Moderate Glucose Target May Reduce Deaths

Moderate blood glucose control was linked to a significant 40% reduced mortality after CABG.

BY MITCHEL L. ZOLER

FROM THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

TORONTO — Moderate glucose control during the first days following coronary artery bypass graft surgery led to better outcomes than did liberal control, judging by a review of more than 4,000 patients at one U.S. center.

Patients who were maintained on tight glucose control, however, with an average blood glucose level of less than 126 mg/dL during the first 3 days after undergoing CABG, had no significant outcome advantage over those who were maintained on liberal control at a mean glucose level of more than 180 mg/dL.

On the basis of these findings as well as those of previous published studies, the ideal blood glucose target after CABG is 150 mg/dL, with a target range of 120-150 mg/dL, Dr. Gorav Ailawadi said.

Moderate glucose control, defined by Dr. Ailawadi as a mean blood glucose level during the first 3 days after surgery of 126-179 mg/dL, was linked to a significant reduction in both mortality and major complications, compared with liberal control, said Dr. Ailawadi, who is a cardiothoracic surgeon at the University of Virginia in Charlottesville.

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DR. AILAWADI

"At our institution, our postoperative glucose control policy as of January 2010 has been a target range of 120-150 mg/dL hospital-wide," not just in cardiac surgery patients, he said in an interview.

"The previous goal had been 80-110 mg/dL, but we felt there were enough data, including our own data, to support the change. We're not saying that you can be lax about glucose, but that you don't need to be as tight as 80-110 mg/dL. The goal is 120-150 mg/dL, and be sure it doesn't go above 180 mg/dL."

Although it's unclear why tight control may not be as effective as moderate control, Dr. Ailawadi suggested that perhaps patients in the tight-control group have more hypoglycemic episodes.

In this series, the incidence of first postoperative glucose levels that measured 60 mg/dL or less ran 1.5% in the tight-control patients, 0.4% in the moderate-control group, and 0.1% in the liberal-control group, a significant difference for the tight-control patients compared with the other two groups.

Unadjusted mortality rates during hospitalization were 2.9% in the tight-control group, 2.0% in the moderate-control group, and 3.4% in the liberal-control group.

Dr. Ailawadi said that the evidence in favor of moderate control confirms results from several recent randomized, controlled studies, including:

- The Normoglycemia in Intensive Care Evaluation—Survival Using Glucose Algorithm Regulation (NICE-SUGAR) study, which included 6,100 intensive care unit patients and found that a glucose target of less than 180 mg/dL led to significantly better survival than did a target of 81-108 mg/dL (N. Engl. J. Med. 2009;360:1283-97).
- A study that randomized 400 on-pump cardiac surgery patients to tight postoperative glucose control with a target of 80-100 mg/dL or to conventional treatment with a blood glucose goal of less than 200 mg/dL and an achieved mean level of 157 mg/dL.

At 30 days' follow-up, the incidence of the primary end point—a composite of death, sternal infections, prolonged ventilation, cardiac arrhythmias, stroke, and renal failure—was identical in the two groups.

But the group on tight control had a trend toward more deaths that neared significance ($P = .061$) and a significantly higher rate of stroke (Ann. Intern. Med. 2007;146:233-43).

- An unpublished study that randomized cardiac surgery patients to tight postoperative glucose control with a target mean level of 90-120 mg/dL, compared with a target mean of 120-180 mg/dL, and showed no significant difference in the rates of major adverse cardiovascular events between the two groups.

Dr. Harold L. Lazar, professor of cardiothoracic surgery at Boston University and lead investigator of that study, summarized the results during the discussion of Dr. Ailawadi's report.

Dr. Lazar also noted that the 2009 report from the Blood Glucose Guideline Task Force of the Society of Thoracic Surgeons set an "optimal glucose range" of 120-180 mg/dL for the peroid during and after adult cardiac surgery (Ann. Thorac. Surg. 2009;87:663-9).

A reason the task force selected this range was "to make it easier for people to be in compliance," he said.

The study by Dr. Ailawadi and his associates included patients at the University of Virginia during 1995-2008 who underwent CABG and either had known type 2 diabetes preoperatively or developed perioperative hyperglycemia, defined as a blood glucose level of 126 mg/dL or higher at their first postoperative glucose measurement or a mean glucose of at least 126 mg/dL during the first 3 days after surgery. Their average age was 64 years, and about 70% were men.

During the first 3 postoperative days, average blood glucose levels were 118.9 mg/dL in the tight-control group, 152.5 mg/dL in the moderate-control group, and 214.6 mg/dL in the liberal-control group.

Unadjusted mortality rates during hospitalization were 2.9% in the tight-control group, 2.0% in the moderate-control group, and 3.4% in the liberal-control group.

The unadjusted rates of the combined complication end point were 19.4%, 11.1%, and 14.2% in the three groups, respectively.

Multivariate analysis that controlled for clinical and demographic differences revealed that moderate glucose control was linked to a significant 40% reduced mortality and a 30% reduced rate of complications compared with the liberal-control group.

The tight-control group had a 50% reduced mortality compared with the liberal-control group, but the difference was not significant.

Patients in the tight-control group had the same rate of complications as those in the liberal-control group, said Dr. Ailawadi. ■

VITALS

Major Finding: After receiving a coronary artery bypass graft, patients who maintained a moderate blood glucose level of 126-179 mg/dL had a significant 40% lower mortality and a significant 30% lower rate of major complications, compared with patients whose mean blood glucose was 180 mg/dL or higher. Mortality and morbidity were not significantly lower in patients who maintained a blood glucose level of less than 126 mg/dL, compared with patients with levels that were 180 mg/dL or higher.

Data Source: Review of more than 4,600 post-CABG patients at a single U.S. center during 1995-2008.

Disclosures: Dr. Ailawadi said that he and his associates had no disclosures. Dr. Lazar disclosed that he has received research support from Eli Lilly & Co.

MY TAKE

Study Did Not Prove Moderate Better Than Tight Glucose Control

Neither the title of this paper nor the conclusions are in any way supported by the data. Nor is it possible that any difference between the tight- and moderate-control groups, if it did actually exist, could have been statistically detected in this study.

Due to the lack of sufficient numbers of patients in the tight-control group, the study was markedly underpowered to detect any difference between the tight- and moderate-control groups. The power of this study to detect an absolute 1% reduction in mortality between the two groups was only 3%. Furthermore, these were entirely retrospective data from an administrative database, not a clinical database. Clinical outcomes are assumed by interpolating coding information.

What this report has shown is that moderate control is better than no control at all, a finding supported by 15 years of published literature. Moderate control reduced mortality by 40% compared with no control. Interestingly, the point estimate for tight control in the multivariate mortality analysis shows a 50% reduction in mortality compared with no control, but with not enough patients to bring the point estimate to statistical significance. To imply that moderate control is superior to tight control when they weren't even directly compared is either wishful thinking or misleading marketing rhetoric that is not supported by the statistical data.

I have similar concerns about the morbidity conclusions. Of the five major complications included in the morbidity end point, three—stroke, prolonged ventilation, and reoperation—have never been shown to be associated with or caused by glycemia in cardiac surgery patients. Thus, glycemic control is unrelated to the complications studied.

ANTHONY P. FURNARY, M.D., *is a cardiothoracic surgeon in Portland, Ore. He disclosed that he has served on the speakers bureau for and has received research grants and honoraria from Lifescan and Sanofi-Aventis. Dr. Furnary made these remarks as the designated discussant for the paper.*