stresses

MDPI

Brief Report

COVID-19 Mortality in Patients with a Ward-Based Ceiling of Care

Matthew Ingram [1,2,*], Ellen Tullo [1,3], Laura Mackay [1], Avinash Aujayeb [1] and Northumbria COVID-19 Audit Collaborative [†]

[1] Northumbria Healthcare NHS Foundation Trust, North Shields NE1 7RU, UK; ellen.tullo@nhct.nhs.uk (E.T.); laura.mackay@nhct.nhs.uk (L.M.); avinash.aujayeb@nhct.nhs.uk (A.A.)
[2] Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne NE1 7RU, UK
[3] NIHR Newcastle Biomedical Research Centre, Newcastle upon Tyne NE1 7RU, UK
* Correspondence: matthewj.ingram@outlook.com
† See Appendix A for Collaborator List.

Abstract: Objectives: COVID-19 patients thought unlikely to benefit from organ support, thereby having a ward-based ceiling of care (WBCoC), represent a distinct subgroup. There are no associated studies in mortality. We sought to identify clinical risk factors for inpatient COVID-19 mortality. Design and setting: this was a retrospective observational study of patients admitted to Northumbria Healthcare NHS Foundation Trust. Clinical variables were associated with inpatient mortality via logistic regression. Participants: all patients admitted with COVID-19 infection and who had a WBCoC at point of admission were included (n = 114). Main outcome measures: the outcome measure was inpatient death.

Keywords: COVID-19; clinical epidemiology; assisted ventilation; emergency medicine

Citation: Ingram, M.; Tullo, E.; Mackay, L.; Aujayeb, A.; Northumbria COVID-19 Audit Collaborative. COVID-19 Mortality in Patients with a Ward-Based Ceiling of Care. *Stresses* **2021**, *1*, 277–284. https://doi.org/10.3390/stresses1040020

Academic Editors: Pinar Uysal Onganer and Daria Bottai

Received: 14 October 2021
Accepted: 4 November 2021
Published: 17 November 2021

1. Summary

What is already known on this subject?

Frailer and more elderly patients are at increased risk of COVID-19 mortality and are also more likely to have a ward-based ceiling of care (WBCoC).

Being better able to prognosticate patients with a WBCoC would allow more informed discussions with patients and relatives and would better enable services to provide holistic and end-of-life cares, such as family visits.

What are the new findings?

Mortality rate in this patient group was 48.2%.

Risk factors for inpatient mortality included increasing clinical frailty, raised inflammatory markers, increasing oxygen requirement and increasing serum creatinine.

Within this patient group, age and residential status were not risk factors for inpatient mortality.

How might it impact clinical practice in the foreseeable future?

More objective means to prognosticate COVID-19 patients with a WBCoC would allow strained healthcare systems to appropriately allocate resources and would enable clinicians to provide better holistic and clinical care.

2. Introduction

Older, frailer and co-morbid patients are disproportionately affected by COVID-19 [1–3]. Guidance from the National Institute of Clinical Excellence suggests that such individuals are less likely to benefit from organ support on intensive care and high-dependency units, thus being more likely to have a ward-based ceiling of care (WBCoC) [4]. Patients with a WBCoC represent a distinct clinical subgroup, which has become increasingly relevant during the COVID-19 pandemic. Whilst it is anticipated that those patients with severe

COVID-19 infection and a WBCoC will have a guarded prognosis, to our knowledge there are no studies outlining their risk factors for mortality.

3. Methods

Northumbria Healthcare NHS Foundation Trust (NHCT) serves a population of 600,000 in the North East of England with care organized across four sites, including a purpose built acute care center [5]. All NHCT COVID-19 inpatients admitted between 1 March 2020 and 27 April 2020 were identified. With local Caldicott approval, data and outcomes were collected retrospectively from clinical records. Rockwood clinical frailty scores (CFS) [6] were individually checked by two consultants in geriatric medicine.

