GLUCOSE VARIABILITY AND CARDIOVASCULAR RISK

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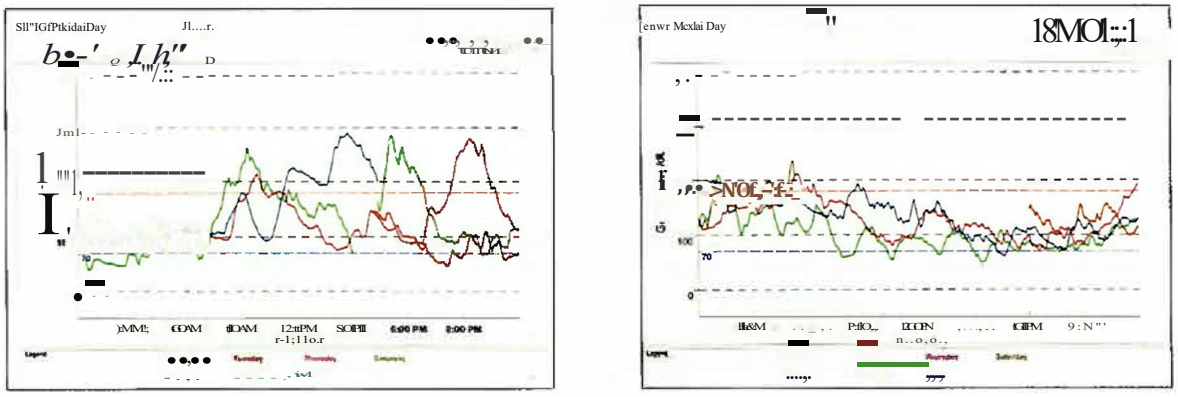
INTRODUCTION

Controlling blood glucose in patients with diabetes mellitus reduces the risk of cardiovascular (CV) complications.1 While the UK Prospective Diabetes Study and others have related fasting plasma glucose level (FPG) and hemoglobin A_c (HbA_c) to CV outcomes, a recent interim analysis of the major NIH-funded study of patients with type 2 diabetes, the ACCORD trial, now indicates that there might be a limit to the benefits and degree of HbA_c reduction. Although specifics of the trial are yet to be published, the data analysis and safety board terminated the tight control arm of this treatment trial because of a small but significant increase in mortality. As a result, the target HbA,c for many patients with CVD will, in all likelihood, remain above the nondiabetic range.

Glucose variability, another measure of glycemic control, also relates to CV outcomes. This metric quantitates the change in glucose concentration from before a meal to that obtained afterwards and can be used to assess risk and monitor treatment effectiveness. When control is targeted to minimize glucose fluctuations, even if the HbA_c is above normal, there are cardiovascular advantages.

Consider an example of two patients with type 2 diabetes and similar HbA,c results: one patient with the continuous glucose monitoring (CGMS) tracing A, the other with tracing B (Figure 1). The tracings record three days each. Then ask, "Do these two patients have the same cardiovascular risk?" Current evidence suggests the answer is no! The patient with tracing A, with greater variability, carries a two- to three-fold increased risk of primary and secondary macrovascular disease.2•3 The purpose of this review is to examine the relationship between glucose variability and cardiovascular disease.



Tracing A **Tracing B**

Figure 1. Three-day continuous glucose monitoring (CGMS) tracings.

CLINICAL ASSESSMENT: VARIABILITY VS. TIME AVERAGE

Time-averaged mean levels of glycemia as measured by HbA_1c strongly correlates with diabetic complications.[1,4] Various methods for daily glucose assessment, including laboratory measurement of fasting plasma glucose level (FPG) and patient self-monitored blood glucose (SMBG), have made it possible for patients to achieve lower HbA_1c. Analysis of these glucose measurements reveals substantial differences in daily glucose patterns, differences that neither the HbA_1c measurement nor the FPG distinguish. Some have wider fluctuations throughout the day.

Glucose variability and the magnitude fluctuations can be quantified. Calculation of the mean amplitude of glucose excursion (MAGE), a cool first described in 1970,[5] and the use of CGMS (Figure 1) provide parameters that, in addition to HbA_1c, yield a detailed assessment of the level of control. The MAGE calcula-