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Short Report

Sixty-day consequences of COVID-19 in patients discharged from hospital: an electronic health records study

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Data on patients discharged following COVID-19 hospitalization is scarce. We conducted an electronic health records study of community-acquired COVID-19 patients discharged between 15 March and 14 July 2020 from hospitals in Oxfordshire, UK. Of 403 discharged patients, 114 (28%) were readmitted or died within 60 days (incidence rate 18/100 person-months). Rates of readmission or death were twice as high among those ≥ 65 years as those < 65 years [standardized rate ratio: 2.21 (95% CI: 1.45–3.56)] and among women than men [2.25 (1.05–4.18)]. These findings suggest important sex differences in 60-day outcomes following COVID-19 hospitalization that have not previously been well described.

Introduction

Among patients hospitalized for COVID-19, more severe clinical outcomes (such as admission to critical care and death) have been associated with higher age, male sex and the presences of one or more major comorbidities, such as diabetes.^{1,2} However, data on patients discharged following hospitalization for COVID-19 are scarce. In particular, there is limited information on risk factors for adverse outcomes following discharge, such as readmission or death; previous studies have tended to be too small to assess variation by patient characteristics.^{3,4} This study describes the variation in the risk of readmission or death within 60 days of discharge following hospitalization for COVID-19, by age, sex and ethnicity.

Methods

Study population

We conducted a study using routinely-collected data on patients discharged between 15 March and 14 July 2020 to National Health Service (NHS) hospitals in Oxfordshire (UK) with a diagnosis of community-acquired COVID-19 (ICD-10 codes U07.1 and U07.2). Patients were followed up using linked hospital records for Oxfordshire and national death registries. Data were obtained from the Oxford University Hospital (OUH) NHS Foundation Trust as part of the National Institute of Health Research (NIHR) Health Informatics Collaborative. Details on data collection procedures, including data security and governance, are available online (<https://hic.nihr.ac.uk/COVID>).

Statistical analyses

Analyses were restricted to patients who received a positive SARS-CoV-2 polymerase chain reaction (PCR) test within seven days of

their initial hospital admission (for consistency with the NHS definition of community-acquired COVID-19 infection), and excluded those with < 60 days of follow-up. The primary outcome of analyses was incidence of hospital readmission or death within 60 days post-discharge. Patients were followed up from the day of discharge until readmission, death or 60 days post-discharge, whichever occurred first.

We calculated standardized incidence rates per 100 person-months for readmission or death, by age (< 65 years, ≥ 65 years), sex and ethnicity; rates were standardized, where appropriate, to the distribution of age (five-year age groups), sex and ethnicity of the total cohort, using the direct standardization. The variance of the standardized incidence rates was estimated assuming modified gamma distribution proposed by Fay and Feuer, and modified by Tiwari et al.⁵ All the statistical analyses were conducted in RStudio Server (Version 1.3.959) and Stata SE (v.15.1; College Station, TX: StataCorp LLC).

The database was reviewed by the National Research Ethics Service (reference: 16/HRA/3327). All data used in this analysis were provided in fully anonymized form, following a data protection impact assessment. Additional ethics committee or institutional review board approval was not required.

Results

After exclusions (two patients had < 60 days of follow-up), 403 patients were discharged following admission for community-acquired COVID-19. Median age at discharge was 66 years [interquartile range (IQR): 52–80], 192 (48%) were women, 268 (67%) were White and 273 (68%) had one or more major chronic conditions (table 1). Median duration of hospital stay was six days

(IQR: 1–13); women and men had median hospital stays of five (1–12) and six (2–14) days, respectively. However, more men ($n=25$, 12%) than women ($n=6$, 3%) had undergone invasive mechanical ventilation during their admission. Women and men had comparable distributions of age, ethnicity and prevalence of comorbidities at discharge (except for acute myocardial infarction which was more prevalent in men than in women).

Overall, 114 patients (28%) were readmitted or died within 60 days (644 person-months) following discharge (incidence rate: 17.7/100 person-months) (table 2). Median time to readmission or death was 11 days (IQR: 3–30). The standardized incidence rate (per 100 person-months) of readmission or death within 60 days of discharge was twice as high among those aged ≥ 65 years as those < 65 years [23.4 vs 10.6; standardized incidence rate ratio 2.21 (95% CI: 1.45–3.56)] and among women as men [34.9 vs 15.5; standardized incidence rate ratio 2.25 (1.05–4.18)]. There was no evidence of variation in incidence by ethnicity (table 2).

Of the 85 patients readmitted within 60 days of discharge, 35 (41%) had COVID-19 listed as a comorbidity at readmission, and breathing difficulty and fatigue was among the most common presentation among those without COVID-19 listed as a

comorbidity; 70 (82%) of the readmissions were emergencies. There were 29 deaths recorded during follow-up, with a higher proportion of deaths among women ($n=18$, 9%) than among men ($n=11$, 5%).

Discussion

Among patients discharged following admission for community-acquired COVID-19, there was a high rate of major adverse events, with about 30% of patients readmitted or dead within 60 days. Rates of readmission or death were higher among older than younger adults, and among women than men, but there was no evidence of disparities by ethnicity.

The higher rates of adverse clinical outcomes following discharge for COVID-19 hospitalization at older age is in keeping with studies of the relation between age and adverse clinical outcomes during first hospitalization for COVID-19.^{1,2} However, the higher rates of readmission or death in women than men contrasts with studies of within-hospital mortality and morbidity for COVID-19, which have tended to find that men had higher rates of admission to critical care or death than women.