WBCoC was defined as not being for level 2 and 3 care (not for non-invasive ventilation or admission to intensive care), as established at admission (Supplemental Information). We analyzed all COVID-19 inpatients with a WBCoC and for whom infection was confirmed by polymerase chain reaction (PCR) swab within the week preceding presentation, or within five days following presentation.

We carried out univariate logistic regression of common clinical variables against inpatient mortality (Supplemental Information). Significance was inferred if $p < 0.05$. We included significant variables in a progressive multivariate logistic regression analysis, adjusted to optimize the Akaike information criterion (AIC).

Patient and public bodies were not consulted regarding study design or reporting.

4. Results

114 patients were identified, 61 (53.5%) were male and 55 patients (48.2%) died. Median age was 83 (IQR 78–87, range 58–100). Of the 109 patients for whom data was available, 60 (55.0%) lived at a private residence, with 49 (45.0%) living in care homes or supported accommodation prior to admission.

Results from univariate logistic regression are displayed in Tables 1 and 2. ACE-inhibitor use was associated with reduced odds of inpatient death (odds ratio 0.354, 95% confidence interval 0.145–0.863; $p = 0.022$) (Table 1). Increased odds of inpatient death were seen with admission high FiO_2 requirements of 60% or more (23.111, 5.087–104.989; $p < 0.0001$) and 28% or more (15.562, 5.738–42.202; $p < 0.0001$). Chest X-ray changes at presentation (2.684, 1.232–5.847; $p = 0.013$) and requirement of antibiotics for suspected bacterial infection (2.355, 1.028–5.392; $p = 0.042$) were also associated. No association with inpatient death was seen with either male gender (0.817, 0.391–1.708; $p = 0.591$) or living in a private residence (0.898, 0.422–1.911; $p = 0.780$).

Table 1. Results of univariate logistical regression of categorical variables against inpatient death. OR, Odds ratio; CI, Confidence interval. ǂ, As opposed to care home residence or supported living. *, $p < 0.05$; ***, $p < 0.001$.

	Total (Died)	Percent Positive (%)	OR (95% CI)	*p*-Value
All patients	114 (55)			
Demographics				
Male Gender	114 (55)	53.5	0.817 (0.391–1.708)	0.591
Living in private residence ǂ	109 (54)	55.0	0.898 (0.422–1.911)	0.780
Clinical history				
Atrial Fibrillation	114 (55)	33.3	1.111 (0.510–2.422)	0.791
Chronic Kidney Disease	114 (55)	46.5	0.828 (0.395–1.950)	0.617
Dementia	114 (55)	29.8	0.666 (0.296–1.499)	0.326
Diabetes Mellitus	114 (55)	33.3	0.949 (0.435–2.069)	0.895
Hypertension	114 (55)	41.2	0.503 (0.235–1.076)	0.076
Ischaemic Heart Disease	114 (55)	33.3	0.690 (0.315–1.513)	0.354
ACE-inhibitor	114 (55)	26.3	0.354 (0.145–0.863)	0.022 *
Smoking history	82 (42)	52.4	0.818 (0.343–1.950)	0.651

Table 1. *Cont.*

	Total (Died)	Percent Positive (%)	OR (95% CI)	*p*-Value
Admission history				
Admission high FiO_2 requirement $\geq$ 28%	103 (53)	43.7	15.562 (5.738–42.202)	$p < 0.001$ ***
Admission high FiO_2 requirement $\geq$ 60%	103 (53)	27.2	23.111 (5.087–104.988)	$p < 0.001$ ***
Antibiotics for lower respiratory tract infection	113 (55)	69.0	2.355 (1.028–5.392)	0.042 *
Chest X-ray changes at presentation	108 (53)	51.9	2.684 (1.232–5.847)	0.013 *

Table 2. Results of univariate logistical regression of continuous variables against inpatient death. All odds ratios given as per unit increase. OR, Odds ratio; CI, Confidence interval. *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$.

