The rate of COVID-19 and associated mortality after elective hip and knee arthroplasty prior to cessation of elective services in UK

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A multicentre study conducted during March 2020

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ABSTRACT

Aims

The primary aim was to assess the rate of postoperative COVID-19 following hip and knee arthroplasty prior to the cessation of elective orthopaedic services in the UK. The secondary aims were to assess (1) whether there were clinical factors associated with COVID19 status, (2) the mortality rate of patients with COVID-19, and (3) the rate of potential COVID-19 in patients not representing to healthcare services.

Methods

A multicentre retrospective study was conducted of all patients undergoing hip or knee arthroplasty during the early stages of the COVID-19 pandemic (1st to 31st of March 2020) with a minimum of 60-days follow up. Patient demographics, ASA grade, procedure type, primary or revision, length of stay (LOS), COVID-19 test status and postoperative mortality were recorded. A subgroup of patients that had not represented to healthcare services after discharge were contacted and questioned as to whether they had symptoms of COVID-19 and a positive predictive value (PPV) was assigned.

Results

During the study period 1072 patients underwent hip or knee arthroplasty. Five (0.5%) patients that tested positive for SARS-CoV-2 postoperative (swab n=4, antibody n=1). Unadjusted analysis demonstrated that TKA (p=0.029), a revision procedure (p=0.003) and a longer LOS (p=0.015) were associated with developing COVID-19 postoperatively. However, when adjusting for confounding the only significant factor associated with developing COVID-19 following surgery was increased LOS (p=0.022). A LOS greater than 3-days was a reliable

predictor of developing COVID-19 postoperatively with an area under the curve of 81% (95% CI 64 to 98, p=0.018). There were three (0.3%) deaths in the study cohort within 60-days of surgery. The overall mortality rate attributable to COVID-19 was 0.09% (n=1/1072), with one (20%) to the five patients with COVID-19 dying postoperatively. Of the 212 patients contacted eight (3.8%) declared symptoms within 60 days of discharge from surgery, but only two had symptoms within 2 to 14 days postoperatively with a PPV of 31% i.e. one (0.5%) patient may had COVID-19.

Conclusion

The rate of postoperative COVID-19 was 0.5% but may have been as high as 1% when accounting for those not presenting to healthcare services. A LOS more than 3-days was associated with an increased risk of acquiring COVID-19 postoperatively. The overall mortality rate secondary to COVID-19 was low (0.09%).

INTRODUCTION

Routine elective orthopaedic operating in the UK stopped in March due to the COVID-19 pandemic.[1, 2] There is now a gradual restoration of elective orthopaedic services as the prevalence of COVID-19 pandemic continues to fall.[3, 4] There are suggested guidelines in regard to preoperative screening and patient pathways to limit the risk of acquiring COVID-19 postoperatively.[5-8] However, there may be a proportion patients that do not wish to proceed with surgery in view of the perceived increased mortality risk associated with developing COVID-19 postoperatively.[9] Currently communication of this potential risk is difficult in elective orthopaedic practice due to the limited evidence.

Lei et al[10] described a postoperative mortality rate of 21% in a group of 34 who developed COVID-19 following elective surgery, of which seven were orthopaedic procedures, during the pandemic in Wuhan. The international multicentre COVIDSurg study reported a 19% 30-day postoperative mortality rate in 278 patients that developed COVID-19 perioperative after undergoing elective surgery, however only five patients underwent elective hip or knee replacement surgery.[11] Therefore the findings of the COVIDSurg study[11] are generalisable to patients undergoing lower limb elective arthroplasty. An early report of return to elective operating on phase one patients has been encouraging with no postoperative COVID-19 infections and a high rate of patient satisfaction.[4] The risk of a patient developing COVID-19 postoperatively after elective hip and knee arthroplasty and the associated mortality rate should this occur is not clear from the current literature.

