Perioperative Glucose Control and Infection Risk in Older Surgical Patients

Pearl Lee · Lillian Min · Lona Mody

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Abstract The aging of the U.S. population is leading to an increasing number of surgical procedures performed on older adults. At the same time, the quality of medical care is being more closely scrutinized. Surgical site infection is a widely-assessed outcome. Evidence suggests that strict perioperative serum glucose control among patients with or without diabetes can lower the risk of these infections, but it is unclear whether this control should be applied to older surgical patients. In this clinical review, we discuss current research on perioperative serum glucose management for cardiothoracic, orthopedic, and general/colorectal surgery. In addition, we summarize clinical recommendations and quality-of-care process indicators provided by surgical, diabetes, and geriatric medical organizations.

Keywords Hyperglycemia · Geriatrics · Surgical site infections

Introduction

Improved life expectancy in the United States has resulted in a substantial increase in the number of surgeries performed on older adults. Over one-third of all surgical procedures occur in adults aged 65 years and older [1], and this proportion is

expected to increase in the coming decades. Because certain cardiothoracic, orthopedic, and general surgical procedures are performed predominantly on older patients, these are surgical areas with particularly high expectations for increased utilization [2].

With the rising number of surgical procedures, prevention of surgical complications such as surgical site infections (SSIs) is becoming increasingly critical. A recent observational study found that SSIs were the most common healthcare-associated infection (HAI), accounting for 31 % of all HAIs among hospitalized patients [3]. SSIs are also costly, as they lead to prolonged hospitalization and high mortality [3]. According to The Joint Commission Surgical Care Improvement Project (SCIP, 2011), these infections are responsible of over 8,200 deaths each year. The Centers for Disease Control and Prevention (CDC) estimates between \$2,734 and \$26,019 of additional cost to the American healthcare system associated with each SSI, with an annual system-wide cost estimate of \$130–\$845 million. SSIs in older patients are likely to involve a prolonged hospital course. For example, SSIs due to *Staphylococcus aureus* are associated with more than five times greater mortality and more than double the postoperative duration of hospitalization of elderly patients without SSIs [4].

Both age and diabetes are two important risk factors for SSIs [5, 6]. Aging is also associated with a high prevalence of diabetes. Type 2 diabetes is one of the most prevalent chronic diseases in the U.S., affecting 13.7 % of adults aged 45–64 years and 27 % aged ≥65 years [7], with an additional 50 % of those aged ≥65 years at risk for developing diabetes [7]. Thus it is critically important to investigate how to best reduce the rate of SSIs among older adults, particularly those with diabetes mellitus. Research has demonstrated that patients with postoperative hyperglycemia, even those with no previous diabetes diagnosis, are at higher risk of SSIs, and therefore current efforts to improve perioperative

P. Lee (✉) · L. Min (✉) · L. Mody
Divisions of Geriatric and Palliative Care Medicine, University of Michigan, Ann Arbor, MI, USA
e-mail: pearllee@umich.edu
e-mail: lmin@med.umich.edu

L. Mody
e-mail: lonamody@umich.edu

P. Lee · L. Min · L. Mody
Geriatric Research Education and Clinical Center, Veteran Affairs
Ann Arbor Healthcare System, Ann Arbor, MI 48109, USA

glucose management target both patients with and without diabetes.

SSI incidence data is widely collected as an outcome measure of surgical quality, an effort spearheaded by the American College of Surgeons (ACS) through the National Surgical Quality Improvement Program (NSQIP). In addition, of nine publicly-reported SCIP measures, six focus on postoperative infection prevention, including control of blood glucose <200 mg/dL during the immediate postoperative period for all cardiothoracic surgery patients [8].

In this paper, we discuss recent evidence with regard to the risk of hyperglycemia and SSIs in older surgical patients during the perioperative period, with a focus on general, cardiothoracic, and orthopedic surgical procedures. We also review care process guidelines and quality indicators, as well as strategies and goals for management of hyperglycemia during perioperative periods in patients with or without diabetes.

Hyperglycemia as a Risk Factor for Surgical Site Infections

Hyperglycemia occurs frequently in critically ill patients both with and without diabetes mellitus, leading to significant morbidity and mortality. Uncontrolled hyperglycemia is a well-established risk factor for postoperative infection following various surgical procedures [9, 10]. The literature shows that over one-third of all patients admitted to the hospital without a history of diabetes are hyperglycemic [11]. These patients are also at risk of longer hospital stays, higher intensive care unit (ICU) admissions, and increased morbidity and mortality [12].