	Total (Died)	OR (95% CI)	*p*-Value
All patients	114 (55)		
Demographics			
Age (years)	114 (55)	0.997 (0.951–1.045)	0.908
Number of hospital admissions in preceding 12 months	114 (55)	1.318 (1.012–1.718)	0.041 *
Rockwood clinical frailty score	108(54)	1.308 (1.002–1.705)	0.048 *
Physiological measurements at presentation			
Bodyweight (kg)	84 (35)	1.002 (0.979–1.025)	0.879
Body mass index (kg/m^2)	84 (35)	1.027 (0.962–1.097)	0.428
Peripheral oxygen saturation (%)	113 (54)	0.891 (0.807–0.984)	0.023 *
Heart rate (beats/minute)	114 (55)	1.009 (0.993–1.026)	0.271
Respiratory rate (breaths/minute)	114 (55)	1.206 (1.099–1.323)	<0.001 ***
Systolic blood pressure (mmHg)	114 (55)	0.989 (0.975–1.002)	0.100
Diastolic blood pressure (mmHg)	114 (55)	0.992 (0.968–1.017)	0.517
Temperature (°C)	114 (55)	1.110 (0.791–1.559)	0.546
Inhaled FiO_2 (%)	114 (55)	1.072 (1.025–1.122)	0.003 **
Venous blood at presentation			
Neutrophils (10^9/L)	113 (54)	1.099 (1.008–1.198)	0.033 *
Lymphocytes (10^9/L)	113 (54)	0.709 (0.313–1.605)	0.410
Platelets (10^9/L)	113 (54)	0.998 (0.994–1.003)	0.476
C-reactive protein (mg/L)	111 (52)	1.009 (1.004–1.015)	<0.001 ***
Procalcitonin (ng/mL)	43 (22)	1.610 (0.646–4.013)	0.307
Urea (mmol/L)	113 (54)	1.039 (0.994–1.087)	0.089
Creatinine (µmol/L)	113 (54)	1.009 (1.002–1.016)	0.017 *
ALT (IU/L)	109 (53)	1.003 (0.999–1.007)	0.205
Bilirubin (µmol/L)	106 (51)	1.030 (0.972–1.091)	0.315
Fibrinogen (g/L)	63 (35)	1.143 (0.809–1.613)	0.449
Lactate (mmol/L)	91 (47)	1.374 (0.995–1.896)	0.053
Blood gas at presentation			
pH	63 (34)	2.506 (0.007–965.303)	0.763
pO2 (arterial blood gases only, kPa)	46 (27)	0.971 (0.884–1.066)	0.532
pCO_2 (kPa)	62 (34)	0.428 (0.248–0.739)	0.002 **
Bicarbonate (mmol/L)	61 (32)	0.858 (0.763–0.964)	0.010 *
Base excess (mmol/L)	60 (31)	0.894 (0.806–0.993)	0.036 *

Table 2. *Cont.*

	Total (Died)	OR (95% CI)	*p*-Value
During admission			
Peak C-reactive protein (mg/L)	111 (52)	1.009 (1.005–1.014)	<0.001 ***
Peak creatinine (μmol/L)	113 (54)	1.009 (1.002–1.015)	0.012 *
Number of affected zones on worst chest X-ray	108 (53)	1.532 (1.170–2.009)	0.002 **

Age was not associated with inpatient mortality (0.997, 0.951–1.045, per year increase; $p = 0.908$), whereas Rockwood CFS was (1.308, 1.002–1.705, per unit increase; $p = 0.048$) (Table 2). At presentation, lower peripheral oxygen saturations (0.891, 0.807–0.984, per % increase; $p = 0.023$), requirement of higher inhaled FiO_2 (1.072, 1.025–1.122, per % increase; $p = 0.003$) and increased respiratory rate (1.206, 1.099–1.323, per beath per minute increase; $p < 0.0001$) were associated with inpatient mortality.