This study reports the findings of International Multicentre Project Auditing COVID-19 in Trauma & Orthopaedics (IMPACT) Restart project from centres in Scotland and England contributing data to the collaborative. The primary aim was to assess the rate of postoperative COVID-19 following hip and knee arthroplasty prior to the cessation of elective orthopaedic services. The secondary aims were to assess (1) whether there were factors associated with COVID19 status, (2) the mortality rate of patients with COVID-19, and (3) the rate of potential symptomatic COVID-19 in patients not representing to healthcare services.

PATIENTS AND METHODS

A multicentre emergency clinical audit response was initiated and supported by the Scottish Hip Fracture Audit[12], Scottish Government and the Scottish Committee for Orthopaedics & Trauma in response to the need for urgent clinical audit into COVID-19 and restarting elective orthopaedic surgery. A multicentre observational study was conducted of data collected retrospectively from all 15 NHS health boards in Scotland and five NHS trusts in England providing elective hip and knee arthroplasty. Data from these centres were recorded retrospectively for all orthopaedic patients undergoing elective hip or knee surgery. Data were collected in accordance with UK Caldicott principles and local data governance guidance, and no patient-identifiable data were transferred out with the local units or accessed by the central IMPACT audit team.

All patients undergoing elective hip or knee arthroplasty surgery at any of the participating centres over the study period (1st to 31st of March 2020) were included, however the majority of centres stopped elective operating on the 16th of March.[13] This period was chosen as it was thought to represented the peak transmission rate of COVID-19.[14] This was also supported by the observed peak rate of COVID-19 associated mortality that was observed in the UK at the beginning of April 2020[15], which suggests the peak infection rate was two to three weeks earlier in the middle of March 2020 as this is the average time taken from infection to death.[16] Patients were followed up for a minimum of 60 days following their surgery.

A priori aims were developed before the collection of data. Data were collected using a bespoke digital IMPACT Restart Audit data collection tool comprising data-validated fields to ensure accuracy and consistency of coding, thus increasing intra- and inter-observer reliability. Additionally, data collectors were provided with an IMPACT Restart Audit user guide and had continuous access for queries to the audit designers (NDC).

Patient demographics and surgical data were collected from the databases which included: age, sex, body mass index (BMI), diabetes mellitus status, American Society of Anaesthesiologists (ASA) grade, date of surgery, primary or revision surgery, procedure type

(hip or knee replacement), length of hospital stay (LOS), COVID-19 testing and mortality. ASA classification was recorded on the theatre database or operation note at time of surgery and used to assign physical status.[12] Procedure type was subclassified into three groups: total hip arthroplasty (THA), total knee arthroplasty (TKA) and partial knee arthroplasty (PKA). Patients were defined to be COVID-19 positive if they had a positive SARS-CoV-2 swab test (antigen polymerase chain reaction test) or a positive serum SARS-CoV-2 antibody test in their postoperative period. The results of SARS-CoV-2 testing was collected from local microbiology laboratory databases and was used to determine COVID-19 status: positive, negative, or not tested. Swabs were obtained via the standard oropharyngeal and nasopharyngeal swab technique as part of the patients' clinical management. Mortality status was obtained from the patient's medical records and by direct contact for those that underwent symptom questionnaire assessment, with a minimum follow-up of 60 postoperative days. Postoperative complications were recorded as part of the data collection tool. Patients that developed lower respiratory tract infections (LRTI) postoperatively were identified and, for the purpose of calculating a "worst-case scenario" for the rate of postoperative COVID-19, it was assumed that these patients had COVID-19.

To assess the potential rate of unidentified COVID-19 in patients not representing to healthcare services a telephone symptom questionnaire was undertaken in three centres (XXX, XXX, XXX). This questionnaire was designed to record whether a patient had symptoms of COVID-19 or not postoperatively and assign a probability (specificity and positive predictive value [PPV]) of having COVID-19 according to the patients stated symptoms within six weeks of surgery (Figure 1).[17] The PPV for each symptom or cluster of symptoms for each patient was used to assign an overall probability of the group having COVID-19 postoperatively.