The perioperative period is often associated with poor oral intake in the setting of increased metabolic demand. The human body generally responds by resorting to gluconeogenesis from various amino acids and glycerol glycogenolysis, as well as utilization of fat stores. Patients with reduced glucose tolerance can be “pushed over” into hyperglycemia by this increase. This phenomenon can occur irrespective of a preexisting history of diabetes [13–15]. In addition, the physiologic stress response to surgery (or the acute condition leading up to surgery) results in alteration of endogenous hormone production, including increased serum cortisol production, insulin resistance, release of proinflammatory cytokines, and nervous system signals on metabolic pathways. Thus hyperglycemia can occur even in patients with previously undiagnosed diabetes [13]. Hyperglycemia, in turn, is known to interfere with monocyte and neutrophil function, which increases the risk of infection [16].

Elevated serum glucose levels after injury are associated with several adverse events, including a substantially increased risk of infectious complications, prolonged hospital

stay, and death [12]. What is less clear is whether hyperglycemia leads to an infection or whether an infection reflects the magnitude of systemic inflammation due to an injury. Patients with posttraumatic sepsis may demonstrate hyperglycemia that requires new or escalating insulin therapy [13].

Hyperglycemia increases the risks of infections in surgical patients. A large prospective randomized clinical trial of patients in a surgical critical care unit found that intensive insulin therapy to maintain blood glucose ≤ 110 mg/dL reduces mortality and morbidity, including bloodstream infections. SSIs were not assessed [17]. The findings on the association between hyperglycemia and SSIs are primarily based on studies on cardiothoracic patients [21, 28, 30]. Kao et al. [18] performed a systematic review of randomized controlled trials addressing perioperative glycemic control among surgical patients, and identified that three out of five trials were conducted among cardiothoracic patients.

Perioperative Hyperglycemia and Surgical Site Infections

Cardiothoracic Surgery

The majority of cardiothoracic surgeries are performed on patients aged 65 years or older. Due to the aging of the U.S. population, the number of cardiothoracic surgeries is forecast to be 42 % higher in 2020 than in 2001 [2]. The most common comorbidity among patients undergoing coronary artery bypass grafting (CABG) is diabetes, with a prevalence reported as high as 34 % [19]. Historically, diabetic patients have had poorer post-CABG outcomes, such as superficial and deep sternal wound infections, urinary tract infections, postoperative stroke, and early mortality, when compared to patients without diabetes [20–22]. Patients who have no previous diabetes diagnosis but who develop hyperglycemia during cardiac surgeries such as CABG also suffer poor outcomes [23]. Perioperative hyperglycemia is associated with greater healthcare utilization in patients undergoing CABG as well [24].

In a retrospective chart review of diabetic patients undergoing CABG (mean age 65 years), the risk of sternal wound infections increased from 1.3 % in patients with mean postoperative glucose values of 100–150 mg/dL to 6.7 % in patients with mean postoperative glucose values of 250–300 mg/dL [25]. Additionally, among CABG patients with diabetes (mean age 62 years), a continuous insulin infusion maintaining glucose levels at 120–160 mg/dL was associated with a significant reduction in the incidence of sternal wound infections compared with intermittent subcutaneous injections [26].

A number of randomized controlled trials and observational studies [21, 27–29] have demonstrated that keeping perioperative serum glucose levels below 200 mg/dL can help reduce the risk of deep sternal wound infections. However,

these studies have substantial heterogeneity with regard to their study protocols and primarily involve younger adults (mean age 63–65 years). Some studies, for example, exclusively enrolled patients with diabetes, whereas others included patients both with and without diabetes. Protocols varied from initiation of tight glycemic control at 24 hours prior to surgery to concurrent with surgery. The end time for tight glucose control varied from 18 to 24 hours after surgery. Serum glucose levels were managed by either continuous insulin infusion or by sliding-scale insulin. The target serum glucose levels ranged from 80–100 mg/dL in one study to <200 mg/dL in another. While most studies found reduced risk of SSIs with glucose control, it is important to note that tight glucose control during cardiac surgery may lead to higher rates of other types of adverse outcomes, including stroke and death [30].

Based on the above findings, the Society of Thoracic Surgeons (STS) [31] recommends maintaining serum glucose levels below 180 mg/dL for the duration of postoperative care for all adults, both with and without diabetes mellitus, who undergo cardiac surgery. Furthermore, insulin infusions, as opposed to intermittent subcutaneous insulin injections or intermittent IV insulin boluses, are the preferred method to manage hyperglycemia during this period. All patients with diabetes undergoing cardiac surgical procedures should receive an insulin infusion in the operating room and for at least 24 hours postoperatively to maintain serum glucose levels ≤ 180 mg/dL.

