Maturitas 161 (2022) 40–43

Contents lists available at ScienceDirect

Maturitas

journal homepage: www.elsevier.com/locate/maturitas

Effects of malnutrition on mortality in oldest-old inpatients with COVID-19 in the GERIA-COVID cohort

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ARTICLE INFO

Keywords:
COVID-19
Malnutrition
GNRI
Mortality
Oldest-old
GERIA-COVID

ABSTRACT

We assessed the impact of malnutrition on 14-day, 28-day, and 3-month mortality risk in oldest-old inpatients aged ≥80 years with COVID-19 in the hospital-based GERIA-COVID cohort. Malnutrition was assessed on hospital admission using the Geriatric Nutritional Risk Index (GNRI). Potential confounders were age, sex, functional abilities, number of acute health issues, CRP level, hypertension, cardiomyopathy, malignancies, use of antibiotics, and respiratory treatments. Seventy-eight participants (88.9 ± 4.3 years old, 55% women) were included. Of these, 82.1% had survived at day 14, 78.2% at day 28, and 70.5% after 3 months. No association between malnutrition according to the GNRI and 14-day ($P = 0.324$), 28-day ($P = 0.166$), or 3-month mortality ($P = 0.109$) was found. Thus, malnutrition according to the GNRI was not associated with mortality within the first 3 months of diagnosis of COVID-19 among oldest-old inpatients.

1. Introduction

The coronavirus disease identified in 2019 (COVID-19) is associated with greater mortality risk [1,2], the highest impact being reported in oldest-old patients (i.e., aged 80 years and older) with 6-fold higher mortality-risk [OR=6.25 (95%CI 5.38–7.25), $P<0.001$] compared to the general population [2]. Better understanding, identifying, and treating modifiable prognostic factors in this population is highly desirable to prevent mortality [1,2].

Early detection and treatment of malnutrition, a potent prognostic factor for health outcomes in oldest-old adults, is considered an essential prerequisite in geriatric medicine. The Geriatric Nutritional Risk Index (GNRI) estimates nutrition-related mortality-risk in older patients [3]. The GNRI consists of anthropometric measures and serum albumin levels, assessed in acute healthcare settings. The GNRI also could be an adequate screening tool to identify those oldest-old inpatients with COVID-19 at higher mortality risk. However, its impact on COVID-19-related mortality in oldest-old adults remains unexplored.

The main objective of the present study was to determine whether the presence of malnutrition on hospital admission according to the GNRI was associated to increased 14-day mortality in oldest-old inpatients with COVID-19 in the GERIA-COVID cohort (GERIAtric Patients Hospitalized for COVID-19), and also whether malnutrition according to the GNRI was associated to 28-day and 3-month mortality.

2. Methods

2.1. Study population

The study consisted of a longitudinal observational analysis of a

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https://doi.org/10.1016/j.maturitas.2021.11.016
Received 19 July 2021; Received in revised form 11 November 2021; Accepted 12 November 2021
Available online 24 February 2022

subset of the GERIA-COVID cohort, a study carried out in the geriatric acute care unit dedicated to COVID-19 patients in the University Hospital of Angers, France (ClinicalTrials.gov NCT04560608) [4]. Data from the GERIA-COVID study were retrospectively collected from patient records. The inclusion criteria were as follows: 1) consecutive ≥75-year-old patients hospitalized in the geriatric acute care unit of Angers University Hospital, France, in March-May 2020 during the first wave of the pandemic; 2) no objection from the patients and/or relatives to the use of anonymized clinical and biological data for research purposes. Inclusion criteria for the present analysis were as follows: 1) COVID-19 diagnosed with RT-PCR and/or chest CT-scan; 2) age ≥80 years; 3) availability of data about the GNRI on hospital admission; 4) availability of data on vital status at 14-day, 28-day, and 3-month follow-up after COVID-19 diagnosis.

2.2. Main and secondary outcome

Main outcome: 14-day all-cause mortality. **Secondary:** 28-day and 3-month all-cause mortality. Vital status was collected from medical records and/or follow-up telephone calls.

2.3. GNRI

GNRI was calculated upon hospital admission from serum albumin levels (g/L), present body weight (PBW, kg), and ideal body weight (IBW=height^2(m^2)×22) [3], according to the following formula: *GNRI=1.489×albumin+41.7×PBW/IBW*. When PBW exceeded IBW, PBW/IBW was considered equal to 1 [3]. The study sample was categorized into patients at risk (GNRI≤98) and patients without risk (GNRI>98) [3].