Statistical methods. Statistical analysis was performed using Statistical Product and Service Solutions version 17.0 (SPSS Inc. Released 2008. SPSS Statistics for Windows, Version 17.0. Chicago: SPSS Inc.). Age and BMI were compared between groups assessed using an unpaired t-test (normally distributed data). LOS was compared between groups assessed

using a Mann Whitney test (skewed distributed). Dichotomous variables (sex, diabetes mellitus status, ASA grade, primary or revision, procedure, mortality) were assessed using a chi square test or a Fisher's exact test (if 5 or less in one cell) between group comparisons. Logistic regression analysis was used to assess the independence of predictors associated with a patient developing COVID-19 postoperatively. Only variables with a trend ($p<0.1$) or significant ($p<0.05$) on unadjusted analysis were included in the multivariable model. Receiver operating characteristic (ROC) curve analysis was used to identify a threshold value in LOS that was predictive of developing COVID-19 postoperatively. The area under the ROC curve (AUC) ranges from 0.5 (no accuracy) to 1.0 (test identifies all COVID-19 positive patients, and the minimum AUC for reliability is defined as 0.7 or more.[18] The threshold value was defined as the point at which the sensitivity and specificity were maximal in predicting a COVID-19 positive patient.[19] A p-value of <0.05 was defined as statistically significant.

RESULTS

There were 1073 patients who underwent hip or knee arthroplasty during the study period, of which three patients underwent bilateral THA, one underwent bilateral TKA and the remainder had single joint surgery. A single patient was excluded from analysis after they had moved to a different area postoperatively and was not contactable. There were 624 (58.2%) female and 448 (41.8%) male patients with a mean age of 68 (range 22 to 95) years old.

Primary aim: rate of postoperative COVID-19 following hip and knee arthroplasty

There were five patients that tested positive for SARS-CoV-2 in the postoperative period (antigen PCR swab test n=4, serum antibody n=1), which resulted in an overall 0.5% rate of developing COVID-19 in the 60 days following elective hip or knee arthroplasty during the study period. One of these patients was thought to have contracted the infection following contact with a COVID-19 positive family member (Table I). The remaining four patients were diagnosed with COVID-19 either as an inpatient (n=1), during a readmission (n=1) or within 14-days of discharge (Table I).

Worst case scenario analysis for the rate of COVID-19 postoperatively identified an additional seven patients that had a LRTI (hospital acquired pneumonia (HAP) n=5, community acquired pneumonia (CAP) n=2), three of whom had negative COVID-19 swabs and another two had a CT scan (to exclude a pulmonary embolism) which were consistent with LRTI. One patient represented to the Emergency Department with generalised fatigue 14-days following surgery but was not thought to have COVID-19 and therefore did not undergo COVID-19 testing. This resulted in a total of 13 patients that were potentially COVID-19 positive which increased the overall potential postoperative rate to 1.2%.

Secondary aim: clinical predictors of postoperative COVID19 status

Five patients tested positive for SARS-CoV-2 and were assigned the diagnosis of COVID-19. Unadjusted analysis identified patients undergoing a TKA (p=0.029), a revision procedure (p=0.003) and a longer length of hospital stay (p=0.015) were associated with developing COVID-19 postoperatively (Table II). There was also a trend toward significance (p=0.086) for older age to be associated with COVID-19 following surgery (Table II). These variables were entered into a logistic regression model and when adjusting for confounding the only significant factor associated with developing COVID-19 following surgery was increased LOS (Table III). ROC curve analysis illustrated that LOS was a reliable predictor of developing COVID-19 postoperatively with an AUC of 81% (95% CI 64 to 98, p=0.018) (Figure 2). Using the point of maximum sensitivity and specificity as the threshold value a LOS longer than 3-days was associated with an approximate 70% sensitivity and 70% specificity of predicting postoperative COVID-19 (Figure 3).