The Society for Healthcare Epidemiology of America (SHEA) has slightly different recommendations [32]. They recommend controlling glucose levels during the immediate postoperative period for patients undergoing cardiac surgery by maintaining a postoperative serum glucose level of less than 200 mg/dL. The measurement starts at 6:00 a.m. on postoperative days (PODs) 1 and 2, with the procedure day considered as postoperative day 0. One of the core SCIP measures is the percentage of cardiothoracic surgery patients with 6:00 a.m. serum glucose levels <200 mg/dL on PODs 1 and 2. Compliance with this quality measure is publicly reported on the Centers for Medicare and Medicaid Services website and is used to determine monetary reimbursement for participating hospitals.

Orthopedic Surgery

In 2003 in the U.S., 202,500 primary total hip arthroplasties and 402,100 primary total knee arthroplasties were performed, as well as 36,000 revision total hip arthroplasties and 32,700 revision total knee arthroplasties. By 2030, the number of primary total knee and hip arthroplasties is projected to reach 4 million [33]. Among Medicare beneficiaries, 188,000 underwent primary hip arthroplasty in 1991, and this number grew to 279,000 in 2008 [34•]. The prevalence of concurrent diabetes mellitus in these patients increased from 7 % to 15 %

between 1991 and 2008 [34•]. Retrospective data analysis of orthopedic spinal surgeries (mean age 52.4 years, range 15.2–94.4 years) found that diabetes and perioperative hyperglycemia were the two leading risk factors for SSIs [9].

From 1991 to 2008, the postoperative infection rate among patients who underwent primary hip arthroplasty improved significantly, from 0.8 % to 0.6 % ($p < .0001$), while the rate increased among those who underwent revision of arthroplasty [34•]. Among those who underwent primary hip arthroplasty during this period, the number of comorbidities increased from 1.1 to 2.0, and the proportion of patients with comorbid diabetes increased from 7.3 % to 15 % (all $p < .001$) [34•]. In the U.S., more than 8 % of patients undergoing primary or revision total hip and knee arthroplasty had diabetes [35]. Similar to diabetic patients who underwent cardiothoracic surgeries, these patients had increased odds of specific perioperative complications such as pneumonia and need for transfusion, and experienced greater incidence of stroke, urinary tract infection, and ileus ($p > .001$), as well as a number of other perioperative complications [36]. Hyperglycemia is associated with increased risk of infectious complications in nondiabetic hyperglycemic trauma patients [37, 38]. In a large retrospective review of adults (mean age 47.7 years) without diabetes and requiring acute orthopedic intervention, hyperglycemia (serum glucose ≥ 140 mg/dL) was an independent predictor of 30-day SSI [39]. Patients in intensive care were excluded in this study.

We were unable to identify any randomized controlled trials that investigated the effect of perioperative glucose control in reducing the risk of SSIs. Due to a lack of evidence, there is no consensus on glycemic goals for the perioperative period in patients undergoing orthopedic surgery. For patients who are critically ill, a consensus statement of the American Association of Clinical Endocrinologists and the American Diabetes Association recommends initiating hyperglycemia treatment at a threshold of 180 mg/dL, preferably with IV insulin therapy, and maintaining glucose level at 140–180 mg/dL [40].

General Surgery

In 1996, over half of the general surgeries in the U.S. were performed on patients aged 65 years or older. The aging of the population is anticipated to lead to at least a 30 % increase in colorectal surgeries from 2005 to 2025 [41]. Perioperative hyperglycemia is common among patients who undergo general surgeries. In one series, postoperative serum glucose levels greater than 140 mg/dL were present in as many as 40 % of non-cardiac surgery patients, and 25 % of those patients had serum glucose levels above 180 mg/dL [42].

Several recent studies link perioperative hyperglycemia with increased risk of SSI among general surgery patients. Kwon et al. [43••] analyzed data from the Surgical Care and

Outcomes Assessment Program (SCOAP), a statewide quality improvement activity implemented in hospitals in Washington. They evaluated the relationship of perioperative hyperglycemia (>180 mg/dL) and insulin administration on mortality, reoperative interventions, and infections for patients undergoing elective colorectal and bariatric surgery between 2005 and 2010. Patients with perioperative hyperglycemia (>180 mg/dL) from the day of surgery to POD 2 were older than those with normal glucose level (age 58 ± 14 years vs. 53 ± 16 years, $p < .001$). The unadjusted rate of composite infections (6.0 % vs. 3.4 %, $p < .001$) was higher among those who had hyperglycemia at any of the three time points: day of surgery, POD 1, or POD2. After controlling for clinical factors, those with hyperglycemia had a significantly increased risk of infection (odds ratio [OR] 2.0; 95 % confidence interval [CI], 1.63–2.44), and this was true for patients both with and without diabetes. Those with hyperglycemia on the day of surgery who received insulin had no significant increase in infections (OR 1.01; 95 % CI, 0.72–1.42). A dose-effect relationship was found between the effectiveness of insulin-related glucose control and increased risk of infection, a 1.07-fold increase in the odds per 10-unit increase in highest postoperative glucose between <130 and >250 mg/dL.