From serum blood tests at presentation, neutrophilia (1.099, 1.008–1.198, per 10^9/L increase; $p = 0.033$), increasing C-reactive protein (CRP; 1.009, 1.004–1.015, per mg/L; $p = 0.0003$) and increasing creatinine (1.009, 1.002–1.016, per μmol/L; 0.017) associated with later mortality. In the smaller number of patients with blood gases at presentation, odds of inpatient death increased with decreasing pCO_2 (0.428, 0.248–0.739, per kPa; $p = 0.002$), bicarbonate (0.858, 0.763–0.964, per mmol/L; $p = 0.010$) and base excess (0.894, 0.806–0.993, per mmol/L; $p = 0.036$).

During admission, number of affected zones on worst chest X-ray (1.532, 1.170–2.009, per zone; $p = 0.002$), and higher peak measurements of CRP (1.009, 1.005–1.014, per mg/L; $p < 0.001$) and creatinine (1.009, 1.002–1.015, per μmol/L; $p = 0.012$) all associated with increased odds of death.

For multivariate logistic regression, we selected from variables with significant univariate relationships and included all patients for whom we had data for all selected variables (n = 95). After optimizing AIC, we observed adjusted odds ratios as shown in Table 3. Inpatient requirement of FiO_2 greater than or equal to 28% (10.479, 2.888–38.023; $p < 0.001$), respiratory rate at presentation (1.181, 1.030–1.353, per breaths per minute; $p = 0.017$), Rockwood CFS (1.612, 1.040–2.499, per unit increase; $p = 0.033$), admission high CRP (1.010, 1.002–1.019, per mg/L; $p = 0.010$) and admission high creatinine (1.011, 1.001–1.020, per μmol/L; $p = 0.029$) all increased odds of inpatient mortality.

Table 3. Adjusted odds ratios of variables from adjusted multivariate logistical regression against inpatient death, in the 95 patients for whom data for all patients was available. OR, Odds ratio; CI, Confidence interval. ǂ, continuous variable, OR presented as per unit increase. *, $p < 0.05$; ***, $p < 0.001$.

	Adjusted OR (95% CI)	*p*-Value
Admission high FiO_2 requirement ≥ 28%	10.479 (2.888–38.023)	<0.001 ***
Respiratory rate ǂ (breaths/minute)	1.181 (1.030–1.353)	0.017 *
Peak C-reactive protein ǂ (mg/L)	1.010 (1.002–1.018)	0.010 *
Peak creatinine ǂ (μmol/L)	1.011 (1.001–1.020)	0.029 *
Rockwood clinical frailty score ǂ	1.612 (1.040–2.499)	0.033 *

5. Discussion

The mortality rate (48.2%) in this patient group was higher than in previous studies [1–3]. Whilst our population was clearly elderly when compared to the general COVID-19 population [1–3], we did not find any association of age with mortality within our group. In contrast to previous studies [1], care home or supported residence were not associated with inpatient mortality. Additionally, no significant association was seen with any individual comorbidity.

Our strongest predictors of mortality were those reflective of respiratory distress, as were clinical frailty and biomarkers indicative of inflammatory response, such as neutrophilia, CRP and chest X-ray changes. These findings are consistent with previous clinical studies and autopsy reports [1,3,7]. The results of multivariate analysis evidence organ failure (in the form of type 1 respiratory failure and declining creatinine clearance) as implicit in mortality risk, which is especially pertinent in those unlikely to benefit from organ support.

Limitations to this analysis include our reliance on retrospective data collected from clinical records, which resulted in missing data and may result in errors in the effect sizes of some variables. However, our main conclusions are based upon objective measures within which there were minimal missing data. Additionally, it is possible that not all WBCoC patients were successfully identified. However, data selection is unlikely to have been biased towards either outcome, minimizing effects on our findings. Another limitation was our reliance on laboratory tests that were collected during routine clinical care; inclusion of investigations such as serum cardiac troponin, brain natriuretic protein (BNP), D-dimer and procalcitonin may further aid prognostication [3,8–10].

