) was higher than in the non-COVID-19 group (0%). In a recent retrospective study in China, Lei et al[7] described the clinical outcomes of elective general surgical patients within the incubation period of COVID-19. In that study, the rate of ICU admission was 44%. Patients in that study underwent elective surgeries, whereas our patients had an emergency or urgent surgeries. In addition, the number of patients with at least one morbidity was higher in the current study. Hypertension was the most common comorbidity in our cohort, which is consistent with other studies.[3,7] The median EuroSCORE of our patients was 7.50 (IQR, 6.5-8.5), indicating that the risk of morbidity and mortality was high. The overall mortality of our patients was 16%, which is higher than the non-COVID-19 cardiac surgery patients ($P = .040$). Hemodynamic complications, as well as cardiogenic and septic shocks, are not uncommon in patients with COVID-19.[7,14] In a study by Lei, 53% of the patients admitted to the ICU had shock, and 33% had cardiac arrhythmias. As inotropes are usually used to support hemodynamics in cardiac surgery patients, it is difficult to compare the incidence rate of

shock between that study and ours. Nonetheless, overall, our patients were relatively hemodynamically stable after surgery, as 14 (56%) patients received the usual doses of inotropes and only 4 (16%) patients received high doses. One of our valve surgery patients needed an IABP in the operating theater. Another patient that underwent on-pump CABG needed defibrillation twice, which was because of sustained episodes of ventricular fibrillation.

Schumer et al[15] compared postoperative outcomes between patients undergoing emergency CABG and those undergoing elective CABG surgeries. They found that the mean CPB time was 80.2 ± 39.7 minutes, which is shorter than in our study (99.75 ± 63.5 minutes). Nevertheless, given the complexity and diversity in our surgical operations, a longer CPB time is expected. The mean CPB time was not different from non-COVID-19 cardiac surgery patients (Table 3). The rate of AKI on the third postoperative day was 40% in our patients, which is higher than the rates seen in either the study by Lei et al[7] or Schumer et al.[15]

Although some anesthetic agents may pose anti-inflammatory effects, the surgery itself, especially cardiac surgery, and CPB causes an inflammatory response and acute lung injury.[16,17] The median airway pressure and FiO_2 of intubated patients were 10 cm H_2O (IQR, 9.50-10.50) and 0.64 (IQR, 0.60-0.64), respectively, which are lower than the values reported in the study by Grasselli et al.[3] Also, the severity of ARDS was lower in our patients. This may be explained by the fact that our patients were asymptomatic and that postoperative anesthetics and residual muscular relaxants might affect the compliance and resistance of the lung. The median PEEP in our patients (6 cmH_2O,[IQR, 5-6]) was lower compared to the nonsurgical ICU COVID-19 patients in the study by Grasselli et al.[3] Emergency or urgent surgery, old age, comorbidities, and high frailty scores are associated with a longer mechanical ventilation time in cardiac surgery patients.[18] The initial intubation time in the present study was not different from our non-COVID-19 cardiac surgery patients (Table 3), indicating that the early respiratory course was unremarkable. We had only one case of extubation failure in the ICU. This patient was reintubated in 8 hours, extubated 2 days later, and discharged from ICU but was then readmitted after 5 days. In addition, we could not wean and extubate another one of our patients and he died during the first 7 days of his stay in ICU. Unlike the postsurgery patients in the study by Lei et al,[7] in which fever was the most common symptom, in the present study, low SpO_2 (<87%) was the most common first sign (80%). Fever (72%), respiratory distress (64%), headache (28%), and cough (28%) were also common signs and symptoms. The majority of the patients improved with routine supportive care. However, four patients were readmitted to the ICU due to respiratory and hemodynamic problems. The respiratory and ventilator indices in the readmitted group were unfavorable during their second ICU stay (Table 2). Three (75%) of these patients suffered from severe ARDS and one had moderate ARDS. The mean PEEP and mean airway pressure values were higher than the nonreadmitted group ($P = .01$).

The median ICU LOS in the readmitted group was 6.5 (IQR, 5.25-23.23), which was longer than that of the nonreadmitted group. Three (75%) of these patients died, which, by comparison with our nonreadmitted group and the nonsurgical ICU admitted patients in the study by Grasselli et al,[3] is high. This indicates that symptomatic postcardiac surgery patients have a very high risk of mortality.

This study has several limitations. First, this study is a retrospective study, and the data was collected from the medical records and flow sheets. As such, some of the data was missing. Second, the sample size was too small to make an accurate comparison between the groups. Third, patients in post ICU and other wards were not monitored to the same extent as those in the cardiothoracic ICU. Fourth, at the peak of the COVID-19 pandemic, we did not always have enough test kids to test our patients.

5 | CONCLUSION

Even though the respiratory outcomes of asymptomatic COVID-19 patients that underwent early postcardiac surgery appeared to be satisfactory, the rate of readmission to the ICU was high. The patients that were readmitted to ICU had high rates of severe ARDS and mortality. Therefore, we suggest postponing cardiac operations on patients with COVID-19 unless they require emergency surgery.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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