MAYO CLINIC

REVIEW

New-Onset Diabetes After Acute and Critical Illness: A Systematic Review

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Abstract

Hyperglycemia is commonly observed during acute and critical illness. Recent studies have investigated the risk of developing diabetes after acute and critical illness, but the relationship between degree of in-hospital hyperglycemia and new-onset diabetes has not been investigated. This study examines the evidence for the relationship between in-hospital hyperglycemia and prevalence of new-onset diabetes after acute and critical illness. A literature search was performed of the MEDLINE, EMBASE, and Scopus databases for relevant studies published from January 1, 2000, through August 4, 2016. Patients with no history of diabetes before hospital discharge were included in the systematic review. In-hospital glucose concentration was classified as normoglycemia, mild hyperglycemia, or severe hyperglycemia for the meta-analysis. Twenty-three studies were included in the systematic review, and 18 of these (111,078 patients) met the eligibility criteria for the meta-analysis. The prevalence of new-onset diabetes was significantly related to in-hospital glucose concentration and was 4% (95% CI, 2%-7%), 12% (95% CI, 9%-15%), and 28% (95% CI, 18%-39%) for patients with normoglycemia, mild hyperglycemia, and severe hyperglycemia, respectively. The prevalence of new-onset diabetes was not influenced by disease setting, follow-up duration, or study design. In summary, this study found stepwise growth in the prevalence of new-onset diabetes with increasing in-hospital glucose concentration. Patients with severe hyperglycemia are at the highest risk, with 28% developing diabetes after hospital discharge.

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Acute and critical illness describes a group of life-threatening conditions that affect millions of people around the world every year. In 2013 alone, 8.6 million people experienced acute myocardial infarction, 10.3 million stroke, 17.2 million pancreatitis, and 33.4 million burns.[1] The mortality of acute and critical illness ranges from 7% in patients with ST-segment elevation myocardial infarction to 50% to 60% in patients with septic shock.[2] In addition, acute and critical illness carries a large economic burden, with the average cost of treatment in an intensive care unit ranging from $4000 to $8500 per day.[3,4] Moreover, the global burden of acute and critical illness is expected to increase as the population ages and nonfatal outcomes require more resources from health care systems.[1]

Transient elevations in blood glucose concentration during acute and critical illness have been recognized for decades.[5,6] This response in patients without a known history of diabetes was classically considered benign[7,8] and commonly referred to as *stress hyperglycemia*.[9] In recent years, the focus has shifted from immediate health outcomes to long-term outcomes, including the development of new-onset diabetes after acute and critical illness. Several studies have reported that acute and critically ill patients may have a greater risk of subsequent diabetes than the general population.[10,11] However, evidence is conflicting,[12] even within the same disease setting.[13,14] A recent systematic review found that hyperglycemia in patients admitted to intensive care units was associated with an increased risk of subsequent diabetes[15]; however, this association has not been explored in broader settings of acute and critical illness. In addition, the relationship between degree of hyperglycemia and development of new-onset diabetes remains largely unknown. Therefore, the aim of this study was to systematically review the best available evidence on the relationship between degree of in-hospital

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ARTICLE HIGHLIGHTS

- The relationship between degree of in-hospital hyperglycemia and development of new-onset diabetes is largely unknown.
- This study found that hyperglycemia in acute and critically ill patients increases the risk of new-onset diabetes after hospital discharge.
- The prevalence of new-onset diabetes increases with the degree of in-hospital hyperglycemia. Patients with severe hyperglycemia have the greatest risk, with 28% developing diabetes after hospital discharge.
- These findings suggest that prevention programs after hospital discharge might need to be considered in patients with acute and critical illness.

hyperglycemia and prevalence of new-onset diabetes after acute and critical illness.

METHODS

Search Criteria and Identification

A search strategy was developed to identify all clinical studies that reported the prevalence of new-onset diabetes after hospital discharge following acute and critical illness. Three major electronic databases (MEDLINE, EMBASE, and Scopus) were searched to identify relevant literature from January 1, 2000, through August 4, 2016. The following key words were searched: *(blood glucose or hyperglycemia)* AND *diabetes* AND *(acute or critically) ill* AND *clinical studies* AND *(predict or risk)* AND *hospital*. See the Supplemental Appendix (available online at http://www.mayoclinicproceedings.org) for the full search strategy. Abstracts were reviewed for relevance, and full-text articles were obtained for potentially eligible studies. References in the included studies were also reviewed for eligibility.

Eligibility Criteria

The study inclusion criteria were diabetes onset after hospitalization, no history of diabetes (including the need for insulin therapy or oral hypoglycemic agents during hospitalization), older than 17 years, and hospital admission with acute and critical illness. The study exclusion criteria were in-hospital glucose concentration not reported, pediatric or transplant patients, and reviews, commentaries, and letters to the editor.

If data from the same cohort had been reported in multiple studies, only the most recent study or the most detailed population (with respect to relevant methods and results) was included. Eligibility assessment was conducted by 2 of us (C.J.J. and V.M.A.), and discrepancies were resolved by discussion with the senior author (M.S.P.) or via e-mail with authors of primary studies.

Data Extraction and Reporting

Data were extracted from all eligible studies and entered into a predesigned data collection form. The following study and patient characteristics were extracted: author(s), year of publication, country, study design, disease setting, follow-up duration, total study population, age, percentage males, number of patients who met the inclusion criteria, in-hospital glucose categorization, and prevalence of new-onset diabetes. Patients with incomplete data sets were not eligible for analysis (ie, patients unable to complete follow-up or without an in-hospital glucose concentration measured). For studies that included patients with and without diabetes or that had multiple study arms, only patients without a history of diabetes, an in-hospital diabetes diagnosis (including those discharged on insulin therapy), or a need for intensive glucose-lowering therapy during hospitalization were eligible for analysis. The conventional treatment arms of randomized controlled trials were considered prospective cohorts for the purpose of this systematic review.

Reporting of this study was in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocols statement and checklist.[16]

Quality Assessment

The methodological quality of studies was assessed by the Newcastle-Ottawa Scale.[17] Studies were allocated a maximum of 9 points based on 3 perspectives of study design: the selection of the study groups, the comparability of the study groups, and the ascertainment of the outcome of interest. Studies were considered to be of high quality if 5 or more points were scored and of low quality if 4 or fewer points were scored.[18]