Table 1 Characteristics of patients discharged following COVID-19 hospitalisation

	Female	Male	Overall
Patients, number	192	211	403
Age, years			
< 65	101 (52.6)	102 (48.3)	203 (50.4)
≥ 65	91 (47.4)	109 (51.7)	200 (49.6)
Age, years; median (IQR)	63.6 (50.9–80.6)	65.8 (52.9–78.9)	64.7 (52.4–79.7)
Ethnicity			
White	127 (66.1)	141 (66.8)	268 (66.5)
Other	28 (14.6)	33 (15.6)	61 (15.1)
Unknown	37 (19.3)	37 (17.5)	74 (18.4)
Major comorbidities			
Diabetes	43 (22.4)	49 (23.2)	92 (22.8)
Acute myocardial infarction	11 (5.7)	20 (9.5)	31 (7.7)
Congestive heart failure	20 (10.4)	23 (10.9)	43 (10.7)
Cerebrovascular disease	13 (6.8)	16 (7.6)	29 (7.2)
Dementia	24 (12.5)	19 (9.0)	43 (10.7)
Chronic obstructive pulmonary disease	46 (24.0)	53 (25.1)	99 (24.6)
Renal disease	32 (16.7)	29 (13.7)	61 (15.1)
Any of the above	115 (59.9)	128 (60.7)	243 (60.3)
Charlson Comorbidity Index^a			
0	63 (32.8)	67 (31.8)	130 (32.3)
1	62 (32.3)	73 (34.6)	135 (33.5)
≥ 2	67 (34.9)	71 (33.6)	138 (34.2)

Note: Data are n (%) unless otherwise specified.

a: Index score based on presence of major co-morbid conditions.

Table 2 Incidence rate and rate ratio of 60-day hospital readmission or death among patient discharged following COVID-19 hospitalisation

	Number of readmission or deaths	Follow-up, person-months	Crude incidence rate, per 100 person-months ^a	Standardized incidence rate (95% CI), per 100 person-months ^a	Standardized incidence rate ratio (95% CI)
Age, years					
<65	38	350	10.9	10.6 (7.4–14.7)	Ref
≥ 65	76	294	25.9	23.4 (18.2–31.2)	2.21 (1.45–3.56)
Sex					
Male	51	351	14.5	15.5 (11.3–20.8)	Ref
Female	63	293	21.5	34.9 (17.5–59.1)	2.25 (1.05–4.18)
Ethnicity					
White	83	420	19.8	20.5 (15.5–26.6)	Ref
Other	12	105	11.4	13.7 (2.5–35.3)	0.67 (0.12–1.80)
Unknown	19	119	16.0	76.2 (19.5–174.9)	3.72 (0.92–8.97)

a: Rates standardized, where appropriate, to the distribution of age (five-year age groups), sex and ethnicity of the cohort, using the direct method; confidence intervals were calculated assuming modified gamma distribution.

The reason for higher rates of readmission or death among women than men is unclear. In the present study, there was no evidence of differences between sexes in the prevalence of major comorbidities, although it was not possible to assess severity. Aspects of lifestyle or biological differences between the sexes may also affect the natural history of SARS-CoV-2 infection. Understanding outcomes by sex will be informed by detailed assessments of COVID-19 survivors, such as a recent study in China that reports worse lung diffusion impairment on CT scan among women than men.⁶

Previous studies of outcomes following COVID-19 have focused mainly on survival during hospitalization, and the few studies that have linked discharged patient to longer-term outcomes have been too small to assess differences by demographic factors^{3,4}; neither have such studies tended to consider the importance of death as a competing risk when analyzing readmissions post-discharge.^{7–9} A recent study in Michigan State (USA) found a high rate of major adverse events following admission for COVID-19, with one-fifth (22%) of patients readmitted or dead within 60 days,¹⁰ but risk factors for such outcomes were not assessed.

It is a particular strength of this study that linkage to laboratory data allowed analyses to be restricted to patients who were admitted for COVID-19, so as not to conflate outcomes in this patient group with those infected whilst in hospital. The linkage of participants to readmission throughout the region and to national death registries is also a significant strength of this study. It is a limitation that data were from a single region and that there was few non-White patients, so it was not possible to examine robustly the ethnic differences in outcomes following COVID-19. There were also too few deaths to reliably assess whether age, sex or ethnicity were related to mortality following discharge.

To the authors' knowledge, this is the first study to describe the clinically meaningful variations by demographics factors in long-term outcomes among patient admitted with community-acquired COVID-19. The findings suggest important difference in the clinical course of infection between the sexes that has not previously been well described. The reasons for higher rates of readmission or death in women require further large-scale studies.

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Conflict of interest

S.L. reports grants from the Medical Research Council (MRC), and research funding from the US Centers for Disease Control and Prevention Foundation (with support from Amgen) unrelated to this study. Other authors declare no relevant conflicts of interest.

Key points

- Patients discharged (March–July 2020) following hospitalization for COVID-19 in Oxfordshire, UK, were followed up using linked hospital records.
- Of 403 discharged COVID-19 patients, about 30% were readmitted or dead within 60 days.
- The incidence rate ratio (standardized for age, sex and ethnicity) of readmission or death within 60 days of discharge was about twice as high among women than men [ratio 2.25 (95% CI: 1.05–4.18)] and among those aged ≥ 65 than those < 65 years [ratio 2.21 (1.45–3.56)].
- The findings suggest important difference in the clinical course of COVID-19 between men and women following discharge that has not previously been well described.

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