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Outcomes of COVID-19 in patients with skin cancer

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Dear Editor, The effect of a skin cancer diagnosis on the risk of adverse outcomes from COVID-19 remains unknown. Few studies have shown that patients with cancer and COVID-19 have higher rates of mortality and hospitalizations than those without cancer, perhaps due to a combination of delayed diagnosis and pre-existing comorbidities from chemotherapy and radiation treatments.[1] However, some studies suggest cancer may be protective against mortality from COVID-19, possibly from natural immunosuppression reducing the negative effects of a cytokine storm.[2] Therefore, the aim of this study was to evaluate the risk of complications in patients with COVID-19 with a history of skin cancer, the most common form of cancer.

A retrospective cohort analysis was conducted using TriNetX (Cambridge, MA, USA), a real-time federated database of > 60 million unique electronic patient medical records from around 48 healthcare organizations. Patients aged ≥ 18 years and diagnosed with COVID-19 between 20 January 2020 and 10 January 2021 were included for analysis. COVID-19 infections were confirmed using validated codes and serology values, as recommended by the Centers for Disease Control and Prevention and the World Health Organization. Patients with COVID-19 were divided into two groups (history of skin cancer and no history of skin cancer), identified by International Classification of Diseases, 10th Revision codes. To be included, the diagnosis of skin cancer must have occurred prior to the date of COVID-19 diagnosis. A 1 : 1 propensity score-matching (PSM) analysis was conducted using the greedy nearest neighbour algorithm to balance baseline confounders between the cohorts. PSM included demographics and comorbidities such as hypertension, chronic lung disease, heart disease, diabetes, cerebrovascular disease, chronic kidney disease, nicotine and alcohol dependence, transplant status and HIV status. Thirty-day outcomes were assessed post-COVID-19 diagnosis, including all-cause mortality, mechanical ventilation, severe COVID (composite of morality and mechanical ventilation), hospitalization, acute respiratory distress syndrome (ARDS) and sepsis. Subgroup analyses were determined a priori and conducted for melanoma, basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (SCC). Statistical analyses were performed using previously reported methodology on the TriNetX platform, and further details regarding the database are explained elsewhere.[3]

In total, 455 505 patients with COVID-19 were identified (skin cancer, n = 7681; no skin cancer, n = 447 824). Before PSM, the skin cancer cohort was older [mean (SD) age 69 (14) vs. 47 (19) years; $P < 0{\cdot}001$] and there was a higher proportion of males (52% vs. 44%; $P < 0{\cdot}001$), people with white skin (91% vs. 60%; $P < 0{\cdot}001$) and comorbidities. After PSM, two well-matched cohorts of 7663 patients were created. Outcomes before and after PSM are given in Table S1 (see Supporting Information). After PSM, the skin cancer group had improved outcomes than controls regarding mortality (4·5% vs. 5·7%; $P < 0{\cdot}001$), mechanical ventilation (3·8% vs. 4·8%; $P = 0{\cdot}002$), hospitalization (21% vs. 28%; $P < 0{\cdot}001$), severe COVID (6·7% vs. 8·4%; $P < 0{\cdot}001$) and ARDS (1·8% vs. 2·3%; $P = 0{\cdot}023$), with no differences seen between the groups with regard to sepsis. In matched subgroup analysis, patients with melanoma and SCC had decreased hospitalization rates vs. controls [21% vs. 25% ($P = 0{\cdot}002$) and 28% vs. 32% ($P = 0{\cdot}001$), respectively]. There were no differences in matched analyses for all other outcomes between the melanoma and SCC cohorts. In the matched BCC cohorts, patients with BCC had improved outcomes vs. controls with regard to mortality (4·0% vs. 5·6%; $P < 0{\cdot}001$), mechanical ventilation (3·2% vs. 4·9%; $P < 0{\cdot}001$), hospitalization (18% vs. 27%; $P < 0{\cdot}001$), severe COVID (5·8% vs. 8·4%; $P < 0{\cdot}001$), ARDS (1·5% vs. 2·2%; $P = 0{\cdot}012$) and sepsis (4·7% vs. 5·8%; $P = 0{\cdot}028$).

Until now, the information on the effect of skin cancer on COVID-19 outcomes has been scant. Matching revealed that the skin cancer cohort demonstrated a significantly reduced risk of adverse outcomes, which was most pronounced in the BCC subgroup. While the pathophysiological basis of this finding is unclear, research has shown increased mortality in patients with COVID-19 with low serum 25-hydroxyvitamin

D levels.[4] Therefore, we hypothesize that patients with BCC have higher vitamin D levels, which may protect against severe COVID-19 outcomes. While serum 25-hydroxyvitamin D has been positively associated with melanoma and keratinocyte carcinoma, particularly BCC,[5,6] there may be other residual confounders in patients with COVID-19 with SCC and melanoma that were impossible to elucidate from the data, such as duration of immunosuppression, severity of chronic skin inflammation and genetic make-up, which could have contributed to the findings of the given outcomes. A limitation of this study is that because vitamin D levels are not routinely assessed in either in- or outpatients, there were incomplete records of vitamin D levels in the database and so pre-existing levels could not be examined. Other limitations include possible errors in coding/data entry, a bias towards sicker patients and the inability to monitor progression through the clinical course of the disease. Further studies are warranted in patients with skin cancer to validate this finding.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Table S1 Thirty-day COVID-19 outcomes for each cohort.

Dysbiotic gut microbiota in patients with inflammatory rosacea: another clue towards the existence of a brain–gut–skin axis

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Dear Editor, Rosacea is a chronic inflammatory disease that primarily affects young and middle-aged white women.[1] Its aetiology is multifactorial and appears to be determined by genetic predisposition, alteration of the neurovascular and immune response, and an altered dialogue with the microbiota.[1,2] Additionally, the disease has been linked to gastrointestinal disorders such as *Helicobacter pylori* infection or small intestine bacterial overgrowth, and even neurological disorders such as Parkinson disease,[3,4] revealing the existence of a brain–gut–skin axis. Currently there is a high suspicion that these different organs are interrelated in their mechanisms of homeostasis and allostasis. They might be involved in the aetiopathogenesis of some chronic inflammatory skin diseases such as rosacea through immune, neuroendocrine and metabolic mechanisms that are not well elucidated.[2,4] The aim of this study was to determine whether the gut microbiome composition of patients with inflammatory rosacea was different from that of healthy controls, and to investigate possible bacterial biomarkers of the disease.

We conducted a cross-sectional study that enrolled 15 patients affected by inflammatory rosacea and 15 healthy controls. The diagnosis of subtype 2 (papulopustular rosacea) was based on typical clinical presentation.[1] The exclusion criteria for all of the patients were use of systemic immunomodulators or antibiotics, extreme diets, pregnancy, intake of prebiotics or probiotics in the previous 12 weeks, and the presence of any comorbidity. Stool samples were collected, processed with the RNase inactivation solution RNAlater® (ThermoFisher Scientific, Waltham, MA, USA) and stored at −80°C at the Biobank of University Hospital Ramon y Cajal. Next-generation sequencing of the V3–V4 region of the 16S rRNA gene was carried out using V3 MiSeq (Illumina, San Diego, CA, USA). We searched for microbiological biomarkers of inflammatory rosacea using the linear discriminant analysis effect size (LEfSe) tool.[5]

The mean age of the case patients was 36·5 years (SD 4·2), and 12 (80%) were female. Regarding controls, the mean age was 39·6 years (SD 6·8), and five of them (33%) were female. Around half of the controls cohabited with the case patients. Alpha diversity, a measure of the richness and evenness of microbiological taxa within a community, was