Ata et al. [44] analyzed a sample of adults from the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database who underwent colorectal or vascular surgery. The mean age of the study sample was not reported. The overall SSI rate in the study sample was 7.42 %. Colorectal surgery patients were 3.6 times more likely (95 % CI, 2.3–5.7 times; infection rate 14 %) to develop an SSI than non-colorectal general surgery patients. The authors found that among colorectal surgery patients, a postoperative serum glucose level higher than 140 mg/dL was the only significant predictor of SSI. The incidence of infection in colorectal surgery patients with postoperative serum glucose levels higher than 140 mg/dL (20.6 %) was 3.2 times (95 % CI, 1.4–7.2 times) that of those with serum glucose levels of 140 mg/dL or less (7.6 %). Kiran et al. [45] performed a retrospective analysis using data from a single tertiary medical center, including over 2,000 consecutive patients who underwent elective colorectal surgeries. They found that among nondiabetic patients, postoperative hyperglycemia was significantly associated with infectious and noninfectious complications and mortality (mean age 50 ± 17 years). As noted by Ata et al. [44], there is a need for large prospective randomized controlled trials among general surgery patients to investigate whether tighter control of perioperative hyperglycemia may lead to better outcomes. Studies in the literature are either limited in sample size or focused on surgical critical care.

Two groups have proposed measures of appropriate glucose control among older adults undergoing general or colorectal surgery. McGory et al. [46] developed quality indicators using literature review and the RAND /UCLA

Appropriateness Method, convening an expert panel of physicians in surgery, geriatrics, anesthesia, critical care, and internal and rehabilitation medicine. They rated a modestly aggressive measure to maintain POD 1 and 2 serum glucose <200 mg/dL as appropriate for patients with diabetes undergoing elective or urgent surgery [46]. Using similar methods, the Assessing Care of Vulnerable Elders (ACOVE) study found a similar appropriate measure to maintain serum glucose levels of <200 mg/dL among vulnerable diabetic patients who are hospitalized and undergoing surgery (Table 1) [47].

Research Gaps

Older patients with postoperative hyperglycemia are at higher risk of infection, irrespective of preoperative diagnosis of diabetes. In this review, we found a number of clinical trials demonstrating that treatment of perioperative hyperglycemia results in fewer SSIs. However, these trials do not focus on older adults or adults with multiple comorbidities. Older adults undergo the majority of cardiothoracic, orthopedic, and general surgical procedures, but the studies that we reviewed had a mean age of 65 years or younger. The oldest old, or those aged 75 years and older, will constitute a large portion of surgical patients in the near future. Effective and safe strategies to reduce the risk of post-surgical SSIs among these oldest patients have not been addressed in current studies. Furthermore, the optimal target for glucose control remains uncertain. One trial demonstrated that lowering glucose to near normal level (80–100 mg/dL) during cardiac surgery actually led to more strokes and death [30]. A more modest approach (controlling to <200 mg/dL, and for those with diabetes only) was found to be appropriate by two expert panels focused on older surgical patients (Table 1) [46, 47].

From our analysis, we have identified three gaps in the available research. First, in contrast to elective surgeries, emergency surgeries pose a dramatically greater risk of infection [44]. We cannot conclude from the current research whether postoperative glucose control should differ between older patients with elective versus urgent or emergent surgeries. We expect that the greater physiological response to stress due to preoperative emergency would predispose older patients to higher glucose levels, but further research is needed to determine whether this translates into differences in recommended protocols (e.g., tighter control for patients with emergency surgery).

Second, controlled trials are needed with varying postoperative glycemic control as targets, particularly involving elective general and colorectal surgery, and should include older age groups. Current studies have combined different surgeries to ensure adequate sample size. Multi-center collaborations may be necessary to obtain meaningful results.

Table 1 Recommended control of perioperative and postoperative hyperglycemia in selected major guidelines by professional societies