Secondary aim: the mortality rate of patients with COVID-19 postoperatively

There were three (0.3%) deaths in the study cohort within 60-days of surgery. The first was at 17-days after surgery and was due to a pulmonary embolism in a 64-year-old female who underwent a TKA and had a high BMI of 37kg/m^2. The second patient death was 35-days following surgery and related to acute complication of diabetes mellitus in a 72-year-old male

undergoing a TKA and there was no clinical suspicion of COVID-19. The final patient death was 47-days following surgery and the cause of death was attributed to COVID-19 (described above). The overall mortality rate after elective hip and knee arthroplasty secondary to COVID-19 was 0.09% (n=1/1072). Mortality for patients with test proven postoperative COVID-19 was 20% (n=1/5) which was significantly (p=0.014, Fishers exact) greater than those patients without proven COVID-19 postoperatively (n=2/1067). However, when the worst-case scenario is applied for the rate of postoperative COVID-19, then the mortality rate may be as low as 8% (n=1/13).

Secondary aim: the rate of potential symptomatic COVID-19 in patients not representing to healthcare services

Subgroup analysis of postoperative symptoms was conducted in three centres (XXX, XXX, XXX), who contacted patients directly via the telephone. Two patients were not contactable by telephone in one of the centres (XXX), but their GP was contacted, and they had not presented with symptoms of COVID-19 postoperatively and were alive. It was already known that one patient from XXX had a postoperative HAP and one from XXX had a CAP, and a patient from XXX had postoperative COVID-19 and therefore were not asked to complete the symptom survey. There were 212 patients (XXX n=56, XXX n=127, XXX n=39) asked about perioperative symptoms of COVID-19. Eight (3.8%) patients declared symptoms within six weeks of surgery. Three stated they had symptoms immediately or within one day of their surgery (Table IV). Two stated their symptoms were at 7 and 10 days following discharge (Table IV). The remaining three all had symptoms which began beyond 14-days from discharge (Table IV). No patient had a symptom or combination of symptoms that was associated with a PPV of COVID-19 greater than 50%. The PPV of COVID-19 for the two patients that had symptoms at 7 and 10 days following discharge was 31%, therefore it is estimated that one (0.5%) out of the 212 surveyed patients may have acquired a nosocomial COVID-19 infection after surgery and did not present to healthcare services. Whereas the three patients developing symptoms after 14-days acquired this infection in the community.

DISCUSSION

This multicentre study has demonstrated the 60-day rate of postoperative COVID-19 after hip and knee arthroplasty was 0.5% in the UK during a period when the prevalence of COVID-19 was nearing the peak, which was without any preoperative patient screening or precautions using standard patient pathways and operating procedures. The main factor associated with developing COVID-19 in the postoperative period was longer LOS in hospital, with patients staying longer than 3-days being at increased risk. The overall mortality rate secondary to COVID-19 was low (0.09%), however for those patients developing COVID-19 postoperatively the mortality rate was 20%. Potentially 0.5% patients had symptoms consistent with COVID-19 within 14-days of days of discharge and did not represent to healthcare services. When worst-case scenario analysis was applied to estimate the highest rate of symptomatic postoperative COVID-19 the incidence may have been as high 1.2% (when including all patients that developed a LRTI postoperatively) or 1.0% (when including those patients that were symptomatic but did not present to healthcare services within 14-days of their discharge).

The main limitation of the study was the reliance on a positive antigen PCR swab or serum antibody test for SARS-CoV-2 to assign the diagnosis of COVID-19. The study period was at the peak of the UK pandemic and testing pathways for COVID-19 may not have been fully established and patients may not have demonstrated typical symptoms of COVID-19 and therefore not given a diagnosis of COVID-19.[20] This may have resulted in a lower rate of postoperative COVID-19 diagnoses and conversely an over estimation of the mortality rate in patients with postoperative COVID-19. However, the subgroup analysis of patients that did not present to healthcare services and were contacted directly to assess for postoperative symptoms demonstrated a relatively low (0.5%) rate of developing COVID-19 in the 14 days following discharge. The time period assessed in this study was also a limitation as there were no established elective patient pathways in place nor was there any preoperative patient screening.[15] The rate of acquiring COVID-19 postoperative is likely to be less than that demonstrated in the current study as the prevalence decreases in the community and hospital

infection control strategies are introduced and developed to reduce the risk of viral transmission.[5, 7, 15] However, these pathways should undergo auditing to ensure this is the case.

