ORIGINAL ARTICLE

NOVEL USE OF AGE-ADJUSTED CHARLSON COMORBIDITY INDEX (ACCI) AS A RISK STRATIFICATION TOOL FOR DEVELOPMENT OF POSTOPERATIVE SARS-COV-2 INFECTION IN SURGICAL PATIENTS

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Background: Current study documents the role of Age adjusted Charlson Comorbidity Index (ACCI) as a stratification tool for the development of postoperative SARS-CoV-2 infection in surgical patients. **Methods:** This prospective cohort study was conducted over the period of 8 weeks starting on 1st of March 2020. Sampling was convenience and purposive and included all consecutive patients who underwent any surgical procedure. Follow up period was 30 days. Outcomes included postoperative SARS-CoV-2 infection, morbidity and 30-day mortality. Risk factors for development of infection were detected by univariate and multivariate analysis. **Results:** Postoperative SARS-CoV-2 infection developed in 37 cases while 131cases remained confirmed negative. Of 37 patients, 18 were male while 19 were female. Postoperative complications developed in 17 patients (45.9%). In-hospital 30-day mortality was 16.2% (n=6). The factors that increased the chances of postoperative SARS-CoV-2 infection ($p<0{\cdot}00$) included increasing age, higher ACCI Score, emergency surgery, trauma, orthopaedic and vascular procedures, spinal anaesthesia, and surgeries of complex nature. In adjusted analyses, predictors of postoperative infection included ACCI score of 4 or more (5.54 [1·51–20.34], $p<0{\cdot}01$), and orthopaedics or vascular procedures versus others (12.32 [1.98-76.46], $p<0{\cdot}007$). Based on infection rates across the different scores of ACCI, cohort was divided into 3 groups. ACCI score of zero had postoperative SARS-CoV-2 infection rate of 1.9 % (negative predictive value, 98.1%) compared with 36.26% in patients with score of 4 or more (sensitivity, 89.19%). **Conclusion:** Low risk surgical patients (ACCI=0) should have universal precautions, while intermediate risk group (ACCI=1-3) should have extra precautions. The options for high-risk patients (ACCI ≥4) include cancellation of nonurgent surgery; delaying the surgery till optimization of modifiable factors; or reverse isolation/ shielding in perioperative period if surgery cannot be cancelled.

Keywords: COVID-19 Pandemic; Postoperative mortality; Operative Severity Score (OSS); Age adjusted Charlson Comorbidity index (ACCI); Morbidity; Mortality

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INTRODUCTION

Perioperative infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has a high respiratory complications and mortality rate in surgical patients.[1] COVIDSurg Collaborative has reported pulmonary complication rate of 51.2% and 30-day mortality of 23.8%.[2] Similarly, Doglietto F *et al*, in a comparative study, have reported higher frequency of complications and a mortality rate of 19.51%.[3] Poor outcomes associated with covid-19 infection in surgical patients mandates the development and/or validation of a risk stratification tool to allow the early identification of patients at a risk of development of infection with SARS-CoV-2, in postoperative period. Use of such a tool has a pragmatic value as the patients at a higher risk of infection can be managed by more intensive preventive strategies. Most of the prognostic tools developed for COVID-19 are aimed at detection of patients at high risk of complications and mortality, once the infection has already developed.[4–6] Moreover, these tools are more valid for non-surgical patients. Recently reported "4C Mortality Score" is an example of such tools.[7] Before COVID-19 pandemic, one of the prognostic indicators to predict morbidity and mortality in surgical patients, was the Charlson Comorbidity Index.[8] It was developed as a predictor of 1-year mortality based on comorbidities. In its original form, the overall score was derived by the summation of the weighted scores of 19 medical conditions.[9] However, its recent online version, predicts 10-year mortality based on age and 16 other comorbidities. There is a great advantage in producing a summative score through incorporation of weighted scores for age groups and other comorbidities including myocardial infarction (MI), congestive heart failure (CHF), peripheral vascular disease (PVD), cerebrovascular accident (CVA)/ transient ischemic attack (TIA), dementia, chronic cognitive deficit, chronic obstructive pulmonary disease (COPD), connective tissue disease, peptic ulcer disease, liver disease, diabetes mellitus, hemiplegia, moderate to severe chronic kidney disease (CKD), solid tumour, leukaemia, lymphoma, and acquired immunodeficiency syndrome (AIDS). It helps in avoiding the use of individual medical conditions and also adjusts the effects of age on outcomes.[10] Multiple studies have documented the validity of the Charlson Comorbidity Index and its various versions in predicting postoperative complications and mortality.[11,12]

Current study was aimed at reporting the incidence of postoperative SARS-CoV-2 infection; outcomes of these patients; and assessing the role of ACCI as a stratification tool for the development of postoperative SARS-CoV-2 infection. It also provides an account of usage of this stratification tool in management of patients undergoing surgery for various indications.

