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Hospitalization costs and clinical outcomes in CABG patients treated with intensive insulin therapy

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ABSTRACT

Background: The financial impact of intensive (blood glucose [BG] 100–140 mg/dl [5.5–7.8 mM] vs. conservative (141–180 mg/dl (7.9–10.0 mM) glucose control in the ICU in patients, with and without diabetes, undergoing coronary artery bypass graft (CABG) surgery is not known.
Methods: This post-hoc cost analysis determined differences in hospitalization costs, resource utilization and perioperative complications in 288 CABG patients with diabetes ($n = 143$) and without diabetes ($n = 145$), randomized to intensive ($n = 143$) and conservative ($n = 145$) glucose control.
Results: Intensive glucose control resulted in lower BG (131.4 ± 14 mg/dl-(7.2 ± 0.8 mM) vs. 151.6 ± 17 mg/dl (8.4 ± 0.8 mM, $p < 0.001$), a nonsignificant reduction in the median length of stay (LOS, 7.9 vs. 8.5 days, $p = 0.17$) and in a composite of perioperative complications including wound infection, bacteremia, acute renal and respiratory failure, major cardiovascular events (42% vs 52%, $p = 0.10$) compared to conservative control. Median hospitalization costs were lower in the intensive group ($39,366 vs. $42,141, $p = 0.040$), with a total cost savings of $3654 (95% CI: $1780–$3723), than conservative control. Resource utilization for radiology ($p = 0.008$), laboratory ($p = 0.014$), consultation service ($p = 0.013$), and ICU utilization ($p = 0.007$) were also lower in the intensive group. Compared to patients without perioperative complications, those with complications had longer hospital length of stay (10.7 days vs. 6.7 days, $p < 0.001$), higher total hospitalization cost ($48,299 vs. $32,675, $p < 0.001$), and higher resource utilization units (2745 vs. 1710, $p < 0.001$).
Conclusion: Intensive glycemic control [BG 100–140 mg/dl (5.5–7.8 mM)] in patients undergoing CABG resulted in significant reductions in hospitalization costs and resource utilization compared to patients treated with conservative [BG 141–180 mg/dl (7.9–10.0 mM)] glucose control.

1. Introduction

The prevalence of diabetes in patients undergoing cardiac surgery has increased each year during the past four decades (Raza, Sabik, Ainkaran, & Blackstone, 2015). Among patients undergoing coronary artery bypass grafting (CABG), about 30% to 50% of patients have a history of diabetes (McAlister, Man, Bistritz, Amad, & Tandon, 2003; Raza et al., 2015; Schmeltz et al., 2007), and 60% to 90% of them develop hyperglycemia during the perioperative period (McAlister et al., 2003; Schmeltz et al., 2007; Umpierrez et al., 2015). Diabetes has been identified as independent risk factors of morbidity and mortality after cardiac surgery (Carson et al., 2002; Furnary et al., 2003; Thourani et al., 1999). Patients with diabetes have worse surgical outcomes when compared to those without diabetes; specifically higher mortality, deep sternal wound infections, renal failure, postoperative strokes, and longer hospital stay (Carson et al., 2002; Furnary et al., 2003; Guvener, Pasaoglu, Demircin, & Oc, 2002; Herlitz et al., 2000; Thourani et al., 1999), as well as increased resource utilization and hospitalization costs (Estrada, Young, Nifong, & Chitwood, 2003; Greco et al., 2016; Raza et al., 2015).

