

Predictors and Outcomes for COVID-19 Re-Admissions in the Anticipate Cohort

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Abstract

Aims

To describe readmissions of hospitalised patients with COVID-19, define predictors of readmission and explore the long term outcomes using the SF-12 score compared to patients who were not readmitted and those not hospitalised.

Methods

A single centre retrospective in North Inner-City Dublin. Recruitment was done through a COVID follow up clinic. Predictors of readmission and SF-12 scores at two timepoints post follow up at median 3 months and 12 months.

Results

Seventy (45%) participants were admitted, with a median age of 49.5 years (IQR 41.3-56.9), 36(51%) of whom were female. Unscheduled readmissions at ≤ 30 days in COVID-19 patients were 9(12.9%) and length of stay was four days (IQR 2-5). Readmissions were due to ongoing symptoms($n=9(64.3\%)$) or new complications($n=5(35.7\%)$). Mechanical ventilation and having symptoms of nausea and vomiting on index admission were predictive of readmission. ($p=0.002$). SF-12 scores at one year of readmitted patients were not different to patients who were never admitted at median one year follow up, $p=.089$.

Conclusions

Most readmissions were of short duration. Early follow up of patients post MV or who had nausea and vomiting on index admission should be prioritised. Wellbeing of readmitted patients was not different to those never hospitalised, at one year.

Keywords: SARS-CoV-2, COVID-19, Post COVID-19 Syndrome, SF-12, long covid, readmission

Introduction

To date over 519 million infections and over six million deaths due to COVID-19 have been reported by the World Health Organization (May 2022)¹. National data from Ireland between March and June 2020 describe 19,789 cases, 2,811(14.2%) of whom were hospitalised². This is in keeping with a predicted hospitalisation rate between 10 and 20% internationally for those infected prior to the availability of vaccination³. Those who are unvaccinated or partially vaccinated accounted for 63.2% of these ICU admissions between June and October 2021⁴. In essence the pressure applied by COVID-19 to the Irish healthcare system is vast and will continue to be an ongoing issue. This is compounded by the fact that Ireland has proportionally fewer doctors and fewer intensive care unit beds than most European Union (EU) countries⁵.

The stress applied to the Irish hospital network manifests in many ways including; a delay in non-COVID related procedures during wave one⁶⁻⁸, delayed care due to fear of acquiring COVID-19 in a healthcare setting⁹, and also the impact of the pandemic on Irish healthcare workers, who have been shown to have considerable levels of depression, anxiety, stress and post-traumatic stress disorder in this context¹⁰.

Readmission of patients with COVID-19 due to re-infection, complications, or persistence of symptoms are an additional considerable burden on bed days. Data from Madrid show that of 1,368 hospitalised patients between February and April 2020, 61(4.4%) were readmitted¹¹. Other reports quote readmission rates of 19.9% at 60 days for those discharged after acute infection with readmission bed days of 11.9% of total bed days for these patients¹². Early identification of those at risk of readmission and early follow up in the out-patient setting should be at the forefront of COVID-19 management to reduce the ongoing burden of COVID-19 on hospitals.

The aim of this study was to identify patient factors during first hospitalisation that may be predictive of readmission. Other aims include describing readmissions for the Anticipate cohort and exploring outcomes of readmitted and non-readmitted patients at three month and one year follow up after initial infection with COVID-19.

Methods

The Anticipate study is a single centre prospective non-interventional cohort study conducted in the Mater Misericordiae University Hospital (MMUH). Patients were recruited from the 'COVID clinic', created by the Infectious Diseases Directorate, between June and November 2020. Patient cohorts followed in the clinic were those who had been hospitalised, those that were diagnosed in the emergency department and managed with home monitoring through the hospital, and referrals from general practitioners in the catchment area. Between 12 and 15 patients were seen in the clinic weekly, approximating 300 potential participants who were eligible during the enrolment period. HRQoL questionnaires were done at 2-4 month follow up after initial symptoms and at 7-14 months. Follow up and data collection was also done through the clinic. Patients were eligible if they had laboratory confirmed COVID-19, or in those with a clinical diagnosis of COVID-19 which requires individuals to have had typical symptoms of acute COVID-19 in returning travellers or local patients at times where community transmission was known in those respective areas.

Participants also needed to be admitted to hospital for COVID-19 related illness with subsequent discharge home or to a step-down facility. Unplanned readmissions up to 180 days were considered as 'readmissions'. Informed written consent was required to participate.

