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Letters to the editor

Diabetes is not associated with COVID-19-related mortality in older institutionalized people

Several studies have shown that people with diabetes who contract coronavirus disease 2019 (COVID-19) have an increased risk of death [1]. However, most of these findings refer to in-hospital deaths, whereas a significant proportion of COVID-19 deaths have occurred in nursing homes (NHs; Etablissement d’Hébergement pour Personnes Âgées Dépendantes, EHPAD) among people who were not transferred to hospital. In both Europe and the US, it is estimated that up to 40% of all COVID-19 deaths happen among NH residents [2]. Yet, very little is known about COVID-19 mortality in older institutionalized patients. Thus, the aim of the present study was to assess the influence of diabetes on COVID-19-related mortality in older institutionalized people.

This retrospective, multicentre study was carried out in six NHs in the Côte d’Or region of France. All deaths occurring in these NHs between 1 January and 31 May 2020 were collected and classified as either COVID-19-related death or any other cause of death. For COVID-19 to be considered a cause of death, a positive polymerase chain reaction (PCR) test for infection by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was necessary.

The most recent biological data prior to COVID-19 infection were also collected. ‘Neurodegenerative’ diseases included Alzheimer’s disease, Parkinson’s disease and major cognitive dysfunction; ‘cardiovascular’ diseases included coronary disease, heart failure and stroke; ‘pulmonary’ diseases included chronic obstructive pulmonary disease (COPD), asthma, obstructive sleep apnoea and a need for oxygen therapy; and chronic kidney disease (CKD) was defined as a glomerular filtration rate (GFR) < 60 mL/min/1.73 m².

Data are here presented as means ± standard deviation (SD) or as percentages, as appropriate. Differences between groups were evaluated by chi-squared or Kruskal–Wallis tests. Univariate analyses were done using a linear regression model with a robust variance estimator; multivariable analyses were done using a linear regression model. Statistical analyses were performed using Stata version 14.0 software (StataCorp LLC, College Station, TX, USA). Differences with P values < 0.05 were considered statistically significant.

A total of 106 deaths were recorded in the six study NHs: 28.3% of these deaths were related to COVID-19; their mean age was 89.1 ± 10.5 years; 22 patients had diabetes, 30 were overweight or obese, 77 had neurodegenerative disease and 32 had CKD (Table 1). However, the proportion of patients with diabetes did not significantly differ between patients who died of COVID-19 and those who died of other causes. Also, no significant differences were observed in the prevalences of overweight, obesity, cardiovascular disease and hypertension between the two groups of patients. On the other hand, the proportions of male patients, patients with neurodegenerative disease and patients with CKD were significantly higher among COVID-19-related deaths than among other causes of death.

Table 1
Characteristics of the study nursing-home-based population.

|                      | Total (n = 106) | COVID-19-related deaths (n = 30) | Other causes of death (n = 76) |
|----------------------|----------------|---------------------------------|--------------------------------|
| Age, years           | 89.1 ± 10.5    | 88.5 ± 8.1                      | 89.3 ± 11.3                    |
| Female gender, n (%) | 78 (73.6)      | 18 (60)                         | 60 (78.9)*                     |
| Weight, kg (n = 101) | 58.1 ± 14.8    | 62.4 ± 17.8                     | 56.3 ± 14.5                    |
| Body mass index, kg/m² (n = 82) | 23.3 ± 5.6 | 24.4 ± 5.4                      | 22.8 ± 5.6                     |
| 25–29.9, n (%)       | 22 (20.8)      | 9 (30)                          | 13 (17.1)                      |
| > 30, n (%)          | 8 (7.5)        | 4 (13.3)                        | 4 (5.3)                        |
| Hypertension, n (%)  | 76 (71.7)      | 20 (66.7)                       | 56 (73.7)                      |
| Dyslipidaemia, n (%) | 31 (29.2)      | 9 (30)                          | 22 (28.8)                      |
| Diabetes, n (%)      | 22 (20.8)      | 5 (16.7)                        | 17 (22.4)                      |
| Neurodegenerative diseases, n (%) | 77 (72.6) | 27 (90)                          | 50 (65.8)*                     |
| Pulmonary diseases, n (%) | 13 (12.3) | 1 (3.3)                          | 12 (15.8)                      |
| Cardiovascular diseases, n (%) | 50 (47.1) | 11 (36.7)                        | 39 (51.3)                      |
| Chronic kidney failure, n (%) | 32 (30.2) | 13 (43.3)                        | 18 (23.7)*                     |
| Creatinine, μmol/L (n = 96) | 78.6 ± 31.3 | 89.2 ± 36.1                      | 74.0 ± 28.0*                   |
| GFR, mL/min/1.73 m² (n = 96) | 65.8 ± 20.1 | 60.7 ± 19.6                      | 68.0 ± 21.3                    |
| 30–60, n (%)         | 30 (28.3)      | 11 (36.7)                       | 19 (25)                        |
| < 30, n (%)          | 2 (1.9)        | 1 (3.3)                         | 1 (13.1)                       |
| HbA1c %              | 8 ± 1.3        | 8.6 ± 0.8                       | 7.8 ± 1.4                      |
| HbA1c, mmol/mol      | 63.9 ± 10.4    | 70.5 ± 6.6                      | 61.7 ± 11.1                    |
| Serum albumin, g/L (n = 81) | 30.8 ± 6.3 | 31.4 ± 4.1                      | 30.5 ± 7.1                     |
| Prealbumin, g/L (n = 56) | 0.18 ± 0.05 | 0.2 ± 0.03                      | 0.17 ± 0.06                    |