During the past decade, there has been ongoing debate about the benefits of intensive glycemic control in cardiac surgery patients. Many observational studies have reported that intensive control reduces the number of hospital complications, shorter length of stay, and lower mortality in intensive care unit (ICU) and cardiac surgery patients (Cunningham, Daoud, Baimbridge, Baimbridge, & Abdelnour, 2013; Estrada et al., 2003; Furnary et al., 2003; Gandhi et al., 2007). The results of randomized controlled trials; however, have reported

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controversial results; with some showing a reduction in complications with intensive glucose control (Hruska, Smith, Hendy, Fritz, & McAdams, 2005; Lazar et al., 2004; van den Berghe et al., 2001) and others reporting no differences in outcomes (Finfer et al., 2009; Kansagara, Fu, Freeman, Wolf, & Helfand, 2011; Lazar et al., 2011). Adding to the controversy, our group and others recently reported heterogeneity in the treatment effect according to diabetes status in cardiac surgery patients, reporting no differences in the rate of perioperative complications among patients with diabetes treated with intensive or conservative regimens, but a significant lower rate of complications in patients without diabetes treated with intensive compared to conservative treatment (Godinjak et al., 2015; Umpierrez et al., 2015; van den Berghe et al., 2001).

Cross-sectional studies and retrospective claims database analysis have reported higher hospitalization costs in cardiac surgery patients with a history of diabetes and in those with hyperglycemia without diabetes (stress hyperglycemia) compared to patients without diabetes and normoglycemia (Greco et al., 2016; Straka, Liu, Girase, DeLorenzo, & Chapman, 2009). Few randomized controlled trials; however, have reported on financial impact and clinical outcome of insulin treatment in cardiac surgery patients with hyperglycemia and diabetes. Accordingly, this post-hoc cost analysis of the GLUCO-CABG trial (Umpierrez et al., 2015) determined differences in hospitalization costs, resource utilization, and perioperative complications in CABG patients with and without diabetes randomized to intensive or conservative glucose control.

2. Materials and Methods

The GLUCO-CABG trial (Umpierrez et al., 2015) was a randomized open-label clinical study (NCT: 01792830) that included patients with and without diabetes undergoing CABG who experienced perioperative hyperglycemia, defined as a BG >140 mg/dL (>7.8 mM). A total of 302 patients between 18 and 80 years of age were randomized to the intensive glycemic control group [target BG 100 and 140 mg/dL (5.5–7.8 mM)] or to conservative control [BG 141 and 180 mg/dL 7.8–10 mM)] in the ICU. After transition from ICU to telemetry floor, patients were managed with a single treatment protocol aimed to maintain a glucose target <140 mg/dL (<7.8 mM) before meals during the hospital stay. The primary outcome included differences between intensive and conservative glucose control on a composite of perioperative complications including sternal wound infection (deep and superficial), bacteremia, respiratory failure, pneumonia, acute kidney injury, major adverse cardiovascular events including acute myocardial infarction, stroke, heart failure and cardiac arrhythmias.

This study was conducted at three academic medical centers including Emory University Hospital, Emory Midtown Hospital, and Grady Memorial Hospital in Atlanta, Georgia. The study was approved by the institutional review board of Emory University.

In order to determine the financial impact of intensive vs. conservative glucose targets in patients undergoing CABG, this cost analysis compared differences in hospitalization costs and resource utilization, using cost-charge ratios from Centers for Medicare and Medicaid Services. Data identified for extraction included ICD-9, CPT, and MS-DRG codes as well as resource utilization data and related hospital charges. These were obtained from the electronic health record and billing/coding departments. Resources were inventoried and itemized across major utilization categories. These included laboratory, pharmacy, radiology, consultation services, as well as surgical floor and ICU bed days. Units of resource utilization were calculated according to the number of instances or times a particular resource was used during the hospital stay (e.g. each number of times pharmacy dispensed a medication or the number of times a radiologic study was ordered). Charges for individual resource utilization were obtained from the billing departments at each hospital. Once the inventory was compiled, costs by category and cost differences between the treatment arms were calculated. Total charges were adjusted by applying the institution-specific fiscal year (FY) 2012 and 2013 cost-to-charge ratios to the charge data captured in the database. The adjustment ratios were determined from the Medicare Hospital Cost Report published by the Centers of Medicare and Medicaid Services and data available from the participating hospitals. Our data set was also queried for analysis of hospital and ICU length of stay (LOS), number of individual and composite of perioperative complications, and readmission after hospital discharge. The number of hospital inpatient days and ICU LOS were determined based on billing data.