Source	Patients	Hyperglycemia management	Serum glucose goal	Duration of intense glucose management
Society of Thoracic Surgeons (STS) Practice Guidelines [31]	All adults undergoing cardiac surgery, with or without diabetes mellitus	Insulin infusions preferred over intermittent subcutaneous insulin injections or intermittent IV insulin boluses	Maintain serum glucose levels <180 mg/dL	For at least 24 hours postoperatively
American Association of Clinical Endocrinologists and the American Diabetes Association [40]	All critically ill patients Non-critically ill patients	Preferably with IV insulin therapy Scheduled administration of subcutaneous insulin with a basal, a nutritional, and a supplemental (correction) element	Start hyperglycemia treatment at a threshold of 180 mg/dL, and maintain glucose level at 140–180 mg/dL Pre-meal glucose targets should generally be <140 mg/dL (<7.8 mmol/L) in conjunction with random BG values <180 mg/dL (<10.0 mmol/L), as long as these targets can be safely achieved	–
Society for Healthcare Epidemiology of America (SHEA) [32]	All adults undergoing cardiac surgery	NS	<200 mg/dL at 6:00 a.m. PODs 1 and 2	PODs 1 and 2
Surgical Care Improvement Program (SCIP) [8]	All adults undergoing cardiac surgery	NS	<200 mg/dL	PODs 1 and 2
McGory et al. RAND/UCLA quality indicators for postoperative management [46]	Older patients with diabetes mellitus undergoing any inpatient surgery	NS	All postoperative glucose should be <200 mg/dL on PODs 1 and 2	PODs 1 and 2
Medical-surgical hospital indicators from the Assessing Care of Vulnerable Elders (ACOVE) study [47]	Vulnerable ^a older patients with diabetes undergoing surgery	NS	<200 mg/dL	On the day of surgery and PODs 1 and 2

BG blood glucose, PODs postoperative days, NS not specified

^a“Vulnerable” elders are defined by functional and physical impairments, self-rated health, and age, using the Vulnerable Elders-13 Survey [48]

Lastly, there is a need for research on the optimal monitoring of glucose level among older surgery patients to prevent hypoglycemia. While serum glucose is typically reported in the literature as the target glucose level to achieve, it is often measured once a day, and therefore may not be an effective measurement to monitor for hypoglycemia. There is also little evidence of the ideal time of day or length of intervals for collecting postoperative serum glucose measurements and for how many days the tight control should continue. Continuous glucose monitoring system or frequent finger blood glucose checks may need to be implemented to minimize hypoglycemia risk.

Challenges of Glucose Control in Aging Populations

Perioperative glucose control in older adults poses unique challenges. We suggest four caveats that should be contemplated when considering across-the-board protocols regarding glucose control measures for older surgical patients. First, older adults are particularly vulnerable to developing hypoglycemia due to age-associated reduced ability to counter-regulate hypoglycemia. Aging is associated with decreased β -adrenergic receptor function [49]. As a result, the sympathoadrenal system that stimulates catecholamine secretion to induce the rapid elevation of blood glucose levels is less effective. Aging is also associated with reduced glucagon response to hypoglycemia [50], and elderly adults with non-insulin-dependent diabetes have further impaired glucagon response to hypoglycemia when compared to age-matched control subjects [51]. Growth hormone responses to glucagon have been shown to reduce with aging [51], and they are further impaired in older diabetic adults. Epinephrine and cortisol responses are similar or reduced in older adults with diabetes [51].

Second, aging is associated with reduced renal function. Renal function can change rapidly when one is acutely ill or on multiple medications. Insulin is the most common method for controlling perioperative hyperglycemia. There is an inherently higher risk of hypoglycemia due to renal insufficiency [52]. Furthermore, older adults are at greater risk of developing ileus and delirium postoperatively, potentially resulting in poor oral intake and reduced ability to communicate early hypoglycemia symptoms to medical staff, further increasing the risk of hypoglycemia.

Third, increased vigilance is necessary for older patients with postoperative delirium or with preexisting dementia. The disorientation and decreased attention that are hallmarks of delirium may distract from proper medical detection of hypoglycemic symptoms. Patients with advanced dementia may not be able to communicate their symptoms or needs (e.g., symptoms of hypoglycemia or hunger) to healthcare providers [53, 54]. We recommend screening for cognitive impairment in older preoperative patients with diabetes. Nearly one-quarter of older patients with diabetes have cognitive

impairment [55]. Patients undergoing surgery who have a history of cognitive impairment and those with undiagnosed cognitive impairment are at increased risk of delirium. In a small study of diabetic patients undergoing CABG surgery ($n=82$), aggressive serum glucose control (90–120 mg/dL) actually increased the incidence of hypoglycemic events and did not result in any significant improvement in clinical outcomes with moderate control (120–180 mg/dL) [56••]. We posit that older adults on postoperative protocols to tightly control their glucose levels should have regular daily screening for mild symptoms of delirium (such as using the Confusion Assessment Method [Inouye, 1990]). A “geriatric” postoperative glucose control protocol should include increased frequency of glucose monitoring if delirium is detected.

Fourth, multimorbidity (i.e., two or more chronic conditions) is common in older adults. Two-thirds of Medicare beneficiaries have two or more chronic diseases, and 43 % have three or more [58]. Older persons with diabetes are particularly at risk for multiple morbidities and disabilities [59–62]. The presence of multiple concurrent comorbidities such as diabetes, chronic kidney disease, autonomic neuropathy, and dementia or cognitive impairment may complicate both management of glucose levels and detection of hypoglycemia. As patients with multiple conditions have historically not been included in clinical trials, we recommend consideration of individual case complexity and greater caution rather than across-the-board protocols to control glucose levels in older surgical patients.