We conclude that having more objective means to assess risk factors of mortality in patients with a WBCoC would better enable clinicians, patients and relatives to discuss appropriate settings of care, likely trajectories and to balance the provision of holistic care with infection risk. Whilst our results suggest some concordance with mortality risk factors observed in the general COVID-19 population [1,2,11], there is sufficient divergence to warrant investigation with larger prospective studies.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/stresses1040020/s1, Treatment escalation plans at Northumbria Healthcare Trust; Selection of clinical variables.

Author Contributions: Conceptualization, M.I., L.M. and A.A.; methodology, M.I., L.M. and A.A.; software, M.I.; validation, M.I., L.M. and A.A.; formal analysis, M.I.; investigation, M.I., E.T., L.M. and A.A.; resources, L.M. and A.A.; data curation, M.I., E.T., L.M. and A.A.; writing—original draft preparation, M.I.; writing—review and editing, M.I., E.T., L.M. and A.A.; supervision, A.A.; project administration, L.M. and A.A.; funding acquisition, not applicable. Northumbria COVID-19 Audit Collaborative contributed to data collection. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors. This research received no external funding.

Institutional Review Board Statement: The study was registered as a clinical service evaluation with the Northumbria Healthcare NHS Foundation Trust and was exempt from ethical approval, with analysis of anonymized healthcare data approved by the Caldicott Guardian.

Informed Consent Statement: Informed consent was not required for a retrospective anonymized evaluation under the Control of Patient Information Regulations Notice for processing of data in connection to COVID-19.

Data Availability Statement: The data are not publicly available due to patient confidentiality.

Conflicts of Interest: The authors declare no conflict of interest.

Appendix A

Table A1. Northumbria COVID-19 Audit Collaborative.

	Name	Email	Affiliation
1	Karl Jackson	karl.jackson@nhct.nhs.uk	Northumbria, HealthCare, NHS, Foundation, Trust Newcastle, United Kingdom
2	Elinor Edwards	elinor.edwards@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
3	Elizabeth Marsh	elizabeth.marsh4@nhs.net	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
4	Catherine Moores	catherine.moores@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
5	Esther Longden	esther.longden@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
6	Pierre Chinedu	pierre.chinedu@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
7	Matt Ingram	matt.ingram@nhs.net	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
8	Gemma Stonier	gemma.stonier@nhs.net	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
9	Ellen Tullo	ellen.tullo@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
10	Laura Mackay	laura.mackay@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
11	Catherine Dotchin	catherine.dotchin@nhs.net	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
12	Amaani Hussain	amaani.hussain@nhs.net	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
13	Samuel Dale	samuel.dale@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
14	Sarah Manning	sarah.manning@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
15	Lindsey Dew	lindsey.dew@nhs.net	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
16	Thomas Ross	thomas.ross@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
17	Leyla Wannous	leyla.wannous@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
18	Sophia Oxenburgh	sophia.oxenburgh@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
19	Declan Murphy	declan.nurphy@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
20	Richard Gavin	richard.gavin@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
21	Leah Taylor	leah.taylor1@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
22	Sarah Welsh	sarah.welsh1@nhs.net	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
23	Caitlin Carolan	caitlin.carolan@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom

Table A1. *Cont.*

	Name	Email	Affiliation
24	April Donne	april.donne@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
25	Nicholas Moss	nicholas.moss@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
26	Josephine Gwinnell	josephine.gwinnell@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
27	Fiona Starkie	fiona.starkie@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
28	Robert Johnston	robert.johnston@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
29	James Dundas	james.dundas@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
30	Johannna Jones	johanna.jones@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
31	Kristen Davies	kristen.davies@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
32	Richard Anderson	richard.anderson@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
33	Peter Ireland	peter.ireland@ncht.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom
34	Avinash Aujayeb	avinash.aujayeb@nhct.nhs.uk	Northumbria, HealthCare, NHS Foundation Trust Newcastle United Kingdom