2.4. Covariables

Potential confounders were age, sex, functional abilities, number of acute health issues, serum levels of C-reactive protein (CRP, mg/L), hypertension, cardiomyopathy, malignancies, and use of antibiotics and respiratory treatments. Functional abilities prior to COVID-19 were measured from 1 to 6 (best) with the isoresources groups (GIR) [4]. History of hypertension, cardiomyopathy, and malignancies were recorded on admission from medical reports, or patient and caregiver interviews or contact with primary care providers. The number of acute health issues on admission (i.e., diseases with sudden onset and rapid progression, whatever their nature or site) was also recorded [4]. The use of antibiotics and pharmacological treatments of respiratory disorders was systematically recorded from hospital prescriptions.

2.5. Statistics

Unadjusted and adjusted Cox-regression models were used to examine the associations of malnutrition defined as GNRI score <98 (independent variable) with 14-day, 28-day, and 3-month mortality (dependent variables). Statistical significance was set as α=5%. Statistical tests were performed by SAS®v9.4 (Cary, NC).

3. Results

From 246 patients included in the GERIA-COVID, $n = 78$ (88.9 ± 4.3years, 55.1% women) met eligibility criteria. Fourteen deaths were recorded at 14-day follow-up, 3 at day 28, and 6 at 3 months.

No association was found between malnutrition according to the GNRI and 14-day, 28-day, and 3-month mortality (**Table 1**). The history of malignancies [adjusted hazard ratio (HR)=9.11, $P = 0.001$] and the use of antibiotics [HR=10.14, $P = 0.038$] were associated with greater mortality risk.

4. Discussion

We provide here the first assessment to our knowledge of the impact of malnutrition on short- and mid-term mortality in oldest-old inpatients with COVID-19. The results showed that malnutrition did not predict the vital prognosis of COVID-19 after age 80, compared to other recognized prognosis factors such as the history of malignancies. This could be attributed to the high lethality of COVID-19 in this population and also to the characteristics of oldest-old adults, in whom diseases may present in atypical semiological forms and geriatric syndromes.

It should be acknowledged that the lack of association (if any existed) may also be explained by three main limitations of our study. First, the GNRI was chosen to assess malnutrition instead of applying the Global Leadership Initiative of Malnutrition (GLIM) criteria (updated standard) [5]. The requirements of isolation and device sterilization required by COVID-19 protocols hindered applying GLIM, as using bioimpedance was not always feasible. To authors' knowledge, the association between GLIM criteria and COVID-19 outcomes remains unexplored. Second, dietitians were not allowed in COVID-19 units during the first wave. Thus, patients could receive only systematic oral supplementation on demand during hospital stay, rather than professionally tailored nutritional advice. Authors consider that the potential impact of such nutritional supplementation was minimal and would not affect prognosis. Third, the limited sample size might have increased the beta risk of not showing a difference (if any existed); larger samples might counteract this limitation in future studies.

We found no association of malnutrition with mortality in oldest-old inpatients with COVID-19. Malnutrition should not be considered a discriminating, limiting factor in oldest-old inpatients with COVID-19.

Contributors

Dolores Sanchez-Rodriguez contributed to the design and conception of the present research, drafted the manuscript.

Guillaume Sacco substantively revised the manuscript.

Jennifer Gautier substantively revised the manuscript.

Olivier Brière substantively revised the manuscript.

Cédric Annweiler contributed to the design and conception of the present research, drafted the manuscript.

Dolores Sanchez-Rodriguez and Cédric Annweiler equally contributed to the design and conception of the present research. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

Funding

No funding from an external source was received for this study.

Ethical approval

The study was conducted in accordance with the Good Clinical Practice guidelines, the ethical standards of the Helsinki Declaration (1964), and its further amendments. Data were treated following EU Regulation 2016/679. The study was approved by the Ethics Board of Angers University (2020/100) and declared to the French National Commission for Information Technology and Civil Liberties (ar20–0087v0).

Provenance and peer review

This article was not commissioned. Peer review was directed by Leon Flicker independently of Cédric Annweiler, an author and *Maturitas* editor, who was blinded to the process.

Table 1
Multiple Cox proportional-hazards model showing the hazard ratio for mortality risk (dependent variable) according to malnutrition defined as GNRI score <98 (independent variable), adjusted for participant characteristics ($n = 78$).