Conclusion

While there is compelling evidence to support postoperative hyperglycemia control among cardiac surgery patients in order to reduce the risk for SSIs, further studies are needed in older orthopedic and general surgery patients. Future clinical trials should emphasize older adults, including oldest old (>75 years), as well as patients with multiple morbidities. Better protocols and quality measures must be developed to prevent hypoglycemic sequelae in older patients if tight glucose control protocols are implemented across surgery types.

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Compliance with Ethics Guidelines

Conflict of Interest Pearl Lee, Lillian Min, and Lona Mody declare that they have no conflict of interest.

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References

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

1. NCHS National Hospital Discharge Survey. CDC, 2010. 2014, at http://www.cdc.gov/nchs/data/nhds/4procedures/2010pro4_numberprocedureage.pdf.
2. Etzioni DA, Liu JH, Maggard MA, Ko CY. The aging population and its impact on the surgery workforce. *Ann Surg*. 2003;238:170–7.
3. Awad SS. Adherence to surgical care improvement project measures and post-operative surgical site infections. *Surg Infect*. 2012;13:234–7.
4. McGarry SA, Engemann JJ, Schmader K, Sexton DJ, Kaye KS. Surgical-site infection due to *Staphylococcus aureus* among elderly patients: mortality, duration of hospitalization, and cost. *Infect Control Hosp Epidemiol*. 2004;25:461–7.
5. Kaye KS, Schmit K, Pieper C, et al. The effect of increasing age on the risk of surgical site infection. *J Infect Dis*. 2005;191:1056–62.
6. Cheadle WG. Risk factors for surgical site infection. *Surg Infect*. 2006;7 Suppl 1:S7–11.
7. National diabetes fact sheet, 2011. Centers for Disease Control and Prevention. (Accessed May 29, 2012, at http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf).
8. Surgical Care Improvement Program-Inf-4-9. Specifications Manual for National Hospital Quality Indicators. (Accessed January 12, 2014, at http://www.jointcommission.org/specifications_manual_for_national_hospital_inpatient_quality_measures.aspx).
9. Olsen MA, Nepple JJ, Riew KD, et al. Risk factors for surgical site infection following orthopaedic spinal operations. *J Bone Joint Surg Am*. 2008;90:62–9.
10. Rizvi AA, Chillag SA, Chillag KJ. Perioperative management of diabetes and hyperglycemia in patients undergoing orthopaedic surgery. *J Am Acad Orthop Surg*. 2010;18:426–35.
11. Fish LH, Moore AL, Morgan B, Anderson RL. Evaluation of admission blood glucose levels in the intensive care unit. *Endocr Pract*. 2007;13:705–10.
12. Umpierrez GE, Isaacs SD, Bazargan N, You X, Thaler LM, Kitabchi AE. Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. *J Clin Endocrinol Metab*. 2002;87:978–82.
13. Long CL, Spencer JL, Kinney JM, Geiger JW. Carbohydrate metabolism in man: effect of elective operations and major injury. *J Appl Physiol*. 1971;31:110–6.
14. Epstein J, Breslow MJ. The stress response of critical illness. *Crit Care Clin*. 1999;15:17–33.
15. Schricker T, Lattermann R, Schreiber M, Geisser W, Georgieff M, Radermacher P. The hyperglycaemic response to surgery: pathophysiology, clinical implications and modification by the anaesthetic technique. *Clin Intensive Care*. 1998;9:118–28.
16. Delamaire M, Maugendre D, Moreno M, Le Goff MC, Allannic H, Genetet B. Impaired leucocyte functions in diabetic patients. *Diabet Med*. 1997;14:29–34.
17. van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in critically ill patients. *N Engl J Med*. 2001;345:1359–67.
