CRITICAL CARE

COMMENTARY

The good and the bad of diabetes mellitus in the critically ill

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See related research by Siegelaar *et al.*, http://ccforum.com/content/15/5/R205

Abstract

Diabetes mellitus is increasingly prevalent and associated with significant end organ damage that one may presume to impact upon critical illness. However, Siegelaar and colleagues present data that suggest, excepting those patients admitted to a cardiac intensive care unit, the presence of diabetes mellitus is not associated with increased mortality in critically ill patients. It is not possible to unpick how unmeasured parameters such as glycaemic control, the nature of whether type I or type II, or concomitant drug therapy confound the results. Nevertheless, the results are consistent with many risk-adjustment models used in the critically ill, and clinical practice that tolerates mild hyperglycaemia. Is it even possible that diabetes mellitus is protective?

The prevalence of diabetes mellitus is increasing, in part due to aging, obesity, and lower levels of physical activity. The findings of Siegelaar and colleagues presented in the previous issue of *Critical Care* challenge current beliefs but are also relevant to all [1]. Advanced diabetes is associated with end organ damage that is likely to impact upon critically ill patients – nephropathy, autonomic neuropathy, and small-vessel and large-vessel disease. Thus many believe that diabetes is associated with increased mortality and morbidity in patients admitted to an intensive care unit (ICU). Moreover, studies have demonstrated that not addressing severe hyperglycaemia (>10 mmol/l) in critically ill patients is associated with higher mortality [2,3].

Siegelaar and colleagues use meta-analysis techniques to examine the relationship between mortality and diabetes mellitus in patients admitted to an ICU. Pooling data from 141 studies and nearly 12.5 million patients, they demonstrate that, outside the cardiothoracic ICU, diabetes mellitus is not associated with an increased risk of mortality. Their findings were consistent whether mortality was considered at ICU discharge, hospital discharge, or 28/30 days.

The value of the study lies in the large number of patients included, sourced from a broad range of publications most of which were not specific to patients with diabetes mellitus. Moreover, the Forest plots demonstrate consistency between studies. However, unmeasured confounders may influence their results. Whilst a sensitivity analysis using risk-adjusted mortality from five studies encompassing ~15% of the patients demonstrates a similar result, the model is not comprehensive. For example, patients with diabetes mellitus may receive inhibitors of the renin–angiotensin system, HMG-CoA reductase inhibitors, peroxisome proliferator-activated receptor gamma agonists, and aspirin. All of these treatments have been postulated to affect outcome in critically ill patients [4-6]. The study is limited also by considering diabetes mellitus as a homogeneous entity rather than a diagnosis that encompasses two different pathophysiologies and widely ranging therapies and qualities of glycaemic control. How all these parameters impact upon outcome is not explored.

The authors' results are mirrored in current risk-adjustment models. In the cardiothoracic setting, the presence of diabetes mellitus has been used as a risk factor for perioperative mortality in the Parsonnet score [7] but not the EuroSCORE tools [8]. Cardiac revascularisation of patients with diabetes mellitus is complicated by poorer targets and microvascular disease. By contrast, diabetes mellitus does not form part of standard ICU risk-prediction models such as the Acute Physiology and Chronic Health Evaluation score and the Simplified Acute Physiology Score [9-12].

Why does the presence of diabetes mellitus not matter outside the cardiothoracic ICU? As the authors point out, the higher incidence of sepsis in patients with diabetes mellitus may imply a protective effect. Certainly, targeting mild hyperglycaemia in all patients seems

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preferable to strict normoglycaemia control [13]. The effects of insulin may be detrimental in the critically ill [14]. Insulin is anti-inflammatory [15] and switches cells to preferentially metabolise glucose rather than free fatty acids. Alternatively, patients with diabetes mellitus may be taking protective medications or have become accustomed to mild hyperglycaemia, a prooxidant status, or increased levels of advanced glycated end products – all implicated in the pathogenesis of systemic inflammation.

Since few would have cited diabetes mellitus as a contributory reason for defining an ICU admission as futile, Siegelaar and colleagues' study does not change our clinical practice. Nevertheless, the suggestion of a potential protective effect for diabetes mellitus merits further investigation. Unpicking this hypothesis may reveal new therapeutic strategies that we can exploit in other patient populations.

Abbreviations
ICU, intensive care unit.

Competing interests
The author declares that he has no competing interests.

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