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Short Report

Does nosocomial COVID-19 result in increased 30-day mortality? A multi-centre observational study to identify risk factors for worse outcomes in patients with COVID-19

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SUMMARY

This study aimed to determine whether nosocomial coronavirus disease 2019 (COVID-19) has a worse outcome compared with community-acquired COVID-19. This was a prospective cohort study of all hospitalized patients with confirmed COVID-19 in three acute hospitals on 9th April 2020. Patients were followed-up for at least 30 days. Nosocomial infection was defined as a positive swab after 7 days of admission. In total, one hundred and seventy-three patients were identified, and 19 (11.0%) had nosocomial infection. Thirty-two (18.5%) patients died within 30 days (all cause) of a positive swab test; there were no significant differences in 30-day all-cause mortality rates between the three groups (i.e. patients admitted with suspected COVID-19, patients with incidental COVID-19 and patients with nosocomial COVID-19): 21.1% vs 17.6% vs 21.6% ($P=0.755$). Nosocomial COVID-19 is not associated with increased mortality compared with community-acquired COVID-19.

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Introduction

In December 2019, a series of viral pneumonia cases were reported in Wuhan, Hubei Province, China. The World Health

Organization (WHO) named the novel coronavirus ‘severe acute respiratory syndrome coronavirus-2’ (SARS-CoV-2) as the causative virus of coronavirus disease 2019 (COVID-19). On 30th January 2020, WHO declared that this viral outbreak constituted a public health emergency of international concern. The spectrum of disease severity is wide; approximately 81% of cases are mild, 14% are severe and 5% are critical, with outcomes influenced by a range of factors [1]. No vaccine is currently available, and the mainstay of treatment for COVID-19 is supportive [2].

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All age groups are susceptible, but elderly patients are more likely to have severe disease [1]. Co-morbidities that increase mortality have been well described in recent literature. The age-adjusted Charlson co-morbidity index (ACCI) is a widely used prognostic indicator that assesses risk conferred by age and co-morbid disease, and allows a more pragmatic approach to comparisons within populations. The Scottish Index of Multiple Deprivation (SIMD) is a relative measure of seven domains (income, employment, education, health, access to services, crime and housing) used to target policies and funding to more-deprived areas. Whilst the median incubation period of SARS-CoV-2 is approximately 4 days (range 1–14 days), patients can be contagious before the onset of symptoms and the duration of infectivity remains uncertain [3].

The primary aim of this study was to determine whether nosocomial COVID-19 had a higher mortality rate compared with community-acquired COVID-19 after adjusting for covariates. The secondary aim was to identify demographic and other risk factors for severe outcomes of COVID-19.

Methods

Study design and participants

A prospective cohort study was conducted on all hospitalized patients with COVID-19, confirmed by reverse transcription polymerase chain reaction (RT-PCR), on a single day. This was carried out across three acute hospitals in a single National Health Service (NHS) trust in Scotland serving a population of 655,000.

Data collection

Patients with positive RT-PCR swabs were identified from the TrakCare Electronic Medical Record System. Demographic data, SIMD score and ACCI were extracted from electronic case records.

Patients were categorized into three distinct groups based on the reason for admission: Group 1 were admitted with suspicion of COVID-19; Group 2 presented with other pathologies but were incidentally found to have COVID-19 on admission (or within 7 days of admission); and Group 3 were admitted with other pathologies and contracted COVID-19 in hospital (positive RT-PCR after 7 days of admission). In patients with nosocomial COVID-19, day 0 was defined as the date of positive RT-PCR. All

patients were included in the study and followed-up for 30 days from admission or until discharge or death.

Outcome measures

A poor outcome was defined as all-cause 30-day mortality and/or need for critical care admission. Baseline characteristics were compared between survivors and non-survivors.

Statistical analyses

Length of stay (LOS) was calculated from the date of positive COVID-19 diagnosis until discharge or death. Covariates controlled for included ACCI, sex, deprivation decile and admission to critical care.

Multi-variate logistic regression was performed to explore predictors of admission to critical care. Only Group 1 was included in this analysis due to a lack of data for Groups 2 and 3. Covariates included in this analysis were ACCI, sex and deprivation decile. ACCI was categorized as either low (ACCI=0–3) or high (ACCI=4+). A *P*-value <0.05 was considered to indicate significance.

This study was registered with NHS Lanarkshire's Clinical Quality Project (Project ID: 13124).

Results

In total, 173 patients were identified; of these, 108 (62.4%) were male and the mean age was 68 [standard deviation (SD) 14.7] years. Of 173 patients, 31 (17.9%) died within 30 days of positive RT-PCR. All of the Group 3 patients were symptomatic, and the mean time from admission to positive RT-PCR was 36.6 (SD 24.7) days. The reasons for admission were heterogeneous, with common reasons including fall, stroke and fractured neck of femur. Summary baseline patient characteristics for each admission group were calculated, and differences were explored with univariate analyses (Table 1). There was no significant difference in mortality between the groups. Figure 1 shows a Kaplan–Meier plot of Groups 1, 2 and 3 (unadjusted).