MATERIAL AND METHODS

This prospective observational cohort study was conducted at North Cumbria Integrated Care, Carlisle-United Kingdom. The study was registered as a quality improvement project with the local hospital audit department (Project ID: 720). Data collection was routine and anonymised; and the study was in accordance with national and international guidelines, based on Helsinki declaration.[13] No changes were made to clinical care pathways, mandating it a non-interventional study. Ethical approval and patient consent were not required for inclusion in study, however, for every surgical procedure, informed consent was taken.

Since 1st of March 2020, over the period of 8 weeks, all consecutive patients who underwent any surgical procedure (elective/ emergency), operated by any surgical speciality, under any kind of anaesthesia, were included in the study. These patients were followed up for the next 30 days. Variables recorded for each patient included, date of admission, age, gender, Age adjusted Charlson Comorbidity Index (ACCI) score, responsible speciality, surgical condition, indication for surgery, surgical procedure and Operative Severity Score (OSS). All the patients had their COVID status determined during the study period which was categorized into positive, negative and not available. Positive status was based on detection of viral RNA through quantitative real-time polymerase-chain reaction (RT-PCR) laboratory testing on nasal swabs or bronchoalveolar lavage. Patients were labelled as postoperative SARS-CoV-2 positive where infection developed between 7th and 30th day of surgery. Thirty-day mortality was defined as death within 30 days of index procedure. For final analysis only patients with known COVID-19 status (positive/ negative) were included. ACCI was calculated using an online calculator.[10] OSS was based on severity of surgical procedures as defined by Portsmouth-Physiological and Operative Severity Score for the enUmeration of Mortality (P-POSSUM).[14]

Primary outcome was postoperative SARS-CoV-2 infection while secondary outcomes included hospital stay, complications, need and duration of Intensive Therapy Unit (ITU) stay, duration of hospital stay, and 30-day mortality. Data were analysed using the Statistical Package for the Social Sciences (SPSS), Version 20 (IBM, Corp., Chicago, Illinois, USA). Descriptive statistics were used to analyse different variables. Means with standard deviations (SD) were measured for numerical variables with normal distribution while medians and modes were measured for numerical variables with non-parametric distribution. For categorical variables frequencies were determined. Univariate analysis was performed to determine the risk factors for postoperative SARS-CoV-2 infection. After identification of risk factors, multivariate analysis was performed. ACCI as a prognostic indicator was assessed by developing ROC curve, sensitivity, specificity, positive predictive value and negative predictive value. Performance of ACCI was compared with other predictors (Age and OSS).

RESULTS

Over a period of 2 months 550 emergency/elective procedures were performed by seven surgical specialities, in 518 patients. With regards to COVID test, it was performed in 167 patients (32.23%). SARS-COVI-2 infection was detected in 52 cases (31.13% of the tested). Fifteen patients had infection before or at the time of admission. Postoperative infection (between 7 and 30 days) developed in 37 cases while 131cases remained confirmed negative during this period. The median time duration to develop infection was 11 days ± 10 (IQR). Of 37 patients with postoperative SARS-CoV-2 infection, 18 were male and 19 were female. Mean age was 77.78±13.97 (SD). Twenty-three (23) postoperative complications developed in 17 patients (45.9%). These included respiratory complications (n=9), postoperative wound infection (n=4), thrombotic complications (stroke) (n=3), urinary tract infection (n=3), need for intensive therapy unit (ITU)(n=3) and renal failure (n=1). In-hospital 30-day mortality was 16.2% (n=6).

Table-1 documents the results of univariate analysis. The factors that increased the chances of postoperative SARS-CoV-2 infection included increasing age (p<0·00), higher ACCI Score (p<0·00), emergency surgery (p<0·00), trauma (p<0·00), orthopaedic or vascular procedures (p<0·00), spinal anaesthesia (p<0·00), and surgeries of a complex nature (class 3 and 4) (p<0·00).

