COMMENT ON CHEN ET AL.

Clinical Characteristics and Outcomes of Patients With Diabetes and COVID-19 in Association With Glucose-Lowering Medication. Diabetes Care 2020;43: 1399–1407

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Since the beginning of the coronavirus disease 2019 (COVID-19) pandemic, people with diabetes have been rapidly identified as having more vulnerable profiles. Therefore, as highlighted by Riddle et al. (1), specific data providing a better understanding of the relationship between diabetes and COVID-19 are urgently needed. In this context, the retrospective data of Chen et al. (2), published online 14 May 2020, provided important insights that we would like to comment on in light of the results from our CORONADO (CORONAvirus SARS-CoV-2 and Diabetes Outcomes) study that was published online almost simultaneously on 29 May 2020 (3).

Specifically conducted in patients with diabetes and hospitalized for COVID-19 (>90% with positive PCR for severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]), the CORONADO study is an observational, multicenter (67 centers), nationwide (France) study with a prespecified protocol (reg. no. NCT04324736, ClinicalTrials.gov) and standardized data collection. The primary end point combines mortality and tracheal intubation on day 7 (D7) after hospital admission. The first results from an intermediate analysis including 1,317 participants (64.9% men, mean age 69.8 years, median BMI 28.4 kg/m^2) was commented on by Scheen et al. very recently (4).

The retrospective study by Chen et al. (2) included 904 people, of whom only 136 had diabetes (mean age 66.0 years and with a large predominance of type 2 diabetes, as in CORONADO). As had been previously reported (5), the authors confirmed that diabetes was associated with an increased risk (odds ratio 2.51) of in-hospital death. By performing multivariable regression, they found that older age (adjusted P value = 0.001) and elevated CRP (adjusted P value = 0.043) were independently associated with in-hospital death (n = 26 events) in patients with diabetes, in agreement with the findings from CORONADO.

Indeed, we performed similar multivariable analyses with stepwise selection to identify independent predictive factors of death on D7 in CORONADO. Considering the covariables before admission (n = 748 participants, 74 deaths), older age ($P < 0.0001$) and microvascular (P = 0.0153) and macrovascular (P = 0.0013) complications as well as treated obstructive sleep apnea (P = 0.0013) were independently associated with early death. Regarding the covariates on admission (n = 612 participants, 59 deaths), dyspnea (P = 0.0049), increased CRP (P = 0.0052) and AST (P = 0.0003), and decreased estimated glomerular filtration rate ($P < 0.0001$) and platelet count (P = 0.0292) were independently associated with death on D7 (3). The discordant findings regarding the independent prognosis factors of COVID-19 severity between the two studies are probably due to a power issue in the study by Chen et al.

Like Chen et al., we found that patients who died on D7 were more frequently under insulin therapy. However, this probably reflects their advanced stage of diabetes with frequent comorbidities contraindicating the use of other glucose-lowering therapies. In agreement with this hypothesis, insulin therapy was not associated with death on D7 in multivariable analyses in CORONADO (3).

Finally, it is becoming increasingly evident that elevated admission plasma glucose is a marker of severe COVID-19 prognosis (2,3), although it was not independently associated with severe outcomes in either study. In contrast to the study by Chen et al., we demonstrated for the first time in CORONADO that previous glucose control assessed by A1C before admission was not associated with a worse COVID-19 prognosis.

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