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## Calcifediol treatment and COVID-19-related outcomes

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### Abstract

**Context:** COVID-19 is a major health problem because of saturation of intensive care units (ICU) and mortality. Vitamin D has emerged as a potential treatment able to reduce the disease severity.

**Objective:** To elucidate the effect of calcifediol [25OHD3] treatment on COVID-19-related outcomes.

**Design:** Observational cohort study from March to May, 2020.

**Setting:** Patients admitted to COVID-19 wards of Hospital del Mar, Barcelona, Spain.

**Patients:** A total of 930 patients with COVID-19 were included. Ninety-two were excluded due to previous calcifediol intake.

**Intervention:** Of the remaining 838, a total of 447 received calcifediol (532ug on day one plus 266ug on day 3, 7, 15, and 30) whereas 391 were not treated at the time of hospital admission (Intention-to-Treat). Of the latter, 53 patients were treated later during ICU admission and were allocated in the treated group in a second analysis. In healthy subjects, calcifediol is about 3.2-fold more potent on a weight basis than cholecalciferol.

**Main outcome measures:** ICU admission and mortality.

**Results:** ICU assistance was required by 102 (12.2%) participants. Out of 447 patients treated with calcifediol at admission, 20 (4.5%) required ICU, compared to 82 (21%) out of 391 non-treated ( $p$ -value<0.0001). Logistic regression of calcifediol treatment on ICU admission, adjusted by age, gender, linearized 25OHD levels at baseline, and comorbidities showed that treated patients had a reduced risk to require ICU (OR 0.13 [95% CI 0.07;0.23]). Overall mortality was 10%. In the Intention-to-Treat

analysis, 21 (4.7%) out of 447 patients treated with calcifediol at admission died compared to 62 patients (15.9%) out of 391 non-treated ( $p=0.0001$ ). Adjusted results showed a reduced mortality risk with an OR 0.21 [95% CI 0.10; 0.43]). In the second analysis, the obtained OR was 0.52 [95% CI 0.27;0.99].

**Conclusions:** In patients hospitalized with COVID-19, calcifediol treatment significantly reduced ICU admission and mortality.

**Keywords:** COVID-19; Calcifediol; ICU admission; Vitamin D; mortality.

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