In adjusted analyses (Table 2), predictors of postoperative infection included ACCI score of 4 or more versus ACCI score less than 4 (5.54 [1·51–20.34], p<0·01), and surgical speciality orthopaedics and vascular versus others (12.32 [1.98-76.46], p<0·007).

Table-3 documents the performance of ACCI in detection of postoperative SARS-CoV-2 infection across a range of cut-off values. Based on infection rates across the different scores of ACCI, the cohort was divided into 3 groups. Low risk group had score of 0, while intermediate and high-risk groups had scores of 1–3 and 4 or more, respectively. ACCI score of zero had postoperative SARS-CoV-2 infection rate of 1.9 % (negative predictive value, 98.1%) compared with 36.26% in patients with score of 4 or more (sensitivity, 72.97%). The ACCI score had high discrimination for development of postoperative SARS-COVI-2 infection as evident by area under the receiver operating characteristic curve (AUROCC) of 0.797 (95% confidence interval 0.72 to 0.87, *p*<0·03). Its performance was better than other predictors like age alone (AUROCC 0.755, 95% confidence interval 0.67 to 0.83, *p*<0·00) and OSSS (AUROCC 0.67, 95% confidence interval 0.58 to 0.76, *p*<0·00) (Figure-1).

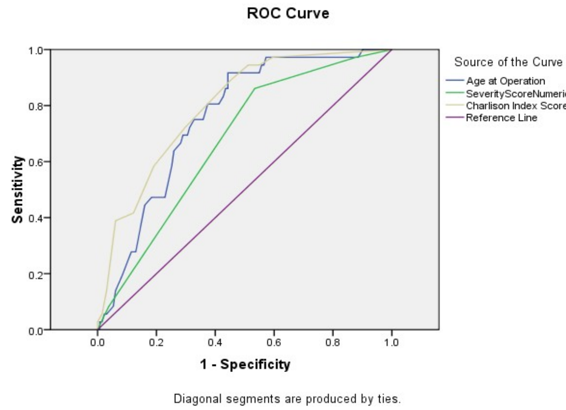

Figure-1: Comparative performance of ACCI

Table-1: Univariate Analysis. a: student t-test, b: Mann-Whitney test, c: Chi-square test/ Fischer's exact test

Variables		**COVID Negative (n=130)**	**COVID Positive (n=37)**	**Total (n=167)**	***p*-value**
Age (years)					
	Mean (SD)	55.01 (25.34)	77.64 (14.14)		0.00[a]
	Median (IQR)[range]	54.50 (49) [2-98]	81 (15) [24-96]		0.00[b]
Age (Years)					
	Less than 65	74 (93.7%)	5 (6.3%)	79	0.00[c]
	65-74	17 (73.9%)	6 (26.1%)	23	
	75-84	20 (60.6%)	13 (39.4%)	33	
	More than 84	19 (59.4%)	13 (40.6%)	32	
Gender					
	Male	52 (74.3%)	18 (25.7%)	70	0.34[c]
	Female	78 (80.4%)	19 (19.6%)	97	
ACCI (Score)					
	Mean (SD)	2.82 (2.85)	6.08 (2.46)		0.03[a]
	Median (IQR)[Range]	2.62 (5) [0-10]	6.12 (4) [0-11]		0.00[b]
ACCI Score Group					
	I (Score=0)	53 (98.1%)	1 (1.9%)	54	0.00[c]
	II (score=1-3)	19 (86.4%)	3 (13.6%)	22	
	III (Score ≥ 4)	58 (63.7%)	33 (36.3%)	91	
CEPOD Code					0.00[c]
	Emergency	104 (74.3%)	36 (25.7%)	140	
	Urgent/ Elective	26 (96.3%)	1 (3.7%)	27	
Pathology					
	Benign	76 (87.4%_	11 (12.6%)	87	0.00[c]
	Trauma	50 (66.7%)	25 (33.3%)	75	
	Cancer	4 (80%)	1(20%)	5	
Speciality					
	Anaesthetics	3 (100%)	0 (0%)	3	0.00[c]
	ENT	6 (100%)	0 (0%)	6	
	General Surgery	33 (91.7%)	3 (8.3)	36	
	OBG	22(100%)	0 (0%)	22	
	Trauma and Orthopaedics	51 (65.4%)	27 (34.6%)	78	
	Urology	9 (100%)	0 (0%)	9	
	Vascular surgery	6 (46.2%)	7 (53.8%)	13	
Anaesthesia					
	Local	2 (100%)	0 (0%)	2	0.02[c]
	Conscious sedation	3 (100%)	0 (0%)	3	
	Spinal	3 (37.5%)	5 (62.5%)	8	
	General	122 (79.2%)	32 (20.8%)	154	
Surgery Severity Score					
	Minor	16 (94.1%)	1 (5.9%)	17	0.00[c]
	Intermediate	45 (91.8%)	4 (8.2%)	49	
	Major	64 (68.8%)	29 (31.2%)	93	
	Major Complex	5 (62.5%)	3 (37.5%)	8	

