BMJ Open

Risk of acute deterioration and care complexity individual factors associated with health outcomes in hospitalised patients with COVID-19.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-041726
Article Type:	Original research
Date Submitted by the Author:	15-Jun-2020
Complete List of Authors:	Adamuz, Jordi; Bellvitge University Hospital, Nursing Knowledge Management and Information Systems Department González-Samartino, Maribel; Bellvitge University Hospital, Nursing knowledge Management and Information Systems Department Jiménez-Martínez, Emilio; Bellvitge University Hospital, Department of Infectious Diseases Tapia-Pérez, Marta; Bellvitge University Hospital, Nursing knowledge Management and Information Systems Department López-Jiménez, María-Magdalena; Bellvitge University Hospital, Nursing knowledge Management and Information Systems Department Rodríguez-Fernández, Hugo; Bellvitge University Hospital, Nursing knowledge Management and Information Systems Department Castro-Navarro, Trinidad; University Hospital Germans Trias i Pujol, Nursing knowledge Management and Information Systems Department Zuriguel-Pérez, Esperanza; Vall d'Hebron Research Institute, Nurse research coordinator Carratala, Jordi; Bellvitge University Hospital, Department of Infectious Diseases Juvé-Udina, Maria-Eulàlia; Catalan Institute of Health
Keywords:	Health informatics < BIOTECHNOLOGY & BIOINFORMATICS, Health & safety < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, INFECTIOUS DISEASES, Respiratory infections < THORACIC MEDICINE

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

ORIGINAL ARTICLE

Risk of acute deterioration and care complexity individual factors associated with health outcomes in hospitalised patients with COVID-19.

Jordi Adamuz, PhD, MSN, RN[1,2,5]; Maribel González-Samartino, PhD, MSN, RN[1,2,5] *; Emilio Jiménez-Martínez, MSN, RN [3,5]; Marta Tapia-Pérez, RN[1,5]; María-Magdalena López-Jiménez, MSN, RN [1,5]; Hugo Rodríguez-Fernández, RN[1,5]; Trinidad Castro-Navarro, RN[6]; Esperanza Zuriguel-Pérez, PhD, MSN, RN[7]; Jordi Carratalà, PhD, MD [3,4,5], Maria-Eulàlia Juvé-Udina, PhD, MSN, RN [2,5,8].

[1]Nursing knowledge Management and Information Systems Department, Bellvitge University Hospital, L'Hospitalet de Llobregat, Barcelona, Catalonia, Spain.

[2]School of Nursing, Medicine and Health Science Faculty, University of Barcelona, L'Hospitalet de Llobregat, Barcelona, Catalonia, Spain.

[3]Department of Infectious Diseases, Bellvitge University Hospital, L'Hospitalet de Llobregat, Barcelona, Catalonia, Spain.

[4]Faculty of Medicine, Department of Clinical Sciences, University of Barcelona, L'Hospitalet de Llobregat, Barcelona, Catalonia, Spain.

[5]Bellvitge Biomedical Research Institute (IDIBELL). L'Hospitalet de Llobregat, Barcelona, Catalonia, Spain.

[6]Nursing knowledge Management and Information Systems Department, Germans Trias i Pujol University Hospital. Badalona, Catalonia, Spain.

[7]Nurse research coordinator, Vall d'Hebron Institute of Biomedical Research (VHIR). Barcelona, Catalonia, Spain.

[8]Catalan Institute of Health. Barcelona, Catalonia, Spain.

*Corresponding Author:

Maribel González-Samartino, PhD, MSN, RN.

Nursing Knowledge Management and Information Systems Department, Bellvitge University Hospital - IDIBELL.

Feixa Llarga s/n, 08907, L'Hospitalet de Llobregat (Barcelona), Spain.

Telephone: +34 93 2602123.

Fax: +34 93 2607561.

E-mail: maribelgonzalez@bellvitgehospital.cat

Conflict of interest disclosures: We declare that we have no competing interests.

Word Count: 3,014 words.

Funding: None.

ABSTRACT

Background: Evidence about the impact of systematic nursing surveillance on acute deterioration risk along with care complexity individual factors on inpatient outcomes, is scarce. The study is aimed at determining the association between acute deterioration risk and care complexity individual factors with unfavourable outcomes in hospitalised patients with COVID-19.

Methods: A multicentre cohort study was conducted from March 1, 2020 to March 31, 2020 at seven hospitals in Catalonia, Spain. All COVID-19 adults patients admitted to hospitals and with completed minimum data set were recruited retrospectively. Patients were classified based on the presence or absence of a composite unfavourable outcome (in-hospital mortality and adverse events [AEs] during hospitalisation). The main measures included acute deterioration risk (as measured with VIDA early warning system) and 28 care complexity individual factors. All data were obtained blinded from electronic health records. Multivariate logistic analysis was performed to identify VIDA score and care complexity factors associated with unfavourable outcomes.

Results: From a total of 1,176 COVID-19 patients, 506 patients (43%) experienced an unfavourable outcome during hospitalisation. The frequency of unfavourable outcomes rose with increasing risk of acute deterioration as measured with VIDA score. Risk factors independently associated with unfavourable outcomes were chronic underlying disease (OR: 1.90, 95% CI: 1.32-2.72: $p < 0.001$), mental status impairment (OR: 2.31, 95% CI: 1.45-23.66; $p < 0.001$), length of hospital stay (OR: 1.16, 95% CI: 1.11-1.21; $p < 0.001$) and high risk of acute deterioration (OR: 4.32, 95% CI: 2.83-6.60; $p < 0.001$). High-tech hospital admission was a protective factor of unfavourable outcomes (OR: 0.57, 95% CI: 0.36-0.89; $p = 0.01$).

Conclusion: The systematic nursing surveillance of the status and evolution of COVID-19 inpatients, including the careful monitoring of acute deterioration risk and care

complexity individual factors may contribute to reduce deleterious health outcomes in COVID-19 inpatients.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This was a multicentre cohort study with a large sample size in hospitalised patients with COVID-19.
- It is the first research evaluating the association of the risk of acute deterioration (as measured with VIDA early warning system), along with care complexity individual factors, with COVID-19 patient outcomes.
- We identify broader health-contributors of care complexity, including psychosocial and mental-cognitive factors.
- No previous studies have demonstrated the effectiveness VIDA early warning system yet. Nevertheless, the results of this study had proved the significant association between the unfavourable outcomes with VIDA score.
- We not evaluate other clinical measures such as the age-adjusted Charlson comorbidity index or patient lab values.

INTRODUCTION

Along with climate change and financial crises, pandemics are one of the major global risks for the 21st century. A 2019 report stated that, in the last decade the World Health Organization (WHO) tracked 1,483 epidemic events, including Sever Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), Ebola or other epidemic-prone diseases, considered harbingers of a new era of high-impact, potentially fast-spreading outbreaks.[1]

The potential thread became real last December 2019, when a severe acute respiratory infection caused by the new coronavirus SARS-CoV-2 began to spread first in Wuhan (China).[2,3] The WHO announced the Wuhan pneumonia as an outbreak of potential danger in December 31st, as an outbreak of global concern in January 31st, and finally the coronavirus disease (COVID-19) was declared a global pandemic in February 2020.

COVID-19 patients frequently require hospital admission as they may rapidly develop severe potential life-threatening complications, such as acute respiratory distress syndrome, sepsis, major thromboembolic events or cardiac injury, requiring intensive care.[3–5] Recent studies have found overall in-hospital mortality rates for COVID-19 inpatients ranging from 15 to 28%.[3,6–8] Therefore, early recognition of patient deterioration and escalation of treatment to reduce the risk of progression to critical complications is a significant issue that may impact patient and organizational outcomes. Screening for acute deterioration implies nursing surveillance, data collection, interpretation and recognition of changes in patients' status, prioritization of patients' problems and decision making on the interventions to perform in order to curb the cascade towards adverse events (AEs) and death.[9]

According to the WHO "*patients hospitalized with COVID-19 require regular monitoring of vital signs and, where possible, utilization of early warning scores that*

facilitate early recognition and escalation of treatment of the deteriorating patient.[10] Early warning systems have become an important component of managing inpatient care, as well as a clinical decision-making support stratification tool to prevent poor health outcomes.[11–13] Previous studies suggested the need for adaptation of these systems to each context.[14] According to these recommendations, several evidence-based algorithms were developed and used to early identify and act upon initial or impending acute deterioration among hospitalised patients. In the context of this study, a nursing surveillance improving program named VIDA (the Catalan acronym for Surveillance and Identification of Acute Deterioration) started in 2013 and has evolved with a multidisciplinary approach, as a daily used early warning score system, contributing to assist clinical decision-making, since then.

It has been described that admitted patients with COVID-19 have a substantial rate of chronic conditions that may affect the complexity of medical and nursing care provision, and patient health outcomes.[15] Nevertheless, care complexity individual factors (CCIF) are related not only to multiple comorbidities but also to mental-cognitive and psychosocial patient features, which in turn are also associated with increased healthcare needs during hospitalization and with selected health outcomes.[16–18]

Only a few studies in COVID-19 inpatients have explored the use of acute deterioration risk stratification[11,19] and to date, none has assessed CCIF as predictors of poor health outcomes. The aim of this study is to determine the association between acute deterioration risk (as measured with VIDA early warning system) and care complexity individual factors with unfavourable outcomes in admitted patients with COVID-19.

METHODS

Setting and Study Design

A retrospective cohort study was carried out at seven public hospitals in Catalonia, Spain: three tertiary metropolitan facilities, three urban university centres and one community hospital. All patients with COVID-19 who were admitted to the hospital from March 1, 2020 to March 31, 2020 with a completed hospital minimum data set report were recruited retrospectively and followed up. Patients' directly admitted and discharged from intensive care units (ICU), as well as those who remained hospitalized after the recruitment end date, were excluded.

We defined the primary endpoint as a composite of unfavourable outcomes including in-hospital mortality and adverse events (AEs), not present on admission and occurring thereafter during hospitalization.

Patient and Public Involvement

This study was approved by The Clinical Research Ethics Committee of the Bellvitge University Hospital (reference 158/20). Informed consent was waived due to the study's retrospective design. Ethical and data protection protocols related to anonymity and data confidentiality (access to records, data encryption and archiving of information) were complied with throughout the whole research process.

Data Collection

Information regarding the demographic and clinical characteristics, continuity of care (discharged to another facility), high-tech hospital, length of hospital stay (LOS) and patient severity and mortality risk were collected from the hospital minimum data set and the clinical data warehouse of the Catalan Institute of Health. Patient severity and risk of mortality was based on the all patient refined diagnosis-related groups (APR-DRG) that categorises both measures in four groups, from low (level 1) to extreme

(level 4). Severity and mortality risk were dichotomized in this study into low risk (levels 1-2) and high risk (levels 3-4).[20]

VIDA score (acute deterioration risk stratification) classifies patients into five groups: no risk (level 0), low risk (level 1), moderate risk (level 2), high risk (impending complication if not stabilized) (level 3), manifested complication initial status (level 4). For the purposes of this study, VIDA score classified into mild (levels 1-2) and high (levels 3-4) risk groups. Patient progress data were extracted from anonymised electronic health records whenever they were e-charted including: respiratory rate (breaths/min), oxygen saturation (%), temperature (ºC), mental status (level of awareness; 1= aware and orientated, >1 = disturbed mental status, including disorientation, acute confusion, etc...), pulse (cardiac rate, beats/min) and systolic and diastolic blood pressure (mmHg).

Care complexity individual factors (CCIF) were classified into five domains: (i) mental-cognitive, (ii) psycho-emotional, (iii) sociocultural, (iv) developmental, and (v) comorbidity/complications, as described in previous studies.[16,18] Each CCIF domain is structured into factors and specifications. Patients were considered within any CCIF domains if they presented at least one factor or specification. These CCIF factors and specifications were obtained from the nursing assessment e-charts, as structured data based on the Architecture, Terminology, Interface, Knowledge (ATIC) terminology.[20]

Outcome measures

The in-hospital mortality accounted the number of deceased COVID-19 patients while in a ward. The AEs included intensive care unit transfer, hospital-acquired infections (HAI) and potentially avoidable critical complications (ACC) during hospitalization. Intensive care unit (ICU) transfer was defined as the number of patient episodes with effective bed change from a general ward to an intensive care area. HAI included the number of episodes of ward patients that developed catheter-related bloodstream

infection, urinary catheter-related infection, aspiration pneumonia and/or sepsis. ACC accounted for the number of episodes of ward patients that experienced a cardiac arrest, shock, thromboembolic event, acute respiratory failure, acute respiratory distress syndrome (ARDS), myocardial injury, liver injury and/or kidney failure, not present on admission.

Statistical Analysis

Descriptive analysis of data using percentage frequencies, median and interquartile range was performed to determine demographic and clinical characteristics, and patients' outcomes. For categorical variables, a comparative analysis for detecting significant differences between groups was carried out using the chi-square test or Fisher's exact test when one or more cells had an expected frequency of five or less. For continuous variables, the Student's t-test or Mann-Whitney U test was used depending on the results of the Kolmogorov-Smirnov normality test. A logistic-regression model of all clinical factors potentially associated with unfavourable outcome measures (AEs and in-hospital mortality) was performed including VIDA score, clinically relevant CCIF and other potential confounders: sex, hospital level and LOS (only covariates with *p*-values less than 0.05 in the univariate analysis were entered in the multivariate model). All potential explanatory variables included in the multivariate analyses were subjected to a correlation matrix for analysis of collinearity. The discriminatory power was evaluated by the area under the receiver operating characteristic (ROC). Results of multivariate analysis was reported as odds ratios (OR) and 95% confidence intervals (CI). We also performed a descriptive analysis to compare unfavourable outcomes in patients admitted in wards with VIDA system and without this system. Statistical analysis will be performed using the SPSS software package version 25.0 (SPSS, Chicago, IL). *P* values less than 0.05 were considered statistically significant.

RESULTS

During the study period, 1,838 patients were hospitalised with COVID-19, among them, 1,176 patients with minimum data set completed were included. The frequency of unfavourable outcomes was 42.8% (506 patients). In-hospital mortality rate was 19.6% (232 patients), and almost 41% (481 patients) experienced an AE while in a ward (2.7% transferred to ICU; 2.5% HAI; 40% ACC). Acute respiratory failure, ARDS, acute kidney failure, urinary catheter-related infection, sepsis, and thrombotic event were the most frequently AEs.

Patient Characteristics

The baseline characteristics of patients with unfavourable and favourable outcome are compared in **Table 1**. COVID-19 hospitalised patients who had an unfavourable outcome were more often male, older, and had one or more underlying chronic conditions (75.5%), mostly arterial hypertension or congestive heart failure and, diabetes or chronic kidney disease. Furthermore, they had longer LOS and high risk of severity or mortality (APR-DRG 3-4). Conversely, patients admitted in high-tech hospitals presented less frequency of unfavourable outcomes.

Regarding VIDA score, most patients with unfavourable outcomes experienced high risk of acute deterioration (41.7% in patients with unfavourable outcomes vs. 9.1% in patients with favourable outcomes).

Comorbidity, sociocultural and developmental domains were the most frequent CCIF domains identified in the studied sample. Mental-cognitive and psycho-emotional domains were less frequent. Patients with unfavourable outcomes exhibited a higher frequency of chronic disease, position impairment, anatomical and functional disorders, communication disorders, old age (>75 years) and mental status impairments, when compared to patients with favourable outcomes. The median of CCIF was also higher in patients with unfavourable outcomes (5 [IQR: 4-6] vs. 4 [IQR: 3-5]) **(Table 1)**.

Risk of acute deterioration and individual complexity factors association with outcomes.

Patients' outcomes of 806 patients with low, mild or high risk of acute deterioration were compared in **Table 2.** The frequency of unfavourable outcomes was nearly 38% in patients with mild risk and almost 80% in the high risk of acute deterioration group (p <.0.001). Similarly, the frequency of in-hospital mortality and AEs rose with increasing VIDA score and reached near 60% and 80% in patients with high risk of acute deterioration, respectively (p <.0.001). Acute respiratory failure, acute kidney failure and ICU transfer were the most frequent AEs.

Among the 1,176 patients analysed in this study, those with four or more CCIF experienced unfavourable outcomes (p <.0.05) **(Table 2)**.

Table 3 shows an adjusted analysis of health outcomes in 486 patients with high risk of mortality (APR-DRG 3-4) to compare patients admitted in wards where registered nurses use or do not use the VIDA early warning score system. In-hospital mortality was more frequent in patients admitted in wards where VIDA was not used (52.5% vs. 41.3%, p <.0.05). Conversely, the frequency of AEs was slightly higher in patients admitted VIDA' wards (p <.0.05).

Risk factors associated with unfavourable outcomes

The results of the multivariable analysis for risk of acute deterioration (as measured with VIDA score) and CCIF potentially associated with unfavourable outcomes, in-hospital mortality and AEs, are summarized in **Table 4**.

After adjustment of potentially confounders, the analysis shows that high risk of acute deterioration was an independent factor associated with unfavourable outcomes, in-hospital mortality, and AEs in COVID-19 ward inpatients. Furthermore, chronic disease, mental status impairments and LOS were risk factors associated with unfavourable outcomes. Conversely, high-tech hospital admission was a protective

factor of unfavourable outcomes. The area under the ROC curve (AUC) was 0.81 (95% CI: 0.78-0.84).

Chronic disease, mental status impairments, old age and male sex were independent risk factors associated with in-hospital mortality for studied COVID-19 inpatients. (AUC 0.91 [95% CI: 0.88-0.93]). Finally, risk factors independently associated with AEs were chronic disease, mental status impairments, old age and LOS; while high-tech hospital admission was a protective factor of AEs (AUC 0.80 [95% CI: 0.77-0.83]).

DISCUSSION

In this study of a large cohort of hospitalised patients with COVID-19, the frequency of unfavourable outcomes (in-hospital mortality and AEs) reached near 80%, in patients scored as at high risk of acute deterioration. In-hospital mortality was higher in wards not using the VIDA early warning system. A wide majority of patients had four or more care complexity individual factors identified. The risk factors independently associated with unfavourable outcomes included chronic disease, mental status impairments, LOS and high risk of acute deterioration. High-tech hospital admission was a protective factor of unfavourable outcomes.

Our findings are consistent with previous COVID-19 reports which have found a similar frequency of in-hospital mortality and AEs.[3,21] In addition, 37% of patients developed respiratory complications (acute respiratory failure or ARDS) during hospitalization. This value is within the range reported in a previous inquiry (29-42%).[3]

The results of this study show that high risk of acute deterioration is a significant risk factor for unfavourable outcomes, as a composite measure for in-hospital mortality, and AEs in admitted COVID-19 patients. Although previous studies have stressed that early warning systems are predictors of in-hospital mortality and health outcomes,[22,23] only a few have evaluated warning score systems in admitted COVID-19 patients.[11,19] These latest studies showed a fair discrimination with adverse outcomes, concluding that the evaluation of the risk for acute deterioration in the COVID-19 hospital population is a priority for the organizations.[19]

In-hospital mortality was more frequent in patients admitted in wards where registered nurses do not use VIDA early warning system. In this regard, other studies show that the use of early systems reinforces collaboration among the multidisciplinary team, and promotes the early identification of clinical deterioration.[24] Similarly,

previous studies have reported less mortality and adverse events when systematic nursing surveillance of patient status and progress is a daily basis practice.[9]

Chronic conditions and mental status impairments were the CCIF independently associated with unfavourable outcomes. Previous reports have shown that chronic diseases were more frequent among deceased COVID-19 patients [15] and older age was a potential risk factor associated with mortality.[6] Although our study has not identified age as a risk factor associated with a composite unfavourable outcome, we acknowledge that old age was an independent risk factor associated with mortality and AE. Furthermore, our findings were also consistent with other studies showing that mental status impairments are associated with hospital-acquired complications,[25] including sepsis.[4]

A wide majority of patients had four or more CCIF. Our findings are consistent with other studies that identified an important rate of chronic conditions in COVID-19 patients[15] and by the other hand, selected organizational issues that may impact care complexity and health outcomes.[26] Previous inquires have demonstrated the association of CCIF and health outcomes,[16] with an average of two CCIF per patient. Our investigation showed that for COVID-19 inpatients, the average of CCIF is four. These results are probably related to the transmissibility of this condition requiring droplet and contact precautions, the pandemics management associated public health measures of population confinement, preventing patients' relatives to visit admitted patients in person, resulting in a lack of family caregiver support during hospitalisation, and the frequency of chronic diseases in the studied sample. The organizational adaptation of hospitals to this pandemic context and the required isolation precautions have been associated with poor outcomes in prior studies.[27,28]

Additionally, we found that LOS was associated with unfavourable outcomes, coinciding with previous studies that associated AEs with increased healthcare costs due

to longer hospital stays.[29] Finally, high-tech hospital admission was a protective factor associated to unfavourable outcomes. High-tech hospitals usually have better nurse-to-patient ratios, than urban or community facilities. In this sense, a couple of recent inquiries in the same context of this study conclude that, on average hospital ward patients require 5.6 hours of RN care per patient day, while the average RN offered hours per patient day is 2.4, and that RN understaffing is a structural issue.[26,30] Nevertheless, to the best of our knowledge, no study on nurse staffing and COVID-19 inpatients' outcomes have been published. Similarly, healthcare clinical leaders and managers have become key role to rapidly adapt organizations to the new reality. Fast and effective decision-making and managerial responses in crisis situations with high levels of uncertainty are essential at immediate and short-term however, they should be accompanied by planning and executing mid-term and long-lasting improvements that positively impact patient, professional and organizational outcomes, such as structural RN understaffing.[26]

The strengths of this study include its multicentre approach, cohort design and large sample size. It is the first research evaluating the association of the risk of acute deterioration, along with care complexity individual factors, with COVID-19 patient outcomes. Importantly, we identify broader health-contributors of care complexity, including psychosocial and mental-cognitive factors. In addition, the VIDA early warning system was developed as an evidence-based algorithm with a multidisciplinary approach, and also according to previous studies that highlighted the importance to adapt surveillance and screening systems to organization and cultural context.[14]

VIDA score and CCIF data were comprehensively collected from clinical data warehouse of the Catalan Institute of Health and all patients included had a completed nurse charting in the patient electronic health record. Nevertheless, there are some limitations that should be acknowledged. We relied a properly compliance on electronic

health records and administrative data, however this statement should be interpreted with caution since voluntary completion of electronic health records show close-to-reality data and information on nurses' observations on patient status and progress, but it not the reality in itself. It should be noted, no previous studies have demonstrated the effectiveness VIDA early warning system yet. Nevertheless, the results of this study had proved the significant association between the unfavourable outcomes with VIDA score. Finally, we acknowledge as a significant limitation that we did not evaluate other clinical measures such as the age-adjusted Charlson comorbidity index or patient lab values.

Conclusion

The risk of acute deterioration and the care complexity individual factors are associated with COVID-19 patient outcomes. The rate of unfavourable outcomes rose with increasing risk of acute deterioration as measured with VIDA score. The risk factors independently associated with poor health outcomes were chronic disease, mental status impairment, length of hospital stay and high risk of acute deterioration. High-tech hospital admission was a protective factor of unfavourable outcomes. The systematic nursing surveillance of patients at risk of acute deterioration and the assessment of CCIF may contribute to reduce deleterious health outcomes in COVID-19 inpatients.

REFERENCES

1 WHO, World Bank. Global preparedness monitoring board. A world at risk. Annual report on global preparedness for health emergencies. 2019. DOI:10.2307/40153772.

2 Li Q, Guan X, Wu P, *et al.* Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N. Engl. J. Med. 2020; **382**: 1199–207.

3 Huang C, Wang Y, Li X, *et al.* Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; **395**: 497–506.

4 Li H, Liu L, Zhang D, *et al.* SARS-CoV-2 and viral sepsis: observations and hypotheses. *Lancet* 2020; **395**: 1517–20.

5 Shi S, Qin M, Shen B, *et al.* Association of Cardiac Injury with Mortality in Hospitalized Patients with COVID-19 in Wuhan, China. *JAMA Cardiol* 2020; published online March 25. DOI:10.1001/jamacardio.2020.0950.