2.1. Insulin Treatment

Patients with glucose >140 mg/dL (>7.8 mM) were randomized after completion of surgery in the post-surgical holding area or in the ICU. Glucommander, a computer-guided continuous insulin infusion (CII) device was used to facilitate glycemic control with a single insulin delivery program in both treatment arms (Davidson, Steed, & Bode, 2005). In brief, this computer-guided insulin algorithm directs the administration of intravenous insulin in response to glucose measurement at the patient's bedside. During CII, glucose levels were entered into the system and the program recommended the infusion rate and a variable time to check the next glucose testing. Intravenous insulin infusion was continued until the patient could eat and/or transferred to non-ICU service.

2.2. Statistical Analysis

We compared baseline clinical characteristics and study outcomes, such as hospitalization costs as well as overall and itemized health care resource utilization costs between treatment groups. We also compared hospitalizations and resource utilization costs between patients with and without diabetes and between patients with and without complications. We made the comparisons with the use of nonparametric Wilcoxon tests (or Kruskal-Wallis tests) for continuous variables and chi-square tests (or Fisher's exact test) for discrete variables. We adopted the nonparametric Hodges-Legmann method to evaluate the cost difference between the treatment groups. The data were generally presented as median (interquartile range) for continuous cost-related variables, mean ± standard deviation for non-cost related continuous variables, and count (percentage) for discrete variables. A p-value of <0.05 was considered significant. Statistical analyses were performed using SAS (v9.2).

3. Results

A total of 288 of 302 patients randomized in the GLUCO-CABG trial were included in this cost analysis. Fourteen patients were excluded because of incomplete financial data. There were 143 patients in the intensive glucose control and 145 patients in the conservative group. The two groups were well balanced in terms of demographics, American Heart Association (AHA) procedure specific cardiac risk category, and American Society of Anesthesiology (ASA) physical status (Table 1). There were no differences between intensive and conservative groups in the mean glucose concentration on admission, at randomization, or during surgery (Table 1). The mean BG during the ICU stay was 132 ± 47 mg/dL (7.3 ± 2.6 mM) in the intensive and 152 ± 17 mg/dL (8.4 ± 0.9 mM) in the conservative group ($p < 0.001$). The duration of CII was 26.3 ± 22 h in the intensive and 22 ± 24 h in the conservative group ($p = 0.001$). There were no differences in the rate of hypoglycemia or in mean daily glucose during the hospital stay between intensive and conservative groups.

Intensive glucose treatment resulted in a non-significant reduction in perioperative complications compared to the conservative group (42% vs. 52%, $p = 0.10$). In addition, there were no differences in the

Table 1
Clinical characteristics on admission and glycemic control.