Table-2: Bi-nominal Regression Analysis

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I for EXP(B)	
							Lower	Upper
Emergency vs Elective	1.82	1.22	2.23	1	0.14	6.22	0.56	68.55
Trauma vs non-trauma	0.85	0.86	0.96	1	0.33	2.33	0.43	12.69
Spinal anaesthesia vs others	1.31	1.28	1.05	1	0.31	3.70	0.30	45.33
Operative Severity Score	0.32	0.47	0.47	1	0.49	1.38	0.55	3.43
ACCI (Groups)	1.71	0.66	6.67	1	***0.01***	5.54	1.51	20.35
Orthopaedic and vascular procedures vs others	2.51	0.93	7.27	1	***0.007***	12.32	1.99	76.47
Constant	-7.28	2.39	9.32	1	***0.002***	0.001		

Table-3: Diagnostic Performance of ACCI at different cut-off scores

ACCI Score	Number of patients	TP	TN	FN	FP	Sensitivity %	Specificity %	PPV	NPV	Incidence of SARS CoV-2
Low Risk Group ACCI score <1										
0	167	36	53	1	77	97.30	40.77	31.86	98.15	1.37%
Intermediate Risk Group ACCI 1-3										
1	167	35	59	2	71	94.59	45.38	33.02	96.72	13.6%
2	167	35	64	2	66	94.59	49.23	34.65	96.97	
3	167	33	72	4	58	89.19	55.38	36.26	94.72	
High Risk Group ACCI ≥4										
4	167	27	92	10	38	72.97	70.77	41.54	90.20	36.3%
5	167	23	105	14	25	62.16	80.77	47.92	88.24	
6	167	22	114	15	16	59.46	87.69	57.89	88.37	
7	167	21	122	16	8	56.76	93.85	72.41	88.41	
8	167	5	126	32	4	13.51	96.92	55.56	79.75	
9	167	2	128	35	2	5.41	98.46	50.00	78.53	
10	167	2	128	35	2	5.41	98.46	50.00	78.53	
11	167	1	130	36	0	2.70	100.00	100.00	78.31%	
12	There were no patients with ACCI more than 11 in this cohort.									

DISCUSSION

Current study reports high morbidity and mortality in surgical patients who developed SARS-CoV-2 infection in postoperative period. It identifies, increasing age, emergency surgery, surgery for trauma, orthopaedic and vascular procedures, spinal anaesthesia, and severity of operative procedures as independent risk factors for development of infection in surgical patients. It also documents ACCI as a predictor of development of postoperative SARS-CoV-2 infection, both in univariate and multivariate fashion, and its potential use a risk stratification tool.

Overall complication rate in surgical patients with SARS-CoV-2 infection was 49.5% while 30-day mortality was 16.2%. Respiratory complications developed in 24.32%. Mortality rate was close to that reported by Doglietto F *et al* (19.51%).[3] However, complication rate and mortality rate were lower than reported by COVIDSurg Collab (Respiratory complication rate of 51.2%; 30-day mortality of 23.8%).[2] This significant difference in incidence can partly be explained by limitations mentioned by authors in that international, multicentre, cohort study recruiting patients from 235 hospitals in 24 countries. Selection bias is one of the plausible explanations.[2]

Among others, age and comorbidities are consistent risk factors for development and progression of SARS-CoV-2 infection in both surgical and non-surgical patients. There are various methods to integrate comorbidities in research studies to assess their role.[15] These can be included as an overall count giving each comorbidity equal weight, or as a summative score.[16] Assigning equal weight does not take different grades of severity of a disease into account and cannot adjust for the confounding effect of comorbidities. Due to these reasons, it is not surprizing that COVIDSurg Collab has not identified comorbidities as a risk factor for severity of COVID19 infection in adjusted analysis.[2] Current study, on the other hand, has utilized age adjusted comorbidity index which is a more comprehensive method. It assigns different weights to each comorbidity, present in a surgical patient, based on severity and then sums the weights to assign a summative score. Integration of age score and different weights for different grades of comorbidities has helped in identification of ACCI as an important predictor of development of COVID 19 infection in surgical patients.

