Associations between recently diagnosed conditions and hospitalization due to COVID-19 in patients aged 50 years and older– A SHARE-based analysis

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Abstract

Background: Only a few studies have been carried out with a large sample size on the relationship between chronic conditions and hospitalization for COVID-19, and there is no research examining recently diagnosed conditions. Our purpose was to evaluate this association in a large sample including the older population from Europe and Israel.

Methods: Data from the SHARE COVID-19 Survey, a representative survey of individuals aged 50 or over residing in 27 European countries and Israel, were retrieved. Associations between recently diagnosed chronic conditions (i.e., conditions detected over the last three years) (exposure) and hospitalization due to COVID-19 (outcome) were assessed using multivariable logistic regression.

Results: 51,514 participants on average 71.0 (SD = 9.2) years old were included. Participants with multimorbidity (i.e., two or more recently diagnosed conditions) had significantly higher odds for COVID-19 hospitalization (AOR = 3.91 [95%CI = 2.14-7.12]). Independent conditions such as lung disease (AOR = 16.94 [95%CI = 9.27-30.95]), heart disease (AOR = 3.29 [95%CI =1.50-7.21]), or cancer (AOR = 3.45 [95%CI = 1.26-9.48]), showed particularly high odds for hospitalization due to COVID-19 disease.

Conclusions: People with recently diagnosed diseases, and in particular those having lung disease, heart disease, or cancer were significantly more likely to be hospitalized for COVID-19.

Key words: SARS-CoV-2, diabetes, hypertension, lung disease, multimorbidity

Background

The SARS-CoV-2 emerged in Wuhan (China) in December 2019 and spread worldwide rapidly causing millions of infections.[1] The World Health Organization (WHO) announced on March 11, 2020, that the outbreak had become a pandemic. One year later, the WHO reported more than 120 million confirmed cases and more than 2.5 million deaths due to COVID-19, the disease caused by SARS-CoV2.

In symptomatic patients, the disease's severity and outcome vary with age and other health conditions.[1,2] Hereditary and acquired factors influence both host sensitivity and disease severity. For example, a study conducted in Northern California reported that, among patients requiring hospitalization, 56.2% were men with a median age of 61 years, with the most prevalent comorbidities being hypertension (43%), diabetes (31%), chronic kidney disease (13%) and chronic obstructive pulmonary disease (COPD) or asthma (7.4%).[2] Moreover, recent meta-analyses reported that hypertension and diabetes were associated with greater risk of admission to intensive care[4] and higher mortality.[5] However, to date, there are only a few studies carried out with a large sample size from Europe on the relationship between chronic conditions and hospitalization due to COVID-19. Moreover, previous studies on this topic incorporated the entire age range of adults and did not focus exclusively on subjects over 50 years of age and with recently diagnosed chronic conditions. It is well known that long-lasting chronic conditions such as diabetes can lead to added health complications which can worsen COVID-19 disease prognostic, but little is known on how a shorter length of experiencing a chronic condition might affect the likelihood of being hospitalized due to COVID-19 disease. Thus, new studies conducted among the older European population are needed, since age is by itself a risk factor for severity of and mortality due to COVID-19,[6] and this might aid in developing specific preventive strategies.

Furthermore, although chronic conditions have shown a role in the severity and mortality of people with COVID-19, these results might vary given the differences in health-related factors among countries.

Given this background, it is important to determine whether chronic conditions, such as those recently diagnosed among older Europeans, which has not been specifically examined thus far, have a similar trajectory in relation to COVID-19 prognosis as in other populations who have had long exposure to chronic conditions. Thus, the objective of this study was to evaluate associations between recently diagnosed chronic conditions and hospitalization for COVID-19 in the older European population. It was hypothesized that those with a chronic disease would be at higher risk for hospitalization due to COVID-19 infection.

Methods

Study design and population

For the present study, data from the Survey of Health, Ageing and Retirement in Europe (SHARE) COVID-19 Survey, a representative survey including individuals with an age of 50 or over residing in 27 European countries and Israel, were retrieved. Representativeness of the different waves of SHARE is ensured using a multi-stage stratified sampling design, in which countries are divided into different strata based on geographical areas, and municipalities or zip codes within those strata are used as Primary Sampling Units (PSUs) with probability of being sampled proportional to their size.[7] Owing to the COVID-19 outbreak, regular data collection for the 8th SHARE ordinary wave was modified and accordingly adapted to the new situation, including new questions on health, infection, healthcare, socioeconomic changes, and social network.[8] The survey was carried out between June and August 2020 through computer-

assisted telephone interviews conducted by trained interviewers. Data from SHARE is collected using ex-ante harmonized interviews and provides calibrated weights to address the potential selection bias associated with non-respondent errors. Moreover, new respondents are also added to compensate for such attrition.

In the used sample, there were 408 participants with any missing values in the examined variables, who were excluded from the study. Moreover, participants with an age less than 50 or over 100 (n = 388) were also excluded owing to the likelihood of misreporting information. Overall, less than 1% of the original sample was excluded from the study. The study followed the World Medical Declaration of Helsinki principles and was approved by the Ethics Committee of Research in Humans of the University of Valencia (register code 1510464).