6 Zhou F, Yu T, Du R, *et al.* Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020; **395**: 1054–62.

7 Wu C, Chen X, Cai Y, *et al.* Risk Factors Associated with Acute Respiratory Distress Syndrome and Death in Patients with Coronavirus Disease 2019 Pneumonia in Wuhan, China. *JAMA Intern Med* 2020; published online March 13. DOI:10.1001/jamainternmed.2020.0994.

8 Zheng Z, Peng F, Xu B, *et al.* Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. *J Infect* 2020; published online April 23. DOI:10.1016/j.jinf.2020.04.021.

9 Juvé-Udina ME, Fabrellas-Padrés N, Adamuz-Tomás J, *et al.* Surveillance nursing diagnoses, ongoing assessment and outcomes on in-patients who suffered a cardiorespiratory arrest. *Rev da Esc Enferm* 2017; **51**: e03286.

10 WHO. Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected. 2020. https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected (accessed May 20, 2020).

11 Hu H, Yao N, Qiu Y. Comparing rapid scoring systems in mortality prediction of critical ill patients with novel coronavirus disease. *Acad Emerg Med* 2020; published online April 20. DOI:10.1111/acem.13992.

12 Liao X, Wang B, Kang Y. Novel coronavirus infection during the 2019–2020 epidemic: preparing intensive care units—the experience in Sichuan Province, China. *Intensive Care Med* 2020; **46**: 357–60.

13 O'Brien C, Goldstein BA, Shen Y, *et al.* Development, Implementation, and Evaluation of an In-Hospital Optimized Early Warning Score for Patient Deterioration. *MDM Policy Pract* 2020; **5**: 1–10.

14 McGaughey J, O'Halloran P, Porter S, Trinder J, Blackwood B. Early warning systems and rapid response to the deteriorating patient in hospital: A realist evaluation. *J Adv Nurs* 2017; **73**: 3119–32.

15 Chen T, Wu D, Chen H, *et al.* Clinical characteristics of 113 deceased patients with coronavirus disease 2019: Retrospective study. *BMJ* 2020; **368**: m1091.

16 Adamuz J, González-Samartino M, Jiménez-Martínez E, *et al.* Care Complexity Individual Factors Associated With Hospital Readmission: A Retrospective

Cohort Study. *J Nurs Scholarsh* 2018; **50**: 411–21.

17 Safford MM. The Complexity of Complex Patients. *J Gen Intern Med* 2015; **30**: 1724–5.

18 Juvé-Udina, M.E., Matud, C., Farrero S., Jiménez, H., Rodríguez, E., Martínez, M. et al. Intensity of nursing care: workloads or individual complexity? *Metas de Enfermería* 2010; **13**: 6–14.

19 Singh K, Valley TS, Tang S, Li BY, Kamran F, Sjoding MW, Wiens J, Otles E, Donnelly JP, Wei MY, McBride JP, Cao J, Penoza C, Ayanian JZ NB. Validating a Widely Implemented Deterioration Index Model Among Hospitalized COVID-19 Patients. *medRxiv* 2020. DOI:10.1101/2020.04.24.20079012.

20 Juvé-Udina ME. What patients' problems do nurses e-chart? Longitudinal study to evaluate the usability of an interface terminology. *Int J Nurs Stud* 2013; **50**: 1698–710.

21 Mao L, Jin H, Wang M, *et al.* Neurologic Manifestations of Hospitalized Patients with Coronavirus Disease 2019 in Wuhan, China. *JAMA Neurol* 2020; published online April 10. DOI:10.1001/jamaneurol.2020.1127.

22 Medic G, Kließ MK, Atallah L, *et al.* Evidence-based clinical decision support systems for the prediction and detection of three disease states in critical care: A systematic literature review. *F1000Research* 2019; **8**: 1728.

23 Kim I, Song H, Kim HJ, *et al.* Use of the national early warning score for predicting in-hospital mortality in older adults admitted to the emergency department. *Clin Exp Emerg Med* 2020; **7**: 61–6.

24 Ashbeck R, Stellpflug C, Ihrke E, *et al.* Development of a Standardized System

to Detect and Treat Early Patient Deterioration. *J Nurs Care Qual* 2020; published online April 6. DOI:10.1097/ncq.0000000000000484.

25 Bail K, Draper B, Berry H, Karmel R, Goss J. Predicting excess cost for older inpatients with clinical complexity: A retrospective cohort study examining cognition, comorbidities and complications. *PLoS One* 2018; **13**: e0193319.

26 Juvé-Udina M, González-Samartino M, López-Jiménez MM, *et al.* Acuity, nurse staffing and workforce, missed care and patient outcomes. A cluster-unit-level descriptive comparison. *J Nurs Manag* 2020; published online May 8. DOI:10.1111/jonm.13040.

27 Purssell E, Gould Di, Chudleigh J. Impact of isolation on hospitalised patients who are infectious: Systematic review with meta-analysis. *BMJ Open* 2020; **10**: e030371.

28 Tran K, Bell C, Stall N, *et al.* The Effect of Hospital Isolation Precautions on Patient Outcomes and Cost of Care: A Multi-Site, Retrospective, Propensity Score-Matched Cohort Study. *J Gen Intern Med* 2017; **32**: 262–8.

29 Rafter N, Hickey A, Condell S, *et al.* Adverse events in healthcare: Learning from mistakes. *Q J Med* 2015; **108**: 273–7.

30 Juvé-Udina M-E, Adamuz J, López-Jimenez M-M, *et al.* Predicting patient acuity according to their main problem. *J Nurs Manag* 2019; **27**: 1845–58.

FOOTNOTES

Author Contributions: All authors had full access to all study data and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Adamuz, González-Samartino, Juvé-Udina. *Coordination team:* Juvé-Udina. *Acquisition of data:* Adamuz, Tapia-Perez, López-Jiménez, Zuriguel-Pérez, Castro-Navarro. *Analysis and interpretation data:* Adamuz, González-Samartino, Jiménez-Martínez. *Drafting of the manuscript:* Adamuz, González-Samartino, Jiménez-Martínez, Juvé-Udina. *Critical revision of the manuscript for important intellectual content:* Tapia-Perez, López-Jiménez, Rodríguez-Fernández, Zuriguel-Pérez, Castro-Navarro, Carratalà. *Statistical analysis:* Adamuz and González-Samartino. *Obtained funding:* - . *Administrative, technical and material support:* López-Jiménez, Rodríguez-Fernández. *Study supervision:* Juvé-Udina, Carratalà.

Funding/Support: No funding.

Declaration of Interests: We declare that we have no competing interests.

Patient and public involvement: Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this inquiry.

Patient consent for publication: Not required**.**

Ethical approval: This study is approved by the Clinical Research Ethics Committee of the Bellvitge University Hospital with a waiver of informed consent (reference 158/20).

Provenance and peer review: Not commissioned; externally peer reviewed.

Data availability statement: All data relevant to the study are included in the article. No additional data are available.

Table 1. Baseline characteristics, VIDA score and care complexity individual factors of admitted COVID-19 patients with unfavourable and favourable outcomes.

Characteristics	Study population n=1,176 No.	%	Unfavourable outcome [a] n=506 (42.8%) No.	%	Favourable outcome n=670 (57.1%) No.	%	*p value*
Demographic characteristics							
Age (years)_median (IQR)	66.5	(51-77)	74	(60-80)	61	(49-74)	<0.001
Male sex	667	(56.7)	192	(37.9)	317	(47.3)	0.001
Clinical characteristics							
LOS_median (IQR)	6	(4-8)	7	(4-10)	5	(4-7)	<0.001
Continuity of care (discharged to another facility)	165	(14)	58	(11.5)	107	(16)	0.02
Severity (APR-GRD 3-4)	503	(42.8)	450	(88.9)	53	(7.9)	<0.001
Mortality risk (APR-DRG 3-4)	486	(41.3)	449	(88.7)	37	(5.5)	<0.001
High-tech hospital	969	(82.4)	389	(76.9)	580	(86.6)	<0.001
Underlying disease	745	(63.4)	382	(75.5)	363	(54.4)	<0.001
Arterial hypertension or chronic heart failure	469	(39.9)	234	(46.2)	235	(35.1)	<0.001
Diabetes or chronic kidney disease	298	(25.3)	165	(32.6)	133	(19.9)	<0.001
Chronic respiratory disease	171	(14.5)	95	(18.8)	76	(11.3)	<0.001
Neurodegenerative disease	63	(5.3)	33	(6.5)	39	(4.5)	0.15
Chronic liver disease	54	(4.6)	30	(5.9)	24	(3.6)	0.07
Cancer	50	(4.3)	31	(6.5)	19	(2.8)	0.008
Immunosuppression	49	(4.2)	23	(4.5)	26	(3.9)	0.66
VIDA score[b]							
Low risk (0)	104	(12.9)	27	(7.1)	77	(18)	<0.001
Moderate risk (1-2)	505	(62.7)	194	(51.2)	311	(72.8)	<0.001
High risk (3-4)	197	(16.7)	158	(41.7)	39	(9.1)	<0.001
Care complexity individual factors (CCIF)							
Comorbidity/complications	1,176	(100)	506	(100)	670	(100)	-
Transmissible infection	1,176	(100)	506	(100)	670	(100)	-
Hemodynamic instability	910	(77.4)	396	(78.3)	514	(76.7)	0.57
Chronic disease	745	(63.4)	382	(75.5)	363	(54.4)	<0.001
Uncontrolled pain	194	(16.5)	82	(16.2)	112	(16.7)	0.87
Extreme weight	168	(14.3)	82	(16.2)	86	(12.8)	0.11
Position impairment	72	(6.1)	52	(10.3)	20	(3.0)	<0.001
Urinary or faecal incontinence	58	(4.9)	31	(6.1)	27	(4.0)	0.10
Immunosuppression	49	(4.1)					
Anatomical and functional disorders	41	(3.5)	30	(5.9)	11	(1.6)	<0.001
Communication disorders	18	(1.5)	13	(2.6)	5	(0.7)	0.01
High risk of hemorrhage	2	(0.2)	1	(0.2)	1	(0.1)	0.68
Vascular fragility	6	(0.5)	4	(0.8)	2	(0.3)	0.41
Involuntary movements	3	(0.3)	3	(0.6)	0	(0.0)	0.08
Dehydration	3	(0.3)	1	(0.2)	2	(0.3)	0.60
Oedema	0	(0)	0	(0.0)	0	(0.0)	-
Developmental	397	(33.8)	244	(48.2)	153	(22.8)	<0.001
Old age (≥75 years)	397	(33.8)	244	(48.2)	153	(22.8)	<0.001
Psycho-emotional	218	(18.5)	86	(17.0)	132	(19.7)	0.13
Fear/anxiety	173	(14.7)	70	(13.8)	103	(15.4)	0.51
Impaired adaptation	54	(4.6)	17	(3.4)	37	(5.5)	0.09
Aggressive behaviour	1	(0.1)	1	(0.2)	0	(0.0)	0.43
Mental-cognitive	240	(20.4)	184	(36.4)	56	(8.4)	<0.001
Mental status impairments	238	(20.2)	183	(36.2)	55	(8.2)	<0.001
Agitation	5	(0.4)	4	(0.8)	1	(0.1)	0.17
Impaired cognitive functions	4	(0.3)	3	(0.6)	1	(0.1)	0.32
Perception of reality disorders	2	(0.2)	0	(0.0)	2	(0.3)	0.51
Sociocultural	1,176	(100)	506	(100)	670	(100)	-
Lack of caregiver support	1,176	(100)	506	(100)	670	(100)	-
Belief conflict	1	(0.1)	0	(0.0)	1	(0.1)	0.57
Language barriers	1	(0.1)	1	(0.2)	0	(0.0)	0.43
Social exclusion	1	(0.1)	0	(0.0)	1	(0.1)	1
Care complexity individual factors (CCIF), median (IQR)	4	(3-6)	5	(4-6)	4	(3-5)	<0.001

Abbreviations: IQR, interquartile range; LOS, length of hospital stay; ICU, intensive care unit; APR-DRG, all patient refined diagnosis-related groups; VIDA, surveillance and identification of acute deterioration.

[a] Unfavourable outcomes included: in-hospital mortality and adverse events during hospitalization.

[b] VIDA score was analysed according to 806 admitted patients in wards with VIDA system.

Table 2. Patients' outcomes according to risk of acute deterioration (VIDA score) and care complexity individual factors.

Outcomes	All n=1,181 N (%)	VIDA_score n=806 (68.5) Low risk (0) n=104 (12.9) N (%)	VIDA_score n=806 (68.5) Mild risk (1-2) n=505 (62.7) N (%)	VIDA_score n=806 (68.5) High risk (3-4) n=197 (16.7) N (%)	CCIF n=1,176 CCIF<4 n=327 (27.8) N (%)	CCIF n=1,176 CCIF≥4 n=849 (72.2) N (%)
Unfavourable outcomes	506 (43.0)	27 (26.0)**	194 (38.4)*	158 (80.2)**	92 (28.1)**	414 (48.8)**
Deceased	232 (19.6)	0 (0.0)**	46 (9.1)**	118 (59.9)**	5 (1.5)**	227 (26.7)**
Adverse event	481 (40.9)	27 (26.0)**	187 (37)*	153 (77.7)**	91 (27.8)**	394 (46.4)**
ICU transfer	32 (2.7)	0 (0.0)*	12 (2.4)	13 (6.6)*	4 (1.2)*	28 (3.3)*
HAI	29 (2.5)	0 (0.0)*	10 (2.0)	12 (6.1)*	1 (1.5)	24 (2.8)
Catheter-related bloodstream infection	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.1)
HA urinary tract infection	19 (1.6)	0 (0.0)	7 (1.4)	8 (4.1)*	3 (0.9)	16 (1.9)
Aspiration pneumonia	3 (0.3)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.4)
Sepsis	7 (0.6)	0 (0.0)	1 (0.2)	3 (1.5)*	2 (0.6)	5 (0.6)
ACC	470 (40.0)	27 (26.0)**	181 (35.8)**	150 (76.1)**	88 (26.6)**	383 (45.1)**
Cardiac arrest	5 (0.4)	1 (1.0)	0 (0.0)*	3 (1.5)*	0 (0.0)	5 (0.6)
Shock	4 (0.3)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	4 (0.5)
Thrombotic event	7 (0.6)	1 (1.0)	1 (0.2)	2 (1)	1 (0.3)	6 (0.7)
Acute respiratory failure[1]	436 (37.0)	27 (26.0)**	164 (32.5)**	144 (73.1)**	84 (25.1)**	353 (41.6)**
Myocardial injury	5 (0.4)	0 (0)	3 (0.6)	1 (0.5)	0 (0.0)	5 (0.6)
Liver injury	2 (0.2)	0 (0)	0 (0)	1 (0.5)	0 (0.0)	2 (0.2)
Renal insufficiency	83 (7.1)	1 (1.0)*	28 (5.5)*	31 (15.7)**	6 (1.8)**	77 (9.1)**

Abbreviations: VIDA, surveillance and identification of acute deterioration; CCIF, care complexity individual factors; ICU, intensive care unit; HAI, hospital-acquired infections; ACC, avoidable critical complications.

* *p* value >0.001 and <0.05.

** *p* value ≤0.001.

[1] Include acute respiratory distress syndrome (ARDS).

Table 3. Adjusted analysis of unfavourable outcomes according to VIDA early warning system in 486 patients with high risk of mortality (APR-DRG 3-4).

Outcomes	Unadjusted n=1,181 N (%)	Adjusted n=486 (41.2) N (%)	With VIDA_system n=368 (75.7) N (%)	Without VIDA_system n=118 (24.3) N (%)	*p value*
Unfavourable outcomes	506 (43.0)	449 (92.4)	345 (93.8)	104 (88.1)	0.07
Deceased	232 (19.6)	214 (44)	152 (41.3)	62 (52.5)	0.02
Adverse event	481 (40.9)	436 (89.7)	337 (91.6)	99 (83.9)	0.02
ICU transfer	32 (2.7)	25 (5.1)	20 (5.4)	5 (4.2)	0.41
HAI	29 (2.5)	19 (3.9)	16 (4.3)	3 (2.5)	0.28
ACC	470 (40.0)	433 (89.1)	334 (90.8)	99 (83.9)	0.31

Abbreviations: VIDA, surveillance and identification of acute deterioration; ICU, intensive care unit; HAI, hospital-acquired infections; ACC, avoidable critical.

Table 4. Multivariate analysis of VIDA score and CCIF in adult COVID-19 hospitalized patients associated with unfavourable outcomes.

Characteristics	Unfavourable outcomes [1] n= 379 (47)		Deceased[2] n= 164 (20.3)		AE[3] n=367 (45.5)	
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Old age (≥75 years)	1.48	(0.99-2.22)	3.04	(1.79-5.15)**	1.52	(1.02-2.26)*
Male sex	1.21	(0.87-1.69)	1.86	(1.11-3.11)*	1.20	(0.87-1.67)
LOS	1.16	(1.11-1.21)**	0.97	(0.93-1.01)	1.17	(1.12-1.22)**
High-tech hospital	0.57	(0.36-0.89)*	1.88	(0.94-3.78)	0.61	(0.39-0.95)*
VIDA score 3-4	4.32	(2.83-6.60)**	13.99	(8.44-23.18)**	4.21	(2.79-6.36)**
Chronic disease	1.90	(1.32-2.72)**	2.01	(1.03-3.90)*	1.81	(1.26-2.59)**
Position impairment	1.19	(0.58-2.44)	1.41	(0.63-3.13)	1.23	(0.62-2.46)
Communication disorders	0.97	(0.24-3.96)	0.87	(0.22-3.41)	0.78	(0.21-2.95)
Mental status impairments	2.31	(1.45-23.66)**	6.21	(3.67-10.50)**	1.72	(1.09-2.69)*

Abbreviations: AE, adverse event; LOS, length of hospital stay; VIDA, surveillance and identification of acute deterioration.
[1]AUC 0.81 (CI 95%; 0.78-0.84).
[2]AUC 0.91 (CI 95%; 0.88-0.93).
[3]AUC 0.80 (CI 95%; 0.77 -0.83).
* *p* value >0.001 and <0.05.
** *p* value ≤0.001.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Pg.3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Pg.3-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Pg.5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	Pg.6
Methods			
Study design	4	Present key elements of study design early in the paper	Pg.7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Pg.7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Pg.7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Pg.7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Pg.7-8
Bias	9	Describe any efforts to address potential sources of bias	Pg.16
Study size	10	Explain how the study size was arrived at	Pg.7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Pg.9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Pg.9
		(*b*) Describe any methods used to examine subgroups and interactions	Pg.9
		(*c*) Explain how missing data were addressed	-
		(*d*) If applicable, explain how loss to follow-up was addressed	-
		(*e*) Describe any sensitivity analyses	-
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Pg.10
		(b) Give reasons for non-participation at each stage	Pg.10-11
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Pg.10
		(b) Indicate number of participants with missing data for each variable of interest	-
		(c) Summarise follow-up time (eg, average and total amount)	Pg.10
Outcome data	15*	Report numbers of outcome events or summary measures over time	Pg10-11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 1&4

		(*b*) Report category boundaries when continuous variables were categorized	Table 1&4
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Pg.11-12
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Pg.11
Discussion			
Key results	18	Summarise key results with reference to study objectives	Pg.13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Pg.16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Pg.14-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	Pg.15-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Pg.21.

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Risk of acute deterioration and care complexity individual factors associated with health outcomes in hospitalised patients with COVID-19: a multicenter cohort study.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-041726.R1
Article Type:	Original research
Date Submitted by the Author:	09-Sep-2020
Complete List of Authors:	Adamuz, Jordi; Bellvitge University Hospital, Nursing Knowledge Management and Information Systems Department González-Samartino, Maribel; Bellvitge University Hospital, Nursing knowledge Management and Information Systems Department Jiménez-Martínez, Emilio; Bellvitge University Hospital, Department of Infectious Diseases Tapia-Pérez, Marta; Bellvitge University Hospital, Nursing knowledge Management and Information Systems Department López-Jiménez, María-Magdalena; Bellvitge University Hospital, Nursing knowledge Management and Information Systems Department Rodríguez-Fernández, Hugo; Bellvitge University Hospital, Nursing knowledge Management and Information Systems Department Castro-Navarro, Trinidad; University Hospital Germans Trias i Pujol, Nursing knowledge Management and Information Systems Department Zuriguel-Pérez, Esperanza; Vall d'Hebron Research Institute, Nurse research coordinator Carratala, Jordi; Bellvitge University Hospital, Department of Infectious Diseases Juvé-Udina, Maria-Eulàlia; Catalan Institute of Health
Primary Subject Heading:	Nursing
Secondary Subject Heading:	Health informatics, Infectious diseases, Nursing, Respiratory medicine
Keywords:	Health informatics < BIOTECHNOLOGY & BIOINFORMATICS, Health & safety < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, INFECTIOUS DISEASES, Respiratory infections < THORACIC MEDICINE

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

ORIGINAL ARTICLE

Risk of acute deterioration and care complexity individual factors associated with health outcomes in hospitalised patients with COVID-19: a multicenter cohort study.

Jordi Adamuz, PhD, MSN, RN[1,2,5]; Maribel González-Samartino, PhD, MSN, RN[1,2,5] *; Emilio Jiménez-Martínez, MSN, RN [3,5]; Marta Tapia-Pérez, RN[1,5]; María-Magdalena López-Jiménez, MSN, RN [1,5]; Hugo Rodríguez-Fernández, RN[1,5]; Trinidad Castro-Navarro, RN[6]; Esperanza Zuriguel-Pérez, PhD, MSN, RN[7]; Jordi Carratalà, PhD, MD [3,4,5], Maria-Eulàlia Juvé-Udina, PhD, MSN, RN [2,5,8].

[1]Nursing knowledge Management and Information Systems Department, Bellvitge University Hospital, L'Hospitalet de Llobregat, Barcelona, Catalonia, Spain.

[2]School of Nursing, Medicine and Health Science Faculty, University of Barcelona, L'Hospitalet de Llobregat, Barcelona, Catalonia, Spain.

[3]Department of Infectious Diseases, Bellvitge University Hospital, L'Hospitalet de Llobregat, Barcelona, Catalonia, Spain.

[4]Faculty of Medicine, Department of Clinical Sciences, University of Barcelona, L'Hospitalet de Llobregat, Barcelona, Catalonia, Spain.

[5]Bellvitge Biomedical Research Institute (IDIBELL). L'Hospitalet de Llobregat, Barcelona, Catalonia, Spain.

[6]Nursing knowledge Management and Information Systems Department, Germans Trias i Pujol University Hospital. Badalona, Catalonia, Spain.

[7]Nurse research coordinator, Vall d'Hebron Institute of Biomedical Research (VHIR). Barcelona, Catalonia, Spain.

[8]Catalan Institute of Health. Barcelona, Catalonia, Spain.

*Corresponding Author:

Maribel González-Samartino, PhD, MSN, RN.

Nursing Knowledge Management and Information Systems Department, Bellvitge University Hospital - IDIBELL.

Feixa Llarga s/n, 08907, L'Hospitalet de Llobregat (Barcelona), Spain.

Telephone: +34 93 2602123.

Fax: +34 93 2607561.

E-mail: mgsamartino67@gmail.com

Conflict of interest disclosures: We declare that we have no competing interests.

Word Count: 3,161 words.

Funding: None.

ABSTRACT

Background: Evidence about the impact of systematic nursing surveillance on acute deterioration risk along with care complexity individual factors on inpatient outcomes, is scarce. The study is aimed at determining the association between acute deterioration risk and care complexity individual factors with unfavourable outcomes in hospitalised patients with COVID-19.

Methods: A multicentre cohort study was conducted from March 1, 2020 to March 31, 2020 at seven hospitals in Catalonia. All COVID-19 adults patients admitted to hospitals and with completed minimum data set were recruited retrospectively. Patients were classified based on the presence or absence of a composite unfavourable outcome (in-hospital mortality and adverse events). The main measures included acute deterioration risk (as measured with VIDA early warning system) and care complexity individual factors. All data were obtained blinded from electronic health records. Multivariate logistic analysis was performed to identify VIDA score and care complexity factors associated with unfavourable outcomes.