Use of ACCI as a predictor of development of infection in postoperative period is novel. Most of the stratification tools reported, have been designed either for early detection of infection or to predict severity of illness in infected patients.[4–6] Model proposed by Sun T *et al* is aimed at early identification while "4-C mortality tool" reported by Knight SR *et al* is an example of mortality predictor tools.[7,17] ACCI proposed in our study is aimed at prevention of infection in surgical patients. In the absence of vaccine and treatment of SARS-CoV-2 infection, this approach is more effective to neutralize the massive impact of COVID pandemic on surgical speciality. According to the statement of the Royal college of surgeons of England, more than 50,000 patients have waited over 52 weeks and these figures in June 2020 are thirty times higher than those in February 2020.[18] Besides stress on resources, fear of development of infection in perioperative period is a possible contributor. The policy of cancelling all surgical procedures due to this fear is not practical.[19] On the contrary, the strategy of approaching every surgical patient as a high risk is resource intensive. We propose a different solution to the situation at hand.

Based on statistics of current study, surgical patients with ACCI score of zero should be managed with standard precautions. Application of this strategy means that 32.33% of the patients can be managed on general wards. Such patients from the waiting list should be prioritised and surgery should be performed with no need for delaying. Absence of risk factors means that turnover for such patients will be high with minimal strain on resources. This strategy will also reduce hospital stay for such patients. Patients at moderate risk of infection (ACCI 1-3) will require extra precautions and use of certain strategies. Grouping patients with moderate risk of infection together and keeping them away from hot zones, are a few of the suggestions.[19] Similarly, some of the comorbidities are modifiable. Optimization of such morbidities may transfer patients from moderate risk to low risk.[20]

High risk group (ACCI 4 of more) is a special group of patients. More than one third of such patients may develop postop SARS-CoV-2 infection. Optimization and group de-escalation could be part of the solution. However, more intensive preventive strategies may be needed. Options of cancellation of surgery should be discussed with the patients where the risk of infection outweighs the benefits of surgery. In cases where surgery cancellation is not in the best interest of the patient, reverse isolation options should be seriously considered.[21] Shielding high risk patients, requiring urgent surgery, during perioperative period will prevent development of SARS-CoV -2 infection which in turn will reduce the risk of complications and mortality.

Current study is a single centre experience that minimizes the bias introduced due to variation in practices in multicenter design. It has documented the validity of an already existing tool for a novel use as a predictor of development of SARS-CoV-2 infection in surgical patients. The tool utilized is cost effective as it does not require any expensive laboratory testing and can be easily calculated by using an online application and patient records. Nonetheless, there are few limitations of the study.

Potential factors that can affect the infection rate include; prevalence of disease, nature of the preventive measures and effectiveness of such strategies. As these factors vary from one centre to another, generalizability and applicability of the results should be carefully assessed. Another aspect of the study is a limitation on development of a newer predictor tool incorporating other factors. Orthopaedic and vascular procedures have been identified as high risk for the development of postoperative SARS-CoV-2 infection. There could be many reasons for these findings. For example, such patients may have higher number of comorbidities; are of advanced age; have prolonged hospital stay; and may need multiple procedures. However, current study has not performed subgroup analysis. Incorporation of speciality score in ACCI can potentially improve the performance of this prognostic tool which can be investigated in future studies utilizing a large database. Currently available literature is inconclusive in this regard and further trials are in process[22,23]

CONCLUSION

Current study has validated an easily available and user-friendly stratification tool for the prevention of postoperative SARS-CoV-2 infection in surgical patients. Based on ACCI score, low risk surgical patients should have universal precautions, while intermediate risk group should have extra precautions. The options for high-risk patients include cancellation of nonurgent surgery; delaying the surgery until optimization of modifiable factors; or reverse isolation/ shielding in perioperative period if surgery cannot be cancelled. Further studies, using this model, should document the effectiveness of preventive strategies mentioned.

AUTHORS' CONTRIBUTION

Prof RC and MA conceived the idea of the research work. BH, SR, EB and WL collected the data. KB analysed and interpreted the data; drafted and revised the content; and submitted for publication. All the authors agreed with the final version of the manuscript.

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