Higher clinical acuity and 7-day hospital mortality in non-COVID-19 acute medical admissions: prospective observational study

Marcus J Lyall, Nazir I Lone

ABSTRACT

Objectives To understand the effect of COVID-19 lockdown measures on severity of illness and mortality in non-COVID-19 acute medical admissions.

Design A prospective observational study.

Setting 3 large acute medical receiving units in NHS Lothian, Scotland.

Participants Non-COVID-19 acute admissions (n=1682) were examined over the first 31 days after the implementation of the COVID-19 lockdown policy in the UK on 23 March 2019. Patients admitted over a matched interval in the previous 5 years were used as a comparator cohort (n=14 954).

Main outcome measures Patient demography, biochemical markers of clinical acuity and 7-day hospital inpatient mortality.

Results Non-COVID-19 acute medical admissions reduced by 44.9% across all three sites in comparison with the mean of the preceding 5 years (p<0.001). Patients arriving during this period were more likely to be male, of younger age and to arrive by emergency ambulance transport. Non-COVID-19 admissions during lockdown had a greater incidence of acute kidney injury, lactic acidaemia and an increased risk of hospital death within 7 days (4.2% vs 2.5%), which persisted after adjustment for confounders (OR 1.87, 95% CI 1.43 to 2.41, p<0.001).

Conclusions These data demonstrate a significant reduction in non-COVID-19 acute medical admissions during the early weeks of lockdown. Patients admitted during this period were of higher clinical acuity with a higher incidence of early inpatient mortality.

INTRODUCTION

COVID-19, the disease manifestation of the SARS-CoV-2 virus, global pandemic in 2020 enforced unprecedented change on how the people of the UK live their lives. From 23 March 2020, measures were taken to slow the spread of SARS-CoV-2 with the closure of entertainment, hospitality and indoor leisure premises, the advice to stay home and limit all but essential travel and to work from home where at all possible.1

Self-attendance rates to emergency medicine services sharply declined during this phase, with a marked reduction in patients presenting with a possible myocardial infarction prompting concern that patients with significant acute illness may not be attending hospital for acute medical care.2 The reasons for this are unclear but may have been due to concerns about being infected with SARS-CoV-2 or burdening the health service during the pandemic. Concerns that this change in healthcare-seeking behaviour was resulting in public harm were raised following weekly data reports during the first month of lockdown from the National Records of Scotland demonstrating a 79% increase in all-cause mortality for the same week, with 23% of the excess mortality not attributed to COVID-19.3 This was supported by data from the Office of National Statistics UK, recording deaths of 22 351 for week 16 in 2020 in England and Wales, 11 854 more than the 5-year average for this week. While COVID-19 is listed on the death certificate in 8758 deaths for this period, this does not represent all of the excess.4

Community testing for presumed SARS-CoV-2 infection was not adopted in this period. As such, it is unclear whether a proportion of this excess mortality results from delayed presentation to healthcare services with potentially life-threatening conditions unrelated to SARS-CoV-2 infection or due to undiagnosed COVID-19 disease. To investigate this further, we prospectively examined the
demography, route of admission, blood markers of medical acuity and adjusted hospital 7-day mortality of non-COVID-19 acute medical admissions to three large acute medical units in a health board in Scotland during the lockdown period. Admissions to the same units over the same time frame in the preceding 5 years were used as comparison.

Study design, setting and participants
We conducted a cohort study using data obtained from Trakcare inpatient management system (Intersystems, Illinois). Patients resident in the NHS Lothian Health Board area who were admitted to the three acute medical units during the 31-day period were examined following the first week of lockdown (23 March 2020). Patients testing positive for SARS-CoV-2 infection were excluded. This was compared with the same 31-day period beginning the same week from the preceding 5 years (13th week of the years 2015–2019).