	All	Intensive	Conventional	p-value
Number of patients	288	143	145	
Gender				0.39
Male, n	206	99	105	
Female, n	82	44	38	
Age, years	64 ± 9	64 ± 9	64 ± 10	0.86
Race				0.99
Caucasian	216 (75)	109 (75)	107 (75)	
African American	60 (21)	30 (21)	30 (21)	
Other	12 (4)	6 (4)	6 (4)	
Body weight, kg	92 ± 21	93 ± 21	91 ± 21	0.68
BMI, kg/m^2	31 ± 7	31 ± 7	31 ± 7	0.55
Type of Surgery				
Primary isolated CABG	233 (81)	121 (85)	112 (77)	0.11
CABG + Valve repair	45 (16)	18 (13)	27 (19)	0.16
Re-do CABG	19 (7)	9 (6)	10 (7)	1
History of diabetes	143 (50)	71 (50)	72 (50)	1
Home diabetes therapy				
No antidiabetic agents	11 (8)	6 (9)	5 (7)	1
Oral agents	65 (47)	33 (47)	32 (47)	
Insulin alone	27 (20)	13 (19)	14 (21)	
Insulin + oral agents	35 (25)	18 (26)	17 (25)	
Glycemic control				
Admission HbA1C, %	6.8 ± 1.8	6.8 ± 1.8	6.7 ± 1.7	0.62
Randomization BG, mg/dl (mM)	164 ± 26 (9.1 ± 1.4)	161 ± 21 (8.9 ± 1.2)	168 ± 29 (9.3 ± 1.6)	0.09
BG during surgery, mg/dl (mM)	148 ± 29 (8.2 ± 1.6)	146 ± 25 (8.1 ± 1.4)	150 ± 30 (8.3 ± 1.7)	0.65
BG during ICU stay, mg/dl (mM)	142 ± 18 (7.8 ± 1.0)	131 ± 14 (7.3 ± 0.7)	152 ± 17 (8.4 ± 0.9)	<0.001
BG readings >200 mg/dl (>11.1 mM) during CII, %	6 ± 10	3 ± 8	9 ± 11	<0.001
Patients with BG < 70 mg/dl (<3.9 mM) during ICU	14 (5)	11 (8)	3 (2)	0.03
BG readings during ICU < 70 mg/dl (<3.9 mM), %	0.3 ± 1.7	0.4 ± 2.4	0.1 ± 0.6	0.025
BG after transition, non-ICU, mg/dl (mM)	142 ± 29 (7.9 ± 1.6)	143 ± 28 (7.9 ± 1.5)	141 ± 29 (7.8 ± 1.6)	0.43
BG readings >200 mg/dl (>11.1 mM) non-ICU, %	13 ± 17	12.2 ± 18	12 ± 17	0.71
Patients with BG < 70 mg/dl(<3.9 mM) non-ICU	54 (19)	27 (19)	27 (19)	0.95
BG readings non-ICU < 70 mg/dl (<3.9 mM), %	1 ± 3	1 ± 2	1 ± 3	0.82
Insulin therapy				
Patients treated with CII	265 (92)	138 (97)	127 (88)	0.008
Duration of CII, hours	24 ± 23	25 ± 21	22 ± 24	0.003
Total insulin therapy in the ICU, unit/day	1 ± 1	1 ± 1	1 ± 2	0.24
ICU LOS, days	2 [1.1–3.7]	1.9 [1.1–3.1]	2.3 [1.4–3.8]	0.08
Hospital LOS, days	8.1 [6.2–11.8]	8 [6–10]	8 [6–12]	0.12

Data are n (%), mean ± standard deviation, or median [IQR]. IQR = interquartile range; BG = blood glucose; BMI = body mass index; CII = continuous insulin infusion; ICU = intensive care unit; LOS = length of stay; SC = subcutaneous.

ICU or hospital length of stay (LOS), duration of surgery, need for vasopressors, or readmissions after hospital discharge between treatment groups. Although there were no differences in the overall rate of complications among patients with and without diabetes ($p = 0.82$), we observed heterogeneity in treatment effect according to diabetes status. There were no differences in the rate of

Table 2
Hospitalization costs and resource utilization by treatment group.