Regarding variables recorded, age, sex, date of symptom onset and confirmatory testing in those with a positive polymerase chain reaction (PCR) test, comorbidities, hospitalisation, complications, length of stay, ICU admission and need for mechanical intervention (MV), readmission symptoms, complications and time, duration of readmissions, vital signs at 3 month follow up were all recorded from patient notes. Results of X-ray chest and computerised tomography (CT) thoraces were recorded from the electronic hospital record.

Outcomes include incidence of readmission, identifying predictive factors for readmission, and also long term outcomes of readmitted patients. SF-12 scores are used to assess well-being at one year and compare this to non-readmitted and those who were not hospitalised. SF-12 is a HRQoL questionnaire which is a shortened and validated version of the SF-36 questionnaire¹³. Two scores are generated from the SF-12, a Physical Composite Score (PCS) and a Mental Composite Score (MCS). This is done using an algorithm which compares patients to a standardised otherwise well population normalised on a scale of 0-100 with a mean (SD) for PCS and MCS of 50¹⁰. Scores below or above 50 for patients in the cohort confer greater or worse well-being relative to the standardised population. Although not yet validated for COVID-19 the score is well validated and reliable^{14, 15}.

Data was pseudo anonymised and collected on Redcap®, an on-line password protected research tool only accessible by members of the research team. Statistical analysis was done using IBM SPSS V24.0 (IBM Corporation, Armonk, NY, USA). Categorical data are presented as number, percentages and 95% Confidence intervals (CI). Numeric data are presented as median and interquartile range (IQR). Chi squared testing and Fisher's exact test was used to identify any differences in categorical variables. Independent T-testing and Mann Whitney U testing was used to explore parametric and non-parametric numeric data (length of stay, PCS and MCS scores). Univariate and multivariate binary logistic regression was done to assess for predictors of readmission. P values <0.05 were deemed significant.

Results

In total 155 of a potential approximation of 300 participants were included in the Anticipate cohort, 105(68%, of whom were female) with a median age of 43.3 (IQR 30.9-51.9) years. SARS-CoV2 PCR positivity was seen in 150(96.8%). The most common symptoms on initial presentation were cough n=82(53%, CI 45-60.8%), shortness of breath n=71(45.8%, CI 38-53.7%), and Fever >38°C n=70(45.2%, CI 37.3-53%).

In total 70 (45%, CI 37.3-53%) of patients were admitted to hospital, with a median age of 49.5 years (IQR 41.3-56.9), 36(51%) of whom were female. The median length of stay (LOS) was 7 days (IQR 3-15 days) with a total of 781 bed days. Radiologically 10(14.2%) patients had evidence of pneumonitis on X-ray or CT thorax. The overall complication rate on index admission was low; Table 1.

Table 1: Reasons for readmission and Length of stay.

	N (%)	95%CI
Symptomatic		
Worsening shortness of breath	5(35.7%)	7-64%
Chest pain	2(14.3%)	0-35%
Dizziness/palpitations/presyncope	1(7.1%)	0-23%
Loss of consciousness	1(7.1%)	0-23%
Length of stay in days (IQR)	2(1-3)	
Complications		
Bacterial infection	2(14.3%)	0-35%
Chronic thromboembolic pulmonary HTN	1(7.1%)	0-23%
Seizure	1(7.1%)	0-23%
Pericarditis	1(7.1%)	0-23%
Length of stay in days (IQR)	6(5-9)	

Nine (12.9%, CI 5-21%) patients required intensive care admission for a median of 13 days (IQR 9.5-19.5 days), and five (7%, CI 0-13%) required MV. No patients received remdesivir or tocilizumab.

Of all hospitalised patients, 17(24.3%, CI 14-34%) were readmitted within 180 days. Three patients were admitted for elective procedures; cholecystectomy, breast mass biopsy, and lower limb angioplasty planned pre acquisition of COVID-19 and were further excluded from the readmission cohort. The remaining 14(20%, CI 11-29%) readmissions were admitted through the emergency department or direct to ward through the home monitoring service. Nine patients (12.9%, CI 5-21%) were admitted \leq 30 days. Readmissions appear to be bimodal, either because of symptoms (SOB, chest pain) and change in vitals on home monitoring, or due to complications (pericarditis, bacterial infection, thrombosis, seizure), Table 1.