Results: From a total of 1,176 COVID-19 patients, 506 patients (43%) experienced an unfavourable outcome during hospitalisation. The frequency of unfavourable outcomes rose with increasing risk of acute deterioration as measured with VIDA score. Risk factors independently associated with unfavourable outcomes were chronic underlying disease (OR: 1.90, 95% CI: 1.32-2.72: $p < 0.001$), mental status impairment (OR: 2.31, 95% CI: 1.45-23.66; $p < 0.001$), length of hospital stay (OR: 1.16, 95% CI: 1.11-1.21; $p < 0.001$) and high risk of acute deterioration (OR: 4.32, 95% CI: 2.83-6.60; $p < 0.001$). High-tech hospital admission was a protective factor of unfavourable outcomes (OR: 0.57, 95% CI: 0.36-0.89; $p = 0.01$). Area under the receiver-operating-characteristic curve was 0.81 (95% CI: 0.78-0.84).

Conclusion: The systematic nursing surveillance of the status and evolution of COVID-19 inpatients, including the careful monitoring of acute deterioration risk and care complexity individual factors may contribute to reduce deleterious health outcomes in COVID-19 inpatients.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- We performed a multicentre cohort study with a large sample size in patients with COVID-19.
- This novel research assessed the impact of the risk of acute deterioration and broader health contributors of care complexity with COVID-19 patient outcomes.
- We do not evaluate other clinical measures such as the age-adjusted Charlson comorbidity index or patient lab values.
- Futures studies should validate the model.

INTRODUCTION

Along with climate change and financial crises, pandemics are one of the major global risks for the 21st century. A 2019 report stated that, in the last decade the World Health Organization (WHO) tracked 1,483 epidemic events, including Sever Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), Ebola or other epidemic-prone diseases, considered harbingers of a new era of high-impact, potentially fast-spreading outbreaks.[1]

The potential thread became real last December 2019, when a severe acute respiratory infection caused by the new coronavirus SARS-CoV-2 began to spread first in Wuhan (China).[2,3] The WHO announced the Wuhan pneumonia as an outbreak of potential danger in December 31st, as an outbreak of global concern in January 31st, and finally the coronavirus disease (COVID-19) was declared a global pandemic in February 2020.

COVID-19 patients frequently require hospital admission as they may rapidly develop severe potential life-threatening complications, such as acute respiratory distress syndrome, sepsis, major thromboembolic events or cardiac injury, requiring intensive care.[3–5] Recent studies have found overall in-hospital mortality rates for COVID-19 inpatients ranging from 15 to 28%.[3,6–8] Therefore, early recognition of patient deterioration and escalation of treatment to reduce the risk of progression to critical complications is a significant issue that may impact patient and organizational outcomes. Screening for acute deterioration implies nursing surveillance, data collection, interpretation and recognition of changes in patients' status, prioritization of patients' problems and decision making on the interventions to perform in order to curb the cascade towards adverse events (AEs) and death.[9]

According to the WHO "*patients hospitalized with COVID-19 require regular monitoring of vital signs and, where possible, utilization of early warning scores that*

facilitate early recognition and escalation of treatment of the deteriorating patient.[10] Early warning systems have become an important component of managing inpatient care, as well as a clinical decision-making support stratification tool to prevent poor health outcomes.[11–13] Previous studies suggested the need for adaptation of these systems to each context.[14] According to these recommendations, several evidence-based algorithms were developed and used to early identify and act upon initial or impending acute deterioration among hospitalised patients. In the context of this study, a nursing surveillance improving program named VIDA (the Catalan acronym for Surveillance and Identification of Acute Deterioration) started in 2013 and has evolved with a multidisciplinary approach, as a daily used early warning score system, contributing to assist clinical decision-making, since then.

It has been described that admitted patients with COVID-19 have a substantial rate of chronic conditions that may affect the complexity of medical and nursing care provision, and patient health outcomes.[15] Nevertheless, care complexity individual factors (CCIF) are related not only to multiple comorbidities but also to mental-cognitive and psychosocial patient features, which in turn are also associated with increased healthcare needs during hospitalization and with selected health outcomes.[16–18]

Only a few studies in COVID-19 inpatients have explored the use of acute deterioration risk stratification[11,19] and to date, none has assessed CCIF as predictors of poor health outcomes. The aim of this study is to determine the association between acute deterioration risk (as measured with VIDA early warning system) and care complexity individual factors with unfavourable outcomes in admitted patients with COVID-19.

METHODS

Setting and Study Design

A retrospective cohort study was carried out at seven public hospitals in Catalonia, Spain: three tertiary metropolitan facilities, three urban university centres and one community hospital. All patients with a medical diagnosis of COVID-19 infection whether they were admitted for COVID-19 or other causes from March 1, 2020 to March 31, 2020 with a completed hospital minimum data set report were recruited retrospectively and followed up during the hospitalization until discharge or deceased. Patients' directly admitted and discharged from intensive care units (ICU), as well as those who remained hospitalized after the recruitment end date, were excluded.

We defined the primary endpoint as a composite of unfavourable outcomes including in-hospital mortality or adverse events (AEs), not present on admission and occurring thereafter during hospitalization.

Patient and Public Involvement

This study was approved by The Clinical Research Ethics Committee of the Bellvitge University Hospital (reference 158/20). Informed consent was waived due to the study's retrospective design. Ethical and data protection protocols related to anonymity and data confidentiality (access to records, data encryption and archiving of information) were complied with throughout the whole research process.

Data Collection

Information regarding the demographic and clinical characteristics, continuity of care (discharged to another facility), high-tech hospital (referral centre that provides tertiary care for either open-heart surgery or major organ transplants or both, or other centre), length of hospital stay (LOS) and patient severity and mortality risk were collected from the hospital minimum data set and the clinical data warehouse of the Catalan Institute of Health. Patient severity and risk of mortality was based on the all patient refined

diagnosis-related groups (APR-DRG) that categorises both measures in four groups, from low (level 1) to extreme (level 4). Severity and mortality risk were dichotomized in this study into low risk (levels 1-2) and high risk (levels 3-4).[20]

VIDA score (acute deterioration risk stratification) classifies automatically patients into five groups according to patient progress data: no risk (level 0), low risk (level 1), moderate risk (level 2), high risk (impending complication if not stabilized) (level 3), manifested complication initial status (level 4). Levels 2 to 4 make an alert in the electronic health records with clinical recommendations. These recommendations were standardized for each context in line to intensify the measurement of vital signs and notify to medical team. The health team (nurse and specialist) had the final clinical decision-making. For the purposes of this study, VIDA score classified into mild (levels 1-2) and high (levels 3-4) risk groups. Patients were classified in each group according the highest degree of VIDA score obtained during their hospitalization. Patient progress data were extracted from anonymised electronic health records whenever they were e-charted including: respiratory rate (breaths/min), oxygen saturation (%), temperature (ºC), mental status (level of awareness; 1= aware and orientated, >1 = disturbed mental status, including disorientation, acute confusion, etc...), pulse (cardiac rate, beats/min) and systolic and diastolic blood pressure (mmHg) (Supplementary file 1).

Care complexity individual factors (CCIF) were classified into five domains: (i) mental-cognitive, (ii) psycho-emotional, (iii) sociocultural, (iv) developmental, and (v) comorbidity/complications, as described in previous studies.[16,18] Each CCIF domain is structured into factors and specifications. Patients were considered within any CCIF domains if they presented at least one factor or specification. These CCIF factors and specifications were obtained from the nursing assessment e-charts, as structured data based on the Architecture, Terminology, Interface, Knowledge (ATIC) terminology[20] (Supplementary file 2).

Outcome measures

The main end point was a composite of unfavourable outcomes including in-hospital mortality and adverse events [AEs] during hospitalization. The in-hospital mortality accounted the number of deceased COVID-19 patients while in a ward. The AEs included intensive care unit transfer, hospital-acquired infections (HAI) and potentially avoidable critical complications (ACC) during hospitalization. Intensive care unit (ICU) transfer was defined as the number of patient episodes with effective bed change from a general ward to an intensive care area. HAI included the number of episodes of ward patients that developed catheter-related bloodstream infection, urinary catheter-related infection, aspiration pneumonia and/or sepsis. ACC accounted for the number of episodes of ward patients that experienced a cardiac arrest, shock, thromboembolic event, acute respiratory failure, acute respiratory distress syndrome (ARDS), myocardial injury, liver injury and/or kidney failure, not present on admission.

Statistical Analysis

Descriptive analysis of data using percentage frequencies, median and interquartile range was performed to determine demographic and clinical characteristics, and patients' outcomes. For categorical variables, a comparative analysis for detecting significant differences between groups was carried out using the chi-square test or Fisher's exact test when one or more cells had an expected frequency of five or less. For continuous variables, the Student's t-test or Mann-Whitney U test was used depending on the results of the Kolmogorov-Smirnov normality test. A logistic-regression model of all clinical factors potentially associated with unfavourable outcome measures (AEs and in-hospital mortality) was performed including VIDA score, clinically relevant CCIF and other potential confounders: sex, hospital level and LOS. All potential explanatory variables included in the multivariate analysis were subjected to a correlation matrix for analysis of collinearity. The discriminatory power was evaluated by the area under the receiver

operating characteristic (ROC). Results of multivariate analysis was reported as odds ratios (OR) and 95% confidence intervals (CI). We also performed an adjusted analysis to compare unfavourable outcomes in patients admitted in wards with VIDA system and without this system. Statistical analysis will be performed using the SPSS software package version 25.0 (SPSS, Chicago, IL). *P* values less than 0.05 were considered statistically significant.

RESULTS

During the study period, 1,838 patients were hospitalised with COVID-19, among them, 1,176 patients met inclusion criteria. The frequency of unfavourable outcomes was 42.8% (506 patients). In-hospital mortality rate was 19.6% (232 patients), and almost 41% (481 patients) experienced an AE while in a ward (2.7% transferred to ICU; 2.5% HAI; 40% ACC). Acute respiratory failure, ARDS, acute kidney failure, urinary catheter-related infection, sepsis, and thrombotic event were the most frequently AEs.

Patient Characteristics

The baseline characteristics of patients with unfavourable and favourable outcome are compared in **Table 1**. COVID-19 hospitalised patients who had an unfavourable outcome were more often male, older, and had one or more underlying chronic conditions (75.5%), mostly arterial hypertension or congestive heart failure and, diabetes or chronic kidney disease. Furthermore, they had longer LOS and high risk of severity or mortality (APR-DRG 3-4). Conversely, patients admitted in high-tech hospitals presented less frequency of unfavourable outcomes.

Regarding 806 patients hospitalised with VIDA early warning system, most patients with unfavourable outcomes experienced high risk of acute deterioration (41.7% in patients with unfavourable outcomes vs. 9.1% in patients with favourable outcomes).

Comorbidity, sociocultural and developmental domains were the most frequent CCIF domains identified in the studied sample. Mental-cognitive and psycho-emotional

domains were less frequent. Patients with unfavourable outcomes exhibited a higher frequency of chronic disease, position impairment, anatomical and functional disorders, communication disorders, old age (>75 years) and mental status impairments, when compared to patients with favourable outcomes. The median of CCIF was also higher in patients with unfavourable outcomes (5 [IQR: 4-6] vs. 4 [IQR: 3-5]) **(Table 1)**.

Risk of acute deterioration and individual complexity factors association with outcomes.

Patients' outcomes of 806 patients with low, mild or high risk of acute deterioration were compared in **Table 2.** The frequency of unfavourable outcomes was nearly 38% in patients with mild risk and almost 80% in the high risk of acute deterioration group (p <.0.001). Similarly, the frequency of in-hospital mortality and AEs rose with increasing VIDA score and reached near 60% and 80% in patients with high risk of acute deterioration, respectively (p <.0.001). Acute respiratory failure, acute kidney failure and ICU transfer were the most frequent AEs.

Among the 1,176 patients analysed in this study, those with four or more CCIF experienced unfavourable outcomes (p <.0.05) **(Table 2)**.

Table 3 shows an adjusted analysis of health outcomes in 486 patients with high risk of mortality (APR-DRG 3-4) to compare patients admitted in wards where registered nurses use or do not use the VIDA early warning score system. In-hospital mortality was more frequent in patients admitted in wards where VIDA was not used (52.5% vs. 41.3%, p <.0.05). Conversely, the frequency of AEs was slightly higher in patients admitted VIDA' wards (p <.0.05).

Risk factors associated with unfavourable outcomes

The results of the multivariable analysis for risk of acute deterioration (as measured with VIDA score) and CCIF potentially associated with unfavourable outcomes, in-hospital mortality and AEs, are summarized in **Table 4**.

After adjustment of potentially confounders, the analysis shows that high risk of acute deterioration was an independent factor associated with unfavourable outcomes, in-hospital mortality, and AEs in COVID-19 ward inpatients. Furthermore, chronic disease, mental status impairments and LOS were risk factors associated with unfavourable outcomes. Conversely, high-tech hospital admission was a protective factor of unfavourable outcomes. The area under the ROC curve (AUC) was 0.81 (95% CI: 0.78-0.84).

Chronic disease, mental status impairments, old age and male sex were independent risk factors associated with in-hospital mortality for studied COVID-19 inpatients (AUC 0.91 [95% CI: 0.88-0.93]). Finally, risk factors independently associated with AEs were chronic disease, mental status impairments, old age and LOS; while high-tech hospital admission was a protective factor of AEs (AUC 0.80 [95% CI: 0.77-0.83]). The AUC of the three outcomes analysed were > 0.80, showing a fair discriminatory power.

DISCUSSION

In this study of a large cohort of hospitalised patients with COVID-19, the frequency of in-hospital mortality and AEs reached near 60% and 80%, in patients scored as at high risk of acute deterioration, respectively. In-hospital mortality was higher in wards not using the VIDA early warning system. A wide majority of patients had four or more care complexity individual factors identified. The risk factors independently associated with unfavourable outcomes included chronic disease, mental status impairments, LOS and high risk of acute deterioration. High-tech hospital admission was a protective factor of unfavourable outcomes.

Our findings are consistent with previous COVID-19 reports which have found a similar frequency of in-hospital mortality and AEs.[3,21] In addition, 37% of patients developed respiratory complications (acute respiratory failure or ARDS) during hospitalization. This value is within the range reported in a previous inquiry (29-42%).[3]

The results of this study show that high risk of acute deterioration is a significant risk factor for unfavourable outcomes, as a composite measure for in-hospital mortality, and AEs in admitted COVID-19 patients. Although previous studies have stressed that early warning systems are predictors of in-hospital mortality and health outcomes,[22,23] only a few have evaluated warning score systems in admitted COVID-19 patients.[11,19] These latest studies showed a fair discrimination with adverse outcomes, concluding that the evaluation of the risk for acute deterioration in the COVID-19 hospital population is a priority for the organizations.[19]

In-hospital mortality was more frequent in patients admitted in wards where registered nurses do not use VIDA early warning system. In this regard, other studies show that the use of early systems reinforces collaboration among the multidisciplinary team, and promotes the early identification of clinical deterioration.[24] Similarly, previous

studies have reported less mortality and adverse events when systematic nursing surveillance of patient status and progress is a daily basis practice.[9]

Chronic conditions and mental status impairments were the CCIF independently associated with unfavourable outcomes. Previous reports have shown that chronic diseases were more frequent among deceased COVID-19 patients [15] and older age was a potential risk factor associated with mortality.[6] Although our study has not identified age as a risk factor associated with a composite unfavourable outcome, we acknowledge that old age was an independent risk factor associated with mortality and AE. Furthermore, our findings were also consistent with other studies showing that mental status impairments are associated with hospital-acquired complications,[25] including sepsis.[4]

A wide majority of patients had four or more CCIF. Our findings are consistent with other studies that identified an important rate of chronic conditions in COVID-19 patients[15] and by the other hand, selected organizational issues that may impact care complexity and health outcomes.[26] Previous inquires have demonstrated the association of CCIF and health outcomes,[16] with an average of two CCIF per patient. Our investigation showed that for COVID-19 inpatients, the average of CCIF is four. These results are probably related to the transmissibility of this condition requiring droplet and contact precautions, the pandemics management associated public health measures of population confinement, preventing patients' relatives to visit admitted patients in person, resulting in a lack of family caregiver support during hospitalisation, and the frequency of chronic diseases in the studied sample. The organizational adaptation of hospitals to this pandemic context and the required isolation precautions have been associated with poor outcomes in prior studies.[27,28]

Additionally, we found that LOS was associated with unfavourable outcomes, coinciding with previous studies that associated AEs with increased healthcare costs due to longer hospital stays.[29] Finally, high-tech hospital admission was a protective factor

associated to unfavourable outcomes. High-tech hospitals usually have better nurse-to-patient ratios, than urban or community facilities. In this sense, a couple of recent inquiries in the same context of this study conclude that, on average hospital ward patients require 5.6 hours of RN care per patient day, while the average RN offered hours per patient day is 2.4, and that RN understaffing is a structural issue.[26,30] Nevertheless, to the best of our knowledge, no study on nurse staffing and COVID-19 inpatients' outcomes have been published. Similarly, healthcare clinical leaders and managers have become key role to rapidly adapt organizations to the new reality. Fast and effective decision-making and managerial responses in crisis situations with high levels of uncertainty are essential at immediate and short-term however, they should be accompanied by planning and executing mid-term and long-lasting improvements that positively impact patient, professional and organizational outcomes, such as structural RN understaffing.[26]

The strengths of this study include its multicentre approach, cohort design and large sample size. It is the first research evaluating the association of the risk of acute deterioration, along with care complexity individual factors, with COVID-19 patient outcomes. Importantly, we identify broader health-contributors of care complexity, including psychosocial and mental-cognitive factors. In addition, the VIDA early warning system was developed as an evidence-based algorithm with a multidisciplinary approach, and also according to previous studies that highlighted the importance to adapt surveillance and screening systems to organization and cultural context.[14]

VIDA score and CCIF data were comprehensively collected from clinical data warehouse of the Catalan Institute of Health and all patients included had a completed nurse charting in the patient electronic health record. Nevertheless, there are some limitations that should be acknowledged. We relied a properly compliance on electronic health records and administrative data, however this statement should be interpreted with caution since voluntary completion of electronic health records show close-to-reality data

and information on nurses' observations on patient status and progress, but it not the reality in itself. It should be noted, no previous studies have demonstrated the effectiveness VIDA early warning system yet. Nevertheless, the results of this study had proved the significant association between the unfavourable outcomes with VIDA score and CCIF, although a validate the model in external samples is still needed. Finally, we acknowledge as a significant limitation that we did not evaluate other clinical measures such as the age-adjusted Charlson comorbidity index or patient lab values.

Conclusion

The risk of acute deterioration and the care complexity individual factors are associated with COVID-19 patient outcomes. The rate of unfavourable outcomes rose with increasing risk of acute deterioration as measured with VIDA score. The risk factors independently associated with poor health outcomes were chronic disease, mental status impairment, length of hospital stay and high risk of acute deterioration. High-tech hospital admission was a protective factor of unfavourable outcomes. The systematic nursing surveillance of patients at risk of acute deterioration and the assessment of CCIF may contribute to reduce deleterious health outcomes in COVID-19 inpatients.

REFERENCES

1 WHO, World Bank. Global preparedness monitoring board. A world at risk. Annual report on global preparedness for health emergencies. 2019. DOI:10.2307/40153772.

2 Li Q, Guan X, Wu P, *et al.* Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N. Engl. J. Med. 2020; **382**: 1199–207.

3 Huang C, Wang Y, Li X, *et al.* Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; **395**: 497–506.

4 Li H, Liu L, Zhang D, *et al.* SARS-CoV-2 and viral sepsis: observations and hypotheses. *Lancet* 2020; **395**: 1517–20.

5 Shi S, Qin M, Shen B, *et al.* Association of Cardiac Injury with Mortality in Hospitalized Patients with COVID-19 in Wuhan, China. *JAMA Cardiol* 2020; published online March 25. DOI:10.1001/jamacardio.2020.0950.

6 Zhou F, Yu T, Du R, *et al.* Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020; **395**: 1054–62.

7 Wu C, Chen X, Cai Y, *et al.* Risk Factors Associated with Acute Respiratory Distress Syndrome and Death in Patients with Coronavirus Disease 2019 Pneumonia in Wuhan, China. *JAMA Intern Med* 2020; published online March 13. DOI:10.1001/jamainternmed.2020.0994.

8 Zheng Z, Peng F, Xu B, *et al.* Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. *J Infect* 2020; published online April 23. DOI:10.1016/j.jinf.2020.04.021.

9 Juvé-Udina ME, Fabrellas-Padrés N, Adamuz-Tomás J, *et al.* Surveillance nursing diagnoses, ongoing assessment and outcomes on in-patients who suffered a cardiorespiratory arrest. *Rev da Esc Enferm* 2017; **51**: e03286.

10 WHO. Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected. 2020. https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected (accessed May 20, 2020).

11 Hu H, Yao N, Qiu Y. Comparing rapid scoring systems in mortality prediction of critical ill patients with novel coronavirus disease. *Acad Emerg Med* 2020; published online April 20. DOI:10.1111/acem.13992.

12 Liao X, Wang B, Kang Y. Novel coronavirus infection during the 2019–2020 epidemic: preparing intensive care units—the experience in Sichuan Province, China. *Intensive Care Med* 2020; **46**: 357–60.

13 O'Brien C, Goldstein BA, Shen Y, *et al.* Development, Implementation, and Evaluation of an In-Hospital Optimized Early Warning Score for Patient Deterioration. *MDM Policy Pract* 2020; **5**: 1–10.

14 McGaughey J, O'Halloran P, Porter S, Trinder J, Blackwood B. Early warning systems and rapid response to the deteriorating patient in hospital: A realist evaluation. *J Adv Nurs* 2017; **73**: 3119–32.

15 Chen T, Wu D, Chen H, *et al.* Clinical characteristics of 113 deceased patients with coronavirus disease 2019: Retrospective study. *BMJ* 2020; **368**: m1091.

16 Adamuz J, González-Samartino M, Jiménez-Martínez E, *et al.* Care Complexity Individual Factors Associated With Hospital Readmission: A Retrospective

Cohort Study. *J Nurs Scholarsh* 2018; **50**: 411–21.

17 Safford MM. The Complexity of Complex Patients. *J Gen Intern Med* 2015; **30**: 1724–5.

18 Juvé-Udina, M.E., Matud, C., Farrero S., Jiménez, H., Rodríguez, E., Martínez, M. et al. Intensity of nursing care: workloads or individual complexity? *Metas de Enfermería* 2010; **13**: 6–14.

19 Singh K, Valley TS, Tang S, Li BY, Kamran F, Sjoding MW, Wiens J, Otles E, Donnelly JP, Wei MY, McBride JP, Cao J, Penoza C, Ayanian JZ NB. Validating a Widely Implemented Deterioration Index Model Among Hospitalized COVID-19 Patients. *medRxiv* 2020. DOI:10.1101/2020.04.24.20079012.

20 Juvé-Udina ME. What patients' problems do nurses e-chart? Longitudinal study to evaluate the usability of an interface terminology. *Int J Nurs Stud* 2013; **50**: 1698–710.

21 Mao L, Jin H, Wang M, *et al.* Neurologic Manifestations of Hospitalized Patients with Coronavirus Disease 2019 in Wuhan, China. *JAMA Neurol* 2020; published online April 10. DOI:10.1001/jamaneurol.2020.1127.

22 Medic G, Kließ MK, Atallah L, *et al.* Evidence-based clinical decision support systems for the prediction and detection of three disease states in critical care: A systematic literature review. *F1000Research* 2019; **8**: 1728.

23 Kim I, Song H, Kim HJ, *et al.* Use of the national early warning score for predicting in-hospital mortality in older adults admitted to the emergency department. *Clin Exp Emerg Med* 2020; **7**: 61–6.

24 Ashbeck R, Stellpflug C, Ihrke E, *et al.* Development of a Standardized System to

Detect and Treat Early Patient Deterioration. *J Nurs Care Qual* 2020; published online April 6. DOI:10.1097/ncq.0000000000000484.

25 Bail K, Draper B, Berry H, Karmel R, Goss J. Predicting excess cost for older inpatients with clinical complexity: A retrospective cohort study examining cognition, comorbidities and complications. *PLoS One* 2018; **13**: e0193319.

26 Juvé-Udina M, González-Samartino M, López-Jiménez MM, *et al.* Acuity, nurse staffing and workforce, missed care and patient outcomes. A cluster-unit-level descriptive comparison. *J Nurs Manag* 2020; published online May 8. DOI:10.1111/jonm.13040.

27 Purssell E, Gould Di, Chudleigh J. Impact of isolation on hospitalised patients who are infectious: Systematic review with meta-analysis. *BMJ Open* 2020; **10**: e030371.