Recently diagnosed conditions (exposure)

The participants' recently diagnosed conditions were assessed through the following questions; first, participants were asked "Since we last interviewed you, were you diagnosed with a major illness or health condition?". If the answer was affirmative, then the interviewer asked a second question: "Do you have any of the following illnesses or health conditions? With this we mean that a doctor has told you that you have this condition, and that you are either currently being treated for or bothered by this condition.", "Hip fracture?", "Diabetes or high blood sugar?", "High blood pressure or hypertension?", "A heart attack including myocardial infarction or coronary thrombosis or any other heart problem including congestive heart failure?", "Chronic lung disease such as chronic bronchitis or emphysema?", "Cancer or malignant tumor, including leukemia or lymphoma, but excluding minor skin cancers?", and "Another illness or health condition?". Potential answers comprised "Yes", "No", "Doesn´t know", or

"Refusal". Those who answered affirmative to any of the conditions diagnosed from the last interview (i.e., wave 7 of SHARE carried out in 2017) were considered to have a recently diagnosed condition. Multimorbidity was defined as having answered "Yes" to two or more than the aforementioned conditions.

Hospitalization due to COVID-19 (outcome)

Hospitalization due to COVID-19 was self-reported by the participants through the following question: "Have you or anyone close to you been hospitalized due to an infection from the Coronavirus?". Potential answers comprised "Yes", "No", "Doesn´t know", or "Refusal". If the answer was affirmative, then the following question was asked: "Who was hospitalized? Please tell me their relationship to you", and possible answers consisted of "Respondent", "Spouse or partner", "Parent", "Child", "Other household member", "Other relative outside household", "Neighbor, friend or colleague", "Caregiver", or "Other". Only those who answered "Respondent" were considered as hospitalized due to COVID-19 in the present study.

Statistical analyses

The statistical analyses were performed with Stata v16.1 (Stata Corporation, College Station, TX, USA). To ensure enough statistical power, we used the average age of the study sample as the cut-off point for categorizing age. To check associations of multimorbidity and each of the aforementioned conditions (exposures) with hospitalization due to COVID-19 (outcome), we conducted binary logistic regression analysis adjusted for sex and age as covariates. Additionally, the potential interaction between age and chronic conditions was also examined through a likelihood-ratio test which showed no statistical differences between the models with and without the

interaction term, thus we decided not to include it in the used model. The level of statistical significance was set at $P < 0.05$.

Results

A total of 51,514 participants with an average age of 71.0 (SD = 9.2) years were included in the analysis. Of those, 57.7% were women, and 0.2% (n = 77) were hospitalized due to COVID-19. Table 1 displays the basic characteristics of the study sample, including the percentage of participants experiencing any chronic condition.

Table 2 shows adjusted models for the association between any chronic condition and hospitalization due to COVID-19 disease. Participants with multimorbidity had significant higher odds for COVID-19 hospitalization (AOR = 3.91 [95%CI =2.14-7.12]). Independent conditions including lung disease (AOR = 16.94 [95%CI =9.27-30.95]), heart disease (AOR = 3.29 [95%CI =1.50-7.21]), and cancer (AOR = 3.45 [95%CI = 1.26-9.48]) showed higher odds for COVID-19 hospitalization.

Discussion

The main finding of this study was the significant association between having a recently diagnosed chronic condition and higher odds for hospitalization due to COVID-19.

Previous studies have reported an association between having a chronic condition and hospitalization.[9] Additionally, in line with our results, two recent systematic reviews identified that chronic conditions are associated with increased risk for severity and mortality due to COVID-19.[5] However, these studies incorporated the entire age range of adults. The presence of these chronic conditions is directly related to age,[10] so it seems logical that age itself has been found to be the most significant risk factor for becoming seriously ill or dying from COVID-19.[6] However, our study suggests that

specific chronic conditions are associated with COVID-19 hospitalization independently of age among individuals aged ≥50 years, which indicates that it might be the condition *per se* which contributes to the increase in risk of hospitalization.

Our study found that individual chronic conditions such as lung disease, heart disease, and cancer, as well as multimorbidity showed higher odds for hospitalization due to COVID-19. Another study carried out among patients with COVID-19 requiring treatment in intensive care units in Italy reported that a history of COPD, hypercholesterolemia, or diabetes, were independently associated with mortality.[11] Importantly, it has been found that lung disease (which has a particularly high OR in our study), is linked with increased risk of developing severe pneumonia, which is related to mortality due to COVID-19.[5] For instance, in COPD, it appears that the spike protein of the virus binds to ACE2 (angiotensin-converting enzyme 2) during viral attachment to host cells and that viral entry is also facilitated by TMPRSS2 (transmembrane serine protease 2).[12] Differences in the expression of ACE2 and TMPRSS2 may modulate the individual susceptibility to and clinical course of SARS-CoV-2 infection.