	Intensive	Conventional	p-value
Number of patients	143	145	
Total hospital charges, $ [IQR]	99,661 [81,065–125,995]	106,685 [87,242–147,796]	0.036
Pharmacy, $	8210 [6397–12,846]	10,242 [7129–20,477]	0.005
Radiology, $	1967 [1287–3031]	2381 [1582–4822]	0.008
Laboratory, $	12,879 [10,232–18,326]	15,235 [11,489–22,200]	0.005
Consultations, $	2031 [1068–3771]	2560 [1500–5606]	0.013
ICU, $	7990 [4195–13,215]	11,415 [4405–19,975]	0.006
Total hospital costs, $ [IQR]	36,681 [28,488–46,074]	40,913 [31,464–56,629]	0.040
Pharmacy, $	2316 [1808–3559]	2865 [2011–5334]	0.004
Radiology, $	694 [434–960]	818 [526–1324]	0.018
Laboratory, $	2313 [1808–3559]	3141 [1619–5134]	0.09
Consultations, $	755 [493–1424	986 [615–2018]	0.014
ICU, $	4087 [2276–7000]	5540 [2333–10,093]	0.008
Resource utilization, units [IQR]	1919 [1566–2730]	2066 [1641–3223]	0.17
Pharmacy, units	640 [361–1145]	731 [402–1449]	0.13
Radiology, units	15 [12–21]	20 [13–27]	0.002
Laboratory, units	213 [175–294]	246 [195–345]	0.014
Consultations, units	9 [4–23]	14 [6–34]	0.013
ICU, units	2 [1–3]	3 [1–5]	0.007

Data are median [IQR].
ICU = intensive care unit; IQR = interquartile range.

complications among patients with diabetes treated with intensive or conservative regimens (49.3% vs. 45.8%, p = 0.68); however, in patients without DM, intensive treatment was associated with significantly lower rate of complications compared to the conservative group (35% vs. 58%, p = 0.006).

Hospitalization costs were lower in the intensive group (median [IQR] $36,681 [28,488–46,074] vs. $40,913 [31,464–56,629], p = 0.040), with an average total cost savings of $3654 per case compared to conservative glucose control (Table 2). Resource utilization was also lower in the intensive group for radiology (p = 0.002), laboratory (p = 0.014), consultation service (p = 0.013), and ICU utilization (p = 0.007), resulting in an overall lower median total resource costs ($14,060 vs. $16,170, p = 0.004) compared to conservative control. After adjusting for length of stay, the cost savings between intensive and conservative treatment was no longer significant [$1500.35 ($1081–$3333)]. In addition, patients with perioperative complications had longer median hospital LOS (10.7 [7.8–15.7] vs. 6.7 [5.0–8.4] days, p < 0.001), higher total hospitalization cost ($48,299 [37,221–62,905] vs. $32,675 [27,195–39,549], p < 0.001). Similarly, patients with complications had higher unit resource utilization (2745 [1890–3959] vs. 1710 [1497–2135], p < 0.001) compared to those without complications.

The overall hospitalization costs were not different between patients with and without diabetes ($38,321 [29,685–52,514] vs. $37,386 [30,178–52,103], p = 0.65). Among patients with diabetes, intensive control resulted in a non-significant reduction in the total cost of hospitalization ($40,884 [31,216–49,992] vs. $42,052 [32,858–56,421], p = 0.18), total units of resource utilization (1911 [1009–21,694, p = 0.26), and hospitalization LOS 8.2 days [6.4–11.3] vs. 8.9 days [6–12.2], p = 0.64) compared to conservative control. Similarly, in patients without diabetes with hyperglycemia, there was a non-significant trend in reducing hospitalization cost with intensive compared to conservative treatment ($35,389 [28,671–44,602] vs $40,202 [31,134–59,062], p = 0.15) (Table 3).

4. Discussion

This post-hoc cost analysis of the GLUCO-CABG trial determined the financial impact, resource utilization, and clinical outcomes of intensive compared to conservative glycemic control in patients undergoing CABG. Our results indicate that intensive insulin treatment resulted in a trend in reducing perioperative complications, which significantly reduced total hospitalization costs and resource utilization when compared to conservative insulin treatment. Patients with perioperative complications had significantly longer median hospital LOS, higher total hospitalization cost, and resource utilization compared to patients without complications.

