



# The effectiveness of tight glycemic control on decreasing surgical site infections and readmission rates in adult patients with diabetes undergoing cardiac surgery: A systematic review



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## ABSTRACT

**Objective:** A systematic review of the effects of tight glycemic control with a continuous insulin infusion to achieve blood glucose levels  $\leq 200$  mg/dL on surgical site infections and readmission rates in adult patients with diabetes after cardiac surgery.

**Methods:** A quantitative systematic review of the literature. Databases, including PubMed, CINAHL, EMBASE, and CENTRAL, were searched for relevant studies from database inception through August 2014. Randomized and quasi-experimental studies were included.

**Results:** A meta-analysis of ten studies demonstrated that glycemic control with a continuous insulin infusion to achieve blood glucose levels  $\leq 200$  mg/dL significantly reduced surgical site infection rates (odds ratio 0.35, 95% confidence interval 0.25–0.49;  $Z = 6.0$ ,  $P < 0.00001$ ) compared with standard diabetes management.

**Conclusions:** Maintaining blood glucose levels  $\leq 200$  mg/dL with a continuous insulin infusion in all stages of the perioperative period in cardiac surgery patients with diabetes can reduce the incidence of surgical site infections.

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## Introduction

As of 2012, 29.1 million people, representing 9.3% of the United States' (US) population, have been diagnosed with diabetes mellitus (DM).<sup>1</sup> Patients with DM have a 2- to 4-fold greater risk for developing coronary heart disease (CHD) compared to patients without DM and suffer more multi-vessel CHD that leads to invasive revascularization procedures including coronary artery bypass surgery (CABG).<sup>2</sup>

Of the approximately 397,000 CABG procedures performed in the US,<sup>3</sup> as many as 31% of patients develop hospital acquired

infections within 30 days of the operation.<sup>4</sup> DM, obesity, high preoperative serum glucose levels ( $>200$  mg/dL), and female gender are among the risk factors for surgical site infections following CABG surgery.<sup>5</sup> Serum glucose levels  $> 200$  mg/dL in the immediate ( $<48$  h) postoperative period contribute to increased risk of surgical site infections.<sup>6,7</sup> Poor glycemic control prior to surgery contributes to poor control after hospital discharge and increases the incidence of complications such as poor wound healing and higher rates of surgical site infections, and ultimately readmission to the hospital and increased mortality.<sup>8</sup>

Increased hospital readmissions can be used as indicators of poor quality care and are major concerns for health care organizations due to substantial incurred losses in revenue.<sup>9,10</sup> A readmission can be the result of incomplete treatment, poor care of the underlying problem, poor discharge coordination of services, incomplete discharge planning, and/or inadequate access to care.<sup>11,12</sup> Hannan et al.<sup>13</sup> showed a 16.5% all-cause readmission rate within 30 days of CABG surgery and Li et al.<sup>14</sup> showed a 13.2% readmission rate. The authors of both studies identified post-operative infection as the most common reason for readmission.

**Abbreviations:** AACE, American Association of Clinical Endocrinologists; ADA, American Diabetes Association; BMI, body mass index; CABG, coronary artery bypass graft; CHD, coronary heart disease; CI, confidence interval; DM, diabetes mellitus; ICU, Intensive care unit; JBI-MAStARI, Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instrument; NA, not applicable; N, no; OR, odds ratio; RCT, randomized controlled trial; RR, relative risk; SCIP, surgical care improvement project; SE, standard error; U, unclear; US, United States; Y, yes.

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To address the problem of poor glycemic control in acutely ill patients with diabetes, the American Association of Clinical Endocrinologists (AACE) and the American Diabetes Association (ADA) recommend intravenous insulin infusions for achieving and maintaining tight glycemic control in critically ill patients who have DM.<sup>15</sup> The recommendation is to initiate the insulin infusion at a blood glucose threshold no greater than 180 mg/dL for the treatment of persistent hyperglycemia in critically ill inpatients with a target blood glucose of 140–180 mg/dL for the majority of these patients.<sup>15,16</sup> The 2015 ADA practice guidelines<sup>16</sup> suggest that a target of 110–140 mg/dL may be appropriate for select critically ill patients when there is no increased risk of hypoglycemia and recommended the use of subcutaneous insulin with basal and corrective doses in non-critically ill patients, with the goal of a preprandial glucose of <140 mg/dL. However, there are no uniform guidelines defining a desired target range for optimal postoperative blood glucose. The Surgical Care Improvement Project (SCIP), which was developed in 2003 as a national quality partnership of organizations committed to improving the safety of surgical care through the reduction of postoperative complications, developed a core measure to maintain blood glucose at a level  $\leq 180$  mg/dL during the perioperative and postoperative period based on evidence of decreased surgical site infections with this target.<sup>17,18</sup> The Society of Thoracic Surgeons also recommends a target of  $\leq 180$  mg/dL in the immediate postoperative period.<sup>19</sup> In contrast, the Portland Diabetic Project<sup>20</sup> evaluated the effects of the Portland Protocol, a now widely used intravenous insulin protocol to maintain blood glucose < 150 mg/dL, in a randomized controlled trial (RCT) of 5510 cardiac surgery patients with DM. It was demonstrated that the use of this protocol was safe and led to a 77% reduction in surgical site infections.<sup>20</sup>