28 Tran K, Bell C, Stall N, *et al.* The Effect of Hospital Isolation Precautions on Patient Outcomes and Cost of Care: A Multi-Site, Retrospective, Propensity Score-Matched Cohort Study. *J Gen Intern Med* 2017; **32**: 262–8.

29 Rafter N, Hickey A, Condell S, *et al.* Adverse events in healthcare: Learning from mistakes. *Q J Med* 2015; **108**: 273–7.

30 Juvé-Udina M-E, Adamuz J, López-Jimenez M-M, *et al.* Predicting patient acuity according to their main problem. *J Nurs Manag* 2019; **27**: 1845–58.

FOOTNOTES

Author Contributions: All authors had full access to all study data and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Adamuz, González-Samartino, Juvé-Udina. *Coordination team:* Juvé-Udina. *Acquisition of data:* Adamuz, Tapia-Perez, López-Jiménez, Zuriguel-Pérez, Castro-Navarro. *Analysis and interpretation data:* Adamuz, González-Samartino, Jiménez-Martínez. *Drafting of the manuscript:* Adamuz, González-Samartino, Jiménez-Martínez, Juvé-Udina. *Critical revision of the manuscript for important intellectual content:* Tapia-Perez, López-Jiménez, Rodríguez-Fernández, Zuriguel-Pérez, Castro-Navarro, Carratalà. *Statistical analysis:* Adamuz and González-Samartino. *Obtained funding:* - . *Administrative, technical and material support:* López-Jiménez, Rodríguez-Fernández. *Study supervision:* Juvé-Udina, Carratalà.

Funding/Support: No funding.

Declaration of Interests: We declare that we have no competing interests.

Patient and public involvement: Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this inquiry.

Patient consent for publication: Not required**.**

Ethical approval: This study is approved by the Clinical Research Ethics Committee of the Bellvitge University Hospital with a waiver of informed consent (reference 158/20).

Provenance and peer review: Not commissioned; externally peer reviewed.

Data availability statement: All data relevant to the study are included in the article. No additional data are available.

Table 1. Baseline characteristics, VIDA score and care complexity individual factors of admitted COVID-19 patients with unfavourable and favourable outcomes.

Characteristics	Study population n=1,176 No.	%	Unfavourable outcome [a] n=506 (42.8%) No.	%	Favourable outcome n=670 (57.1%) No.	%	*p value*
Demographic characteristics							
Age (years)_median (IQR)	66.5	(51-77)	74	(60-80)	61	(49-74)	<0.001
Male sex	667	(56.7)	192	(37.9)	317	(47.3)	0.001
Clinical characteristics							
LOS_median (IQR)	6	(4-8)	7	(4-10)	5	(4-7)	<0.001
Continuity of care (discharged to another facility)	165	(14)	58	(11.5)	107	(16)	0.02
Severity (APR-GRD 3-4)	503	(42.8)	450	(88.9)	53	(7.9)	<0.001
Mortality risk (APR-DRG 3-4)	486	(41.3)	449	(88.7)	37	(5.5)	<0.001
High-tech hospital	969	(82.4)	389	(76.9)	580	(86.6)	<0.001
Underlying disease	745	(63.4)	382	(75.5)	363	(54.4)	<0.001
Arterial hypertension or chronic heart failure	469	(39.9)	234	(46.2)	235	(35.1)	<0.001
Diabetes or chronic kidney disease	298	(25.3)	165	(32.6)	133	(19.9)	<0.001
Chronic respiratory disease	171	(14.5)	95	(18.8)	76	(11.3)	<0.001
Neurodegenerative disease	63	(5.3)	33	(6.5)	39	(4.5)	0.15
Chronic liver disease	54	(4.6)	30	(5.9)	24	(3.6)	0.07
Cancer	50	(4.3)	31	(6.5)	19	(2.8)	0.008
Immunosuppression	49	(4.2)	23	(4.5)	26	(3.9)	0.66
VIDA score[b]							
Low risk (0)	104	(12.9)	27	(7.1)	77	(18)	<0.001
Moderate risk (1-2)	505	(62.7)	194	(51.2)	311	(72.8)	<0.001
High risk (3-4)	197	(16.7)	158	(41.7)	39	(9.1)	<0.001
Care complexity individual factors (CCIF)							
Comorbidity/complications	1,176	(100)	506	(100)	670	(100)	-
Transmissible infection	1,176	(100)	506	(100)	670	(100)	-
Hemodynamic instability	910	(77.4)	396	(78.3)	514	(76.7)	0.57
Chronic disease	745	(63.4)	382	(75.5)	363	(54.4)	<0.001
Uncontrolled pain	194	(16.5)	82	(16.2)	112	(16.7)	0.87
Extreme weight	168	(14.3)	82	(16.2)	86	(12.8)	0.11
Position impairment	72	(6.1)	52	(10.3)	20	(3.0)	<0.001
Urinary or faecal incontinence	58	(4.9)	31	(6.1)	27	(4.0)	0.10
Immunosuppression	49	(4.1)					
Anatomical and functional disorders	41	(3.5)	30	(5.9)	11	(1.6)	<0.001
Communication disorders	18	(1.5)	13	(2.6)	5	(0.7)	0.01
High risk of hemorrhage	2	(0.2)	1	(0.2)	1	(0.1)	0.68
Vascular fragility	6	(0.5)	4	(0.8)	2	(0.3)	0.41
Involuntary movements	3	(0.3)	3	(0.6)	0	(0.0)	0.08
Dehydration	3	(0.3)	1	(0.2)	2	(0.3)	0.60
Oedema	0	(0)	0	(0.0)	0	(0.0)	-
Developmental	397	(33.8)	244	(48.2)	153	(22.8)	<0.001
Old age (≥75 years)	397	(33.8)	244	(48.2)	153	(22.8)	<0.001
Psycho-emotional	218	(18.5)	86	(17.0)	132	(19.7)	0.13
Fear/anxiety	173	(14.7)	70	(13.8)	103	(15.4)	0.51
Impaired adaptation	54	(4.6)	17	(3.4)	37	(5.5)	0.09
Aggressive behaviour	1	(0.1)	1	(0.2)	0	(0.0)	0.43
Mental-cognitive	240	(20.4)	184	(36.4)	56	(8.4)	<0.001
Mental status impairments	238	(20.2)	183	(36.2)	55	(8.2)	<0.001
Agitation	5	(0.4)	4	(0.8)	1	(0.1)	0.17
Impaired cognitive functions	4	(0.3)	3	(0.6)	1	(0.1)	0.32
Perception of reality disorders	2	(0.2)	0	(0.0)	2	(0.3)	0.51
Sociocultural	1,176	(100)	506	(100)	670	(100)	-
Lack of caregiver support	1,176	(100)	506	(100)	670	(100)	-
Belief conflict	1	(0.1)	0	(0.0)	1	(0.1)	0.57
Language barriers	1	(0.1)	1	(0.2)	0	(0.0)	0.43
Social exclusion	1	(0.1)	0	(0.0)	1	(0.1)	1
Care complexity individual factors (CCIF), median (IQR)	4	(3-6)	5	(4-6)	4	(3-5)	<0.001

Abbreviations: IQR, interquartile range; LOS, length of hospital stay; ICU, intensive care unit; APR-DRG, all patient refined diagnosis-related groups; VIDA, surveillance and identification of acute deterioration.

[a] Unfavourable outcomes included: in-hospital mortality and adverse events during hospitalization.

[b] VIDA score was analysed according to 806 admitted patients in wards with VIDA system.

Table 2. Patients' outcomes according to risk of acute deterioration (VIDA score) and care complexity individual factors.

Outcomes	All n=1,1176 N (%)	VIDA_score n=806 (68.5) Low risk (0) n=104 (12.9) N (%)	Mild risk (1-2) n=505 (62.7) N (%)	High risk (3-4) n=197 (16.7) N (%)	CCIF n=1,176 CCIF<4 n=327 (27.8) N (%)	CCIF≥4 n=849 (72.2) N (%)
Unfavourable outcomes	506 (43.0)	27 (26.0)**	194 (38.4)*	158 (80.2)**	92 (28.1)**	414 (48.8)**
Deceased	232 (19.6)	0 (0.0)**	46 (9.1)**	118 (59.9)**	5 (1.5)**	227 (26.7)**
Adverse event	481 (40.9)	27 (26.0)**	187 (37)*	153 (77.7)**	91 (27.8)**	394 (46.4)**
ICU transfer	32 (2.7)	0 (0.0)*	12 (2.4)	13 (6.6)*	4 (1.2)*	28 (3.3)*
HAI	29 (2.5)	0 (0.0)*	10 (2.0)	12 (6.1)*	1 (1.5)	24 (2.8)
Catheter-related bloodstream infection	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.1)
HA urinary tract infection	19 (1.6)	0 (0.0)	7 (1.4)	8 (4.1)*	3 (0.9)	16 (1.9)
Aspiration pneumonia	3 (0.3)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.4)
Sepsis	7 (0.6)	0 (0.0)	1 (0.2)	3 (1.5)*	2 (0.6)	5 (0.6)
ACC	470 (40.0)	27 (26.0)**	181 (35.8)**	150 (76.1)**	88 (26.6)**	383 (45.1)**
Cardiac arrest	5 (0.4)	1 (1.0)	0 (0.0)*	3 (1.5)*	0 (0.0)	5 (0.6)
Shock	4 (0.3)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	4 (0.5)
Thrombotic event	7 (0.6)	1 (1.0)	1 (0.2)	2 (1)	1 (0.3)	6 (0.7)
Acute respiratory failure[1]	436 (37.0)	27 (26.0)**	164 (32.5)**	144 (73.1)**	84 (25.1)**	353 (41.6)**
Myocardial injury	5 (0.4)	0 (0)	3 (0.6)	1 (0.5)	0 (0.0)	5 (0.6)
Liver injury	2 (0.2)	0 (0)	0 (0)	1 (0.5)	0 (0.0)	2 (0.2)
Renal insufficiency	83 (7.1)	1 (1.0)*	28 (5.5)*	31 (15.7)**	6 (1.8)**	77 (9.1)**

Abbreviations: VIDA, surveillance and identification of acute deterioration; CCIF, care complexity individual factors; ICU, intensive care unit; HAI, hospital-acquired infections; ACC, avoidable critical complications.

* *p* value >0.001 and <0.05.

** *p* value ≤0.001.

[1] Include acute respiratory distress syndrome (ARDS).

Table 3. Adjusted analysis of unfavourable outcomes according to VIDA early warning system in 486 patients with high risk of mortality (APR-DRG 3-4).

Outcomes	Unadjusted n=1,1176		Adjusted n=486 (41.2)		With VIDA_system n=368 (75.7)		Without VIDA_system n=118 (24.3)		
	N	(%)	N	(%)	N	(%)	N	(%)	*p value*[1]
Unfavourable outcomes	506	(43.0)	449	(92.4)	345	(93.8)	104	(88.1)	0.07
Deceased	232	(19.6)	214	(44)	152	(41.3)	62	(52.5)	0.02
Adverse event	481	(40.9)	436	(89.7)	337	(91.6)	99	(83.9)	0.02
ICU transfer	32	(2.7)	25	(5.1)	20	(5.4)	5	(4.2)	0.41
HAI	29	(2.5)	19	(3.9)	16	(4.3)	3	(2.5)	0.28
ACC	470	(40.0)	433	(89.1)	334	(90.8)	99	(83.9)	0.31

Abbreviations: VIDA, surveillance and identification of acute deterioration; ICU, intensive care unit; HAI, hospital-acquired infections; ACC, avoidable critical.
[1]All variables were compared using the Fisher exact test.

Table 4. Multivariate analysis of VIDA score and CCIF in 806 adult COVID-19 hospitalized patients associated with unfavourable outcomes, deceased and AE.

Characteristics	**Unfavourable outcomes [1] n= 379/806 (47%)**		**Deceased[2] n= 164/806 (20.3%)**		**AE[3] n=367/806 (45.5%)**	
	OR	**(95% CI)**	**OR**	**(95% CI)**	**OR**	**(95% CI)**
Old age (≥75 years)	1.48	(0.99-2.22)	3.04	(1.79-5.15)**	1.52	(1.02-2.26)*
Male sex	1.21	(0.87-1.69)	1.86	(1.11-3.11)*	1.20	(0.87-1.67)
LOS	1.16	(1.11-1.21)**	0.97	(0.93-1.01)	1.17	(1.12-1.22)**
High-tech hospital	0.57	(0.36-0.89)*	1.88	(0.94-3.78)	0.61	(0.39-0.95)*
VIDA score 3-4	4.32	(2.83-6.60)**	13.99	(8.44-23.18)**	4.21	(2.79-6.36)**
Chronic disease	1.90	(1.32-2.72)**	2.01	(1.03-3.90)*	1.81	(1.26-2.59)**
Position impairment	1.19	(0.58-2.44)	1.41	(0.63-3.13)	1.23	(0.62-2.46)
Communication disorders	0.97	(0.24-3.96)	0.87	(0.22-3.41)	0.78	(0.21-2.95)
Mental status impairments	2.31	(1.45-23.66)**	6.21	(3.67-10.50)**	1.72	(1.09-2.69)*

Abbreviations: AE, adverse event; LOS, length of hospital stay; VIDA, surveillance and identification of acute deterioration. Multivariate analysis included: high risk of acute deterioration (VIDA score 3-4), clinically relevant care complexity individual factors (old age, chronic disease, position impairment, communication disorders and mental status impairments) and potential confounders (sex, hospital level and LOS).

[1]AUC 0.81 (CI 95%; 0.78-0.84).

[2]AUC 0.91 (CI 95%; 0.88-0.93).

[3]AUC 0.80 (CI 95%; 0.77 -0.83).

* *p* value >0.001 and <0.05.

** *p* value ≤0.001.

Supplementary file 1. Juvé-Udina ME. VIDA score for acute deterioration in the current *human* algorithm.

H1, H2, H3		
Punctuation	**Risk score**	**Definition**
0 – 1	0	No risk of complication (at that particular moment)
2 – 3	1	Low risk
4	2	Moderate risk (very probable complication)
5 – 6	3	High risk (imminent complication if not stabilized)
>= 7	4	Critical complication status
H4		
Punctuation	**Risk score**	**Definition**
0 – 1	0	No risk of complication (at that particular moment)
2 – 3	1	Low risk
4 – 6	2	Moderate risk (very probable complication)
7 – 9	3	High risk (imminent complication if not stabilized)
>= 10	4	Critical complication status
H5		
Punctuation	**Risk score**	**Definition**
0 – 2	0	No risk of complication (at that particular moment)
3 – 4	1	Low risk
5 – 6	2	Moderate risk (very probable complication)
7 – 8	3	High risk (imminent complication if not stabilized)
>= 9	4	Critical complication status
H6		
Punctuation	**Risk score**	**Definition**
0 – 2	0	No risk of complication (at that particular moment)
3 – 4	1	Low risk
5 – 6	2	Moderate risk (very probable complication)
7 – 9	3	High risk (imminent complication if not stabilized)
>= 10	4	Critical complication status
H7		
Punctuation	**Risk score**	**Definition**
<= 3	1	Low risk
4 – 6	2	Moderate risk (very probable complication)
7 – 8	3	High risk (imminent complication if not stabilized)
>= 9	4	Critical complication status

Abbreviations: H, hospital.

Supplementary file 2. Care complexity individual factors.

Domains	Factors	Specifications
Comorbidity/ Complications	Transmissible infection	Isolation measures
	Hemodynamic instability	Intensive control of vital signs or state of shock
	Chronic disease	Conditions (organ failure, degenerative process or oncological disease) that require ongoing medical attention and limit activities of daily living.
	Uncontrolled pain	Verbal numerical rating scale above three points
	Extreme weight	Low weight, obesity
	Position impairment	Includes any position impairment
	Urinary or faecal incontinence	Loss of bladder control or failure to control bowel movements
	Immunosuppression	Neutropenia, immunodeficiency or immunosuppressive therapy
	Anatomical and functional disorders	Amputation, deformities, joint stiffness
	Communication disorders	Aphasia, dysphasia, dysarthria, laryngectomy, tracheostomy
	High risk of haemorrhage	Coagulation disorders, thrombocytopenia, anticoagulant therapy
	Vascular fragility	Capillary fragility, tortuous veins
	Involuntary movements	Continuous involuntary movements
	Dehydration	Skin turgor
	Oedema	An accumulation of an excessive amount of watery fluid in cells, tissues, or serous cavities
Developmental	Old age	≥75 years
Psycho-emotional	Fear/anxiety	Fear or anxiety (moderate or intense)
	Impaired adaptation	Disruptive behaviour, hopelessness or surrender
	Aggressive behaviour	Physical or verbal aggressive behaviour (moderate or intense)
Mental-cognitive	Mental status impairments	Confusion, disorientation, stupor, transient loss of consciousness
	Agitation	Psychomotor agitation
	Impaired cognitive functions	Intellectual disability, amnesia
	Perception of reality disorders	Delirium, hallucinations, disconnection from reality
Sociocultural	Lack of caregiver support	Without caregiver support or caregiver burnout
	Belief conflict	Spiritual distress
	Language barriers	Barrier to communication resulting from speaking different languages than Spanish or Catalan without translator.
	Social exclusion	Extreme poverty

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Pg.3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Pg.3-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Pg.5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	Pg.6
Methods			
Study design	4	Present key elements of study design early in the paper	Pg.7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Pg.7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Pg.7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Pg.7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Pg.7-8
Bias	9	Describe any efforts to address potential sources of bias	Pg.16
Study size	10	Explain how the study size was arrived at	Pg.7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Pg.9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Pg.9
		(*b*) Describe any methods used to examine subgroups and interactions	Pg.9
		(*c*) Explain how missing data were addressed	-
		(*d*) If applicable, explain how loss to follow-up was addressed	-
		(*e*) Describe any sensitivity analyses	-
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Pg.10
		(b) Give reasons for non-participation at each stage	Pg.10-11
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Pg.10
		(b) Indicate number of participants with missing data for each variable of interest	-
		(c) Summarise follow-up time (eg, average and total amount)	Pg.10
Outcome data	15*	Report numbers of outcome events or summary measures over time	Pg10-11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 1&4

		(*b*) Report category boundaries when continuous variables were categorized	Table 1&4
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Pg.11-12
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Pg.11
Discussion			
Key results	18	Summarise key results with reference to study objectives	Pg.13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Pg.16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Pg.14-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	Pg.15-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Pg.21.

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Risk of acute deterioration and care complexity individual factors associated with health outcomes in hospitalised patients with COVID-19: a multicenter cohort study.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-041726.R2
Article Type:	Original research
Date Submitted by the Author:	22-Dec-2020
Complete List of Authors:	Adamuz, Jordi; Bellvitge University Hospital, Nursing Knowledge Management and Information Systems Department González-Samartino, Maribel; Bellvitge University Hospital, Nursing knowledge Management and Information Systems Department Jiménez-Martínez, Emilio; Bellvitge University Hospital, Department of Infectious Diseases Tapia-Pérez, Marta; Bellvitge University Hospital, Nursing knowledge Management and Information Systems Department López-Jiménez, María-Magdalena; Bellvitge University Hospital, Nursing knowledge Management and Information Systems Department Rodríguez-Fernández, Hugo; Bellvitge University Hospital, Nursing knowledge Management and Information Systems Department Castro-Navarro, Trinidad; University Hospital Germans Trias i Pujol, Nursing knowledge Management and Information Systems Department Zuriguel-Pérez, Esperanza; Vall d'Hebron Research Institute, Nurse research coordinator Carratala, Jordi; Bellvitge University Hospital, Department of Infectious Diseases Juvé-Udina, Maria-Eulàlia; Catalan Institute of Health
Primary Subject Heading:	Nursing
Secondary Subject Heading:	Health informatics, Infectious diseases, Nursing, Respiratory medicine
Keywords:	Health informatics < BIOTECHNOLOGY & BIOINFORMATICS, Health & safety < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, INFECTIOUS DISEASES, Respiratory infections < THORACIC MEDICINE

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

ORIGINAL ARTICLE

Risk of acute deterioration and care complexity individual factors associated with health outcomes in hospitalised patients with COVID-19: a multicenter cohort study.

Jordi Adamuz, PhD, MSN, RN[1,2,5]; Maribel González-Samartino, PhD, MSN, RN[1,2,5] *; Emilio Jiménez-Martínez, MSN, RN [3,5]; Marta Tapia-Pérez, RN[1,5]; María-Magdalena López-Jiménez, MSN, RN [1,5]; Hugo Rodríguez-Fernández, RN[1,5]; Trinidad Castro-Navarro, RN[6]; Esperanza Zuriguel-Pérez, PhD, MSN, RN[7]; Jordi Carratalà, PhD, MD [3,4,5], Maria-Eulàlia Juvé-Udina, PhD, MSN, RN [2,5,8].

[1]Nursing knowledge Management and Information Systems Department, Bellvitge University Hospital, L'Hospitalet de Llobregat, Barcelona, Catalonia, Spain.

[2]School of Nursing, Medicine and Health Science Faculty, University of Barcelona, L'Hospitalet de Llobregat, Barcelona, Catalonia, Spain.

[3]Department of Infectious Diseases, Bellvitge University Hospital, L'Hospitalet de Llobregat, Barcelona, Catalonia, Spain.

[4]Faculty of Medicine, Department of Clinical Sciences, University of Barcelona, L'Hospitalet de Llobregat, Barcelona, Catalonia, Spain.

[5]Bellvitge Biomedical Research Institute (IDIBELL). L'Hospitalet de Llobregat, Barcelona, Catalonia, Spain.

[6]Nursing knowledge Management and Information Systems Department, Germans Trias i Pujol University Hospital. Badalona, Catalonia, Spain.

[7]Nurse research coordinator, Vall d'Hebron Institute of Biomedical Research (VHIR). Barcelona, Catalonia, Spain.

[8]Catalan Institute of Health. Barcelona, Catalonia, Spain.

*Corresponding Author:

Maribel González-Samartino, PhD, MSN, RN.

Nursing Knowledge Management and Information Systems Department, Bellvitge University Hospital - IDIBELL.

Feixa Llarga s/n, 08907, L'Hospitalet de Llobregat (Barcelona), Spain.

Telephone: +34 93 2602123.

Fax: +34 93 2607561.

E-mail: mgsamartino67@gmail.com

Conflict of interest disclosures: We declare that we have no competing interests.

Word Count: 3,389 words.

Funding: None.

ABSTRACT

Background: Evidence about the impact of systematic nursing surveillance on acute deterioration risk along with care complexity individual factors on inpatient outcomes, is scarce. The study is aimed at determining the association between acute deterioration risk and care complexity individual factors with unfavourable outcomes in hospitalised patients with COVID-19.

Methods: A multicentre cohort study was conducted from March 1, 2020 to March 31, 2020 at seven hospitals in Catalonia. All COVID-19 adults patients admitted to hospitals and with completed minimum data set were recruited retrospectively. Patients were classified based on the presence or absence of a composite unfavourable outcome (in-hospital mortality and adverse events). The main measures included acute deterioration risk (as measured with VIDA early warning system) and care complexity individual factors. All data were obtained blinded from electronic health records. Multivariate logistic analysis was performed to identify VIDA score and care complexity factors associated with unfavourable outcomes.

Results: From a total of 1,176 COVID-19 patients, 506 patients (43%) experienced an unfavourable outcome during hospitalisation. The frequency of unfavourable outcomes rose with increasing risk of acute deterioration as measured with VIDA score. Risk factors independently associated with unfavourable outcomes were chronic underlying disease (OR: 1.90, 95% CI: 1.32-2.72: $p < 0.001$), mental status impairment (OR: 2.31, 95% CI: 1.45-23.66; $p < 0.001$), length of hospital stay (OR: 1.16, 95% CI: 1.11-1.21; $p < 0.001$) and high risk of acute deterioration (OR: 4.32, 95% CI: 2.83-6.60; $p < 0.001$). High-tech hospital admission was a protective factor of unfavourable outcomes (OR: 0.57, 95% CI: 0.36-0.89; $p = 0.01$).