	14-day mortality				28-day mortality				3-month mortality			
	Unadjusted model HR [95% CI]	*P*-value	Adjusted model HR [95% CI]	*P*-value	Unadjusted model HR [95% CI]	*P*-value	Adjusted model HR [95% CI]	*P*-value	Unadjusted model HR [95% CI]	*P*-value	Adjusted model HR [95% CI]	*P*-value
GNRI score <98	1.16 [0.40–23.33]	0.282	3.19 [0.32–31.9]	0.324	3.83 [0.51–28.86]	0.193	4.70 [0.53–41.92]	0.166	2.61 [0.61–11.14]	0.195	3.74 [0.75–18.72]	0.109
Age	0.98 [0.87–1.10]	0.722	0.93 [0.81–1.08]	0.343	1.01 [0.91–1.12]	0.888	0.98 [0.87–1.10]	0.700	1.01 [0.92–1.12]	0.853	0.99 [0.89–1.09]	0.825
Female sex	1.09 [0.38–3.15]	0.870	1.21 [0.32–4.61]	0.776	0.92 [0.36–2.39]	0.866	0.84 [0.27–2.62]	0.768	0.62 [0.27–1.41]	0.250	0.53 [0.20–1.36]	0.186
GIR score	0.66 [0.44–0.98]	0.041	0.77 [0.51–1.15]	0.200	0.70 [0.49–1.01]	0.059	0.85 [0.59–1.24]	0.394	0.68 [0.50–0.94]	0.021	0.81 [0.58–1.14]	0.232
Number of acute issues on admission	1.10 [0.79–1.55]	0.569	1.04 [0.68–1.59]	0.866	1.19 [0.88–1.62]	0.258	1.16 [0.81–1.67]	0.414	1.24 [0.95–1.61]	0.116	1.17 [0.88–1.56]	0.281
C-reactive protein	1.00 [0.99–1.01]	0.126	1.00 [0.99–1.01]	0.180	1.00 [0.99–1.01]	0.229	1.00 [0.99–1.01]	0.405	1.00 [0.99–1.01]	0.151	1.00 [0.99–1.01]	0.395
History of arterial hypertension	0.99 [0.33–2.96]	0.986	0.64 [0.14–2.88]	0.561	1.01 [0.37–2.73]	0.987	0.81 [0.23–2.83]	0.735	0.85 [0.37–1.97]	0.712	0.85 [0.31–2.31]	0.747
History of cardiomyopathy	1.17 [0.40–3.36]	0.778	1.20 [0.36–3.94]	0.769	1.00 [0.39–2.59]	0.995	1.08 [0.37–3.18]	0.893	0.80 [0.35–1.82]	0.599	0.79 [0.31–1.98]	0.607
History of malignancies	5.71 [1.79–18.22]	0.003	9.11 [2.14–34.95]	0.001	4.41 [1.63–11.94]	0.004	7.37 [2.35–23.07]	0.001	3.35 [1.46–7.65]	0.004	6.32 [2.35–16.96]	<0.001
Use of antibiotics[a]	6.43 [0.84–49.14]	0.073	10.14 [1.14–90.56]	0.038	3.78 [0.86–16.52]	0.078	5.80 [1.15–29.26]	0.033	3.52 [1.04–11.84]	0.042	5.63 [1.39–22.77]	0.016
Use of pharmacological treatments for respiratory disorders[b]	1.52 [0.34–6.79]	0.586	2.01 [0.35–11.54]	0.434	1.22 [0.28–5.35]	0.790	1.44 [0.27–7.56]	0.669	0.86 [0.20–3.68]	0.841	1.10 [0.23–5.21]	0.910

CI: confidence interval; GIR: isoresource groups; HR: hazard ratio; GNRI: Geriatric Nutrition risk index.

[a] Aminoglycosides, beta-lactams, lincosamides, macrolides, quinolones, sulphonamides, among others.

[b] Antihistamines, Beta2-adrenergic agonists, inhaled corticosteroids inhaled, among others.

Research data (data sharing and collaboration)

There are no linked research data sets for this paper. Data will be made available on request.

Declaration of competing interests

The authors declare that they have no competing interests.

Acknowledgments

The authors wish to thank the GERIA-COVID study group. GERIA-COVID study group: Cédric Annweiler, Marine Asfar, Mélinda Beaudenon, Jean Barré, Antoine Brangier, Mathieu Corvaisier, Guillaume Duval, Jennifer Gautier, Mialy Guenet, Jocelyne Loison, Frédéric Noublanche, Marie Otekpo, Hélène Rivière, Guillaume Sacco, Romain Simon. Affiliation: Department of Geriatric Medicine, University Hospital, Angers, France. The authors have listed everyone who contributed significantly to the work in the Acknowledgments section. Permission was obtained from all persons named in the Acknowledgments section. There was no compensation for this contribution. The authors gratefully acknowledge Elaine Lilly PhD for language revisions and unfailing support.

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