The risk of developing COVID-19 after hip and knee arthroplasty was demonstrated to be low, with only five (0.5%) patients testing positive for SARS-CoV-2. Patients with a LOS longer than 3 days were shown to be at an increased risk of developing COVID-19 postoperatively. Nosocomial transmission of SARS-CoV-2 was likely in four of the test proven COVID-19 positive patients, since they received the diagnosis whilst as in inpatient or within 14-days of discharge, which is within the incubation period of the disease).[21] Patient factors that are currently limitations to go forward with surgery such as older age, diabetes mellitus and higher BMI were not associated with developing COVID-19 postoperatively in the current study.[4, 5] However, these factors may be associated with an increased mortality rate should a patient develop COVID-19 postoperatively but due to the low number of deaths in the current cohort analysis of this was not possible. LOS was the only factor associated with the risk of developing postoperative COVID-19, therefore patients may benefit from strategies to reduce LOS such as enhanced recovery programs and short stay or day case arthroplasty in the future.[22, 23]

Due to the limited number of patients developing COVID-19 postoperatively this study did not help to quantify the postoperative mortality risk for elective orthopaedic patients who develop COVID-19 after surgery. It could have been expected that the rate of postoperative COVID-19 would have been higher in the study group due to the fact the time period assessed was at the height of the UK pandemic, and during a period in there were no enhanced infection prevention and control precautions, screening or protective patient pathways in place to mitigate the transmission of SARS-CoV-2 within hospitals. However, the 20% mortality rate observed in the current study was similar to that reported by the COVIDSurg study of 19% at 30-days for patients that developed COVID-19 perioperative after undergoing various elective surgery.[11] A limitation of the COVIDSurg study was that only patients with COVID-19 were

included and there was no reference group with which the relative mortality risk could be calculated. The first study by the IMPACT-Restart group, that included both trauma and elective orthopaedic patients, demonstrated that the mortality risk of a patient doubles should they develop COVID-19 postoperatively.[24] Therefore a patient developing COVID-19 postoperatively following primary total knee or total hip arthroplasty will have an average all-cause mortality rate at 30-days of between 0.2%[25] to 0.3%[26] that may be double to 0.4% and 0.6%, respectively.

Conclusions

The rate of postoperative COVID-19 was 0.5% following elective hip and knee replacement surgery at the height of the COVID-19 pandemic in the UK in March 202 without any preoperative patient screening or precautions using standard patient pathways and operating procedures. The main factor associated with developing COVID-19 postoperatively was longer LOS, with patients staying longer than 3-days being at increased risk. The overall mortality rate attributable to COVID-19 was low (0.09%), however one (20%) of the five patients who developed COVID-19 postoperatively subsequently died.

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TABLES

Table I. Patient demographics, priority, ASA grade, procedure and COVID status according to postoperative mortality.