Variables and data sources
The primary outcome was 7-day hospital mortality obtained from Trakcare. Potential confounders included age, sex and socioeconomic deprivation. Age was categorised into 10-year age bands for graphical presentation and entered as a continuous term into models. Socioeconomic deprivation was represented as quintiles of the Scottish Index of Multiple Deprivation (SIMD) and was obtained from the SIMD database 2020 version published by the Scottish government. Population estimates were obtained from the National Records of Scotland database. Clinical laboratory test results provided measurements for blood lactate, serum creatinine and SARS-CoV-2 test results. Blood lactate was dichotomised at the reference range threshold (≥2.4–>2.4). Baseline creatinine was obtained on the most recent blood test at least 7 days from hospital admission within the year prior to the patient’s admission in order to determine Acute Kidney Injury Network (AKIN) stage (four categories: no acute kidney injury (AKI) and AKI stages 1–3). This was analysed as a binary variable based on severity of renal injury (no AKI/Risk:stage 1 vs ‘Injury’:Stage 2/Failure:Stage 3). Where baseline creatinine was not available, the median value of the population without known renal impairment was used (69µmol/L). All admitted patients were screened for signs and symptoms of SARS-CoV-2 infection using local guidelines (online supplemental material 1) and tested using rtPCR nose and throat combined swab where criteria are met. If this was negative and clinical suspicion persisted, a second swab was performed. Any patients testing positive at any stage during admission were removed from the study.

Statistical methods
Analyses were undertaken using R V.3.6.1. Graphical outputs were performed using ggplot2 package. Missing data for renal biochemistry and lactate were included in the analysis as being ‘no AKI’ or ≤2.4 mmol/L as consultation with clinicians indicated that these tests were considerably more likely to be omitted where there is clinically no indication to perform the test. Baseline characteristics and mode of admission were compared between lockdown and prelockdown cohorts using Mann-Whitney U or χ² tests as indicated. Admission rate and 7-day hospital mortality per head of population were calculated using the number of admissions of events per head of population for the region for the lockdown period relative to the mean of the previous 5 years, and p value was determined using Poisson regression. Seven-day hospital mortality, severity of acute kidney injury and lactic acidemia on admission was compared for the admitted population in the lockdown period relative to previous years using binary logistic regression and adjusted for age, sex and deprivation. To evaluate the robustness of the missingness mechanism for acute kidney injury and lactic acidemia (not missing at random assumption), we conducted a complete case analysis for the association between lockdown period and these two variables in sensitivity analyses. The project was reviewed by NHS Lothian Research and Development Department and Caldicott and deemed not to require ethical approval. The project was undertaken in line with local information governance procedures.

RESULTS
One thousand and eighty-two non-COVID-19 medical admissions were identified during the 2020 lockdown period and compared with 14954 acute medical admissions from a matched period in the previous 5 years. Non-COVID-19 admissions to acute medical units fell by 44.9% in comparison with the mean of the preceding 5 years (p<0.001, figure 1). Numerical data for demographics, source of referral, incidence of AKI, lactic acidemia and 7-day mortality during the lockdown period and compared with the previous 5 years are demonstrated in table 1. Patients admitted during the lockdown period were younger (median 69 vs 72, IQR 26, p<0.001) (figure 2), more likely to be male (49.5% vs 45.5%, p<0.001) and more likely to arrive by emergency ambulance than other modes of attendance (53% vs 37.7%, p<0.001). When examining acuity of illness, there was a small but significant increase in patients with AKI (6.7% vs 4.7%) and lactic acidemia (12.4% vs 7.3%), which persisted after adjustment for confounders (AKI=OR 1.44, 95%CI 1.26 to 1.62, p<0.001; lactic acidaemia=OR 1.79, 95%CI 1.52 to 2.09, p<0.001). In sensitivity analyses using a complete case approach to assess the impact of missing values, the lockdown period was still associated with a higher incidence of AKI (OR 1.42, 95%CI 1.17 to 1.77, p<0.001; lactic acidaemia=OR 1.79, 95%CI 1.52 to 2.09, p<0.001). Patients admitted to acute medical units during the COVID-19 lockdown period had over twice the risk of death within 7 days of admission when compared with the previous
5 years (4.2% vs 2.5%), which persisted after adjustment for confounders (OR 1.87, 95% CI 1.43 to 2.41, p<0.001) (figure 3). However, there was no increase in the absolute rate of patients dying 7 days following acute medical admission as a proportion of the whole population (8.43 vs 7.82 per 100 000 population, p=0.57) (figure 4).