18. Kao LS, Meeks D, Moyer VA, Lally KP. Peri-operative glycaemic control regimens for preventing surgical site infections in adults. *The Cochrane database of systematic reviews* 2009;8:CD006806.
19. Lauruschkat AH, Arnrich B, Albert AA, et al. Prevalence and risks of undiagnosed diabetes mellitus in patients undergoing coronary artery bypass grafting. *Circulation*. 2005;112:2397–402.
20. Guvener M, Pasaoglu I, Demircin M, Oc M. Perioperative hyperglycemia is a strong correlate of postoperative infection in type II diabetic patients after coronary artery bypass grafting. *Endocr J*. 2002;49:531–7.
21. Furnary AP, Zerr KJ, Grunkemeier GL, Starr A. Continuous intravenous insulin infusion reduces the incidence of deep sternal wound infection in diabetic patients after cardiac surgical procedures. *Ann Thorac Surg*. 1999;67:352–60. discussion 60–2.
22. Krinsley JS. Association between hyperglycemia and increased hospital mortality in a heterogeneous population of critically ill patients. *Mayo Clin Proc*. 2003;78:1471–8.
23. Doenst T, Wijesundera D, Karkouti K, et al. Hyperglycemia during cardiopulmonary bypass is an independent risk factor for mortality in patients undergoing cardiac surgery. *J Thorac Cardiovasc Surg*. 2005;130:1144.
24. Estrada CA, Young JA, Nifong LW, Chitwood Jr WR. Outcomes and perioperative hyperglycemia in patients with or without diabetes mellitus undergoing coronary artery bypass grafting. *Ann Thorac Surg*. 2003;75:1392–9.
25. Zerr KJ, Furnary AP, Grunkemeier GL, Bookin S, Kanhere V, Starr A. Glucose control lowers the risk of wound infection in diabetics after open heart operations. *Ann Thorac Surg*. 1997;63:356–61.
26. Hruska LA, Smith JM, Hendy MP, Fritz VL, McAdams S. Continuous insulin infusion reduces infectious complications in diabetics following coronary surgery. *J Cardiac Surg*. 2005;20:403–7.
27. Gandhi GY, Nuttall GA, Abel MD, et al. Intraoperative hyperglycemia and perioperative outcomes in cardiac surgery patients. *Mayo Clin Proc*. 2005;80:862–6.
28. Lazar HL, Chipkin SR, Fitzgerald CA, Bao Y, Cabral H, Apstein CS. Tight glycemic control in diabetic coronary artery bypass graft patients improves perioperative outcomes and decreases recurrent ischemic events. *Circulation*. 2004;109:1497–502.
29. Li JY, Sun S, Wu SJ. Continuous insulin infusion improves post-operative glucose control in patients with diabetes mellitus undergoing coronary artery bypass surgery. *Tex Heart Inst J*. 2006;33:445–51.
30. Gandhi GY, Nuttall GA, Abel MD, et al. Intensive intraoperative insulin therapy versus conventional glucose management during cardiac surgery: a randomized trial. *Ann Intern Med*. 2007;146:233–43.
31. Lazar HL, McDonnell M, Chipkin SR, et al. The Society of Thoracic Surgeons practice guideline series: blood glucose management during adult cardiac surgery. *Ann Thorac Surg*. 2009;87:663–9.
32. Anderson DJ, Kaye KS, Classen D, et al. Strategies to prevent surgical site infections in acute care hospitals. *Infect Control Hosp Epidemiol*. 2008;29 Suppl 1:S51–61.
33. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am*. 2007;89:780–5.
34. Wolf BR, Lu X, Li Y, Callaghan JJ, Cram P. Adverse outcomes in hip arthroplasty: long-term trends. *J Bone Joint Surg Am*. 2012;94:e103. *In a retrospective, observational study of a large cohort of >1 million Medicare patients who underwent primary total hip arthroplasty and revision total hip arthroplasty between 1991 and 2008, the authors identified that these patient are having increasing number of medical co-morbidities. While the surgical outcomes from primary hip arthroplasty are improving, outcomes from*