Conclusion: The systematic nursing surveillance of the status and evolution of COVID-19 inpatients, including the careful monitoring of acute deterioration risk and care

complexity individual factors may contribute to reduce deleterious health outcomes in COVID-19 inpatients.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- We performed a multicentre cohort study with a large sample size in patients with COVID-19.
- This novel research assessed the impact of the risk of acute deterioration and broader health contributors of care complexity with COVID-19 patient outcomes.
- We do not evaluate other clinical measures such as the age-adjusted Charlson comorbidity index or patient lab values.
- Futures studies should validate the model.

INTRODUCTION

Along with climate change and financial crises, pandemics are one of the major global risks for the 21st century. A 2019 report stated that, in the last decade the World Health Organization (WHO) tracked 1,483 epidemic events, including Sever Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), Ebola or other epidemic-prone diseases, considered harbingers of a new era of high-impact, potentially fast-spreading outbreaks.[1]

The potential thread became real last December 2019, when a severe acute respiratory infection caused by the new coronavirus SARS-CoV-2 began to spread first in Wuhan (China).[2,3] The WHO announced the Wuhan pneumonia as an outbreak of potential danger in December 31st, as an outbreak of global concern in January 31st, and finally the coronavirus disease (COVID-19) was declared a global pandemic in February 2020.

COVID-19 patients frequently require hospital admission as they may rapidly develop severe potential life-threatening complications, such as acute respiratory distress syndrome, sepsis, major thromboembolic events or cardiac injury, requiring intensive care.[3–5] Recent studies have found overall in-hospital mortality rates for COVID-19 inpatients ranging from 15 to 28%.[3,6–8] Therefore, early recognition of patient deterioration and escalation of treatment to reduce the risk of progression to critical complications is a significant issue that may impact patient and organizational outcomes. Screening for acute deterioration implies nursing surveillance, data collection, interpretation and recognition of changes in patients' status, prioritization of patients' problems and decision making on the interventions to perform in order to curb the cascade towards adverse events (AEs) and death.[9]

According to the WHO "*patients hospitalized with COVID-19 require regular monitoring of vital signs and, where possible, utilization of early warning scores that*

facilitate early recognition and escalation of treatment of the deteriorating patient.[10] Early warning systems have become an important component of managing inpatient care, as well as a clinical decision-making support stratification tool to prevent poor health outcomes.[11–13] Previous studies suggested the need for adaptation of these systems to each context.[14] According to these recommendations, several evidence-based algorithms were developed and used to early identify and act upon initial or impending acute deterioration among hospitalised patients. In the context of this study, a nursing surveillance improving program named VIDA (the Catalan acronym for Surveillance and Identification of Acute Deterioration) started in 2013 and has evolved with a multidisciplinary approach, as a daily used early warning score system, contributing to assist clinical decision-making, since then.

It has been described that admitted patients with COVID-19 have a substantial rate of chronic conditions that may affect the complexity of medical and nursing care provision, and patient health outcomes.[15] Nevertheless, care complexity individual factors (CCIF) are related not only to multiple comorbidities but also to mental-cognitive and psychosocial patient features, which in turn are also associated with increased healthcare needs during hospitalization and with selected health outcomes.[16–18]

Only a few studies in COVID-19 inpatients have explored the use of acute deterioration risk stratification[11,19] and to date, none has assessed CCIF as predictors of poor health outcomes. The aim of this study is to determine the association between acute deterioration risk (as measured with VIDA early warning system) and care complexity individual factors with unfavourable outcomes in admitted patients with COVID-19.

METHODS

Setting and Study Design

A retrospective cohort study was carried out at seven public hospitals in Catalonia, Spain: three tertiary metropolitan facilities, three urban university centres and one community hospital. All patients with a medical diagnosis of COVID-19 infection whether they were admitted to a ward or intermediate unit for COVID-19 or other causes from March 1, 2020 to March 31, 2020 with a completed hospital minimum data set report were recruited retrospectively and followed up during the hospitalization until discharge or deceased. Patients' directly admitted and discharged from intensive care units (ICU) were excluded because VIDA early warning system was not implemented on ICU. Also patients who remained hospitalized after the recruitment end date were excluded due the data of hospital minimum data set was not available.

We defined the primary endpoint as a composite of unfavourable outcomes including in-hospital mortality or adverse events (AEs), not present on admission and occurring thereafter during hospitalization.

Patient and Public Involvement

This study was approved by The Clinical Research Ethics Committee of the Bellvitge University Hospital (reference 158/20). Informed consent was waived due to the study's retrospective design. Ethical and data protection protocols related to anonymity and data confidentiality (access to records, data encryption and archiving of information) were complied with throughout the whole research process.

Data Collection

Information regarding the demographic and clinical characteristics, continuity of care (discharged to another facility), high-tech hospital (referral centre that provides tertiary care for either open-heart surgery or major organ transplants or both), length of hospital stay (LOS) and patient severity and mortality risk were collected from the hospital

minimum data set and the clinical data warehouse of the Catalan Institute of Health. Patient severity and risk of mortality was based on the all patient refined diagnosis-related groups (APR-DRG) that categorises both measures in four groups, from low (level 1) to extreme (level 4). Severity and mortality risk were dichotomized in this study into low risk (levels 1-2) and high risk (levels 3-4).[20] All variables were collected during hospitalisation.

VIDA score (acute deterioration risk stratification) classifies automatically patients into five groups according to patient progress data: no risk (level 0), low risk (level 1), moderate risk (level 2), high risk (impending complication if not stabilized) (level 3), manifested complication initial status (level 4). Levels 2 to 4 make an alert in the electronic health records with clinical recommendations. These recommendations were standardized for each context in line to intensify the measurement of patients status surveillance and notify to medical team. The health team (nurse and specialist) had the final clinical decision-making. For the purposes of this study, VIDA score classified into mild (levels 1-2) and high (levels 3-4) risk groups. Patients were classified in each group according the highest degree of VIDA score obtained during their hospitalization. Patient progress data were extracted from anonymised electronic health records whenever they were e-charted including: respiratory rate (breaths/min), oxygen saturation (%), temperature (ºC), mental status (level of awareness; 1= aware and orientated, >1 = disturbed mental status, including disorientation, acute confusion, etc...), pulse (cardiac rate, beats/min) and systolic and diastolic blood pressure (mmHg) (Supplementary file 1).

Care complexity individual factors (CCIF) were classified into five domains: (i) mental-cognitive, (ii) psycho-emotional, (iii) sociocultural, (iv) developmental, and (v) comorbidity/complications, as described in previous studies.[16,18] Each CCIF domain is structured into factors and specifications. Patients were considered within any CCIF

domains if they presented at least one factor or specification during their hospitalisation. These CCIF factors and specifications were obtained from the nursing assessment e-charts, as structured data based on the Architecture, Terminology, Interface, Knowledge (ATIC) terminology[20] (Supplementary file 2).

Outcome measures

The main end point was a composite of unfavourable outcomes including in-hospital mortality and adverse events [AEs] during hospitalization. The in-hospital mortality accounted the number of deceased COVID-19 patients while in a ward. The AEs included intensive care unit transfer, hospital-acquired infections (HAI) and potentially avoidable critical complications (ACC) during hospitalization. Intensive care unit (ICU) transfer was defined as the number of patient episodes with effective bed change from a general ward to an intensive care area. HAI included the number of episodes of ward patients that developed catheter-related bloodstream infection, urinary catheter-related infection, aspiration pneumonia and/or sepsis. ACC accounted for the number of episodes of ward patients that experienced a cardiac arrest, shock, thromboembolic event, acute respiratory failure, acute respiratory distress syndrome (ARDS), myocardial injury, liver injury and/or kidney failure, not present on admission.

Statistical Analysis

Descriptive analysis of data using percentage frequencies, median and interquartile range was performed to determine demographic and clinical characteristics, and patients' outcomes. For categorical variables, a comparative analysis for detecting significant differences between groups was carried out using the chi-square test or Fisher's exact test when one or more cells had an expected frequency of five or less. For continuous variables, the Student's t-test or Mann-Whitney U test was used depending on the results of the Kolmogorov-Smirnov normality test. A logistic-regression model of all clinical factors potentially associated with unfavourable

outcome measures (AEs and in-hospital mortality) was performed including VIDA score, clinically relevant CCIF and other potential confounders: sex, hospital level and LOS. All potential explanatory variables included in the multivariate analysis were subjected to a correlation matrix for analysis of collinearity. The discriminatory power was evaluated by the area under the receiver operating characteristic (ROC). Results of multivariate analysis was reported as odds ratios (OR) and 95% confidence intervals (CI). We also performed an adjusted analysis to compare unfavourable outcomes in patients admitted in wards with VIDA system and without this system. Statistical analysis will be performed using the SPSS software package version 25.0 (SPSS, Chicago, IL). *P* values less than 0.05 were considered statistically significant.

RESULTS

During the study period, 1,838 patients were hospitalised with COVID-19, among them, 1,176 patients met inclusion criteria (**Figure 1**). The frequency of unfavourable outcomes was 42.8% (506 patients). In-hospital mortality rate was 19.6% (232 patients), and almost 41% (481 patients) experienced an AE while in a ward (2.7% transferred to ICU; 2.5% HAI; 40% ACC). Acute respiratory failure, ARDS, acute kidney failure, urinary catheter-related infection, sepsis, and thrombotic event were the most frequently AEs.

Patient Characteristics

The baseline characteristics of patients with unfavourable and favourable outcome are compared in **Table 1**. COVID-19 hospitalised patients who had an unfavourable outcome were more often male, older, and had one or more underlying chronic conditions (75.5%), mostly arterial hypertension or congestive heart failure and, diabetes or chronic kidney disease. Furthermore, they had longer LOS and high risk of severity or mortality (APR-DRG 3-4). Conversely, patients admitted in high-tech hospitals presented less frequency of unfavourable outcomes.

Regarding 806 patients hospitalised with VIDA early warning system, most patients with unfavourable outcomes experienced high risk of acute deterioration (41.7% in patients with unfavourable outcomes vs. 9.1% in patients with favourable outcomes).

Comorbidity, sociocultural and developmental domains were the most frequent CCIF domains identified in the studied sample. Mental-cognitive and psycho-emotional domains were less frequent. Patients with unfavourable outcomes exhibited a higher frequency of chronic disease, position impairment, anatomical and functional disorders, communication disorders, old age (>75 years) and mental status impairments, when compared to patients with favourable outcomes. The median of CCIF was also higher in patients with unfavourable outcomes (5 [IQR: 4-6] vs. 4 [IQR: 3-5]) **(Table 1)**.

Risk of acute deterioration and individual complexity factors association with outcomes.

Patients' outcomes of 806 patients with low, mild or high risk of acute deterioration were compared in **Table 2.** The frequency of unfavourable outcomes was nearly 38% in patients with mild risk and almost 80% in the high risk of acute deterioration group (p <.0.001). Similarly, the frequency of in-hospital mortality and AEs rose with increasing VIDA score and reached near 60% and 80% in patients with high risk of acute deterioration, respectively (p <.0.001). Acute respiratory failure, acute kidney failure and ICU transfer were the most frequent AEs.

Among the 1,176 patients analysed in this study, those with four or more CCIF experienced unfavourable outcomes (p <.0.05) **(Table 2)**.

Table 3 shows an adjusted analysis of health outcomes in 486 patients with high risk of mortality (APR-DRG 3-4) to compare patients admitted in wards where registered nurses use or do not use the VIDA early warning score system. In-hospital mortality was more frequent in patients admitted in wards where VIDA was not used

(52.5% vs. 41.3%, p <.0.05). Conversely, the frequency of AEs was slightly higher in patients admitted in VIDA' wards (p <.0.05).

Risk factors associated with unfavourable outcomes

The results of the multivariate analysis for risk of acute deterioration (as measured with VIDA score) and CCIF potentially associated with unfavourable outcomes, in-hospital mortality and AEs are summarized in **Table 4**.

After adjustment of potentially confounders, the analysis shows that high risk of acute deterioration was an independent factor associated with unfavourable outcomes, in-hospital mortality and AEs in COVID-19 ward inpatients. Furthermore, chronic disease, mental status impairments and LOS were risk factors associated with unfavourable outcomes. Conversely, high-tech hospital admission was a protective factor of unfavourable outcomes. The area under the ROC curve (AUC) was 0.81 (95% CI: 0.78-0.84).

Chronic disease, mental status impairments, old age and male sex were independent risk factors associated with in-hospital mortality for studied COVID-19 inpatients (AUC 0.91 [95% CI: 0.88-0.93]). Finally, risk factors independently associated with AEs were chronic disease, mental status impairments, old age and LOS; while high-tech hospital admission was a protective factor of AEs (AUC 0.80 [95% CI: 0.77-0.83]). The AUC of the three outcomes analysed were > 0.80, showing a fair discriminatory power.

DISCUSSION

In this study of a large cohort of hospitalised patients with COVID-19, the frequency of in-hospital mortality and AEs reached near 60% and 80%, in patients scored as at high risk of acute deterioration respectively. In-hospital mortality was higher in wards not using the VIDA early warning system. A wide majority of patients had four or more care complexity individual factors identified. The risk factors independently associated with unfavourable outcomes included chronic disease, mental status impairments, LOS and high risk of acute deterioration. High-tech hospital admission was a protective factor of unfavourable outcomes.

Our findings are consistent with previous COVID-19 reports which have found a similar frequency of in-hospital mortality and AEs.[3,21] In addition, 37% of patients developed respiratory complications (acute respiratory failure or ARDS) during hospitalization. This value is within the range reported in a previous inquiry (29-42%).[3]

The results of this study show that high risk of acute deterioration is a significant risk factor for unfavourable outcomes, as a composite measure for in-hospital mortality, and AEs in admitted COVID-19 patients. Although previous studies have stressed that early warning systems are predictors of in-hospital mortality and health outcomes,[22,23] only a few have evaluated warning score systems in admitted COVID-19 patients.[11,19] These latest studies showed a fair discrimination with adverse outcomes, concluding that the evaluation of the risk for acute deterioration in the COVID-19 hospital population is a priority for the organizations.[19]

In-hospital mortality was more frequent in patients admitted in wards where registered nurses do not use VIDA early warning system. In this regard, other studies showed that the use of early systems reinforces collaboration among the multidisciplinary team, and promotes the early identification of clinical deterioration.[24]

Similarly, previous studies have reported less mortality and adverse events when systematic nursing surveillance of patient status and progress is a daily basis practice.[9]

Chronic conditions and mental status impairments were the CCIF independently associated with unfavourable outcomes. Previous reports have shown that chronic diseases were more frequent among deceased COVID-19 patients [15] and aging was a potential risk factor associated with mortality.[6] Although our study has not identified age as a risk factor associated with a composite unfavourable outcome, we acknowledge that old age was an independent risk factor associated with mortality and AE. Furthermore, our findings were also consistent with other studies demonstrating that mental status impairments are associated with hospital-acquired complications,[25] including sepsis.[4]

A wide majority of patients had four or more CCIF. Our findings are consistent with other studies that identified a significant rate of chronic conditions in COVID-19 patients[15] and by the other hand, selected organizational issues that may impact care complexity and health outcomes.[26] Previous inquires have demonstrated the association of CCIF and health outcomes,[16] with an average of two CCIF per patient. Our investigation showed that for COVID-19 inpatients, the average of CCIF is four. These results are probably related to the transmissibility of this condition requiring droplet and contact precautions, the pandemics management associated public health measures of population confinement, preventing patients' relatives to visit admitted patients in person, resulting in a lack of family caregiver support during hospitalisation, and the frequency of chronic diseases in the studied sample. The organizational adaptation of hospitals to this pandemic context and the required isolation precautions have been associated with poor outcomes in prior studies.[27,28]

Additionally, we found that LOS was associated with unfavourable outcomes, coinciding with previous studies that associated AEs with increased healthcare costs due

to longer hospital stays.[29] Finally, high-tech hospital admission was a protective factor associated to unfavourable outcomes. High-tech hospitals usually have better nurse-to-patient ratios, than urban or community facilities. In this sense, a couple of recent inquiries in the same study setting conclude that on average, hospital ward patients require 5.6 hours of RN care per patient day, while the average of available RN hours per patient day is 2.4, and that RN understaffing is a structural issue.[26,30] Nevertheless, to the best of our knowledge, no study on nurse staffing and COVID-19 inpatients' outcomes have been published. Similarly, healthcare clinical leaders and managers have become key role to rapidly adapt organizations to the new reality. Fast and effective decision-making and managerial responses in crisis situations with high levels of uncertainty are essential at immediate and short-term however, they should be accompanied by planning and executing mid-term and long-lasting improvements that positively impact patient, professional and organizational outcomes, such as structural RN understaffing.[26]

The strengths of this study include its multicentre approach, cohort design and large sample size. It is the first research evaluating the association of the risk of acute deterioration, along with care complexity individual factors, with COVID-19 patient outcomes. Importantly, we identify broader health-contributors of care complexity, including psychosocial and mental-cognitive factors. In addition, the VIDA early warning system was developed as an evidence-based algorithm with a multidisciplinary approach, and also according to previous studies that highlighted the importance to adapt surveillance and screening systems to organization and cultural context.[14]

This study is not exempt of some limitations. First, VIDA score and CCIF data were comprehensively collected from clinical data warehouse of the Catalan Institute of Health and all patients included had a completed nurse charting in the patient electronic health record but we relied a proper compliance of electronic health records and

administrative data. This is acknowledged as a significant limitation since voluntary completion of patient electronic documentation during the initial weeks of COVID-19 first wave in our country, might have been negatively influenced by the peak rising hospital system burden, the need for patient direct care activity prioritization, as well as the physical and emotional stress experienced by bedside healthcare professionals. Second, regarding the study selection criteria, patients directly admitted and discharged from intensive care unit were excluded, since no early warning system was use at the critical care setting at the outset of the pandemics in our context. In this sense, the results of this study only apply to adult ward and intermediate care inpatients. Third, it should be noted that unpublished face validity studies have demonstrated the effectiveness VIDA early warning system. A full evaluation of its psychometric properties, in general medical-surgical inpatients, is pending and this must be acknowledged as a significant limitation. To minimize the potential effect of this limitation, this inquiry considered an adjusted analysis performed with patients in higher risk mortality (APR-DRG 3-4) comparing the ones admitted in wards with VIDA fully implemented and those being treated in units with no VIDA early warning system. The results proved a significant association of VIDA score and CCIF with unfavourable outcomes. Finally, we acknowledge as a potential limitation that other clinical measures such as the age-adjusted Charlson comorbidity index or patient lab values were not assessed. Selected lab values such as lactate, ferritin or calciferol have been studied as indicators of COVID-19 prognosis and severity. Combining point of care lab data with clinical data from nurses' observations and judgments on patient complexity factors, status and progress would probably result in a improved system for early detection and prevention of critical complications and other unfavourable outcomes in COVID-19 inpatients.

Conclusion

The risk of acute deterioration and the care complexity individual factors are associated with COVID-19 patient outcomes. The rate of unfavourable outcomes rose with increasing risk of acute deterioration as measured with VIDA score. The risk factors independently associated with poor health outcomes were chronic disease, mental status impairment, length of hospital stay and high risk of acute deterioration. High-tech hospital admission was a protective factor of unfavourable outcomes. The systematic nursing surveillance of patients at risk of acute deterioration and the assessment of CCIF may contribute to reduce deleterious health outcomes in COVID-19 adult inpatients.

REFERENCES

1 WHO, World Bank. Global preparedness monitoring board. A world at risk. Annual report on global preparedness for health emergencies. 2019. DOI:10.2307/40153772.

2 Li Q, Guan X, Wu P, *et al.* Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N. Engl. J. Med. 2020; **382**: 1199–207.

3 Huang C, Wang Y, Li X, *et al.* Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; **395**: 497–506.

4 Li H, Liu L, Zhang D, *et al.* SARS-CoV-2 and viral sepsis: observations and hypotheses. *Lancet* 2020; **395**: 1517–20.

5 Shi S, Qin M, Shen B, *et al.* Association of Cardiac Injury with Mortality in Hospitalized Patients with COVID-19 in Wuhan, China. *JAMA Cardiol* 2020; published online March 25. DOI:10.1001/jamacardio.2020.0950.

6 Zhou F, Yu T, Du R, *et al.* Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020; **395**: 1054–62.

7 Wu C, Chen X, Cai Y, *et al.* Risk Factors Associated with Acute Respiratory Distress Syndrome and Death in Patients with Coronavirus Disease 2019 Pneumonia in Wuhan, China. *JAMA Intern Med* 2020; published online March 13. DOI:10.1001/jamainternmed.2020.0994.

8 Zheng Z, Peng F, Xu B, *et al.* Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. *J Infect* 2020; published online April 23. DOI:10.1016/j.jinf.2020.04.021.

9 Juvé-Udina ME, Fabrellas-Padrés N, Adamuz-Tomás J, *et al.* Surveillance nursing diagnoses, ongoing assessment and outcomes on in-patients who suffered a cardiorespiratory arrest. *Rev da Esc Enferm* 2017; **51**: e03286.

10 WHO. Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected. 2020. https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected (accessed May 20, 2020).

11 Hu H, Yao N, Qiu Y. Comparing rapid scoring systems in mortality prediction of critical ill patients with novel coronavirus disease. *Acad Emerg Med* 2020; published online April 20. DOI:10.1111/acem.13992.

12 Liao X, Wang B, Kang Y. Novel coronavirus infection during the 2019–2020 epidemic: preparing intensive care units—the experience in Sichuan Province, China. *Intensive Care Med* 2020; **46**: 357–60.

13 O'Brien C, Goldstein BA, Shen Y, *et al.* Development, Implementation, and Evaluation of an In-Hospital Optimized Early Warning Score for Patient Deterioration. *MDM Policy Pract* 2020; **5**: 1–10.

14 McGaughey J, O'Halloran P, Porter S, Trinder J, Blackwood B. Early warning systems and rapid response to the deteriorating patient in hospital: A realist evaluation. *J Adv Nurs* 2017; **73**: 3119–32.

15 Chen T, Wu D, Chen H, *et al.* Clinical characteristics of 113 deceased patients with coronavirus disease 2019: Retrospective study. *BMJ* 2020; **368**: m1091.

16 Adamuz J, González-Samartino M, Jiménez-Martínez E, *et al.* Care Complexity Individual Factors Associated With Hospital Readmission: A Retrospective

Cohort Study. *J Nurs Scholarsh* 2018; **50**: 411–21.

17 Safford MM. The Complexity of Complex Patients. *J Gen Intern Med* 2015; **30**: 1724–5.

18 Juvé-Udina, M.E., Matud, C., Farrero S., Jiménez, H., Rodríguez, E., Martínez, M. et al. Intensity of nursing care: workloads or individual complexity? *Metas de Enfermería* 2010; **13**: 6–14.

19 Singh K, Valley TS, Tang S, Li BY, Kamran F, Sjoding MW, Wiens J, Otles E, Donnelly JP, Wei MY, McBride JP, Cao J, Penoza C, Ayanian JZ NB. Validating a Widely Implemented Deterioration Index Model Among Hospitalized COVID-19 Patients. *medRxiv* 2020. DOI:10.1101/2020.04.24.20079012.

20 Juvé-Udina ME. What patients' problems do nurses e-chart? Longitudinal study to evaluate the usability of an interface terminology. *Int J Nurs Stud* 2013; **50**: 1698–710.

21 Mao L, Jin H, Wang M, *et al.* Neurologic Manifestations of Hospitalized Patients with Coronavirus Disease 2019 in Wuhan, China. *JAMA Neurol* 2020; published online April 10. DOI:10.1001/jamaneurol.2020.1127.

22 Medic G, Kließ MK, Atallah L, *et al.* Evidence-based clinical decision support systems for the prediction and detection of three disease states in critical care: A systematic literature review. *F1000Research* 2019; **8**: 1728.

23 Kim I, Song H, Kim HJ, *et al.* Use of the national early warning score for predicting in-hospital mortality in older adults admitted to the emergency department. *Clin Exp Emerg Med* 2020; **7**: 61–6.

24 Ashbeck R, Stellpflug C, Ihrke E, *et al.* Development of a Standardized System

to Detect and Treat Early Patient Deterioration. *J Nurs Care Qual* 2020; published online April 6. DOI:10.1097/ncq.0000000000000484.

25 Bail K, Draper B, Berry H, Karmel R, Goss J. Predicting excess cost for older inpatients with clinical complexity: A retrospective cohort study examining cognition, comorbidities and complications. *PLoS One* 2018; **13**: e0193319.