The median time to readmission was 11 days (IQR 6-64 days) and length of stay was four days (IQR 2-5 days). Of the nine 'symptomatic' patients; bloods, XR chest, ECG (and CTPA if d-dimer raised) did not yield alternative diagnoses. The median LOS for this symptomatic cohort was two days(IQR 1-3). The 'complications' cohort of five patients had a longer LOS of 6 days (IQR 5-9 days). Readmissions accounted for 79 bed days (9.2% of total bed days). No significant demographic factors were identified between patients that required unscheduled admission and those that were not re-admitted, Table 2. The only statistically significant differences in symptoms were seen with nausea and vomiting which was more common in the readmission group ($p=0.021$), and myalgia which was a more common initial symptom in patients that were not re-admitted. Regarding severity indices, the requirement for MV during index admission was significant ($p=0.016$), and there was a trend to higher complication rate in the re-admission cohort, Table 3.

Table 2: Demographics, comorbidities, symptoms on index admission.

	Readmission N=14	95%CI	No readmission N=53	95%CI	P value
Age					
Female	57%	27-87%	51%	37-65%	
Comorbidities					
Malignancy	0%	-	6%	0-12%	1.0
Pregnancy	0%	-	4%	0-9%	1.0
DM	14%	0-35%	9%	1-18%	0.63
Heart disease	14%	0-35%	11%	3-20%	0.669
Asthma	7%	0-23%	13%	4-23%	1.0
Chronic lung disease	14%	0-35%	2%	0-6%	0.11
Chronic neurological condition	7%	0-23%	9%	1-18%	1.0
Chronic haematological condition	0%	-	2%	0-6%	0.762
HTN	36%	7-64%	25%	13-37%	0.5
DM	14%	0-35%	9%	0-17%	.63
Arrhythmia	0%	-	2%	0-6%	1
PAD	0%	-	2%	0-6%	1
Anaemia	0%	-	2%	0-6%	1
Hyperlipidaemia	14%	0-35%	19%	8-30%	1
Mood disorder	21%	0-46%	13%	4-23%	0.425
Obesity	7%	0-23%	4%	0-9%	0.511
Previous thrombosis	7%	0-23%	4%	0-9%	0.511
Rheumatological condition	7%	0-23%	8%	0-15%	1
Chronic GI issue	0%	-	17%	7-27%	0.186
Endocrinological condition	7%	0-23%	2%	0-6%	0.377
Surgery requiring GA	14%	0-35%	15%	5-25%	1.0
Infection requiring admission	7%	0-35%	11%	3-20%	1.0
Symptoms on index admission					
Fever >38C	7 (50%)	20-80%	30 (57%)	43-70%	0.659
Sore throat	4 (29%)	2-56%	9 (17%)	7-27%	0.447
Rhinorrhoea	0	-	2%	0-6%	1.0
Myalgia	2 (14%)	0-35%	25 (47%)	33-61%	0.026
SOB	9(64%)	36-93%	31(58%)	45-72%	0.694
Chest pain	4(29%)	2-56%	9(17%)	7-27%	0.447
Abdominal pain	1(7%)	0-23%	3(6%)	0-12%	1.0
Nausea and vomiting	4(29%)	2-56%	2(4%)	0-9%	0.015
Joint pain	0(0%)	-	1(2%)	0-6%	1.0
Headaches	5(36%)	7-64%	13(25%)	13-27%	0.5
Weakness	0(0%)	-	2(4%)	0-9%	1.0
Cough	10(71%)	44-98%	36(68%)	55-81%	1.0
Diarrhoea	2(14%)	0-35%	6(11%)	3-20%	0.669
Anosmia	2(14%)	0-35%	8(15%)	5-25%	1.0

Table 3: Severity indices and complication rates of re-admitted and non re-admitted patients.