- revisions are worsening, probably a reflection of more complex medical and surgical conditions among these patients.
35. Bolognesi MP, Marchant Jr MH, Viens NA, Cook C, Pietrobon R, Vail TP. The impact of diabetes on perioperative patient outcomes after total hip and total knee arthroplasty in the United States. *J Arthroplasty*. 2008;23:92–8.
 36. Wimmer C, Gluch H, Franzreb M, Ogon M. Predisposing factors for infection in spine surgery: a survey of 850 spinal procedures. *J Spinal Disord*. 1998;11:124–8.
 37. Mraovic B, Suh D, Jacovides C, Parvizi J. Perioperative hyperglycemia and postoperative infection after lower limb arthroplasty. *J Diabetes Sci Technol*. 2011;5:412–8.
 38. Karunakar MA, Staples KS. Does stress-induced hyperglycemia increase the risk of perioperative infectious complications in orthopaedic trauma patients? *J Orthop Trauma*. 2010;24:752–6.
 39. Richards JE, Kauffmann RM, Zuckerman SL, Obremskey WT, May AK. Relationship of hyperglycemia and surgical-site infection in orthopaedic surgery. *J Bone Joint Surg Am*. 2012;94:1181–6.
 40. Moghissi ES, Korytkowski MT, DiNardo M, et al. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. *Endocr Pract*. 2009;15:353–69.
 41. Etzioni DA, Beart Jr RW, Madoff RD, Ault GT. Impact of the aging population on the demand for colorectal procedures. *Dis Colon Rectum*. 2009;52:583–90. discussion 60–2.
 42. Frisch A, Chandra P, Smiley D, et al. Prevalence and clinical outcome of hyperglycemia in the perioperative period in noncardiac surgery. *Diabetes Care*. 2010;33:1783–8.
 43. Kwon S, Thompson R, Dellinger P, Yanez D, Farrohi E, Flum D. Importance of perioperative glycemic control in general surgery: a report from the Surgical Care and Outcomes Assessment Program. *Ann Surg*. 2013;257:8–14. *In a retrospective cohort study of over 11,000 patients in the Surgical Care and Outcomes Assessment Program from 2005–2010, the authors found that perioperative hyperglycemia (>180 mg/dL) was associated with worse outcomes (e.g., infections) following elective colorectal or bariatric surgeries. This result was similar among both diabetic and non-diabetic patients, supporting the treatment of perioperative hyperglycemia.*
 44. Ata A, Lee J, Bestle SL, Desemone J, Stain SC. Postoperative hyperglycemia and surgical site infection in general surgery patients. *Arch Surg*. 2010;145:858–64.
 45. Kiran RP, Turina M, Hammel J, Fazio V. The clinical significance of an elevated postoperative glucose value in nondiabetic patients after colorectal surgery: evidence for the need for tight glucose control? *Ann Surg*. 2013;258:599–604. discussion 60–2.
 46. McGory ML, Kao KK, Shekelle PG, et al. Developing quality indicators for elderly surgical patients. *Ann Surg*. 2009;250:338–47.
 47. Arora VM, McGory ML, Fung CH. Quality indicators for hospitalization and surgery in vulnerable elders. *J Am Geriatr Soc*. 2007;55 Suppl 2:S347–58.
 48. Saliba D, Elliott M, Rubenstein LZ, et al. The Vulnerable Elders Survey: a tool for identifying vulnerable older people in the community. *J Am Geriatr Soc*. 2001;49:1691–9.
 49. Heinsimer JA, Lefkowitz RJ. The impact of aging on adrenergic receptor function: clinical and biochemical aspects. *J Am Geriatr Soc*. 1985;33:184–8.
 50. Marker JC, Cryer PE, Clutter WE. Attenuated glucose recovery from hypoglycemia in the elderly. *Diabetes*. 1992;41:671–8.
 51. Meneilly GS, Cheung E, Tuokko H. Counterregulatory hormone responses to hypoglycemia in the elderly patient with diabetes. *Diabetes*. 1994;43:403–10.
 52. Rabkin R, Ryan MP, Duckworth WC. The renal metabolism of insulin. *Diabetologia*. 1984;27:351–7.
 53. Brauner DJ, Muir JC, Sachs GA. Treating nondementia illnesses in patients with dementia. *JAMA*. 2000;283:3230–5.
 54. Murdoch BE, Chenery HJ, Wilks V, Boyle RS. Language disorders in dementia of the Alzheimer type. *Brain Lang*. 1987;31:122–37.
 55. Lee PG, Cigolle CT, Ha J, et al. Physical function limitations among middle-aged and older adults with prediabetes: one exercise prescription may not fit all. *Diabetes Care*. 2013;36:3076–83.
 56. Lazar HL, McDonnell MM, Chipkin S, Fitzgerald C, Bliss C, Cabral H. Effects of aggressive versus moderate glycemic control on clinical outcomes in diabetic coronary artery bypass graft patients. *Ann Surg*. 2011;254:458–63; discussion 63–4. *In a sample of 82 diabetic patients who underwent coronary artery bypass grafts, sternal infection rate and 30-day mortality were similar for two glycemic groups (90–120mg/dL vs. <180 mg/dL). However, the more aggressive groups (i.e., glucose 90–120mg/dL) had significantly more hypoglycemic events, suggesting that lowering post-operative glucose to near normal range may not be beneficial for CABG patients, and actually may be harmful.*
 57. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegel AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Ann Intern Med*. 1990;113:941–8.
 58. Wolff JL, Starfield B, Anderson G. Prevalence, expenditures, and complications of multiple chronic conditions in the elderly. *Arch Intern Med*. 2002;162:2269–76.
 59. Schwartz AV, Hillier TA, Sellmeyer DE, et al. Older women with diabetes have a higher risk of falls: a prospective study. *Diabetes Care*. 2002;25:1749–54.
 60. Songer TJ. Disability in diabetes. In: Harris MICCC, Stern MP, et al., editors. *Diabetes in America*. 2nd ed. Bethesda: National Institutes of Health; 1995. p. 259–82.
 61. Gavard JA, Lustman PJ, Clouse RE. Prevalence of depression in adults with diabetes: an epidemiological evaluation. *Diabetes Care*. 1993;16:1167–78.
 62. Gregg EW, Yaffe K, Cauley JA, et al. Is diabetes associated with cognitive impairment and cognitive decline among older women? *Arch Intern Med*. 2000;160:174.