Symptom onset following (days)		Description of Patient Journey
Surgery	Discharge	
13	10	Three day LOS for a TKA. Readmitted hospital 20 days after surgery with a seven day history of symptoms and had a positive swab for COVID-19. The patient's partner had been diagnosed with COVID-19 and the patient subsequently visited them in hospital postoperatively. Discharged home after four day hospital stay.
18	15	Three day LOS for a TKA. Readmitted 12 days after surgery with wound dehiscence and underwent a DAIR and liner exchange. During the readmission they developed COVID-19 with a positive swab 18 days after surgery. Discharged with guidance to self-isolate and for outpatient antibiotics.
20	14	Six day LOS for a revision TKA. Readmitted with typical symptoms of COVID-19, but had a negative swab 20 days following surgery. Patient underwent a CTPA which was also typical of COVID-19 and the patient was managed as a positive COVID-19 clinical diagnosis. They subsequently tested positive for SARS-CoV-2 antibodies.
39	N/A	Forty-seven day LOS for a TKA. Had a prolonged admission that was initially due to non-COVID-19 respiratory problems, but subsequently developed COVID-19 with a positive swab 39 days after surgery. This patient was recognised as high risk preoperatively with an ASA grade of 3. They subsequently died 47 days following surgery.
57	6	Sixty-seven day LOS for a revision TKA. Had a prolonged admission due to rehabilitation issues but had a swab positive for SARS-CoV-2 57 days after surgery (screening swab as an impatient). They had no symptoms at this time and a normal chest radiograph and was discharged 10 days later. Readmitted six days later with delirium, pyrexia and cough, with changes on the chest radiograph. Patient remains as an inpatient in rehabilitation unit with an improving clinical picture.

Table II. Patient demographics, priority, ASA grade, procedure according to postoperative COVID status.

Demographic	Descriptive	Postoperative COVID-19		Difference / Odds Ratio (95% CI)	p-value*
		No (n=1067)	**Yes** (n=5)		
Age (years: mean, SD)		68.3 (10.3)	76.3 (8.1)	7.9 (-1.1 to 17.0)	0.086**
BMI (kg/m^2: mean, SD)		30.4 (5.4)	28.4 (7.8)	2.0 (-2.8 to 6.8)	0.413**
Sex	Female	621 (58.20	3 (60.0)	Reference	0.935
(n, %)	Male	446 (41.8)	2 (40.0)	1.08 (0.18 to 6.47)	
Diabetes	No	862 (80.8)	4 (80.0)	Reference	
(n, %)	Yes	104 (9.7)	1 (20.0)	2.07 (0.23 to 18.72)	0.999
	Missing***	101 (9.5)	0	N/A	0.999
Procedure	THA	507 (47.5)	0	Reference	
(n, %)	TKA	531 (49.8)	5 (100)	N/A	0.029
	PKA	29 (2.7)	0	N/A	N/A
Revision	No	997 (93.4)	3 (60.0)	Reference	
(n, %)	Yes	70 (6.6)	2 (40.0)	9.50 (1.56 to 57.76)	0.003
ASA Grade	I	87 (8.2)	1 (20.0)	3.89 (0.35 to 43.36)	0.307
(n, %)	II	677 (63.4)	2 (40.0)	Reference	N/A
	III	236 (22.1)	2 (40.0)	2.86 (0.40 to 20.48)	0.578
	IV	9 (0.8)	0	N/A	0.999
	V	0	0	N/A	N/A
	Missing***	58 (5.4)	0	N/A	0.999
LOS (days: median, IQR)		3 (2 to 4)	6 (3 to 57)	3	0.015β

* Fishers exact test unless otherwise stated
**unpaired Students t-test
***not included in chi square test
β Mann Whitney Test

Table III. Logistic regression analysis for factors associated with the risk of developing COVID-19 postoperatively (Nagelkerke R^2=0.34).

Predictors in model		**Odds Ratio**	**95% CI**		**p-value**
			Lower	Upper	
Age		1.08	0.96	1.23	0.214
Sex	Female	Reference			
	Male	0.95	0.53	1.69	0.850
LOS		1.06	1.01	1.11	**0.022**
Procedure	THA	Reference			
	TKA	3.11	-	-	0.991
	PKA	7.10	-	-	0.999
Revision	No	Reference			
	Yes	4.91	0.40	59.70	0.212

Bold signifies statistical significance

Table IV. Eight patients declared symptoms of COVID-19 of the 215 patients contacted postoperatively at three study centres with the sensitivity and positive predictive values (PPV) of their symptoms. The time from surgery and discharge to symptom onset is also stated.