We found a significant association between heart disease and COVID-19 hospitalization. Patients with cardiovascular disease appear to have heightened vulnerability to COVID-19 infection and tend to have more severe disease with worse clinical outcomes. A meta-analysis of 1527 patients with COVID-19 found that the prevalence of cardiac disease was 16.4%, and that these patients were more likely to require critical care.[13] The cardiovascular system may be affected in several ways: direct myocardial injury, systemic inflammation, altered myocardial demand, plaque rupture, coronary thrombosis, or electrolyte imbalances.[14]

In our study, although the prevalence of hospitalization due to COVID-19 was higher among those with diabetes, this did not reach statistical significance. A previous study reported that patients with diabetes had an increased risk of serious complications from COVID-19, such as adult respiratory distress syndrome and multiple organ failure.[15] The fact that our results did not reach statistical significance may be due to lack of statistical power, but it could also be explained by the focus of our study on recently diagnosed conditions. As for hypertension, we found no significant association with hospitalization due to COVID. Partly in line, it was found that hypertension was not an independent factor associated with mortality despite being the most frequent chronic condition in patients with COVID-19.[11] However, other studies have found that those with hypertension are at increased risk for adverse COVID-19 related outcomes.[13] It has been hypothesized that those with hypertension may be at increased risk for adverse COVID related outcomes since SARS-CoV-2 was observed to use ACE 2 to enter the host cell.[16] Paradoxically, it appears that ACE 2 not only acts as an entry receptor for SARS-CoV-2, but also protects the lung from injury.[16] Given that our study only focused on recently diagnosed conditions, it is possible that diabetes and hypertension with a longer clinical course would be associated with increased risk for adverse COVID outcomes. Clearly, more research is needed in this area.

Our study results are in line with a previous study which showed that patients with cancer appear to have an increased risk of mortality and severe disease from COVID-19 regardless of whether they have active cancer, are undergoing cancer treatment, or both.[18] Likewise, a recent meta-analysis with 63,019 participants[19] concluded that cancer patients were more susceptible to COVID-19 and increased mortality, especially among those with lung cancer. However, more studies are required to clarify which types of cancer patients are at higher risk, it seems logical that cancer patients need to

be considered as a high-risk group due to their general advanced age, comorbidities and poor performance status.[20]

This study has several limitations. First, the data collection was self-reported which might increase the possibility of recall bias. Second, the effect of other variables that could provide important information, such as physical inactivity, body mass index, smoking or taking medication, was not examined since that would have substantially reduced the study sample due to an important increase in the missing values. Thus, the chance of a confounding bias exists. In addition, our study focuses on recently diagnosed conditions solely, thus there is still the possibility of a confounding bias with individuals experiencing longer conditions than those examined. Third, the single-item questions used to assess the examined variables were not previously validated, although the necessity of urgent information in the context of a pandemic made their use more appropriate than other tools for ethical reasons. Also, interviews were conducted between June-August 2020, when COVID-19 infection numbers across Europe were lower and government restrictions were less strict than previously and later. Besides, the possibility of a number of missing vulnerable participants from nursing homes exists since interviewers were instructed to avoid unethical situations of pressing when selected participants from those settings or their correspondent proxy refused to answer to the survey, although these losses are likely to be randomly distributed. On the other hand, an important strength of the present study is the large sample size and representation of an important number of countries. Furthermore, this is the first study

conducted evaluating the association of recent diagnosed chronic conditions with odds of hospitalization for COVID-19 comprising older European population. Studies with larger number of individuals hospitalized are required to obtain more stable estimations. Particularly, other exposure variables such as long-term chronic conditions, or other combinations of the current exposure variables such as specific dyads could result in special clinical interest.

In conclusion, people with recently diagnosed multimorbidity or conditions including lung disease, cancer and heart disease are significantly more likely to be hospitalized for COVID-19.

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Table 1. Characteristics of the study sample (N= 51,514).

Characteristics	Category	(%)
Age	50-71 years	52.7
	72-100 years	47.3
Sex	Male	42.3
	Female	57.7
Multimorbidity	No	95.3
	Yes	4.7
Hip fracture	No	99.5
	Yes	0.5
Diabetes	No	98.0
	Yes	2.0
Hypertension	No	95.5
	Yes	4.5
Heart disease	No	97.3

	Yes	2.7
Lung disease	No	98.8
	Yes	1.2
Cancer	No	98.5
	Yes	1.5
Hospitalizations due to COVID-19	No	99.8
disease	Yes	0.2

Table 2. Associations between recently diagnosed conditions and hospitalization due to COVID-19 disease.

Condition	Category	AOR (95% CI) [a]
Multimorbidity	Yes vs No	3.91 (2.14-7.12)
Hip fracture	Yes vs No	2.45 (0.34-17.77)
Diabetes	Yes vs No	2.60 (0.95-7.14)
Hypertension	Yes vs No	1.10 (0.40-3.01)
Heart disease	Yes vs No	3.29 (1.50-7.21)
Lung disease	Yes vs No	16.94 (9.27-30.95)
Cancer	Yes vs No	3.45 (1.26-9.48)

AOR Adjusted Odds Ratio.

CI Confidence Interval.

[a]Adjusted for sex and age.