Length of stay

Data on LOS are only reported for those patients primarily admitted for treatment of COVID-19 or who had incidental COVID-19 on admission (Groups 1 and 2). Admission type was not a predictor of LOS, although ACCI (*P*<0.001), admission to

Table 1

Baseline characteristics and main outcomes: analyses performed included one-way analysis of variance (age), Fisher's exact tests (sex, admission to critical care, death) and Kruskal–Wallis tests [age-adjusted Charlson co-morbidity index (ACCI), deprivation decile]

	Total	Group 1	Group 2	Group 3	<i>P</i> -value
Total number of patients	173	131	23	19	NA
Mean age (SD)	68.44 (14.7)	66.14 (13.8)	78.39 (10.0)	72.26 (19.3)	<0.001
Male (%)	108 (62.4)	90 (68.7)	9 (39.1)	9 (47.4)	<0.01
Median ACCI (IQR)	4 (2–6)	3 (2–5)	6 (4.5–7)	5 (4–7)	<0.001
Median deprivation decile (IQR)	4 (2–6)	5 (2–7)	3 (2–5)	4 (3–5.5)	0.321
Attended critical care (%)	48 (27.7)	45 (34.4)	1 (4.3)	2 (10.5)	<0.01
30-day mortality	32 (18.5)	23 (17.6)	5 (21.7)	4 (21.1)	0.755

Group 1, admitted with coronavirus disease 2019 (COVID-19); Group 2, incidental COVID-19; Group 3, nosocomial COVID-19; SD, standard deviation, IQR, interquartile range.

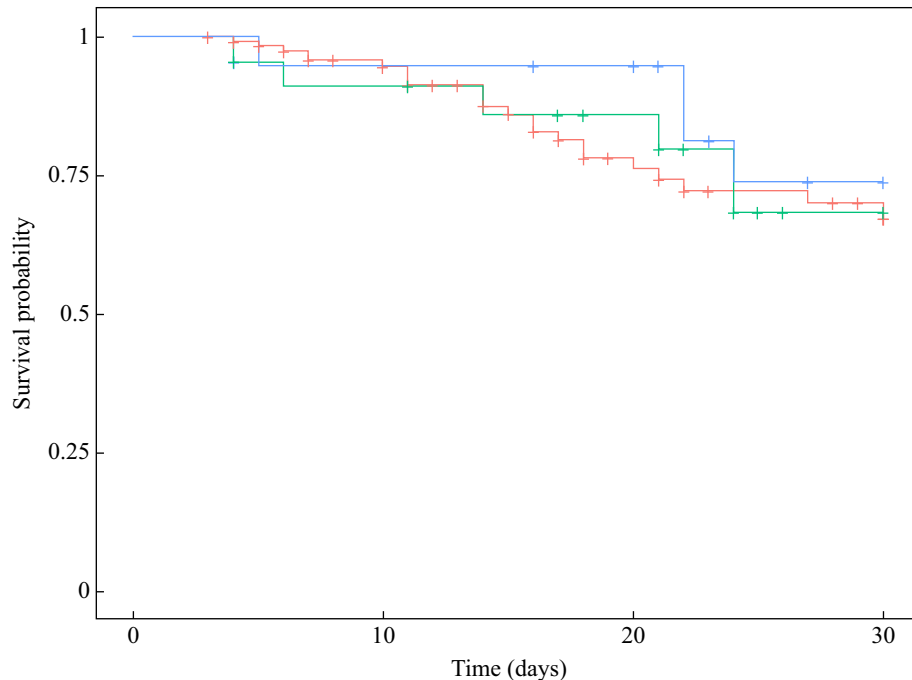


Figure 1. Kaplan–Meier plot stratified by admission group [Group 1 = admitted with coronavirus disease 2019 (COVID-19); Group 2 = incidental COVID-19; Group 3 = nosocomial COVID-19]. Red line, Group 1; green line, Group 2; blue line, Group 3.

critical care ($P < 0.001$) and deprivation decile ($P < 0.05$) were all significant predictors of LOS. Beta estimates and confidence intervals for each covariate can be found in the online supplementary material.

Critical care admission

The overall model was significant ($\chi^2 = 22.98$, $df = 3$; $P < 0.001$) and 70% accurate. Of the included covariates, only ACCI was significant (odds ratio 0.114; $P < 0.001$), suggesting that patients with a higher ACCI were less likely to be admitted to critical care (see online supplementary material).

Survival analysis

Analysis of 30-day mortality was stratified by critical care admission. Of 125 patients not admitted to critical care, there were 19 deaths within 30 days. For this cohort, a Cox proportional hazards model showed that both ACCI [hazard ratio (HR) = 1.29; $P < 0.05$] and male sex (HR = 3.36; $P < 0.05$) were predictive of 30-day mortality. Neither admission status nor deprivation decile were found to be significant. Among 48 patients who were admitted to critical care, there were 13 deaths within 30 days of diagnosis. Neither ACCI nor sex were significant predictors of mortality in this group. The small sample size, however, means that the results from this model should be interpreted with caution. Survival curves for these groups are available in the online supplementary material.