Days from surgery	Days from discharge	Duration and Symptoms	Sensitivity	PPV
0	-3	Persistent postoperative loss of taste and smell	49%	50%
0	-3	Ten days fatigue followed by diarrhoea 5 weeks after surgery	67%	25%
1	1	Two weeks of fever, fatigue and muscle pain, and six weeks of productive cough, dyspnoea, and sore throat	93%	24%
11	7	Four day fever	64%	31%
12	10	Two day fever	64%	31%
21	18	Ten day sore throat	32%	19%
31	30	Five day loss of appetite and fatigue one month after surgery	40%	32%
33	30	Two weeks loss of smell	49%	50%

FIGURE LEGENDS

Figure 1. Telephone patient questionnaire for patients contacted after hip and knee arthroplasty to assess whether they had symptoms of COVID-19 and whether they had been tested for COVID-19.

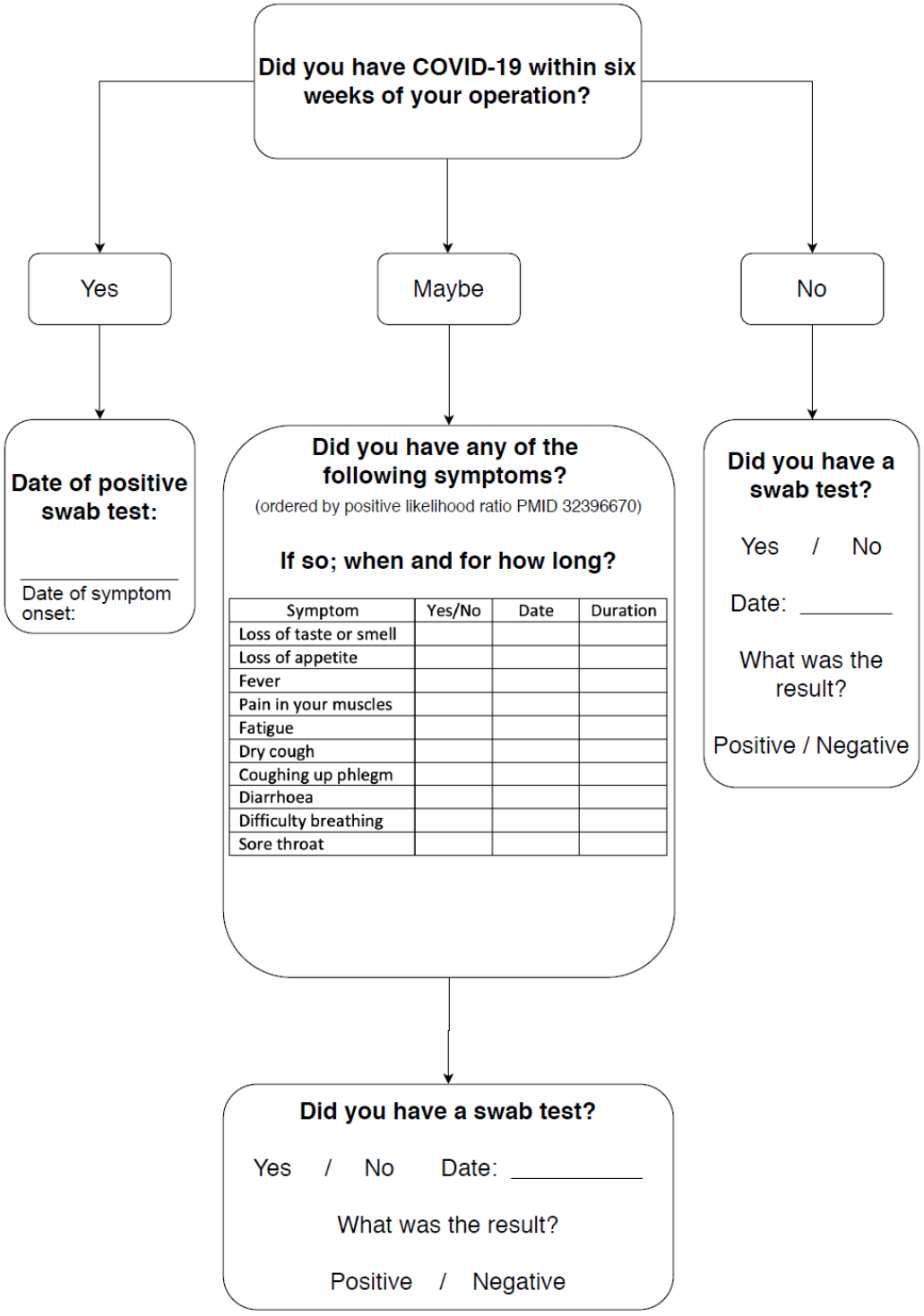

Figure 2. Receiver operating characteristic curve for length of hospital stay as a predictor of developing COVID-19 postoperatively.

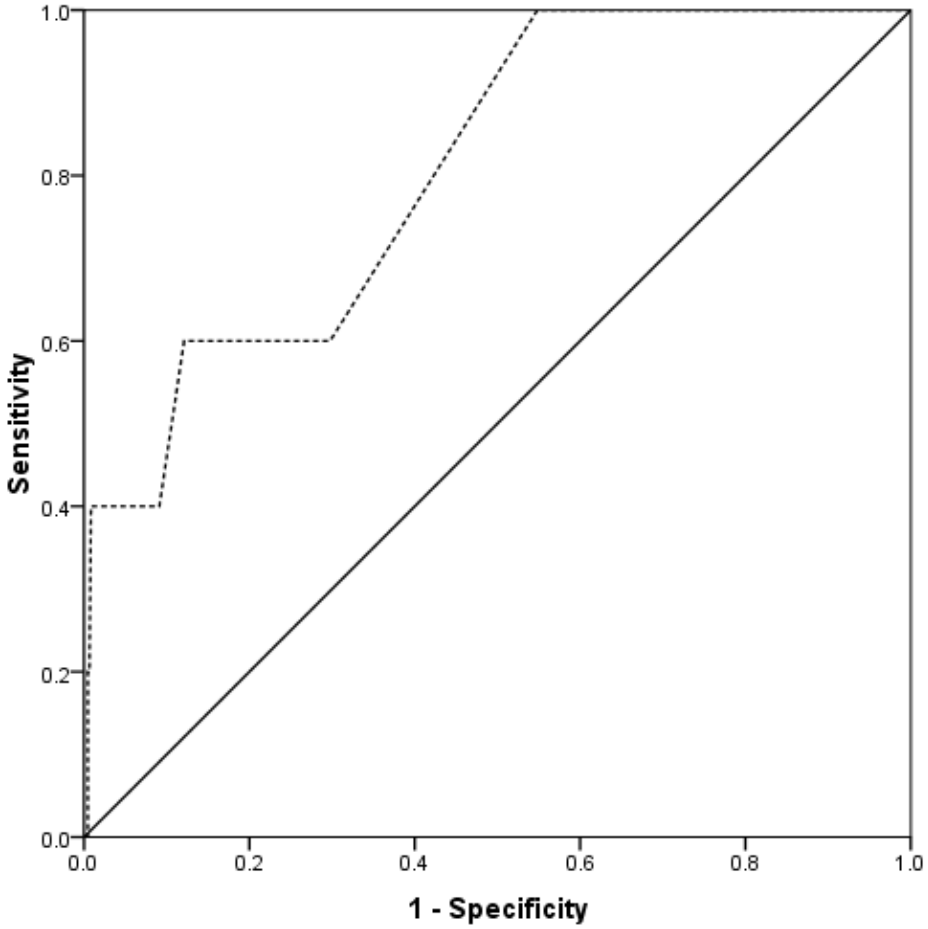

Figure 3. Sensitivity and specificity plot predicting postoperative COVID-19 according to length of hospital stay.