Despite the current recommendations, the most recent systematic review of the effects of tight glycemic control in the postoperative period after surgical procedures was published in 2009<sup>21</sup> and included five RCTs involving 773 adult patients with DM who underwent a variety of surgical procedures. The authors concluded that there was insufficient evidence to support the use of tight glycemic control with continuous insulin infusions to reduce surgical site infections.

Due to the absence of consistent evidence of the effects of tight glycemic control during the postoperative period after cardiac surgery, the purpose of this systematic review was to identify and synthesize the best available evidence on the effectiveness of tight glycemic control interventions using a continuous insulin infusion to achieve blood glucose levels  $\leq 200$  mg/dL on decreasing surgical site infections and readmission rates in adult patients with DM undergoing cardiac surgery.

## Methods

We considered studies on the effectiveness of tight glycemic control interventions in which a continuous insulin infusion was used to control blood glucose to levels  $\leq 200$  mg/dL, for inclusion in this review. The goal of tight glycemic control in the adult patient with DM after cardiac surgery is to obtain a steady serum glucose level to reduce the risk of postoperative complications such as surgical site infections. While current guidelines recommend a target glucose of  $\leq 180$  mg/dL,<sup>16,18,19</sup> some of the studies these guidelines were based on include target ranges up to 200 mg/dL; therefore, a serum glucose target of  $\leq 200$  mg/dL was chosen for this review to capture all studies evaluating tight glycemic control interventions.

We considered studies that compared tight glycemic control interventions with continuous insulin infusions to standard care. Standard care included the administration of bolus dose insulin

subcutaneously on a sliding scale regimen for elevated glucose levels or the administration of diabetes medications in oral form to control serum glucose levels.

Studies included the following outcome measures:

- Surgical site infections within one year after cardiac surgery. For this review a surgical site infection was defined as purulent drainage from the deep incision; an organism isolated from an aseptically obtained wound culture; wound dehiscence; the need for surgical wound revision; or the presence of fever ( $>38$  °C), localized pain or tenderness, an abscess, or any other observable evidence of infection on direct examination, reoperation, histopathology, or radiologic examination.<sup>4,22</sup>
- All cause readmission rates to the same hospital, a different hospital, or another acute care facility within one-year post discharge from the index admission in which the patient underwent cardiac surgery.

## Search strategy

To find both published and unpublished studies, we conducted a comprehensive search of the literature in three steps: 1) We conducted an initial limited search of PubMed and CINAHL using the following initial key words: diabetes, glycemic control, cardiac surgery, insulin, and surgical wound infection. To develop a comprehensive list of key words, we analyzed the text words contained in the title and abstract and the index terms used to describe an article. 2) We conducted a second search across all included databases using all identified keywords and index terms. The databases searched included: PubMed, CINAHL, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Health Source: Nursing/Academic Edition, and Scopus. The search for unpublished studies included: New York Academy of Medicine, ProQuest Dissertation & Thesis, Google Scholar, Virginia Henderson International Library, and the European Society of Cardiology. 3) We searched the reference lists of all identified articles for additional studies. We considered studies published in the English language from the inception of each database through August 2014 for inclusion in this review. Fig. 1 details the PubMed search strategy.

## Study selection

The comprehensive search of the literature yielded 1755 potentially relevant articles. We removed 14 duplicate records and excluded 1701 additional articles after review of the titles and key words. We retrieved 40 full text articles for further review, because additional information beyond the abstract was needed to determine if the article met the inclusion criteria for this review. After reviewing the full text papers for eligibility, we excluded 27 studies that did not meet the inclusion criteria. We identified 13 articles for inclusion in this systematic review. Fig. 2 outlines the stages of the process for identifying relevant studies for inclusion in this systematic review.

## Assessment of methodological quality

Two authors independently assessed each quantitative paper selected for retrieval for methodological quality prior to inclusion in the review. We used standardized critical appraisal instruments from the Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MAStARI).<sup>23</sup>

## Data extraction

Two authors independently extracted data from the included studies using the standardized data collection tool from

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