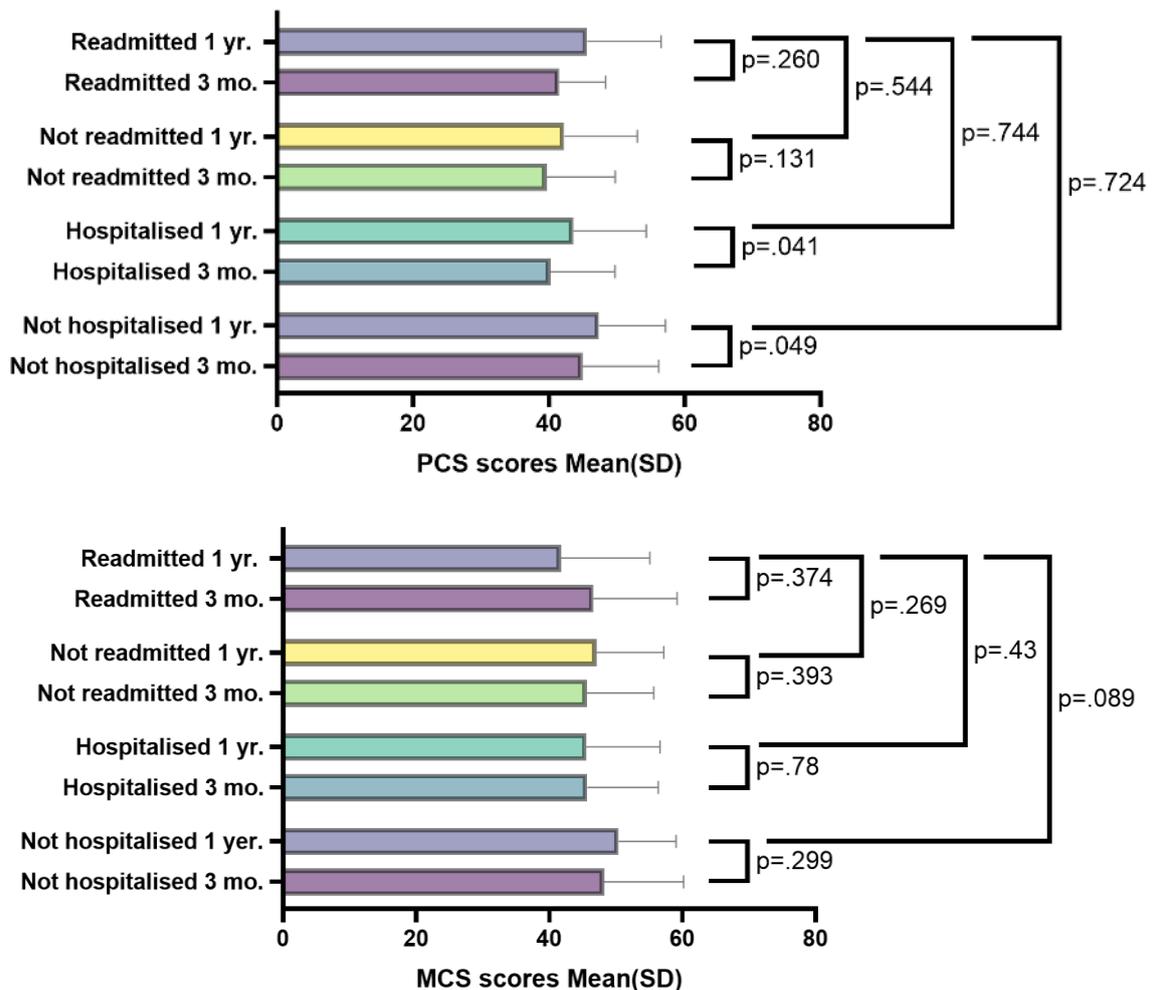
	Unscheduled Readmission N=14	95%CI	No readmission N=53	95%CI	P value
Length of stay in days, IQR)	6(3-11 days)		8(4-23.5 days)		.354
Severity indices					
Intensive care admission	29%	2-56%	8%	0-15%	0.053
HIFLO/NIV*	21%	0-46%	9%	1-18%	0.349
MV	21%	0-46%	2%	0-6%	0.026
Antiviral medication	64%	36-93%	53%	39-67%	0.443
HCQ^+Azithromycin	57%	27-87%	43%	30-57%	0.359
Complications					
Venous thromboembolism	14%	0-35%	2%	0-6%	0.108
Significant bacterial infection	14%	0-35%	2%	0-6%	0.108
Sarcopenia/deconditioning	14%	0-35%	2%	0-6%	0.108
Myocarditis/pericarditis	7%	0-23%	2%	0-6%	0.377
New arrhythmia	7%	0-23%	6%	0-12%	1.00
Pulmonary embolism	7%	0-23%	2%	0-6%	0.377
Myopathy	0%	-	2%	0-6%	1.0
Pneumonitis	14%	0-35%	15%	5-25%	1.0
Acute kidney injury	7%	0-23%	0%	-	0.209

*High flow Oxygen/Non-invasive ventilation.^Hydroxychloroquine

High correlation between ICU admission and Mechanical ventilation was found (Spearman's coefficient 0.722). A Multivariate regression model (with variables that showed significance on univariate analysis) was significant ($\chi^2(2) = 12.23, p=0.002$) and showed MV and N&V predicted 23.9% (Nagelkerke R^2) of variance for readmissions. Patients who were mechanically ventilated were 16 times more likely to be re-admitted than those that were not ($p=0.02, 95\% \text{ CI } 1.55-163.312$), having symptoms of nausea and vomiting were 7.8 times more likely to be readmitted ($p=0.033, 95\% \text{ CI } 1.179-51.416$).

