

# Tight Glucose Control May Harm Critically Ill

BY MARY ANN MOON  
Contributing Writer

**T**ight glucose control does not benefit critically ill patients and may even be harmful because it markedly raises the risk of hypoglycemia, according to a meta-analysis.

Given these findings, "it seems appropriate that the guidelines recommending tight glucose control in all critically ill patients should be reevaluated until the results of larger, more definitive clinical trials are available," said Dr. Renda Soylemez Wiener of the Veterans Affairs Medical Center, White River Junction, Vt., and her associates.

In 2001, a single clinical trial showed that tight glucose control reduced in-hospital mortality by a third among critically ill surgical patients. "The results of this trial were enthusiastically received and rapidly incorporated into guidelines," and tight glucose control is now recommended for all critically ill adults and endorsed by numerous professional societies worldwide.

However, "subsequent large randomized controlled trials of tight glucose control in medical and mixed medical-surgical ICU settings ... have failed to replicate this mortality benefit," and many have reported rates of hy-

poglycemia as high as 40%. "Hypoglycemia is not benign in critically ill patients; it has been linked to serious neurologic events ranging from seizures to coma," the investigators noted.

They conducted a meta-analysis of 29 controlled trials involving 8,432 adult ICU patients with a wide range of disorders who were randomly assigned to either usual care or tight glucose control—a glucose goal of less than 150 mg/dL using an insulin infusion during part or all of the ICU stay.

In-hospital mortality was not significantly different for patients kept on tight glucose control (21.6%) than for those given usual care (23.3%). There also was no difference between the two groups in the need for dialysis, Dr. Soylemez Wiener and her associates said (JAMA 2008;300:933-44).

In subgroup analyses, tight glucose control did not benefit surgical patients vs. medical patients, nor did "very tight" glucose control prove more beneficial than "moderately tight" glucose control. Sensitivity analyses of the data based on several variables that might be clinically relevant, such as disease severity, did not alter these results.

Tight glucose control did reduce the incidence of septicemia, but only among surgical ICU patients.

"On the other hand, we found clear evidence of the

main harm of tight glucose control: Hypoglycemia increased roughly fivefold regardless of the ICU setting and was more common with patients receiving very tight [rather] than moderately tight glucose control," the researchers added.

"Our meta-analysis shows that subsequent trials have not borne out the impressive results of tight glucose control promised by the initial trial" in 2001. In fact, the subjects in that initial trial received early glucose infusions and parenteral nutrition, both of which might artificially induce hyperglycemia and both of which are atypical in clinical practice. This "may have contributed to the outlying results seen in [that] trial," the researchers noted.

In an accompanying editorial comment, Dr. Simon Finfer and Dr. Anthony Delaney of the Royal North Shore Hospital, Sydney, said that the results of this "well-conducted" and "timely" meta-analysis "may surprise many clinicians" (JAMA 2008;300:963-5).

Not only does the meta-analysis call the benefit of tight glucose control into question, it also highlights that there is no agreed standard for glycemic control, that blood glucose levels are extremely variable during the course of an ICU stay, and that bedside measurement of blood glucose can be very inaccurate, Dr. Finfer and Dr. Delaney said. ■

## Vascular Surgery Outcomes Differ by Obesity Classification

BY DOUG BRUNK  
San Diego Bureau

SAN DIEGO — Underweight patients have poorer overall outcomes in vascular surgery, yet morbidly obese patients have increased morbidity, primarily due to wound infections, renal complications, and thromboembolic complications, results from a multicenter analysis showed.

"There are no large studies on the effect of obesity on vascular surgery," Dr. Eleftherios S. Xenos said at the Vascular Annual Meeting. "There is some agreement that wound infection tends to be higher in obese patients, but in terms of mortality there has not been a definite answer."



Dr. Xenos and his associates queried the Patient Safety in Surgery Study Database for a sample of major vascular procedures performed at 14 academic medical centers in the United States between 2002 and 2004. They obtained data on 7,543 vascular surgery patients that included the National Surgical Quality Improvement Program (NSQIP) clinical definitions of patient risk factors and 30-day outcomes.