26 Juvé-Udina M, González-Samartino M, López-Jiménez MM, *et al.* Acuity, nurse staffing and workforce, missed care and patient outcomes. A cluster-unit-level descriptive comparison. *J Nurs Manag* 2020; published online May 8. DOI:10.1111/jonm.13040.

27 Purssell E, Gould Di, Chudleigh J. Impact of isolation on hospitalised patients who are infectious: Systematic review with meta-analysis. *BMJ Open* 2020; **10**: e030371.

28 Tran K, Bell C, Stall N, *et al.* The Effect of Hospital Isolation Precautions on Patient Outcomes and Cost of Care: A Multi-Site, Retrospective, Propensity Score-Matched Cohort Study. *J Gen Intern Med* 2017; **32**: 262–8.

29 Rafter N, Hickey A, Condell S, *et al.* Adverse events in healthcare: Learning from mistakes. *Q J Med* 2015; **108**: 273–7.

30 Juvé-Udina M-E, Adamuz J, López-Jimenez M-M, *et al.* Predicting patient acuity according to their main problem. *J Nurs Manag* 2019; **27**: 1845–58.

FOOTNOTES

Author Contributions: All authors had full access to all study data and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Adamuz, González-Samartino, Juvé-Udina. *Coordination team:* Juvé-Udina. *Acquisition of data:* Adamuz, Tapia-Perez, López-Jiménez, Zuriguel-Pérez, Castro-Navarro. *Analysis and interpretation data:* Adamuz, González-Samartino, Jiménez-Martínez. *Drafting of the manuscript:* Adamuz, González-Samartino, Jiménez-Martínez, Juvé-Udina. *Critical revision of the manuscript for important intellectual content:* Tapia-Perez, López-Jiménez, Rodríguez-Fernández, Zuriguel-Pérez, Castro-Navarro, Carratalà. *Statistical analysis:* Adamuz and González-Samartino. *Obtained funding:* - . *Administrative, technical and material support:* López-Jiménez, Rodríguez-Fernández. *Study supervision:* Juvé-Udina, Carratalà.

Funding/Support: No funding.

Declaration of Interests: We declare that we have no competing interests.

Patient and public involvement: Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this inquiry.

Patient consent for publication: Not required**.**

Ethical approval: This study is approved by the Clinical Research Ethics Committee of the Bellvitge University Hospital with a waiver of informed consent (reference 158/20).

Provenance and peer review: Not commissioned; externally peer reviewed.

Data availability statement: All data relevant to the study are included in the article. No additional data are available.

Table 1. Baseline characteristics, VIDA score and care complexity individual factors of admitted COVID-19 patients with unfavourable and favourable outcomes.

Characteristics	Study population n=1,176 No.	%	Unfavourable outcome [a] n=506 (42.8%) No.	%	Favourable outcome n=670 (57.1%) No.	%	*p value*
Demographic characteristics							
Age (years)_median (IQR)	66.5	(51-77)	74	(60-80)	61	(49-74)	<0.001
Male sex	667	(56.7)	192	(37.9)	317	(47.3)	0.001
Clinical characteristics							
LOS_median (IQR)	6	(4-8)	7	(4-10)	5	(4-7)	<0.001
Continuity of care (discharged to another facility)	165	(14)	58	(11.5)	107	(16)	0.02
Severity (APR-GRD 3-4)	503	(42.8)	450	(88.9)	53	(7.9)	<0.001
Mortality risk (APR-DRG 3-4)	486	(41.3)	449	(88.7)	37	(5.5)	<0.001
High-tech hospital	969	(82.4)	389	(76.9)	580	(86.6)	<0.001
Underlying disease	745	(63.4)	382	(75.5)	363	(54.4)	<0.001
Arterial hypertension or chronic heart failure	469	(39.9)	234	(46.2)	235	(35.1)	<0.001
Diabetes or chronic kidney disease	298	(25.3)	165	(32.6)	133	(19.9)	<0.001
Chronic respiratory disease	171	(14.5)	95	(18.8)	76	(11.3)	<0.001
Neurodegenerative disease	63	(5.3)	33	(6.5)	39	(4.5)	0.15
Chronic liver disease	54	(4.6)	30	(5.9)	24	(3.6)	0.07
Cancer	50	(4.3)	31	(6.5)	19	(2.8)	0.008
Immunosuppression	49	(4.2)	23	(4.5)	26	(3.9)	0.66
VIDA score[b]							
Low risk (0)	104	(12.9)	27	(7.1)	77	(18)	<0.001
Moderate risk (1-2)	505	(62.7)	194	(51.2)	311	(72.8)	<0.001
High risk (3-4)	197	(16.7)	158	(41.7)	39	(9.1)	<0.001
Care complexity individual factors (CCIF)							
Comorbidity/complications	1,176	(100)	506	(100)	670	(100)	-
Transmissible infection	1,176	(100)	506	(100)	670	(100)	-
Hemodynamic instability	910	(77.4)	396	(78.3)	514	(76.7)	0.57
Chronic disease	745	(63.4)	382	(75.5)	363	(54.4)	<0.001
Uncontrolled pain	194	(16.5)	82	(16.2)	112	(16.7)	0.87
Extreme weight	168	(14.3)	82	(16.2)	86	(12.8)	0.11
Position impairment	72	(6.1)	52	(10.3)	20	(3.0)	<0.001
Urinary or faecal incontinence	58	(4.9)	31	(6.1)	27	(4.0)	0.10
Immunosuppression	49	(4.1)					
Anatomical and functional disorders	41	(3.5)	30	(5.9)	11	(1.6)	<0.001
Communication disorders	18	(1.5)	13	(2.6)	5	(0.7)	0.01
High risk of hemorrhage	2	(0.2)	1	(0.2)	1	(0.1)	0.68
Vascular fragility	6	(0.5)	4	(0.8)	2	(0.3)	0.41
Involuntary movements	3	(0.3)	3	(0.6)	0	(0.0)	0.08
Dehydration	3	(0.3)	1	(0.2)	2	(0.3)	0.60
Oedema	0	(0)	0	(0.0)	0	(0.0)	-
Developmental	397	(33.8)	244	(48.2)	153	(22.8)	<0.001
Old age (≥75 years)	397	(33.8)	244	(48.2)	153	(22.8)	<0.001
Psycho-emotional	218	(18.5)	86	(17.0)	132	(19.7)	0.13
Fear/anxiety	173	(14.7)	70	(13.8)	103	(15.4)	0.51
Impaired adaptation	54	(4.6)	17	(3.4)	37	(5.5)	0.09
Aggressive behaviour	1	(0.1)	1	(0.2)	0	(0.0)	0.43
Mental-cognitive	240	(20.4)	184	(36.4)	56	(8.4)	<0.001
Mental status impairments	238	(20.2)	183	(36.2)	55	(8.2)	<0.001
Agitation	5	(0.4)	4	(0.8)	1	(0.1)	0.17
Impaired cognitive functions	4	(0.3)	3	(0.6)	1	(0.1)	0.32
Perception of reality disorders	2	(0.2)	0	(0.0)	2	(0.3)	0.51
Sociocultural	1,176	(100)	506	(100)	670	(100)	-
Lack of caregiver support	1,176	(100)	506	(100)	670	(100)	-
Belief conflict	1	(0.1)	0	(0.0)	1	(0.1)	0.57
Language barriers	1	(0.1)	1	(0.2)	0	(0.0)	0.43
Social exclusion	1	(0.1)	0	(0.0)	1	(0.1)	1
Care complexity individual factors (CCIF), median (IQR)	4	(3-6)	5	(4-6)	4	(3-5)	<0.001

Abbreviations: IQR, interquartile range; LOS, length of hospital stay; ICU, intensive care unit; APR-DRG, all patient refined diagnosis-related groups; VIDA, surveillance and identification of acute deterioration.

[a] Unfavourable outcomes included: in-hospital mortality and adverse events during hospitalization.

[b] VIDA score was analysed according to 806 admitted patients in wards with VIDA system.

Table 2. Patients' outcomes according to risk of acute deterioration (VIDA score) and care complexity individual factors.

Outcomes	All n=1,176 N (%)	VIDA_score n=806 (68.5) Low risk (0) n=104 (12.9) N (%)	Mild risk (1-2) n=505 (62.7) N (%)	High risk (3-4) n=197 (16.7) N (%)	CCIF n=1,176 CCIF<4 n=327 (27.8) N (%)	CCIF≥4 n=849 (72.2) N (%)
Unfavourable outcomes	506 (43.0)	27 (26.0)**	194 (38.4)*	158 (80.2)**	92 (28.1)**	414 (48.8)**
Deceased	232 (19.6)	0 (0.0)**	46 (9.1)**	118 (59.9)**	5 (1.5)**	227 (26.7)**
Adverse event	481 (40.9)	27 (26.0)**	187 (37)*	153 (77.7)**	91 (27.8)**	394 (46.4)**
ICU transfer	32 (2.7)	0 (0.0)*	12 (2.4)	13 (6.6)*	4 (1.2)*	28 (3.3)*
HAI	29 (2.5)	0 (0.0)*	10 (2.0)	12 (6.1)*	1 (1.5)	24 (2.8)
Catheter-related bloodstream infection	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.1)
HA urinary tract infection	19 (1.6)	0 (0.0)	7 (1.4)	8 (4.1)*	3 (0.9)	16 (1.9)
Aspiration pneumonia	3 (0.3)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.4)
Sepsis	7 (0.6)	0 (0.0)	1 (0.2)	3 (1.5)*	2 (0.6)	5 (0.6)
ACC	470 (40.0)	27 (26.0)**	181 (35.8)**	150 (76.1)**	88 (26.6)**	383 (45.1)**
Cardiac arrest	5 (0.4)	1 (1.0)	0 (0.0)*	3 (1.5)*	0 (0.0)	5 (0.6)
Shock	4 (0.3)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	4 (0.5)
Thrombotic event	7 (0.6)	1 (1.0)	1 (0.2)	2 (1)	1 (0.3)	6 (0.7)
Acute respiratory failure[1]	436 (37.0)	27 (26.0)**	164 (32.5)**	144 (73.1)**	84 (25.1)**	353 (41.6)**
Myocardial injury	5 (0.4)	0 (0)	3 (0.6)	1 (0.5)	0 (0.0)	5 (0.6)
Liver injury	2 (0.2)	0 (0)	0 (0)	1 (0.5)	0 (0.0)	2 (0.2)
Renal insufficiency	83 (7.1)	1 (1.0)*	28 (5.5)*	31 (15.7)**	6 (1.8)**	77 (9.1)**

Abbreviations: VIDA, surveillance and identification of acute deterioration; CCIF, care complexity individual factors; ICU, intensive care unit; HAI, hospital-acquired infections; ACC, avoidable critical complications.

* *p* value >0.001 and <0.05.

** *p* value ≤0.001.

[1] Include acute respiratory distress syndrome (ARDS).

Table 3. Adjusted analysis of unfavourable outcomes according to VIDA early warning system in 486 patients with high risk of mortality (APR-DRG 3-4).

Outcomes	Unadjusted n=1,176 N (%)	Adjusted n=486 (41.2) N (%)	With VIDA_system n=368 (75.7) N (%)	Without VIDA_system n=118 (24.3) N (%)	*p value*[1]
Unfavourable outcomes	506 (43.0)	449 (92.4)	345 (93.8)	104 (88.1)	0.07
Deceased	232 (19.6)	214 (44)	152 (41.3)	62 (52.5)	0.02
Adverse event	481 (40.9)	436 (89.7)	337 (91.6)	99 (83.9)	0.02
ICU transfer	32 (2.7)	25 (5.1)	20 (5.4)	5 (4.2)	0.41
HAI	29 (2.5)	19 (3.9)	16 (4.3)	3 (2.5)	0.28
ACC	470 (40.0)	433 (89.1)	334 (90.8)	99 (83.9)	0.31

Abbreviations: VIDA, surveillance and identification of acute deterioration; ICU, intensive care unit; HAI, hospital-acquired infections; ACC, avoidable critical.
[1]All variables were compared using the Fisher exact test.

Table 4. Multivariate analysis of VIDA score and CCIF in 806 adult COVID-19 hospitalized patients associated with unfavourable outcomes, deceased and AE.

Characteristics	Unfavourable outcomes [1] n= 379/806 (47%)		Deceased[2] n= 164/806 (20.3%)		AE[3] n=367/806 (45.5%)	
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Old age (≥75 years)	1.48	(0.99-2.22)	3.04	(1.79-5.15)**	1.52	(1.02-2.26)*
Male sex	1.21	(0.87-1.69)	1.86	(1.11-3.11)*	1.20	(0.87-1.67)
LOS	1.16	(1.11-1.21)**	0.97	(0.93-1.01)	1.17	(1.12-1.22)**
High-tech hospital	0.57	(0.36-0.89)*	1.88	(0.94-3.78)	0.61	(0.39-0.95)*
VIDA score 3-4	4.32	(2.83-6.60)**	13.99	(8.44-23.18)**	4.21	(2.79-6.36)**
Chronic disease	1.90	(1.32-2.72)**	2.01	(1.03-3.90)*	1.81	(1.26-2.59)**
Position impairment	1.19	(0.58-2.44)	1.41	(0.63-3.13)	1.23	(0.62-2.46)
Communication disorders	0.97	(0.24-3.96)	0.87	(0.22-3.41)	0.78	(0.21-2.95)
Mental status impairments	2.31	(1.45-23.66)**	6.21	(3.67-10.50)**	1.72	(1.09-2.69)*

Abbreviations: AE, adverse event; LOS, length of hospital stay; VIDA, surveillance and identification of acute deterioration.
Multivariate analysis included: high risk of acute deterioration (VIDA score 3-4), clinically relevant care complexity individual factors (old age, chronic disease, position impairment, communication disorders and mental status impairments) and potential confounders (sex, hospital level and LOS).
[1]AUC 0.81 (CI 95%; 0.78-0.84).
[2]AUC 0.91 (CI 95%; 0.88-0.93).
[3]AUC 0.80 (CI 95%; 0.77 -0.83).
* *p* value >0.001 and <0.05.
** *p* value ≤0.001.

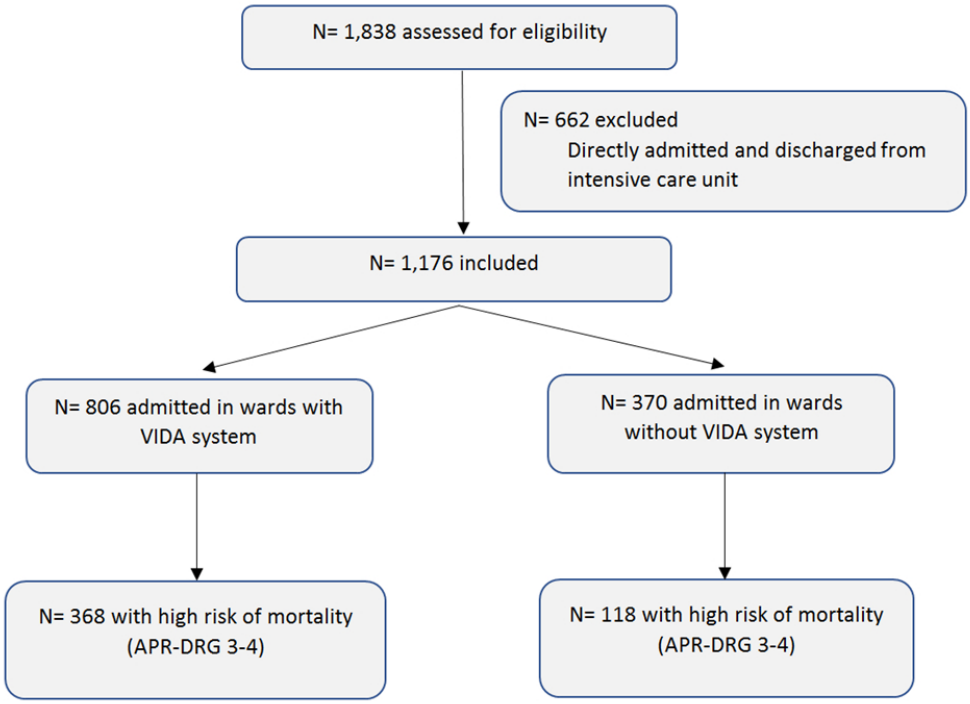

Figure 1. Flow-chart of patient selection process.

Supplementary file 1. Juvé-Udina ME. VIDA score for acute deterioration in the current *human* algorithm.

H1, H2, H3		
Punctuation	**Risk score**	**Definition**
0 – 1	0	No risk of complication (at that particular moment)
2 – 3	1	Low risk
4	2	Moderate risk (very probable complication)
5 – 6	3	High risk (imminent complication if not stabilized)
>= 7	4	Critical complication status
H4		
Punctuation	**Risk score**	**Definition**
0 – 1	0	No risk of complication (at that particular moment)
2 – 3	1	Low risk
4 – 6	2	Moderate risk (very probable complication)
7 – 9	3	High risk (imminent complication if not stabilized)
>= 10	4	Critical complication status
H5		
Punctuation	**Risk score**	**Definition**
0 – 2	0	No risk of complication (at that particular moment)
3 – 4	1	Low risk
5 – 6	2	Moderate risk (very probable complication)
7 – 8	3	High risk (imminent complication if not stabilized)
>= 9	4	Critical complication status
H6		
Punctuation	**Risk score**	**Definition**
0 – 2	0	No risk of complication (at that particular moment)
3 – 4	1	Low risk
5 – 6	2	Moderate risk (very probable complication)
7 – 9	3	High risk (imminent complication if not stabilized)
>= 10	4	Critical complication status
H7		
Punctuation	**Risk score**	**Definition**
<= 3	1	Low risk
4 – 6	2	Moderate risk (very probable complication)
7 – 8	3	High risk (imminent complication if not stabilized)
>= 9	4	Critical complication status

Abbreviations: H, hospital.

Supplementary file 2. Care complexity individual factors.

Domains	Factors	Specifications
Comorbidity/ Complications	Transmissible infection	Isolation measures
	Hemodynamic instability	Intensive control of vital signs or state of shock
	Chronic disease	Conditions (organ failure, degenerative process or oncological disease) that require ongoing medical attention and limit activities of daily living.
	Uncontrolled pain	Verbal numerical rating scale above three points
	Extreme weight	Low weight, obesity
	Position impairment	Includes any position impairment
	Urinary or faecal incontinence	Loss of bladder control or failure to control bowel movements
	Immunosuppression	Neutropenia, immunodeficiency or immunosuppressive therapy
	Anatomical and functional disorders	Amputation, deformities, joint stiffness
	Communication disorders	Aphasia, dysphasia, dysarthria, laryngectomy, tracheostomy
	High risk of haemorrhage	Coagulation disorders, thrombocytopenia, anticoagulant therapy
	Vascular fragility	Capillary fragility, tortuous veins
	Involuntary movements	Continuous involuntary movements
	Dehydration	Skin turgor
	Oedema	An accumulation of an excessive amount of watery fluid in cells, tissues, or serous cavities
Developmental	Old age	≥75 years
Psycho-emotional	Fear/anxiety	Fear or anxiety (moderate or intense)
	Impaired adaptation	Disruptive behaviour, hopelessness or surrender
	Aggressive behaviour	Physical or verbal aggressive behaviour (moderate or intense)
Mental-cognitive	Mental status impairments	Confusion, disorientation, stupor, transient loss of consciousness
	Agitation	Psychomotor agitation
	Impaired cognitive functions	Intellectual disability, amnesia
	Perception of reality disorders	Delirium, hallucinations, disconnection from reality
Sociocultural	Lack of caregiver support	Without caregiver support or caregiver burnout
	Belief conflict	Spiritual distress
	Language barriers	Barrier to communication resulting from speaking different languages than Spanish or Catalan without translator.
	Social exclusion	Extreme poverty

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Pg.3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Pg.3-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Pg.5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	Pg.6
Methods			
Study design	4	Present key elements of study design early in the paper	Pg.7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Pg.7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Pg.7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Pg.7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Pg.7-8
Bias	9	Describe any efforts to address potential sources of bias	Pg.16
Study size	10	Explain how the study size was arrived at	Pg.7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Pg.9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Pg.9
		(*b*) Describe any methods used to examine subgroups and interactions	Pg.9
		(*c*) Explain how missing data were addressed	-
		(*d*) If applicable, explain how loss to follow-up was addressed	-
		(*e*) Describe any sensitivity analyses	-
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Pg.10
		(b) Give reasons for non-participation at each stage	Pg.10-11
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Pg.10
		(b) Indicate number of participants with missing data for each variable of interest	-
		(c) Summarise follow-up time (eg, average and total amount)	Pg.10
Outcome data	15*	Report numbers of outcome events or summary measures over time	Pg10-11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 1&4

		(*b*) Report category boundaries when continuous variables were categorized	Table 1&4
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Pg.11-12
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Pg.11
Discussion			
Key results	18	Summarise key results with reference to study objectives	Pg.13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Pg.16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Pg.14-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	Pg.15-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Pg.21.

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Risk of acute deterioration and care complexity individual factors associated with health outcomes in hospitalised patients with COVID-19: a multicenter cohort study.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-041726.R3
Article Type:	Original research
Date Submitted by the Author:	21-Jan-2021
Complete List of Authors:	Adamuz, Jordi; Bellvitge University Hospital, Nursing Knowledge Management and Information Systems Department González-Samartino, Maribel; Bellvitge University Hospital, Nursing knowledge Management and Information Systems Department Jiménez-Martínez, Emilio; Bellvitge University Hospital, Department of Infectious Diseases Tapia-Pérez, Marta; Bellvitge University Hospital, Nursing knowledge Management and Information Systems Department López-Jiménez, María-Magdalena; Bellvitge University Hospital, Nursing knowledge Management and Information Systems Department Rodríguez-Fernández, Hugo; Bellvitge University Hospital, Nursing knowledge Management and Information Systems Department Castro-Navarro, Trinidad; University Hospital Germans Trias i Pujol, Nursing knowledge Management and Information Systems Department Zuriguel-Pérez, Esperanza; Vall d'Hebron Research Institute, Nurse research coordinator Carratala, Jordi; Bellvitge University Hospital, Department of Infectious Diseases Juvé-Udina, Maria-Eulàlia; Catalan Institute of Health
Primary Subject Heading:	Nursing
Secondary Subject Heading:	Health informatics, Infectious diseases, Nursing, Respiratory medicine
Keywords:	Health informatics < BIOTECHNOLOGY & BIOINFORMATICS, Health & safety < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, INFECTIOUS DISEASES, Respiratory infections < THORACIC MEDICINE

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

ORIGINAL ARTICLE

Risk of acute deterioration and care complexity individual factors associated with health outcomes in hospitalised patients with COVID-19: a multicenter cohort study.

Jordi Adamuz, PhD, MSN, RN[1,2,5]; Maribel González-Samartino, PhD, MSN, RN[1,2,5] *; Emilio Jiménez-Martínez, MSN, RN [3,5]; Marta Tapia-Pérez, RN[1,5]; María-Magdalena López-Jiménez, MSN, RN [1,5]; Hugo Rodríguez-Fernández, RN[1,5]; Trinidad Castro-Navarro, RN[6]; Esperanza Zuriguel-Pérez, PhD, MSN, RN[7]; Jordi Carratalà, PhD, MD [3,4,5], Maria-Eulàlia Juvé-Udina, PhD, MSN, RN [2,5,8].

[1]Nursing Knowledge Management and Information Systems Department, Bellvitge University Hospital, L'Hospitalet de Llobregat, Barcelona, Catalonia, Spain.

[2]School of Nursing, Medicine and Health Science Faculty, University of Barcelona, L'Hospitalet de Llobregat, Barcelona, Catalonia, Spain.

[3]Department of Infectious Diseases, Bellvitge University Hospital, L'Hospitalet de Llobregat, Barcelona, Catalonia, Spain.

[4]Faculty of Medicine, Department of Clinical Sciences, University of Barcelona, L'Hospitalet de Llobregat, Barcelona, Catalonia, Spain.

[5]Bellvitge Biomedical Research Institute (IDIBELL), L'Hospitalet de Llobregat, Barcelona, Catalonia, Spain.

[6]Nursing Knowledge Management and Information Systems Department, Germans Trias i Pujol University Hospital. Badalona, Catalonia, Spain.

[7]Nurse research coordinator, Vall d'Hebron Institute of Biomedical Research (VHIR), Barcelona, Catalonia, Spain.