Anticipate cohort participants had follow-up at the COVID clinic and completed SF-12 questionnaires at median 96(IQR 76-118) days and 364(IQR 304-298) days in total 39(41%, CI 32-51%) admitted patients including 9(9.6%, CI 4-16%) of the readmission cohort attended for follow up. There was no difference in SF-12 wellbeing scores (PCS, MCS) between readmitted, non-readmitted and patients who were never admitted at median one year follow up, Figure 1.

Figure 1: SF-12 components (PCS,MCS) in hospitalised patients who were readmitted at median 3 month and 1 year timepoint compared with participants who were not readmitted.



Discussion

The main findings of the study include an unscheduled readmission rate (20%) at ≤ 180 days for patients hospitalised with COVID-19 and median time to readmission was 11 days. Rates of readmission in current literature appear to be between 2% and 19.9%^{11, 12, 16-22}. Heterogeneity in design, differences in sample sizes, differing populations, local admission and readmission policies may be variables that lead to differing results in these studies. A 30-day readmission rate of 12.9% for this cohort appears to be at the higher end of this spectrum.

Readmissions can be classified into two groups: those with ongoing or worsening symptoms $n=9$ (64%) including breathlessness and chest pain and those with complications $n=5$ (36%) including infection and venous thrombosis. The duration of stay was shorter for those with symptoms, these patients had a median 48 hours stay and had work up to exclude evolving or worsening pneumonitis, pulmonary embolism, acute coronary syndrome or ongoing need for supplemental oxygenation prior to discharge.

Regarding predictors of readmission mechanical ventilation, a marker for disease severity, and symptoms of nausea and vomiting on index admission were the only significant variables found. One year follow up showed no difference in SF-12 physical (PCS) or mental (MCS) scores compared to hospitalised patients who were not readmitted or even those patients with COVID-19 in the cohort who were never admitted.

A study of over 100,000 admissions in an adjacent Dublin Hospital found ≤ 30 day readmission rates were stable over a 16 year period at 10.5%²³. At present readmission rates for COVID-19 vary between 2-20%. Large studies in seasonal influenza show an approximate 30-day readmission rate of 10-14% with most readmissions being most commonly due to bacterial pneumonia or sepsis and are less avoidable^{24, 25}. Thirty-day readmission rate for this cohort fall between these values at 12.9% and most readmissions were due to ongoing respiratory symptoms which is also reflected in the wider literature. In summary although readmission rates were relatively high, most patients had short length of stay which primarily served to diagnose or out rule complications of COVID-19. Anticipation of these issues in COVID-19 patients could be mitigated with early follow up and focused work up in acute medical assessment units or specialist covid clinics which may reduce readmission rates. Special attention should be paid to patients with more severe disease on index admission i.e. those that required mechanical ventilation. Overall patient outcomes are comparable to COVID-19 patients who never needed admission at one year.

The study is limited by small sample size and is from a single centre which make it prone to bias. Also, patients included were recruited from the covid follow up clinic and may not be fully representative of all patients with COVID-19 admitted, for instance many well patients post discharge may not have attended scheduled follow up as they may not have felt the need to attend for ongoing clinical input.

In conclusion readmission rates of COVID-19 patients are most likely to occur in the 30 days post discharge. A ≤ 30 day rate of 12.9% is reported for this cohort. Readmissions were classified into those with worsening thoracic symptoms, in particular SOB, and those with complications of COVID-19. Mechanical ventilation was strongly predictive of readmission. Early follow up of patients post discharge with focused investigation for complications of COVID-19 may mitigate readmissions. One year QoL outcomes of readmitted patients were similar to patients who never required admission or readmission.

Ethical Approval:

The study was approved by the Mater Misericordiae University Hospital Research Ethics Committee (reference number: 1/378/2141).

Patient and Public Involvement:

Neither patients nor the public were involved in the design, conduct, reporting or the dissemination of this study. The results of the study were presented at a Patient and Public Involvement event.

Declaration of Conflicts of Interest:

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