Of the 7,543 patients, 4.6% were underweight (body mass index [BMI] of less than 18.5 kg/m<sup>2</sup>), 34.7% were normal weight (18.5-25 kg/m<sup>2</sup>), 34.9% were overweight (25.1-30 kg/m<sup>2</sup>), 16.3% were obese I (30.1-35 kg/m<sup>2</sup>), 5.7% were obese II (35.1-40 kg/m<sup>2</sup>), and 3.8% were obese III (greater than 40 kg/m<sup>2</sup>), reported Dr. Xenos of the department of surgery at the University of Kentucky, Lexington.

Vascular procedures performed included lower extremity revascularization (24.5%), aneurysm repair (17.4%), cerebrovascular procedures (17.3%), amputations (9.4%), and "other" (31.4%).

Within 30 days after surgery, 1,659 patients (22%) developed complications and 295 (3.9%) died.

As expected, risk factors for hypertension and diabetes increased with increasing BMI. However, rates of smoking, stroke, and recent weight loss—defined as more than 10% of body weight—decreased as BMI increased.

The top three NSQIP predictors of vascular surgery mortality were presence of preoperative sepsis, American Society of Anesthesiologists' physical status classification, and functional de-

pendence. "For these three risk factors, the overweight and obese I patients had the least amount of risk, with the highest risk in the underweight category," Dr. Xenos said.

"The overweight and obese I category patients had a significantly higher albumin level, as compared with normal class patients," Dr. Xenos reported.

The distribution of major complications among patients was U-shaped, with a higher incidence of complications among underweight patients and the lowest among the normal weight, overweight, and obese I category patients.

Obese II and obese III category patients had a significantly higher incidence of wound infections and renal and urinary tract infection complications, while morbidly obese patients had a significantly higher incidence of thromboembolic complications.

After the researchers adjusted for age, gender, and type of operation, the 30-day mortality risk was lowest among the obese I patients (OR 0.53) and highest among the underweight patients (OR 1.48).

"Mild obesity may have an independent protective effect on nutrition, metabolic status, and improved cardiac performance," said Dr. Xenos, who had no conflicts to disclose. ■

## Perioperative Steroids: Use Low Dose for a Short Time

BY KERRI WACHTER  
Senior Writer

WASHINGTON — When administering perioperative steroids to patients with suspected tertiary adrenal insufficiency, it's best to use the smallest possible dose for the shortest possible period of time.

"We should do our best to match the stress of the surgical procedure with the dose," said Dr. Darrell W. Harrington, chief of the division of general internal medicine at Harbor-University of California, Los Angeles Medical Center.

The potential for adrenal crises poses a challenge in patients who are subjected to surgical stress but who are not receiving adequate corticosteroid supplementation. Data are inadequate "to allow reliable prediction of which patients are at risk for tertiary adrenal insufficiency," he said at the annual meeting of the American College of Physicians.

"What we think we know is that there is no significant suppression if patients take a low dose [of steroids] daily." Alternately, if patients take an every-other-day dose—usually less than 10 mg prednisone equivalent—there is little hypothalamic-pituitary-adrenal (HPA) axis suppression. Abbreviated exposures, ranging from 5 days to 3 weeks, are probably not associated with significant HPA axis suppression.

However, significant suppression does occur with high doses, super-potent topical steroids, and inhaled corticosteroids. Recovery after pro-

longed exposure may take as little as 5 days, or as long as a year.

"Unfortunately, there are a lot of patients who fall in between," Dr. Harrington said. The data for these patients are inconsistent. Most patients on chronic steroids or with a history of steroid use do not have an obvious diagnosis of tertiary adrenal insufficiency. "We have to rely on clinical intuition to make this diagnosis."

A random cortisol measurement works well at identifying patients who are likely to have HPA reserve. In addition, an adrenocorticotropic hormone (ACTH) stimulation test resulting in an incremental increase of cortisol greater than 9 mcg/dL indicates adequate HPA reserve. But biochemical abnormalities revealed by such tests "do not correlate or predict safety from a clinical events point of view," Dr. Harrington noted.

The potential for impaired wound healing and increased infection rates related to the perioperative use of exogenous steroids makes some clinicians reluctant to adequately supplement. No clear, consistent evidence shows that wound healing is substantially delayed or impaired when patients are given short courses of perioperative steroids. And data from case series suggest that limited exposure to steroids in surgery patients is associated with a very limited increase in infection risk.

Dr. Harrington reported that he had significant financial relationships with Sanofi-Aventis, Eisai Inc., GlaxoSmithKline, and Pfizer Inc. ■