References

1. Chinnadurai, R.; Ogedengbe, O.; Agarwal, P.; Money-Coomes, S.; Abdurrahman, A.Z.; Mohammed, S.; Kalra, P.A.; Rothwell, N.; Pradhan, S. Older age and frailty are the chief predictors of mortality in COVID-19 patients admitted to an acute medical unit in a secondary care setting—A cohort study. *BMC Geriatr.* **2020**, *20*, 409. [CrossRef] [PubMed]
2. Richardson, S.; Hirsch, J.S.; Narasimhan, M.; Crawford, J.M.; McGinn, T.; Davidson, K.W.; Northwell COVID-19 Research Consortium. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. *JAMA* **2020**, *323*, 2052–2059. [CrossRef] [PubMed]
3. Chen, R.; Liang, W.; Jiang, M.; Guan, W.; Zhan, C.; Wang, T.; Tang, C.; Sang, L.; Liu, J.; Ni, Z.; et al. Risk Factors of Fatal Outcome in Hospitalized Subjects with Coronavirus Disease 2019 From a Nationwide Analysis in China. *Chest* **2020**, *158*, 97–105. [CrossRef] [PubMed]
4. COVID-19 Rapid Guideline: Critical Care in Adults. Available online: https://www.nice.org.uk/guidance/ng159/chapter/4-Clinical-decision-making-and-management (accessed on 22 February 2021).
5. Pioneering New Emergency Care Hospital Close to Completion. Available online: https://www.england.nhs.uk/2015/02/Cramlington-hospital/ (accessed on 14 October 2021).
6. Rockwood, K.; Song, X.; MacKnight, C.; Bergman, H.; Hogan, D.B.; McDowell, I.; Mitnitski, A. A global clinical measure of fitness and frailty in elderly people. *CMAJ* **2005**, *173*, 489–495. [CrossRef] [PubMed]
7. Maiese, A.; Manetti, A.C.; La Russa, R.; Di Paolo, M.; Turillazzi, E.; Frati, P.; Fineschi, V. Autopsy findings in COVID-19-related deaths: A literature review. *Forensic Sci. Med. Pathol.* **2021**, *17*, 279–296. [CrossRef] [PubMed]
8. Arcari, L.; Luciani, M.; Cacciotti, L.; Musumeci, M.B.; Spuntarelli, V.; Pistella, E.; Martolini, D.; Manzo, D.; Pucci, M.; Marone, C.; et al. Incidence and determinants of high-sensitivity troponin and natriuretic peptides elevation at admission in hospitalized COVID-19 pneumonia patients. *Intern. Emerg. Med.* **2020**, *15*, 1467–1476. [CrossRef] [PubMed]
9. Zanza, C.; Racca, F.; Longhitano, Y.; Piccioni, A.; Franceschi, F.; Artico, M.; Abenavoli, L.; Maiese, A.; Passaro, G.; Volonnino, G.; et al. Risk Management and Treatment of Coagulation Disorders Related to COVID-19 Infection. *Int. J. Environ. Res. Public Health* **2021**, *18*, 1268. [CrossRef] [PubMed]

10. Panigada, M.; Bottino, N.; Tagliabue, P.; Grasselli, G.; Novembrino, C.; Chantarangkul, V.; Pesenti, A.; Peyvandi, F.; Tripodi, A. Hypercoagulability of COVID-19 patients in intensive care unit: A report of thromboelastography findings and other parameters of hemostasis. *J. Thromb. Haemost.* **2020**, *18*, 1738–1742. [CrossRef] [PubMed]
11. Knight, S.R.; Ho, A.; Pius, R.; Buchan, I.; Carson, G.; Drake, T.M.; Dunning, J.; Fairfield, C.J.; Gamble, C.; Green, C.A.; et al. Risk stratification of patients admitted to hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: Development and validation of the 4C Mortality Score. *BMJ* **2020**, *370*, m3339. [CrossRef] [PubMed]