**DISCUSSION**

These data suggest that admissions to acute medical units fell considerably during the initial national lockdown phase of the pandemic. We have demonstrated that patients admitted to acute medical units (AMUs) were younger, more likely to be male and were clinically more unwell with more severe renal injury, greater incidence of lactic acidaemia and a significantly higher incidence of in-hospital 7-day mortality.

There are several possible explanations for these findings. The younger demographic could be due to more elderly patients being preferentially managed at home to avoid COVID-19 exposure. This may have been driven by patient preference, primary care physician recommendation or the increased availability of family members to provide support at home. The increase in attendance by emergency ambulance suggests an increase in patient acuity; however, it may also reflect a change in patient behaviour in accessing healthcare during periods that general practices were performing patient care remotely by telephone appointment.

Late presentation with time sensitive pathologies such as sepsis, stroke or myocardial infarction worsens outcome. It is possible that the higher level of illness acuity and higher mortality is due to this phenomenon.
nose and throat swab test for SARS-CoV-2 is widely reported to have sensitivity limitations possibly due to predominance of the infection in the lungs with relatively little in the upper respiratory tract.11 Locally, we have found that 18% of patients admitted to hospital testing positive for SARS-CoV-2 were diagnosed on a subsequent follow-up swab (unpublished data). Local guidelines that require repeat testing in those with a high clinical suspicion of COVID-19 may ameliorate this effect. Furthermore, patients with COVID-19 can present with atypical symptoms and signs, such as rash, seizures and gastrointestinal haemorrhage or stroke, which would not trigger testing under our local guidelines.12-18 It may be therefore that a proportion of the increase in patient acuity and death observed is due to undiagnosed SARS-CoV-2 infection. The expansion of testing to include all hospital admissions in future may help to clarify this.

This study adds to the current literature on non-COVID-19 related healthcare contacts during the pandemic. Previous reports demonstrate active healthcare avoidance with a reduction in paediatric emergency care attendance with minor illnesses and, more demonstrably, evidence of delayed presentation of new-onset type 1 diabetes with diabetic ketoacidosis and acute myocardial infarction.15-18 Riley and colleagues19 describe a reduction in unselected acute medical admission numbers and a change in pathology case mix but no increase in non-COVID-19 related inpatient mortality in comparison with the previous year. We build on this work by analysing admission rates adjusted for regional population size, serum markers of clinical acuity and by extending to the previous 5 years to account for annual variation. In addition, our study reports mortality rates adjusted for age, sex and deprivation quintile that may account for the difference in findings.

There are limitations to this study. For expediency of reporting, disease coding and stratification of presenting pathology is not available at the time of writing and future analysis of case-mix and cause of death in this cohort may allow more detailed understanding of these findings. During the lockdown period, a higher proportion of patients with time-sensitive pathologies such as severe sepsis, myocardial infarction and stroke may bypass acute medical units and be directed to specialist units or critical care units. Furthermore, a higher proportion of patients may die in the community with similar pathologies. However, exclusion of these groups from the study population would bias our mortality findings towards the null.

CONCLUSION

The COVID-19 pandemic has been associated with a significant reduction in acute medical admissions. However, those attending are younger with greater medical acuity and a higher risk of inpatient mortality. Ongoing public health efforts must be made to ensure patients seek medical attention appropriately in the context of acute medical illness during pandemic lockdown periods.

Twitter Marcus J Lyall @marcus_lyall

Acknowledgements Our sincerest thanks go to Stephen Young and Neil Murray and the team from Lothian Analytics Services at NHS Lothian for technical advice and expertise.

Contributors MJL (guarantor); design of study, data collection and linkage, statistical analysis and manuscript preparation. NIL: study design, statistical analysis and manuscript preparation.

Funding MJL is supported by an NHS research Scotland Clinical Fellowship. NIL declares no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work. This project was conducted without influence from the respective funding bodies.

Competing interests None declared.

Patient and public involvement statement We did not directly include PPI in this study, but the database used in the study was developed with PPI and is updated by a committee that includes patient representatives.

Patient consent for publication Not required.