Discussion

Patients in this hospital-based population had a 30-day mortality rate of 18.5%. This study found that male sex and ACCI were predictive of 30-day mortality in patients who were

not admitted to critical care. SMID score and ACCI were also found to be predictive of LOS. Importantly, nosocomial COVID-19 was not associated with increased mortality after adjusting for ACCI. This is likely to be reflective of other parts of the UK. There have been over 15,000 positive cases to date (end May 2020) in Scotland, with a case fatality rate of approximately 15% (vs 18.5% in this study) [4]. This lower figure is likely representative of the increased acuity of hospitalized patients compared with the national population.

Male sex was associated with poor outcomes, as reported previously [2]. No patients with $ACCI \leq 1$ died, yet those with $ACCI \geq 2$ had a chance of mortality $> 25\%$. The median ACCI in this study was 4, equating to an estimated 53% 10-year survival, representing a very high comorbid disease burden in the study population. Similar results have been reported where the incidence of co-morbidities was higher in patients with COVID-19 than the general age-matched population [5]. Interestingly, male sex was only a predictor of mortality in those patients who were not admitted to critical care.

Recent unpublished statistical modelling performed by Public Health England (PHE) predicts that approximately 20% of hospital inpatient cases of COVID-19 are nosocomial [6]. Only 11% of cases in the present study were nosocomial, and stringent isolation practices already implemented may explain these relatively low results. Furthermore, the study hospitals were not fully saturated with COVID-19, and only 55% of beds were occupied (excluding critical care) during the study period. This may, in part, explain lower rates of nosocomial COVID-19 than predicted by PHE.

In this study, the 30-day mortality rate among patients with nosocomial COVID-19 was 21.1%, compared with 17.6% in patients presenting with COVID-19; however, the analysis does not suggest that this difference was significant. However, the sample size was small, and the results should be interpreted

with caution. Compared with patients admitted with symptomatic COVID-19, patients with nosocomial infection were significantly older and had higher ACCI scores. This indicates an ongoing risk for vulnerable patient groups, such as has been demonstrated in care homes across the UK.

One of the greatest challenges of COVID-19 is that it can present with a wide spectrum of illness, including symptoms similar to those of common respiratory viruses, or may be entirely asymptomatic, increasing the risk of nosocomial infection. This presents challenges for availability of isolation and containment rooms in busy hospitals, and many patients admitted without suspicious contact history or characteristic presenting symptoms of COVID-19 may receive care outside dedicated isolation areas.

The initial cross-sectional method of participant identification in this study enables a valid representation of the hospital population in a single health board, and data were collected across all departments. However, this method will be subject to a degree of length–time bias as patients with longer hospital stays would be more likely to be picked up by this method of identification, leading to inaccurate measures of survival/discharge.

A key limitation of this study was the small sample size. The group sizes were not equal; only 19 patients with nosocomial COVID-19 were included in the analysis, which made it difficult to analyse differences with confidence. Collecting data in more than one region and recruiting a larger sample with a control population would improve the validity and generalizability of the data.

A cut-off of 4 days after initial hospitalization and the absence of clinical suspicion of COVID-19 has been used previously [7]. As the incubation period could be up to 14 (interquartile range 2–7) days, it is difficult to be certain that an infection was acquired in hospital [2]. Nosocomial infections may be less advanced when they are detected due to heightened awareness of COVID-19 symptoms among healthcare workers. This means that more mild cases may be identified in Group 3 in comparison with those requiring hospital admission in Groups 1 and 2. Conversely, at the time of data collection, only patients who were symptomatic were tested in hospital, meaning that there may have been a greater number of asymptomatic nosocomial infections who would have been included in Group 3. Patients in Groups 1 and 2 may have different thresholds for self-presentation to hospital. This means the defined day 0 may vary between patients.

This study found that nosocomial COVID-19 is not associated with a significantly higher 30-day mortality rate compared with community-acquired COVID-19. Male sex, age and ACCI are significant predictors of mortality in the whole cohort. A high

degree of vigilance is required by all members of the health-care team to prevent the spread of SARS-CoV-2 within hospitals. Nosocomial infection poses an important challenge to vulnerable hospital populations, and needs to be considered as the NHS attempts to resume elective activities, balancing the risks and benefits whilst the COVID-19 pandemic continues. This study found a relatively low risk of contracting COVID-19 in hospital, with comparable outcomes to when the disease was contracted in the community. Further studies are essential to identify the mechanisms and to gain a greater understanding of how certain risk factors influence outcomes of COVID-19 in order to guide public health initiatives aimed to shield at-risk groups and save lives.

Conflict of interest statement

None declared.

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None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhin.2020.09.017>.

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