[8]Catalan Institute of Health, Barcelona, Catalonia, Spain.

*Corresponding Author:

Maribel González-Samartino, PhD, MSN, RN.

Nursing Knowledge Management and Information Systems Department, Bellvitge University Hospital - IDIBELL.

Feixa Llarga s/n, 08907, L'Hospitalet de Llobregat (Barcelona), Spain.

Telephone: +34 93 2602123.

Fax: +34 93 2607561.

E-mail: mgsamartino67@gmail.com

Conflict of interest disclosures: We declare that we have no competing interests.

Word Count: 3,576 words.

Funding: None.

ABSTRACT

Background: Evidence about the impact of systematic nursing surveillance on risk of acute deterioration of patients with COVID-19 and the effects of care complexity factors on inpatient outcomes is scarce. The aim of this study was to determine the association between acute deterioration risk, care complexity factors and unfavourable outcomes in hospitalised patients with COVID-19.

Methods: A multicentre cohort study was conducted from March 1, 2020 to March 31, 2020 at seven hospitals in Catalonia. All adult COVID-19 patients admitted to hospitals and with a complete minimum data set were recruited retrospectively. Patients were classified based on the presence or absence of a composite unfavourable outcome (in-hospital mortality and adverse events). The main measures included risk of acute deterioration (as measured using the VIDA early warning system) and care complexity factors. All data were obtained blinded from electronic health records. Multivariate logistic analysis was performed to identify the VIDA score and complexity factors associated with unfavourable outcomes.

Results: Out of a total of 1,176 COVID-19 patients, 506 patients (43%) experienced an unfavourable outcome during hospitalisation. The frequency of unfavourable outcomes rose with increasing risk of acute deterioration as measured by the VIDA score. Risk factors independently associated with unfavourable outcomes were chronic underlying disease (OR: 1.90, 95% CI: 1.32–2.72: $p < 0.001$), mental status impairment (OR: 2.31, 95% CI: 1.45–23.66; $p < 0.001$), length of hospital stay (OR: 1.16, 95% CI: 1.11–1.21; $p < 0.001$) and high risk of acute deterioration (OR: 4.32, 95% CI: 2.83–6.60; $p < 0.001$). High-tech hospital admission was a protective factor against unfavourable outcomes (OR: 0.57, 95% CI: 0.36–0.89; $p = 0.01$).

Conclusion: The systematic nursing surveillance of the status and evolution of COVID-19 inpatients, including the careful monitoring of acute deterioration risk and care

complexity factors may help reduce deleterious health outcomes in COVID-19 inpatients.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- We performed a multicentre cohort study with a large sample of patients with COVID-19.
- This novel research assessed the impact of the risk of acute deterioration and broader contributors to care complexity on COVID-19 patient outcomes.
- We did not evaluate other clinical measures such as the age-adjusted Charlson comorbidity index or patient lab values.
- The results of this study only apply to adult wards and intermediate care inpatients.
- The risk of acute deterioration was measured using VIDA, an early warning system not yet fully implemented in all hospitals wards.

INTRODUCTION

Along with climate change and financial crises, pandemics are a major global risk in the 21st century. A 2019 report stated that, in the last decade, the World Health Organization (WHO) had tracked 1,483 epidemic events, including Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), Ebola and other epidemic-prone diseases, considered harbingers of a new era of high-impact, potentially fast-spreading outbreaks.[1]

The potential threat became real in December 2019, when a severe acute respiratory infection caused by the new coronavirus SARS-CoV-2 first began to spread in Wuhan (China).[2,3] The WHO described the 'Wuhan pneumonia' as an outbreak of potential danger on December 31st, and as an outbreak of global concern on January 31st. This coronavirus disease (named COVID-19) was declared a global pandemic in February 2020.

COVID-19 patients frequently require hospital admission as they may rapidly develop severe potentially life-threatening complications, such as acute respiratory distress syndrome, sepsis, major thromboembolic events or cardiac injury, requiring intensive care.[3–5] Recent studies have found overall in-hospital mortality rates for COVID-19 inpatients ranging from 15 to 28%.[3,6–8] Therefore, early recognition of patient deterioration and escalation of treatment to reduce the risk of progression to critical complications is a significant issue that may impact patient and organizational outcomes. Screening for acute deterioration implies nursing surveillance, data collection, interpretation and recognition of changes in patients' status, prioritization of patients' problems and decision-making on the interventions needed in order to curb the cascade towards adverse events (AEs) and death.[9]

According to the WHO "*patients hospitalized with COVID-19 require regular monitoring of vital signs and, where possible, utilization of early warning scores that*

facilitate early recognition and escalation of treatment of the deteriorating patient."[10] Early warning systems have become an important component of managing inpatient care, and are a clinical decision-making support stratification tool used to prevent poor health outcomes.[11–13] Previous studies suggested the need for adaptation of these systems to each context.[14] According to these recommendations, several evidence-based algorithms have been developed and used to identify and act upon initial or impending acute deterioration among hospitalised patients in a timely fashion. In the context of this study, a nursing surveillance improvement programme named VIDA (the Catalan acronym for Surveillance and Identification of Acute Deterioration) was first implemented in 2013 and, through a multidisciplinary approach, has evolved into an early warning score system that is used on a daily basis to assist clinical decision-making.

It has been reported that patients hospitalised with COVID-19 have a substantial rate of chronic conditions that may affect the complexity of medical and nursing care provision and patient health outcomes.[15] Nevertheless, care complexity individual factors (CCIF) are related not only to multiple comorbidities but also to mental-cognitive and psychosocial patient features, which in turn are also associated with increased healthcare needs during hospitalisation and with selected health outcomes.[16–18]

Only a few studies in COVID-19 inpatients have explored the use of acute deterioration risk stratification[11,19] and to date, none has assessed CCIF as predictors of poor health outcomes. The aim of this study was to determine the association between the risk of acute deterioration (as measured using the VIDA early warning system), care complexity individual factors and unfavourable outcomes in patients hospitalised with COVID-19.

METHODS

Setting and Study Design

A retrospective cohort study was carried out at seven public hospitals in Catalonia, Spain: three tertiary metropolitan facilities, three urban university centres and one community hospital. All patients with a medical diagnosis of COVID-19 infection admitted to a ward or intermediate unit for COVID-19 or other causes from March 1, 2020 to March 31, 2020 with a completed hospital minimum data set report were recruited retrospectively and followed up during hospitalisation until discharge or death. Patients' directly admitted and discharged from intensive care units (ICU) were excluded because the VIDA early warning system is not used in the ICU. Patients who remained hospitalised after the recruitment end date were also excluded as the hospital minimum data set was not available.

We defined the primary endpoint as a composite of unfavourable outcomes including in-hospital mortality or adverse events (AEs), not present on admission and occurring thereafter during hospitalisation.

This study was approved by The Clinical Research Ethics Committee of the Bellvitge University Hospital (reference 158/20). Informed consent was waived due to the study's retrospective design. Ethical and data protection protocols related to anonymity and data confidentiality (access to records, data encryption and archiving of information) were complied with throughout the study.

Patient and Public Involvement

Patients were not involved in the design, conduct, or reporting of this study.

Data Collection

Information regarding the demographic and clinical characteristics, continuity of care (discharged to another facility), high-tech hospital (referral centre that provides tertiary care for either open-heart surgery or major organ transplants or both), length of hospital

stay (LOS) and patient severity and mortality risk were collected from the hospital minimum data set and the clinical data warehouse of the Catalan Institute of Health. Patient severity and risk of mortality were based on the all patient refined diagnosis-related group (APR-DRG), which categorises both measures from low (level 1) to extreme (level 4). Severity and mortality risk were dichotomised in this study into low risk (levels 1–2) and high risk (levels 3–4).[20] All variables were collected during hospitalisation.

The VIDA score (acute deterioration risk stratification) automatically classifies patients into five groups according to patient progress data: no risk (level 0), low risk (level 1), moderate risk (level 2), high risk (impending complication if not stabilised) (level 3), manifested complication initial status (level 4). Levels 2 to 4 create an alert in the electronic health records and require action in response to clinical recommendations. These recommendations are standardised for each context and involve intensifying the surveillance of the patients' status and notifying the medical team. The health team (nurse and specialist) are responsible for the final clinical decision-making. For the purposes of this study, the VIDA score was classified as mild (levels 1–2) or high (levels 3–4) risk. Patients were classified according to the highest VIDA score obtained during their hospitalisation. Patient progress data were extracted from anonymised electronic health records whenever they were e-charted, and included: respiratory rate (breaths/min), oxygen saturation (%), temperature (ºC), mental status (level of awareness; 1= aware and orientated, >1 = disturbed mental status, including disorientation, acute confusion, etc.), pulse (cardiac rate, beats/min) and systolic and diastolic blood pressure (mmHg) (Supplementary file 1).

Care complexity individual factors (CCIF) were classified into five domains: (i) mental-cognitive, (ii) psycho-emotional, (iii) sociocultural, (iv) developmental, and (v) comorbidity/complications, as described in previous studies.[16,18] Each CCIF domain is

structured into factors and specifications. Patients were considered to fall within any CCIF domains if they presented at least one factor or specification during their hospitalisation. These CCIF factors and specifications were obtained from the nursing assessment e-charts as structured data based on the Architecture, Terminology, Interface, Knowledge (ATIC) terminology[20] (Supplementary file 2).

Outcome measures

The main end point was a composite of unfavourable outcomes including in-hospital mortality and adverse events (AEs) during hospitalisation. The in-hospital mortality counted the number of COVID-19 patients dying while in a ward. The AEs included intensive care unit transfer, hospital-acquired infections (HAI) and potentially avoidable critical complications (ACC) during hospitalisation. Intensive care unit (ICU) transfer was defined as the number of patient episodes with effective bed change from a general ward to an intensive care area. HAI included the number of episodes of ward patients that developed catheter-related bloodstream infection, urinary catheter-related infection, aspiration pneumonia and/or sepsis. ACC accounted for the number of episodes of ward patients that experienced a cardiac arrest, shock, thromboembolic event, acute respiratory failure, acute respiratory distress syndrome (ARDS), myocardial injury, liver injury and/or kidney failure, not present on admission.

Statistical Analysis

Descriptive analysis of data using percentage frequencies, median and interquartile range was performed to determine demographic and clinical characteristics, and patients' outcomes. For categorical variables, a comparative analysis for detecting significant differences between groups was carried out using the chi-square test or Fisher's exact test when one or more cells had an expected frequency of five or less. For continuous variables, the Student's t-test or Mann-Whitney U test was used depending on the results of the Kolmogorov-Smirnov normality test. A logistic-

regression model of all clinical factors potentially associated with unfavourable outcome measures (AEs and in-hospital mortality) was performed including the VIDA score, clinically relevant CCIF and other potential confounders: sex, hospital level and LOS. All potential explanatory variables included in the multivariate analysis were subjected to a correlation matrix for analysis of collinearity. The discriminatory power was evaluated by the area under the receiver operating characteristic (ROC) curve. The results of the multivariate analysis were reported as odds ratios (OR) and 95% confidence intervals (CI). We also performed an adjusted analysis to compare unfavourable outcomes in patients admitted to wards with and without the VIDA system. Statistical analysis was performed using the SPSS software package version 25.0 (SPSS, Chicago, IL). *P* values less than 0.05 were considered statistically significant.

RESULTS

During the study period, 1,838 patients were hospitalised with COVID-19, of which 1,176 patients met the inclusion criteria (**Figure 1**). The frequency of unfavourable outcomes was 42.8% (506 patients). The in-hospital mortality rate was 19.6% (232 patients), and almost 41% (481 patients) experienced an AE while in a ward (2.7% transferred to ICU; 2.5% HAI; 40% ACC). Acute respiratory failure, ARDS, acute kidney failure, urinary catheter-related infection, sepsis, and thrombotic events were the most frequent AEs.

Patient Characteristics

The baseline characteristics of patients with an unfavourable and favourable outcome are compared in **Table 1**. Hospitalised COVID-19 patients who had an unfavourable outcome were more often male, older, and had one or more underlying chronic conditions (75.5%), mostly arterial hypertension or congestive heart failure, and diabetes or chronic kidney disease. Furthermore, they had a longer LOS and a high risk

of severity or mortality (APR-DRG 3-4). Conversely, patients admitted to high-tech hospitals presented a lower frequency of unfavourable outcomes.

Among the 806 patients in wards where the VIDA early warning system was in use, most patients with unfavourable outcomes experienced a high risk of acute deterioration (41.7% in patients with unfavourable outcomes vs. 9.1% in patients with favourable outcomes).

Comorbidity, sociocultural and developmental domains were the most frequent CCIF domains identified in the studied sample. Mental-cognitive and psycho-emotional domains were less frequent. Patients with unfavourable outcomes exhibited a higher frequency of chronic disease, position impairment, anatomical and functional disorders, communication disorders, old age (>75 years) and mental status impairment, when compared with patients with favourable outcomes. The median CCIF was also higher in patients with unfavourable outcomes (5 [IQR: 4–6] vs. 4 [IQR: 3–5]) **(Table 1)**.

Association of outcomes with risk of acute deterioration and care complexity factors.

The outcomes of 806 patients with low, mild or high risk of acute deterioration are compared in **Table 2.** The frequency of unfavourable outcomes was almost 38% in patients with mild risk and almost 80% in those at high risk of acute deterioration (p <.0.001). Similarly, the frequency of in-hospital mortality and AEs rose with increasing VIDA score and were around 60% and 80%, respectively, in patients with a high risk of acute deterioration (p <.0.001). Acute respiratory failure, acute kidney failure and ICU transfer were the most frequent AEs.

Among the 1,176 patients analysed in this study, those with four or more CCIF experienced unfavourable outcomes (p <.0.05) **(Table 2)**.

Table 3 shows an adjusted analysis of health outcomes in 486 patients with a high risk of mortality (APR-DRG 3-4). In-hospital mortality was more frequent in

patients admitted to wards where VIDA was not used (52.5% vs. 41.3%, p <.0.05). Conversely, the frequency of AEs was slightly higher in patients admitted to wards using VIDA (p <.0.05).

Risk factors associated with unfavourable outcomes

The results of the multivariate analysis for risk of acute deterioration (as measured using the VIDA score) and CCIF potentially associated with unfavourable outcomes, in-hospital mortality and AEs are summarized in **Table 4**.

After adjustment for potential confounders, the analysis showed that a high risk of acute deterioration was an independent factor associated with unfavourable outcomes, in-hospital mortality and AEs in COVID-19 inpatients. Furthermore, chronic disease, mental status impairment and LOS were risk factors associated with unfavourable outcomes. Conversely, high-tech hospital admission was a protective factor against unfavourable outcomes. The area under the ROC curve (AUC) was 0.81 (95% CI: 0.78–0.84).

Chronic disease, mental status impairment, old age and male sex were independent risk factors associated with in-hospital mortality in the studied COVID-19 inpatients (AUC 0.91 [95% CI: 0.88–0.93]). Finally, risk factors independently associated with AEs were chronic disease, mental status impairment, old age and LOS, whereas high-tech hospital admission was a protective factor against AEs (AUC 0.80 [95% CI: 0.77–0.83]). The AUCs of the three outcomes analysed were > 0.80, showing a fair discriminatory power.

DISCUSSION

In this study of a large cohort of hospitalised patients with COVID-19, the frequency of in-hospital mortality and AEs was around 60% and 80%, respectively, in patients scored as at high risk of acute deterioration. In-hospital mortality was higher in wards not using the VIDA early warning system. The majority of patients had four or more care complexity factors identified. The risk factors independently associated with unfavourable outcomes included chronic disease, mental status impairment, LOS and a high risk of acute deterioration. High-tech hospital admission was a protective factor against unfavourable outcomes.

Our findings are consistent with previous COVID-19 reports that found a similar frequency of in-hospital mortality and AEs.[3,21] In addition, 37% of patients developed respiratory complications (acute respiratory failure or ARDS) during hospitalisation. This value is within the range reported in a previous study (29–42%).[3]

The results of this study show that a high risk of acute deterioration is a significant risk factor for unfavourable outcomes, as a composite measure for in-hospital mortality and AEs in COVID-19 inpatients. Although previous studies have stressed that early warning systems are predictors of in-hospital mortality and health outcomes,[22,23] only a few have evaluated warning score systems in COVID-19 inpatients.[11,19] These latest studies showed a fair discrimination with adverse outcomes, illustrating that evaluating the risk for acute deterioration in the COVID-19 hospital population is a priority for healthcare organizations.[19]

In-hospital mortality was more frequent in patients admitted to wards where registered nurses were not using the VIDA early warning system. In this regard, other studies have shown that the use of early warning systems reinforces collaboration among the multidisciplinary team, and promotes the early identification of clinical deterioration.[24] Similarly, previous studies have reported lower mortality and fewer

adverse events when systematic nursing surveillance of patient status and progress is part of the daily routine.[9]

Chronic conditions and mental status impairments were the CCIF independently associated with unfavourable outcomes. Previous reports have shown that chronic diseases were more frequent among deceased COVID-19 patients [15] and that aging was a potential risk factor associated with mortality.[6] Although our study did not identify age as a risk factor associated with a composite unfavourable outcome, we acknowledge that old age was an independent risk factor associated with mortality and AEs. Furthermore, our findings are also consistent with other studies demonstrating that mental status impairment is associated with hospital-acquired complications,[25] including sepsis.[4]

The majority of patients had four or more CCIF. Our findings are consistent with other studies that identified a significant rate of chronic conditions in COVID-19 patients[15] along with various organizational issues that may impact care complexity and health outcomes.[26] Previous studies have demonstrated the association of CCIF and health outcomes,[16] with an average of two CCIF per patient. In our study of COVID-19 inpatients, the average number of CCIF was four. These results are probably related to the transmissibility of this condition, which require droplet and contact precautions; the public health measures of population confinement for pandemic management, which prevent patients' relatives visiting them in person, resulting in a lack of family caregiver support during hospitalisation; and the frequency of chronic diseases in the studied sample. The organisational adaptation of hospitals to this pandemic context and the required isolation precautions have been associated with poor outcomes in prior studies.[27,28]

We also found that LOS was associated with unfavourable outcomes, consistent with previous studies that associated AEs with increased healthcare costs due to longer

hospital stays.[29] Finally, high-tech hospital admission was a protective factor against unfavourable outcomes. High-tech hospitals usually have better nurse-to-patient ratios than urban or community facilities. In this sense, several recent studies in the same study setting concluded that on average, hospital ward patients require 5.6 hours of RN care per patient day, while the average of available RN hours per patient day is 2.4, and that RN understaffing is a structural issue.[26,30] Nevertheless, to the best of our knowledge, no study on nurse staffing and COVID-19 inpatients' outcomes has been published. Similarly, clinical leaders and healthcare managers have a key role to play in rapidly adapting organizations to the new reality. Fast and effective decision-making and managerial responses in crisis situations with high levels of uncertainty are essential both immediately and in the short-term; however, they should be accompanied by planning and executing mid-term and long-lasting improvements that positively impact patient, professional and organisational outcomes, such as structural RN understaffing.[26]

The strengths of this study include its multicentre approach, cohort design and large sample size. It is the first study evaluating the association of the risk of acute deterioration, along with care complexity factors, with COVID-19 patient outcomes. Importantly, we identify the importance of a range of contributors to care complexity, including psychosocial and mental-cognitive factors. In addition, the VIDA early warning system was developed as an evidence-based algorithm using a multidisciplinary approach, based on previous studies that highlighted the importance of adapting surveillance and screening systems to the organizational and cultural context.[14]

This study is not exempt from limitations. First, the VIDA score and CCIF data were comprehensively collected from the clinical data warehouse of the Catalan Institute of Health and all patients included had a completed nurse chart in the patient electronic health record, but we were still reliant on proper compliance with electronic record-keeping and the collection of administrative data. This is acknowledged as a

significant limitation since voluntary completion of patient electronic documentation during the initial weeks of the first wave of COVID-19 in our country might have been negatively influenced by the rising hospital burden, the understandable prioritization of direct patient care, as well as the physical and emotional stress experienced by bedside healthcare professionals. Second, regarding the study selection criteria, patients directly admitted and discharged from the intensive care unit were excluded, since no early warning system was in use in the critical care setting at the outset of the pandemic in our study area. In this sense, the results of this study only apply to adult ward and intermediate care inpatients. Third, it should be noted that of the 1,176 patients included only 806 were hospitalised in wards with a fully implemented VIDA system. Therefore, patients admitted to wards without the VIDA system did not have data available on risk of acute deterioration (VIDA score). This is a significant limitation. The VIDA system was under development in hospitals belonging to the Catalan Institute of Health during the data collection period. Therefore, future studies should corroborate the current results in centres where VIDA has been fully implemented. However, due to the high number of daily admissions the patients' unplanned assignment to the different wards (with or without the VIDA system) means that the patients' clinical characteristics were similar between wards with and without the VIDA system. Fourth, although an unpublished face validity study has demonstrated the effectiveness the VIDA early warning system, full evaluation of its psychometric properties is still pending. To minimize the potential effect of this limitation, we conducted an adjusted analysis performed with 486 patients with a similar higher risk of mortality (APR-DRG 3-4), comparing those admitted to wards using VIDA with those being treated in units with no VIDA early warning system. The results show that in-hospital mortality was more frequent in patients admitted to wards where VIDA had not yet been implemented. This result should be interpreted with caution because this analysis only included patients

with a high risk of mortality and could have been influenced by other variables such as the differences in sample sizes. Finally, we acknowledge as a potential limitation that other clinical measures such as the age-adjusted Charlson comorbidity index or patient lab values were not assessed. Selected lab values such as lactate, ferritin or calciferol have been studied as indicators of COVID-19 prognosis and severity. Combining point of care lab data with clinical data from nurses' observations and judgments on patient complexity factors, status and progress would probably result in an improved system for the early detection and prevention of critical complications and other unfavourable outcomes in COVID-19 inpatients.

Conclusion

The risk of acute deterioration and care complexity individual factors are associated with COVID-19 patient outcomes. The rate of unfavourable outcomes rose with increasing risk of acute deterioration as measured using the VIDA score. The risk factors independently associated with poor health outcomes were chronic disease, mental status impairment, length of hospital stay and high risk of acute deterioration. High-tech hospital admission was a protective factor against unfavourable outcomes. The systematic nursing surveillance of patients at risk of acute deterioration and the assessment of CCIF may help to reduce deleterious health outcomes in adult COVID-19 inpatients.

Figure 1. Flow-chart of patient selection process.

REFERENCES

1 WHO, World Bank. Global preparedness monitoring board. A world at risk. Annual report on global preparedness for health emergencies. 2019. DOI:10.2307/40153772.

2 Li Q, Guan X, Wu P, *et al.* Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N. Engl. J. Med. 2020; **382**: 1199–207.

3 Huang C, Wang Y, Li X, *et al.* Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; **395**: 497–506.

4 Li H, Liu L, Zhang D, *et al.* SARS-CoV-2 and viral sepsis: observations and hypotheses. *Lancet* 2020; **395**: 1517–20.

5 Shi S, Qin M, Shen B, *et al.* Association of Cardiac Injury with Mortality in Hospitalized Patients with COVID-19 in Wuhan, China. *JAMA Cardiol* 2020; published online March 25. DOI:10.1001/jamacardio.2020.0950.

6 Zhou F, Yu T, Du R, *et al.* Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020; **395**: 1054–62.

7 Wu C, Chen X, Cai Y, *et al.* Risk Factors Associated with Acute Respiratory Distress Syndrome and Death in Patients with Coronavirus Disease 2019 Pneumonia in Wuhan, China. *JAMA Intern Med* 2020; published online March 13. DOI:10.1001/jamainternmed.2020.0994.

8 Zheng Z, Peng F, Xu B, *et al.* Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. *J Infect* 2020; published online April 23. DOI:10.1016/j.jinf.2020.04.021.

9 Juvé-Udina ME, Fabrellas-Padrés N, Adamuz-Tomás J, *et al.* Surveillance nursing diagnoses, ongoing assessment and outcomes on in-patients who suffered a cardiorespiratory arrest. *Rev da Esc Enferm* 2017; **51**: e03286.

10 WHO. Clinical management of severe acute respiratory infection when novel

coronavirus (nCoV) infection is suspected. 2020. https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected (accessed May 20, 2020).

