Continuous Glucose Monitoring in Patients With Type 2 Diabetes Receiving Insulin Injections: Does This Mean Continuous Glucose Monitoring for Everyone?

Despite advances in care over the past 2 decades, nearly half of persons living with type 2 diabetes mellitus (T2DM) have uncontrolled disease and are at high risk for complications (1). New technologies aimed at treatment, including advancements in glucose monitoring, may affect control and reduce hypoglycemia risk. Almost 3 decades has passed since the U.S. Food and Drug Administration approved the first continuous glucose monitoring (CGM) system. These devices, introduced in 1999, were uncomfortable, inaccurate, and difficult to use. Now, compact devices can provide consistent and timely data by measuring interstitial fluid every 5 minutes, correlating well with plasma glucose levels; they transmit current and predicted glucose values to cell phones and other devices, providing real-time user feedback. As a result, real-time CGM (RT-CGM) enables both patients and physicians to visualize daily glucose patterns, including variations after meals, exercise, and illness and in response to changes in treatment regimens. Furthermore, device alerts notify users and their support systems of impending hypoglycemia and hyperglycemia.

Because of these advances, randomized controlled trials (RCTs) in patients with type 1 diabetes mellitus (T1DM) have consistently had positive outcomes. The Juvenile Diabetes Research Foundation (2), SWITCH (3), and GOLD (4) studies showed greater reductions in hemoglobin A_{1c} (HbA_{1c}) levels in adults with RT-CGM than with intermittent self-monitoring of blood glucose (SMBG); mean differences were 0.53%, 0.41%, and 0.43%, respectively. In parallel to the trial reported in this issue (5), Beck and colleagues (6) did a 6-month RCT, known as the DIAMOND (Multiple Daily Injections and Continuous Glucose Monitoring in Diabetes) study, in patients with T1DM. They compared the effectiveness of RT-CGM with that of SMBG in patients with T1DM receiving multiple daily injections of insulin. Real-time CGM showed significant improvements in HbA_{1c} levels, hypoglycemia, hyperglycemia, and glucose variability compared with SMBG. At 24 weeks, HbA_{1c} decreased from baseline values of 8.6% in each group by 1% in persons using CGM and 0.4% in those exclusively using SMBG ($P < 0.001$).

Despite the advances achieved with CGM in T1DM, outcomes of clinical trials in T2DM have been mixed. In the largest T2DM study to date, Vigersky and colleagues (7) completed an RCT in 100 adults receiving various antihyperglycemic medications, including basal but not prandial insulin. Compared with SMBG, intermittent RT-CGM use for 12 weeks resulted in significant improvements in HbA_{1c} levels that were sustained during a 40-week follow-up. However, in another RCT of poorly controlled T2DM, Haak and colleagues (8) did not see HbA_{1c} reductions with a flash glucose monitoring system when compared with SMBG.

In this issue, Beck and colleagues report on the T2DM cohort from the DIAMOND study and address whether RT-CGM improves clinical outcomes in patients injecting basal–bolus insulin (5). This 24-week clinical trial randomly assigned 158 patients with T2DM who had varying levels of endogenous insulin production and baseline HbA_{1c} levels of 7.5% to 9.9% to receive CGM ($n = 79$) or SMBG ($n = 79$). At 24 weeks, they noted a modest but statistically significant reduction in HbA_{1c} levels, the primary end point. These levels decreased from a baseline of 8.5% in each group to 7.7% and 8.0% in those using CGM and SMBG, respectively, with a significant difference of −0.3% (95% CI, −0.5% to 0.0%) ($P = 0.022$) favoring CGM. More CGM participants increased time spent with glucose concentrations between 3.89 and 9.99 mmol/L (70 and 180 mg/dL) than did SMBG participants. Similar to outcomes reported in other CGM trials, a high baseline HbA_{1c} level (>9%) was associated with a greater improvement in control (−1.4% vs. −0.7%). Unlike in the T1DM trials, rates of hypoglycemia did not differ, probably because of the low overall frequency at baseline (5).

The evident strength of RT-CGM is its ability to provide timely and accurate glucose readings while reducing the hassle of more frequent SMBG in patients using complicated insulin regimens. Less than 1 year ago, the U.S. Food and Drug Administration allowed "therapeutic CGM" to replace SMBG in treatment decisions. Although this certainly advances diabetes care, many caveats remain to widespread implementation of RT-CGM—primarily those surrounding meaningful glucose monitoring and comprehensive education for patients and the providers overseeing their care. For persons experienced in CGM, the modest outcomes reported in Beck and colleagues' trial may come as no surprise. The DIAMOND trial was designed to simulate "real-world practice" with minimal follow-up. Anecdotal evidence suggests that patients given extensive CGM education may do better. In 1 trial, Allen and colleagues (9) reported on the importance of CGM and diabetes education. They paired RT-CGM with nutritional and exercise feedback and showed significant improvement in physical activity adherence, decreased body mass index, and reduced HbA_{1c} levels (−1.16%) when compared with SMBG.

Additional obstacles to widespread use of RT-CGM are cost-effectiveness and ease of use. Patients and insurance organizations may become more willing to invest in this new technology as it continues to show clin-

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ical benefits, improve quality of life, and reduce long-term health costs related to complications. Currently, insurance coverage for T2DM remains somewhat limited, given the small number of studies in specific diabetic subgroups showing modest improvements in short-term outcomes. Clinicians should carefully select RT-CGM candidates who may achieve maximum clinical utility, such as those who have T1DM, high risk for hypoglycemia, and high medical literacy; those who adhere to medical device instructions; and now patients with T2DM receiving multiple daily injections of insulin (10). However, greater acceptance may also be limited by the requirement for daily calibration and the invasive nature of CGM.

In conclusion, Beck and colleagues should be commended for their well-executed study in patients with poorly controlled T2DM who receive basal–bolus insulin therapy, a study showing that RT-CGM improves diabetes control, albeit modestly, compared with SMBG. With these data, we should seek to further understand patient populations that will benefit most from CGM intervention, such as those with the skills to address glucose variability. Future RT-CGM studies must also assess whether this approach improves health care outcomes for T2DM; its financial effects on the health care system; and further generalizability in T2DM subgroups, such as those with higher risk for hypoglycemia.

Vanessa Arguello, MD
Matthew Freeby, MD
David Geffen School of Medicine at UCLA
Los Angeles, California

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Requests for Single Reprints: Vanessa Arguello, MD, David Geffen School of Medicine at UCLA, 1245 16th Street, Suite 307, Santa Monica, CA 90404; e-mail, varguello@mednet.ucla.edu.

Current author addresses are available at Annals.org.

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Current Author Addresses: Dr. Arguello: David Geffen School of Medicine at UCLA, 1245 16th Street, Suite 307, Santa Monica, CA 90404.
Dr. Freeby: David Geffen School of Medicine at UCLA, 200 Medical Plaza Driveway, Suite 530, Los Angeles, CA 90095.