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LETTER

Systemic glucocorticoid use during ICU admission and symptoms of posttraumatic stress disorder in intensive care unit survivors

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Dear Editor,

Intensive care unit (ICU) survivors are at risk of developing mental health problems, such as symptoms of posttraumatic stress disorder (PTSD), anxiety and depression [1–3]. Glucocorticoid use has been proposed to diminish the risk of these problems, but evidence remains conflicting [4, 5]. This study investigated the association between systemic glucocorticoid use during ICU admission and the incidence of PTSD symptoms in a large population of ICU survivors.

This is a single-center, retrospective cohort study with 1-year follow-up using prospectively collected data. The institution's Medical Research Ethics Committee waived the need for informed consent. Patients alive 1 year after ICU discharge, aged ≥ 18 years and admitted to the ICU > 48 h between January 2011 and February 2020 were included. The cumulative glucocorticoid dose during ICU stay was calculated per subject by (1) obtaining all glucocorticoid administrations (registered in the ICU's Patient Data Management System), (2) converting oral doses to intravenous equivalents, (3) converting different glucocorticoids to prednisolone equivalents and (4) summing these over the period of ICU admission. The primary outcome was PTSD symptoms 1 year after ICU discharge, defined as an Impact of Event Scale (revised) score of ≥ 35 or a mean score of > 1.6, respectively. Secondary outcomes included symptoms of anxiety and depression as measured by the Hospital Anxiety and Depression Scale (sum score of ≥ 8) and Health-Related Quality of Life (HRQoL) as measured with the EuroQol-5D 1 year after discharge. Results were adjusted for age, sex, ICU length of stay, type of admission, referral by a pulmonologist (yes/no), Simplified Acute Physiology Score (SAPS) II, mechanical ventilation, delirium during ICU stay, modified Sequential Organ Failure Assessment (mSOFA) score on day of admission, the difference between the mSOFA score on day of admission and on day 4, cumulative midazolam dosage, cumulative propofol dosage and outpatient use of glucocorticoids / antidepressants / antipsychotics / anxiolytics using a propensity score approach.

In total, 1737 subjects were included of whom 690 (40%) were systemically exposed to glucocorticoids. Subjects who received glucocorticoids were more often female, had a longer ICU length of stay, were more often admitted to the ICU after acute surgery and had a higher mean SAPS II. 187 (11%) Subjects developed PTSD symptoms, 313 (18%) developed symptoms of anxiety and 303 (17%) developed symptoms of depression. Table 1 shows the effect of glucocorticoids on the risk of symptoms of PTSD, anxiety and depression. Adjusted logistic regression analysis showed no beneficial effect on developing PTSD symptoms (adjusted odds ratio (aOR) 0.99, 95% confidence interval (CI) 0.68–1.45) with glucocorticoid use ($n = 81$; 12%) versus non-use ($n = 106$; 11%). Glucocorticoid use was not associated with a decreased incidence of symptoms of anxiety (aOR 0.89, 95% CI 0.65–1.21), symptoms of depression (aOR 0.81, 95% CI

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Table 1 Primary and secondary endpoints

	PTSD symptoms, *n* (%)[a]	Crude OR (95% CI)	Adjusted OR (95% CI)[e]
Glucocorticoid use	81 (12)	1.17 (0.86–1.60)	0.99 (0.68–1.45)
No glucocorticoid use	106 (11)		
	Symptoms of anxiety, *n* (%)[b]	**Crude OR (95% CI)**	**Adj. OR (95% CI)[e]**
Glucocorticoid use	121 (18)	0.95 (0.74–1.23)	0.89 (0.65–1.21)
No glucocorticoid use	192 (19)		
	Symptoms of depression, *n* (%)[c]	**Crude OR (95% CI)**	**Adj. OR (95% CI)[e]**
Glucocorticoid use	106 (16)	0.79 (0.61–1.03)	0.81 (0.59–1.10)
No glucocorticoid use	197 (19)		
	EQ-5D Utility score, median (IQR)[d]	**Change in utility value (crude)**	**Change in utility value (adjusted)[e]**
Glucocorticoid use	0.811 (0.687–1)	− 0.003 (− 0.028–0.022)	0.027 (− 0.003–0.057)
No glucocorticoid use	0.811 (0.687–1)		

Results after multiple imputation

PTSD posttraumatic stress disorder, *OR* odds ratio, *CI* confidence interval, *IQR* interquartile range

[a] Missing for 95 patients (5%)

[b] Missing for 49 patients (3%)

[c] Missing for 42 patients (2%)

[d] Missing for 67 patients (4%)

[e] Adjusted for age, sex, Intensive Care Unit (ICU) length of stay, type of admission, referral by a pulmonologist (yes/no), Simplified Acute Physiology Score II, mechanical ventilation, delirium during ICU stay, modified Sequential Organ Failure Assessment (mSOFA) score on day of admission, difference between mSOFA on day of admission and on day 4, cumulative midazolam dosage, cumulative propofol dosage and outpatient use of glucocorticoids / antidepressants / antipsychotics / anxiolytics

0.59–1.10) or change in HRQoL (adj. linear regression; 0.027 increase in utility value, 95% CI − 0.003–0.057).

Strengths of this study include the large sample size, in particular in the field of mental health disorders post ICU. Also, the mixed ICU population enhances generalizability of the results.

The main limitation of this study was potential confounding by indication, as certain diseases might call for treatment with glucocorticoids and may carry a greater risk of developing mental health problems. Also, no data were available on psychological support received by subjects during follow-up, which might have led to a smaller chance of finding a relationship between exposure and outcome [6].

In conclusion, this study suggests no potential protective effect of systemic exposure to glucocorticoids during ICU admission on the development of PTSD symptoms, nor on symptoms of anxiety and depression or lower HRQoL in ICU survivors. This study does not warrant a randomized controlled trial on glucocorticoids to decrease PTSD symptoms in ICU survivors.

Supplementary Information
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Declarations

Conflicts of interest
None.

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