Data are presented as means ± SD unless otherwise stated; * P < 0.05 vs COVID-19-related deaths.

GFR, glomerular filtration rate.

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higher among those who died due to COVID-19 than because of other causes (Table 1).

On univariate analysis, COVID-19-related death was positively associated with neurodegenerative diseases ($\beta = 0.25, P = 0.001$) and negatively associated with pulmonary diseases ($\beta = -0.23, P = 0.02$). The associations with female gender, body weight and CKD were of borderline significance. On multivariate analysis including age, gender, neurodegenerative diseases, pulmonary diseases, CKD, diabetes and body mass index (BMI) scores as independent variables in the model, COVID-19-related death was independently associated with neurodegenerative diseases ($\beta = 0.28, P = 0.01$).

Our present study also revealed, for the first time, that diabetes was not associated with COVID-19-related mortality in older people living in NHs. As very few studies have evaluated the factors associated with COVID-19 morbidity in institutionalized patients, this makes our present findings particularly novel and informative.

In one meta-analysis including 6452 hospitalized COVID-19-infected patients [1], the association between diabetes and a poor composite outcome, including mortality, was weaker in studies with participants whose median age was $> 55$ years compared to those aged $< 55$ years, which is in line with our present results.

In addition, in our study, the presence of neurodegenerative disease was independently associated with COVID-19 mortality, and one study found cognitive impairment to be a common comorbidity in deceased COVID-19 hospitalized patients [3], which is also in line with our present findings. Thus, our results underscore the fact that neurodegenerative diseases should be taken into account in studies evaluating COVID-19 mortality, and that the influence of such diseases is probably more significant than other comorbidities (hypertension, diabetes, coronary heart disease) associated with in-hospital COVID-19 mortality [4,5].

In conclusion, our study has discovered, for the very first time, that there is no significant association between diabetes and COVID-19 mortality in older institutionalized people. On the other hand, neurodegenerative diseases appear to be a major determinant of COVID-19 death in that frail population, thereby suggesting that such diseases should now be taken into account in analyses of risk factors for COVID-19 mortality.

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### Duality of interest

No potential conflicts of interest relevant to this article are reported.

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### References

[1] Huang J, Lim MA, Pranata R. Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia – a systematic review, meta-analysis, and meta-regression. Diabetes Metab Syndr 2020;14:395–403.

[2] Shi SM, Bakaev I, Chen H, Trivison TG, Berry SD. Risk factors, presentation, and course of coronavirus disease 2019 in a large, academic long-term care facility. J Am Med Dir Assoc 2020;21:1376–83. e1.

[3] Martín-Jiménez P, Muñoz-García MI, Seoane D, Roca-Rodríguez L, García-Reyne A, Laluzoa A, et al. Cognitive impairment is a common comorbidity in deceased covid-19 patients: a hospital-based retrospective cohort study. J Alzheimers Dis 2020;78:1367–72.

[4] Tan W, Jiang W, Yao J, Nicholson CJ, Li RH, Sigurslids HH, et al. Predictors of mortality in hospitalized COVID-19 patients: a systematic review and meta-analysis. J Med Virol 2020;92:1875–83.

[5] Singh AK, Gilles CE, Singh R, Singh AK, Chudasama Y, Coles B, et al. Prevalence of co-morbidities and their association with mortality in patients with COVID-19: a systematic review and meta-analysis. Diabetes Metab 2020;22:1915–24.

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