Cardiovascular disease and specifically coronary artery disease remain the major cause of morbidity and hospital admissions in patients with diabetes (Vamos et al., 2012), and accounts for more than two-third of deaths in individuals with diabetes over 65 years of age in the United States (Fox et al., 2004; Go et al., 2013). The number of patients with diabetes undergoing CABG has increased significantly in recent years. The proportion of patients with diabetes undergoing CABG increased from 7% per year in the 1970s to 37% in the 2000s (Raza et al., 2015). In such patients, diabetes is a marker for resource-intensive and expensive care as well as an independent risk factor for reduced long-term survival. Patients with diabetes experience higher hospital death, renal failure, and deep sternal wound infection results, which lead to prolonged postoperative length of stay and increased hospital resource utilization (Raza et al., 2015).

The diabetes epidemic is one of the most challenging public health issues of the 21st century. Diabetes affects ~415 million adults worldwide, with global health expenditures resulting from diabetes estimated at $673 billion in 2015, and expected to exceed $1197 billion by 2040 (International Diabetes Federation, 2015). Retrospective and claims database analyses have reported higher hospitalization costs in cardiac surgery patients with diabetes and hyperglycemia compared to patients without hyperglycemia (Greco et al., 2016; Straka et al., 2009; Van den Berghe, Wouters, Kesteloot, & Hilleman, 2006). Implementations of glycemic management programs in ICU

Table 3
Hospitalization costs and resource utilization in patients with and without a history of diabetes by treatment group.

	Non-DM		p-value	DM		p-value
	Intensive	Conventional		Intensive	Conventional	
Number of patients	72	73		71	72	
Age, years	63 ± 9	65 ± 11	0.10	66 ± 9	63 ± 9	0.06
BMI, kg/m^2	30 ± 6	29 ± 7	0.31	33 ± 8	32 ± 7	0.87
Glycemic control						
HbA1C, %	5.6 ± 0.4	5.6 ± 0.6	0.79	8 ± 1.8	7.8 ± 1.8	0.23
BG during surgery, mg/dl (mM)	138 ± 20 (7.6 ± 1.1)	140 ± 21 (7.8 ± 1.2)	0.67	155 ± 27 (8.6 ± 1.5)	159 ± 34 (8.8 ± 1.9)	0.67
BG during ICU stay, mg/dl (mM)	127 ± 12 (7.1 ± 0.6)	142 ± 15 (7.8 ± 0.8)	<0.001	136 ± 14 (7.5 ± 0.7)	161 ± 12 (8.9 ± 0.8)	<0.001
BG transition, mg/dl (mM)	126 ± 12 (7.0 ± 0.6)	123 ± 14 (6.8 ± 0.7)	0.19	161 ± 28 (8.9 ± 1.5)	160 ± 29 (8.8 ± 1.6)	0.78
ICU LOS, days	1.8 [1–2.9]	2.1 [1.4–4.8]	0.029	1.9 [1.1–3.8]	2.4 [1.2–3.4]	0.84
Hospital LOS, days	7.4 [5.8–10]	8.1 [6.4–13.3]	0.15	8.2 [6.4–11.3]	8.9 [6–12.2]	0.64
Total hospital costs, $	35,389 [28,671–44,602]	40,202 [31,134–59,062]	0.11	37,473 [28,239–46,725]	42,052 [32,858–56,421]	0.18
Pharmacy, $	2201 [1843–3115]	2884 [1963–5470-]	0.020	2350 [1707–3989]	2859 [2061–5178]	0.11
Radiology, $	640 [430–853]	837 [529–1323]	0.006	796 [487–1099]	802 [515–1323]	0.54
Laboratory, $	3090 [1393–4742]	3120 [1690–5617]	0.42	1994 [1192–4180]	3141 [1578–4627]	0.10
Consultations, $	639 [405–1173]	792 [592–1975]	0.016	837 [616–1646]	1160 [644–2099]	0.24
ICU, $	4062 [2276–6888]	4592 [2276–11,480]	0.10	4087 [2276–8174]	6056 [4062–10,093]	0.05
Resource utilization, units	1924 [1563–2412]	1995 [1545–3248]	0.46	1911 [1569–2773]	2138 [1711–2968]	0.28
Pharmacy, units	623 [303–973]	718 [335–1550]	0.39	664 [388–1371]	777 [501–1400]	0.21
Radiology, units	15 [12–19]	20 [14–29]	0.002	17 [13–23]	19 [13–27]	0.26
Laboratory, units	200 [170–268]	228 [177–327]	0.15	225 [186–319]	267 [206–357]	0.048
Consultations, units	7 [3–19]	13 [6–29]	0.017	12 [5–26]	15 [7–37]	0.20
ICU, units	2 [1–3]	2 [1–5]	0.06	2 [1–4]	3 [2–5]	0.06