Ethics approval The study was reviewed by the Quality Improvement Team and registered in NHS Lothian as a Quality Improvement project. Following the NHS Health Research Authority decision tool and after seeking advice from NHS Lothian Research and Development department, the study was deemed to be service evaluation and therefore formal ethical approval was not required. All data were anonymised before analysis and complied with local data protection requirements.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. Data are obtained from Lothian Analytics Services at NHS Lothian. Subject to appropriate local governance procedures, requests can be made for access. Please contact corresponding author.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

This article is made freely available for use in accordance with BMJ’s website terms and conditions for the duration of the covid-19 pandemic or until otherwise determined by BMJ. You may use, download and print the article for any lawful, non-commercial purpose (including text and data mining) provided that all copyright notices and trade marks are retained.

ORCID iDs

Marcus J Lyall http://orcid.org/0000-0002-2952-2676

Nazir I Lone http://orcid.org/0000-0003-2707-2779

REFERENCES

1 UK Government. Staying at home and away from others (social distancing). Available: https://www.gov.uk/government/publications/full-guidance-on-staying-at-home-and-away-from-others

2 UK Government. Emergency department syndromic surveillance system. emergency department bulletin. Available: www.gov.uk/government/publications/emergency-department-weekly-bulletins-for-2020 [Accessed 23 Apr 2020].
Original research

3 National records of Scotland. deaths involving coronavirus (COVID-19) in Scotland week 16. Available: https://www.nrscotland.gov.uk/statistics-and-data/statistics/statistics-by-theme/vital-events/general-publications/weekly-and-monthly-data-on-births-and-deaths/deaths-involving-coronavirus-covid-19-in-scotland/archive

4 Office for National Statistics. Deaths registered Weekly in England and Wales, provisional. Off Natl Stat 2020 www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsregisteredweekly/englandandwalesprovisional/weekending10april2020

5 Scottish index of multiple deprivation 2020 2012:66:37–9.

6 National records of Scotland. Available: https://www.nrscotland.gov.uk/statistics-and-data/

7 Mehta RL, Kellum JA, Shah SV, et al. Acute kidney injury network: report of an initiative to improve outcomes in acute kidney injury. Crit Care 2007;11:931.

8 Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001;345:1368–77.

9, Sandercock P, Wardlaw JM, et al, IST-3 collaborative group. The benefits and harms of intravenous thrombolysis with recombinant tissue plasminogen activator within 6 h of acute ischaemic stroke (the third international stroke trial [IST-3]): a randomised controlled trial. Lancet 2012;379:2352–63.

10 Cannon CP, Gibson CM, Lambrew CT. Relationship of symptom-onset-to-balloon time and door-to-balloon time with mortality in patients undergoing angioplasty for acute myocardial infarction. J Am Med Assoc 2000.

11 Wang W, Xu Y, Gao R, et al. Detection of SARS-CoV-2 in different types of clinical specimens. JAMA 2020.

12 Doherty AB, Harrison EM, Green CA. Features of 16,749 hospitalised UK patients with COVID-19 using the ISARIC who clinical characterisation protocol.medRxiv 2020.

13 Oxley TJ, Mocco J, Majidi S, et al. Large-Vessel stroke as a presenting feature of Covid-19 in the young. N Engl J Med 2020;382:e60.

14 Klok FA, Kruip M, van der Meer NJM. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res 2020.

15 MÉ C, Marynak K, Clarke KEN. Delay or avoidance of medical care because of COVID-19–Related concerns — United States, June 2020. MMWR Morb Mortal Wkly Rep 2020.

16 Goldman RD, Graifstein E, Barad N, et al. Paediatric patients seen in 18 emergency departments during the COVID-19 pandemic. Emerg Med J 2020;37:emermed-2020-210273.

17 Lawrence C, Seckold R, Smart C, et al. Increased paediatric presentations of severe diabetic ketoacidosis in an Australian tertiary centre during the COVID-19 pandemic. Diabet Med 2021;38:e14417.

18 Choudhary R, Gautam D, Mathur R. Management of cardiovascular emergencies during the COVID-19 pandemic. Emerg Med J 2020;37:778 LP–80.

19 Riley B, Packer M, Gallier S, et al. Acute, non-COVID related medical admissions during the first wave of COVID-19: a retrospective comparison of changing patterns of disease. Acute Med 2020;19:176–82.