Of 668 and 745 glucose observations in the exenatide and MOD groups, respectively, there were numerically fewer overall hypoglycemic episodes in the exenatide group (0.9% vs 1.2%; p=0.57), including severe events (0% vs 0.3%; p=0.18). BG in exenatide-treated patients was more frequently within the target range (100 to 140 mg/dL; 37% vs 29%; p<0.001) and within 71 to 140 mg/dL (48% vs 39%; p<0.001) compared with MOD. No serious adverse events were observed in the exenatide group.

The study objective was to determine the feasibility, efficacy, and safety of glucose-lowering with IV exenatide monotherapy in hyperglycemic patients who were admitted to the CICU. The findings suggest that fixed-dose IV exenatide is feasible in hyperglycemic ICU patients, achieves similar efficacy compared with IV insulin, and does not cause severe hypoglycemia.

## Risk of Mortality Increased with Divergence from Glycemic Target

Written by Lori Alexander

Glucose levels that deviated from established glycemic targets were found to be associated with an increased risk of mortality in an analysis of self-monitoring blood glucose (SMBG) data from a subset of patients in the ACCORD trial.

"The more you diverge from what you're trying to achieve, the higher [the] risk of mortality," said Richard Bergenstal, MD, International Diabetes Center at Park Nicollet, Minneapolis, Minnesota, USA, who reported the findings.

The subanalysis was done in an effort to better understand the excess mortality that was found with intensive therapy (target HbA1C <6%) compared with standard therapy (target HbA1C <7% to 7.9%) in the ACCORD trial. Increased mortality in the study was found to be associated with severe hypoglycemia, but the risk was similar in both groups and could not account for the difference between the groups. The hypothesis was that mild/moderate hypoglycemia may be the cause, leading the investigators to study SMBG data.

Approximately half (52%) of the patients in ACCORD had downloaded any SMBG data; most had downloaded data for at least 2 years. The patients who downloaded SMBG data were representative of the entire study population, as their characteristics were similar to those of the patients who had not downloaded SMBG data.

Subjects in the intensive group tested their glucose levels more frequently (2.7 vs 2 times per day in the standard group). There was a significant correlation between drop in HbA1C and increasing frequency of SMBG tests for both groups (11% reduction in the intensive group and 6% reduction in the standard group; p<0.001 by rank correlation). This finding suggests that more frequent selfmonitoring may be worthwhile.

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The frequency of hypoglycemia (glucose level <70 mg/dL) was 3 times greater in the intensive group than in the standard group, and the frequency of hyperglycemia (glucose level >200 mg/dL) was 2 times greater in the standard group than in the intensive group. However, patients in the intensive group who died were not more likely to have had hypoglycemia than those who remained alive. Instead, the proportion of patients with glucose levels >140 mg/dL was higher among the patients who died.

In evaluating mortality according to the frequency of hypoglycemia, the highest mortality (more than 5%) was found among patients in the intensive group who had fewer than 1% of low glucose levels; the rate was 5 times greater than that for patients in the standard group with few low levels. In the standard group, the highest mortality was associated with the greatest frequency of hypoglycemia; the rate was nearly twice as high as that for patients in the intensive group with the same percentage of low levels.

In terms of hyperglycemia, mortality was highest in both groups when the frequency of high glucose level was greatest; the rate for the intensive treatment group was more than twice that for the standard group.

Dr. Bergenstal recommended setting a glucose goal in addition to an HbA1C goal. "Evaluate the [glucose] profiles, and if you're not achieving the target you set, then be careful and think about whether you want to intensify treatment further if the levels diverge from [the target]." Clinicians should be careful about even mild to moderate hypoglycemia, particularly in people for whom goals have been relaxed, such as frail older patients.

High HbA1C levels are dangerous, not only because of the risk for hyperglycemia but also because patients with high HbA1C levels had the worst frequency of hypoglycemia.

## Depression Increases Risk for Mortality in People with T2DM

Written by Lori Alexander

The ACCORD Health-Related Quality of Life (HRQL) study demonstrated that depression is a strong predictor of increased mortality and may increase the risk of