Data are mean ± standard deviation or median [IQR].
BG = blood glucose; BMI = body mass index; CII = continuous insulin infusion; DM = diabetes mellitus; IQR = interquartile.

and cardiac surgery settings, as well as a post hoc analysis of a randomized controlled trial previously reported reductions in hospitalization costs and resource utilization with intensive glycemic control (Estrada et al., 2003; Krinsley & Jones, 2006; Van den Berghe et al., 2006).

Previous studies in cardiac surgery patients reported several factors that account for the higher hospitalization costs in patients with diabetes including longer ICU and postoperative stays, higher rates of hospital complications, resource utilization, and higher costs of clinical and laboratory testing, diagnostic imaging, pharmacy services, and nursing care (Straka et al., 2009; Zhang et al., 2014). In our study, we found that intensive insulin treatment was associated with lower hospitalization cost including lower pharmacy and laboratory costs compared to patients in the conservative group. We observed a non-significant 20% reduction in perioperative complications in patients treated with intensive insulin treatment. However, in agreement with previous reports, our analysis of the GLUCO-CABG randomized trial indicates a beneficial impact of intensive control in reducing hospitalization costs due to lower number of perioperative complications, ICU utilization, and longer hospital LOS compared to conservative glucose group. An area of great interest in inpatient and critical care is the increasing evidence that stress hyperglycemia in patients without a history of diabetes undergoing cardiac and general surgery patients is associated with higher mortality, hospital complications, and longer length of hospital stay compared to patients with diabetes (Greco et al., 2016; Kansagara et al., 2011; Umpierrez et al., 2015; van den Berghe et al., 2001). In the present analysis, we observed that intensive glucose reduced complications and hospitalization costs in patients without a history of diabetes (stress hyperglycemia) treated with intensive glucose control; however, these differences did not reach significance, likely due to the relative small number of participants. Larger randomized controlled trials are needed to elucidate the impact of intensive vs. conservative glucose control in reducing complications and hospitalization costs in patients without diabetes and stress hyperglycemia.

We acknowledge several limitations in this economic analysis including the post-hoc analysis and the relative small number of participants. Hospitalization cost data were not available for the entire group of patients recruited in the GLUCO-CABG trial. Data on resource utilization were extracted by electronic health record and billing codes, which may have overlooked some costs as well as nursing time and charges. In addition, healthcare cost during follow-up beyond hospitalization was not collected. Finally, the study was conducted at three medical centers from the same academic institution with extensive experience in inpatient management of hyperglycemia and we used a computerized insulin infusion device (Glucommander) to manage patients in the ICU, thus the findings cannot be generalized to all institutions with less clinical experience or nursing support.

5. Conclusions

In summary, our study indicates that intensive glucose control in patients with hyperglycemia undergoing CABG results in lower hospitalization costs and resource utilization compared to conservative glucose control. The lower hospitalization costs was primarily observed in patients without a history of diabetes (stress hyperglycemia), in whom the intensive control resulted in a significant reduction in perioperative complications, shorter hospital stay, and lower resource utilization compared to patients in the conservative treatment group.

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