11 Hu H, Yao N, Qiu Y. Comparing rapid scoring systems in mortality prediction of critical ill patients with novel coronavirus disease. *Acad Emerg Med* 2020; published online April 20. DOI:10.1111/acem.13992.

12 Liao X, Wang B, Kang Y. Novel coronavirus infection during the 2019–2020 epidemic: preparing intensive care units—the experience in Sichuan Province, China. *Intensive Care Med* 2020; **46**: 357–60.

13 O'Brien C, Goldstein BA, Shen Y, *et al.* Development, Implementation, and Evaluation of an In-Hospital Optimized Early Warning Score for Patient Deterioration. *MDM Policy Pract* 2020; **5**: 1–10.

14 McGaughey J, O'Halloran P, Porter S, Trinder J, Blackwood B. Early warning systems and rapid response to the deteriorating patient in hospital: A realist evaluation. *J Adv Nurs* 2017; **73**: 3119–32.

15 Chen T, Wu D, Chen H, *et al.* Clinical characteristics of 113 deceased patients with coronavirus disease 2019: Retrospective study. *BMJ* 2020; **368**: m1091.

16 Adamuz J, González-Samartino M, Jiménez-Martínez E, *et al.* Care Complexity Individual Factors Associated With Hospital Readmission: A Retrospective Cohort Study. *J Nurs Scholarsh* 2018; **50**: 411–21.

17 Safford MM. The Complexity of Complex Patients. *J Gen Intern Med* 2015; **30**: 1724–5.

18 Juvé-Udina, M.E., Matud, C., Farrero S., Jiménez, H., Rodríguez, E., Martínez, M. et al. Intensity of nursing care: workloads or individual complexity? *Metas de Enfermería* 2010; **13**: 6–14.

19 Singh K, Valley TS, Tang S, Li BY, Kamran F, Sjoding MW, Wiens J, Otles E, Donnelly JP, Wei MY, McBride JP, Cao J, Penoza C, Ayanian JZ NB. Validating a Widely Implemented Deterioration Index Model Among Hospitalized COVID-19 Patients. *medRxiv* 2020. DOI:10.1101/2020.04.24.20079012.

20 Juvé-Udina ME. What patients' problems do nurses e-chart? Longitudinal study to evaluate the usability of an interface terminology. *Int J Nurs Stud* 2013; **50**: 1698–710.

21 Mao L, Jin H, Wang M, *et al.* Neurologic Manifestations of Hospitalized Patients with Coronavirus Disease 2019 in Wuhan, China. *JAMA Neurol* 2020; published online April 10. DOI:10.1001/jamaneurol.2020.1127.

22 Medic G, Kließ MK, Atallah L, *et al.* Evidence-based clinical decision support systems for the prediction and detection of three disease states in critical care: A systematic literature review. *F1000Research* 2019; **8**: 1728.

23 Kim I, Song H, Kim HJ, *et al.* Use of the national early warning score for predicting in-hospital mortality in older adults admitted to the emergency department. *Clin Exp Emerg Med* 2020; **7**: 61–6.

24 Ashbeck R, Stellpflug C, Ihrke E, *et al.* Development of a Standardized System to Detect and Treat Early Patient Deterioration. *J Nurs Care Qual* 2020; published online April 6. DOI:10.1097/ncq.0000000000000484.

25 Bail K, Draper B, Berry H, Karmel R, Goss J. Predicting excess cost for older inpatients with clinical complexity: A retrospective cohort study examining

cognition, comorbidities and complications. *PLoS One* 2018; **13**: e0193319.

26 Juvé-Udina M, González-Samartino M, López-Jiménez MM, *et al.* Acuity, nurse staffing and workforce, missed care and patient outcomes. A cluster-unit-level descriptive comparison. *J Nurs Manag* 2020; published online May 8. DOI:10.1111/jonm.13040.

27 Purssell E, Gould Di, Chudleigh J. Impact of isolation on hospitalised patients who are infectious: Systematic review with meta-analysis. *BMJ Open* 2020; **10**: e030371.

28 Tran K, Bell C, Stall N, *et al.* The Effect of Hospital Isolation Precautions on Patient Outcomes and Cost of Care: A Multi-Site, Retrospective, Propensity Score-Matched Cohort Study. *J Gen Intern Med* 2017; **32**: 262–8.

29 Rafter N, Hickey A, Condell S, *et al.* Adverse events in healthcare: Learning from mistakes. *Q J Med* 2015; **108**: 273–7.

30 Juvé-Udina M-E, Adamuz J, López-Jimenez M-M, *et al.* Predicting patient acuity according to their main problem. *J Nurs Manag* 2019; **27**: 1845–58.

FOOTNOTES

Author Contributions: All authors had full access to all study data and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Adamuz, González-Samartino, Juvé-Udina. *Coordination team:* Juvé-Udina. *Acquisition of data:* Adamuz, Tapia-Perez, López-Jiménez, Zuriguel-Pérez, Castro-Navarro. *Analysis and interpretation of data:* Adamuz, González-Samartino, Jiménez-Martínez. *Drafting of the manuscript:* Adamuz, González-Samartino, Jiménez-Martínez, Juvé-Udina. *Critical revision of the manuscript for important intellectual content:* Tapia-Perez, López-Jiménez, Rodríguez-Fernández, Zuriguel-Pérez, Castro-Navarro, Carratalà. *Statistical analysis:* Adamuz and González-Samartino. *Obtained funding:* - . *Administrative, technical and material support:* López-Jiménez, Rodríguez-Fernández. *Study supervision:* Juvé-Udina, Carratalà.

Funding/Support: No funding.

Declaration of Interests: We declare that we have no competing interests.

Patient consent for publication: Not required.

Ethical approval: This study was approved by the Clinical Research Ethics Committee of the Bellvitge University Hospital with a waiver of informed consent (reference 158/20).

Provenance and peer review: Not commissioned; externally peer reviewed.

Data availability statement: All data relevant to the study are included in the article. No additional data are available.

Table 1. Baseline characteristics, VIDA score and care complexity factors of admitted COVID-19 inpatients with unfavourable and favourable outcomes.

Characteristics	Study population n=1,176 No.	%	Unfavourable outcome [a] n=506 (42.8%) No.	%	Favourable outcome n=670 (57.1%) No.	%	*p value*
Demographic characteristics							
Age (years)_median (IQR)	66.5	(51-77)	74	(60-80)	61	(49-74)	<0.001
Male sex	667	(56.7)	192	(37.9)	317	(47.3)	0.001
Clinical characteristics							
LOS_median (IQR)	6	(4-8)	7	(4-10)	5	(4-7)	<0.001
Continuity of care (discharged to another facility)	165	(14)	58	(11.5)	107	(16)	0.02
Severity (APR-GRD 3-4)	503	(42.8)	450	(88.9)	53	(7.9)	<0.001
Mortality risk (APR-DRG 3-4)	486	(41.3)	449	(88.7)	37	(5.5)	<0.001
High-tech hospital	969	(82.4)	389	(76.9)	580	(86.6)	<0.001
Underlying disease	745	(63.4)	382	(75.5)	363	(54.4)	<0.001
Arterial hypertension or chronic heart failure	469	(39.9)	234	(46.2)	235	(35.1)	<0.001
Diabetes or chronic kidney disease	298	(25.3)	165	(32.6)	133	(19.9)	<0.001
Chronic respiratory disease	171	(14.5)	95	(18.8)	76	(11.3)	<0.001
Neurodegenerative disease	63	(5.3)	33	(6.5)	39	(4.5)	0.15
Chronic liver disease	54	(4.6)	30	(5.9)	24	(3.6)	0.07
Cancer	50	(4.3)	31	(6.5)	19	(2.8)	0.008
Immunosuppression	49	(4.2)	23	(4.5)	26	(3.9)	0.66
VIDA score[b]							
Low risk (0)	104	(12.9)	27	(7.1)	77	(18)	<0.001
Moderate risk (1-2)	505	(62.7)	194	(51.2)	311	(72.8)	<0.001
High risk (3-4)	197	(16.7)	158	(41.7)	39	(9.1)	<0.001
Care complexity individual factors (CCIF)							
Comorbidity/complications	1,176	(100)	506	(100)	670	(100)	-
Transmissible infection	1,176	(100)	506	(100)	670	(100)	-
Hemodynamic instability	910	(77.4)	396	(78.3)	514	(76.7)	0.57
Chronic disease	745	(63.4)	382	(75.5)	363	(54.4)	<0.001
Uncontrolled pain	194	(16.5)	82	(16.2)	112	(16.7)	0.87
Extreme weight	168	(14.3)	82	(16.2)	86	(12.8)	0.11
Position impairment	72	(6.1)	52	(10.3)	20	(3.0)	<0.001
Urinary or faecal incontinence	58	(4.9)	31	(6.1)	27	(4.0)	0.10
Immunosuppression	49	(4.1)					
Anatomical and functional disorders	41	(3.5)	30	(5.9)	11	(1.6)	<0.001
Communication disorders	18	(1.5)	13	(2.6)	5	(0.7)	0.01
High risk of haemorrhage	2	(0.2)	1	(0.2)	1	(0.1)	0.68
Vascular fragility	6	(0.5)	4	(0.8)	2	(0.3)	0.41
Involuntary movements	3	(0.3)	3	(0.6)	0	(0.0)	0.08
Dehydration	3	(0.3)	1	(0.2)	2	(0.3)	0.60
Oedema	0	(0)	0	(0.0)	0	(0.0)	-
Developmental	397	(33.8)	244	(48.2)	153	(22.8)	<0.001
Old age (≥75 years)	397	(33.8)	244	(48.2)	153	(22.8)	<0.001
Psycho-emotional	218	(18.5)	86	(17.0)	132	(19.7)	0.13
Fear/anxiety	173	(14.7)	70	(13.8)	103	(15.4)	0.51
Impaired adaptation	54	(4.6)	17	(3.4)	37	(5.5)	0.09
Aggressive behaviour	1	(0.1)	1	(0.2)	0	(0.0)	0.43
Mental-cognitive	240	(20.4)	184	(36.4)	56	(8.4)	<0.001
Mental status impairments	238	(20.2)	183	(36.2)	55	(8.2)	<0.001
Agitation	5	(0.4)	4	(0.8)	1	(0.1)	0.17
Impaired cognitive functions	4	(0.3)	3	(0.6)	1	(0.1)	0.32
Perception of reality disorders	2	(0.2)	0	(0.0)	2	(0.3)	0.51
Sociocultural	1,176	(100)	506	(100)	670	(100)	-
Lack of caregiver support	1,176	(100)	506	(100)	670	(100)	-
Belief conflict	1	(0.1)	0	(0.0)	1	(0.1)	0.57
Language barriers	1	(0.1)	1	(0.2)	0	(0.0)	0.43
Social exclusion	1	(0.1)	0	(0.0)	1	(0.1)	1
Care complexity individual factors (CCIF), median (IQR)	4	(3-6)	5	(4-6)	4	(3-5)	<0.001

Abbreviations: IQR, interquartile range; LOS, length of hospital stay; ICU, intensive care unit; APR-DRG, all patient refined diagnosis-related groups; VIDA, surveillance and identification of acute deterioration.

[a] Unfavourable outcomes included: in-hospital mortality and adverse events during hospitalisation.

[b] VIDA score was analysed according to 806 patients admitted to wards using the VIDA system.

Table 2. Patients' outcomes according to risk of acute deterioration (VIDA score) and care complexity factors.

Outcomes	All n=1,176 N (%)	VIDA_score n=806 (68.5)			CCIF n=1,176	
		Low risk (0) n=104 (12.9) N (%)	Mild risk (1-2) n=505 (62.7) N (%)	High risk (3-4) n=197 (16.7) N (%)	CCIF<4 n=327 (27.8) N (%)	CCIF≥4 n=849 (72.2) N (%)
Unfavourable outcomes	506 (43.0)	27 (26.0)**	194 (38.4)*	158 (80.2)**	92 (28.1)**	414 (48.8)**
Deceased	232 (19.6)	0 (0.0)**	46 (9.1)**	118 (59.9)**	5 (1.5)**	227 (26.7)**
Adverse event	481 (40.9)	27 (26.0)**	187 (37)*	153 (77.7)**	91 (27.8)**	394 (46.4)**
ICU transfer	32 (2.7)	0 (0.0)*	12 (2.4)	13 (6.6)*	4 (1.2)*	28 (3.3)*
HAI	29 (2.5)	0 (0.0)*	10 (2.0)	12 (6.1)*	1 (1.5)	24 (2.8)
Catheter-related bloodstream infection	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.1)
HA urinary tract infection	19 (1.6)	0 (0.0)	7 (1.4)	8 (4.1)*	3 (0.9)	16 (1.9)
Aspiration pneumonia	3 (0.3)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.4)
Sepsis	7 (0.6)	0 (0.0)	1 (0.2)	3 (1.5)*	2 (0.6)	5 (0.6)
ACC	470 (40.0)	27 (26.0)**	181 (35.8)**	150 (76.1)**	88 (26.6)**	383 (45.1)**
Cardiac arrest	5 (0.4)	1 (1.0)	0 (0.0)*	3 (1.5)*	0 (0.0)	5 (0.6)
Shock	4 (0.3)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	4 (0.5)
Thrombotic event	7 (0.6)	1 (1.0)	1 (0.2)	2 (1)	1 (0.3)	6 (0.7)
Acute respiratory failure[1]	436 (37.0)	27 (26.0)**	164 (32.5)**	144 (73.1)**	84 (25.1)**	353 (41.6)**
Myocardial injury	5 (0.4)	0 (0)	3 (0.6)	1 (0.5)	0 (0.0)	5 (0.6)
Liver injury	2 (0.2)	0 (0)	0 (0)	1 (0.5)	0 (0.0)	2 (0.2)
Renal insufficiency	83 (7.1)	1 (1.0)*	28 (5.5)*	31 (15.7)**	6 (1.8)**	77 (9.1)**

Abbreviations: VIDA, surveillance and identification of acute deterioration; CCIF, care complexity individual factors; ICU, intensive care unit; HAI, hospital-acquired infections; ACC, avoidable critical complications.

* *p* value >0.001 and <0.05.

** *p* value ≤0.001.

[1] Include acute respiratory distress syndrome (ARDS).

Table 3. Adjusted analysis of unfavourable outcomes according to VIDA early warning system in 486 patients with high risk of mortality (APR-DRG 3-4).

Outcomes	Unadjusted n=1,176 N (%)	Adjusted n=486 (41.2) N (%)	With VIDA_system n=368 (75.7) N (%)	Without VIDA_system n=118 (24.3) N (%)	*p value*[1]
Unfavourable outcomes	506 (43.0)	449 (92.4)	345 (93.8)	104 (88.1)	0.07
Deceased	232 (19.6)	214 (44)	152 (41.3)	62 (52.5)	0.02
Adverse event	481 (40.9)	436 (89.7)	337 (91.6)	99 (83.9)	0.02
ICU transfer	32 (2.7)	25 (5.1)	20 (5.4)	5 (4.2)	0.41
HAI	29 (2.5)	19 (3.9)	16 (4.3)	3 (2.5)	0.28
ACC	470 (40.0)	433 (89.1)	334 (90.8)	99 (83.9)	0.31

Abbreviations: VIDA, surveillance and identification of acute deterioration; ICU, intensive care unit; HAI, hospital-acquired infections; ACC, avoidable critical complications.
[1]All variables were compared using the Fisher exact test.

Table 4. Multivariate analysis of VIDA score and CCIF in 806 adult COVID-19 inpatients associated with unfavourable outcomes, death and AEs.

Characteristics	Unfavourable outcomes [1] n= 379/806 (47%)		Deceased[2] n= 164/806 (20.3%)		AEs[3] n=367/806 (45.5%)	
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Old age (≥75 years)	1.48	(0.99-2.22)	3.04	(1.79-5.15)**	1.52	(1.02-2.26)*
Male sex	1.21	(0.87-1.69)	1.86	(1.11-3.11)*	1.20	(0.87-1.67)
LOS	1.16	(1.11-1.21)**	0.97	(0.93-1.01)	1.17	(1.12-1.22)**
High-tech hospital	0.57	(0.36-0.89)*	1.88	(0.94-3.78)	0.61	(0.39-0.95)*
VIDA score 3-4	4.32	(2.83-6.60)**	13.99	(8.44-23.18)**	4.21	(2.79-6.36)**
Chronic disease	1.90	(1.32-2.72)**	2.01	(1.03-3.90)*	1.81	(1.26-2.59)**
Position impairment	1.19	(0.58-2.44)	1.41	(0.63-3.13)	1.23	(0.62-2.46)
Communication disorders	0.97	(0.24-3.96)	0.87	(0.22-3.41)	0.78	(0.21-2.95)
Mental status impairments	2.31	(1.45-23.66)**	6.21	(3.67-10.50)**	1.72	(1.09-2.69)*

Abbreviations: AE, adverse event; LOS, length of hospital stay; VIDA, surveillance and identification of acute deterioration.
Multivariate analysis included: high risk of acute deterioration (VIDA score 3–4), clinically relevant care complexity factors (old age, chronic disease, position impairment, communication disorders and mental status impairments) and potential confounders (sex, hospital level and LOS).
[1]AUC 0.81 (CI 95%; 0.78–0.84).
[2]AUC 0.91 (CI 95%; 0.88–0.93).
[3]AUC 0.80 (CI 95%; 0.77–0.83).
* *p* value >0.001 and <0.05.
** *p* value ≤0.001.

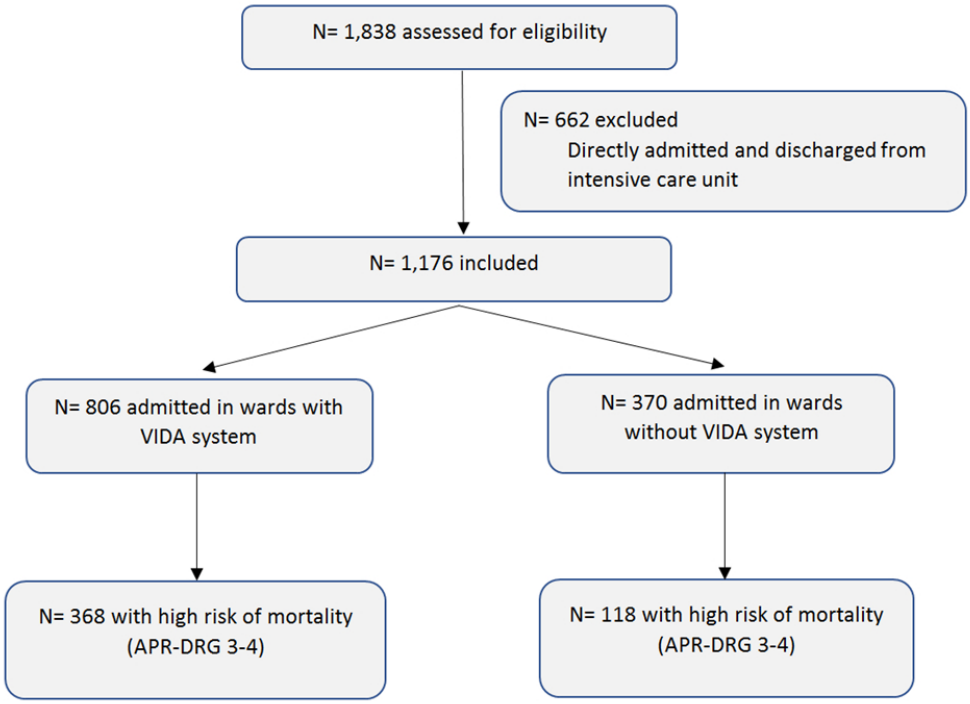

Figure 1. Flow-chart of patient selection process.

Supplementary file 1. Juvé-Udina ME. VIDA score for acute deterioration in the current *human* algorithm.

H1, H2, H3		
Punctuation	**Risk score**	**Definition**
0 – 1	0	No risk of complication (at that particular moment)
2 – 3	1	Low risk
4	2	Moderate risk (very probable complication)
5 – 6	3	High risk (imminent complication if not stabilized)
>= 7	4	Critical complication status
H4		
Punctuation	**Risk score**	**Definition**
0 – 1	0	No risk of complication (at that particular moment)
2 – 3	1	Low risk
4 – 6	2	Moderate risk (very probable complication)
7 – 9	3	High risk (imminent complication if not stabilized)
>= 10	4	Critical complication status
H5		
Punctuation	**Risk score**	**Definition**
0 – 2	0	No risk of complication (at that particular moment)
3 – 4	1	Low risk
5 – 6	2	Moderate risk (very probable complication)
7 – 8	3	High risk (imminent complication if not stabilized)
>= 9	4	Critical complication status
H6		
Punctuation	**Risk score**	**Definition**
0 – 2	0	No risk of complication (at that particular moment)
3 – 4	1	Low risk
5 – 6	2	Moderate risk (very probable complication)
7 – 9	3	High risk (imminent complication if not stabilized)
>= 10	4	Critical complication status
H7		
Punctuation	**Risk score**	**Definition**
<= 3	1	Low risk
4 – 6	2	Moderate risk (very probable complication)
7 – 8	3	High risk (imminent complication if not stabilized)
>= 9	4	Critical complication status

Abbreviations: H, hospital.

Supplementary file 2. Care complexity individual factors.

Domains	Factors	Specifications
Comorbidity/ Complications	Transmissible infection	Isolation measures
	Hemodynamic instability	Intensive control of vital signs or state of shock
	Chronic disease	Conditions (organ failure, degenerative process or oncological disease) that require ongoing medical attention and limit activities of daily living.
	Uncontrolled pain	Verbal numerical rating scale above three points
	Extreme weight	Low weight, obesity
	Position impairment	Includes any position impairment
	Urinary or faecal incontinence	Loss of bladder control or failure to control bowel movements
	Immunosuppression	Neutropenia, immunodeficiency or immunosuppressive therapy
	Anatomical and functional disorders	Amputation, deformities, joint stiffness
	Communication disorders	Aphasia, dysphasia, dysarthria, laryngectomy, tracheostomy
	High risk of haemorrhage	Coagulation disorders, thrombocytopenia, anticoagulant therapy
	Vascular fragility	Capillary fragility, tortuous veins
	Involuntary movements	Continuous involuntary movements
	Dehydration	Skin turgor
	Oedema	An accumulation of an excessive amount of watery fluid in cells, tissues, or serous cavities
Developmental	Old age	≥75 years
Psycho-emotional	Fear/anxiety	Fear or anxiety (moderate or intense)
	Impaired adaptation	Disruptive behaviour, hopelessness or surrender
	Aggressive behaviour	Physical or verbal aggressive behaviour (moderate or intense)
Mental-cognitive	Mental status impairments	Confusion, disorientation, stupor, transient loss of consciousness
	Agitation	Psychomotor agitation
	Impaired cognitive functions	Intellectual disability, amnesia
	Perception of reality disorders	Delirium, hallucinations, disconnection from reality
Sociocultural	Lack of caregiver support	Without caregiver support or caregiver burnout
	Belief conflict	Spiritual distress
	Language barriers	Barrier to communication resulting from speaking different languages than Spanish or Catalan without translator.
	Social exclusion	Extreme poverty

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Pg.3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Pg.3-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Pg.5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	Pg.6
Methods			
Study design	4	Present key elements of study design early in the paper	Pg.7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Pg.7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Pg.7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Pg.7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Pg.7-8
Bias	9	Describe any efforts to address potential sources of bias	Pg.16
Study size	10	Explain how the study size was arrived at	Pg.7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Pg.9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Pg.9
		(*b*) Describe any methods used to examine subgroups and interactions	Pg.9
		(*c*) Explain how missing data were addressed	-
		(*d*) If applicable, explain how loss to follow-up was addressed	-
		(*e*) Describe any sensitivity analyses	-
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Pg.10
		(b) Give reasons for non-participation at each stage	Pg.10-11
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Pg.10
		(b) Indicate number of participants with missing data for each variable of interest	-
		(c) Summarise follow-up time (eg, average and total amount)	Pg.10
Outcome data	15*	Report numbers of outcome events or summary measures over time	Pg10-11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 1&4

		(*b*) Report category boundaries when continuous variables were categorized	Table 1&4
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Pg.11-12
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Pg.11
Discussion			
Key results	18	Summarise key results with reference to study objectives	Pg.13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Pg.16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Pg.14-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	Pg.15-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Pg.21.

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.