Increased Shear Rate Resistance and Fastest Kinetics of Erythrocyte Aggregation in Diabetes Measured With Ultrasound

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OBJECTIVE — To measure with ultrasound the increased erythrocyte aggregation (EA) kinetics and adhesion energy between erythrocytes in patients with type 2 diabetes and poor metabolic control.

RESEARCH DESIGN AND METHODS — Blood samples were analyzed in a Couette rheometer at 32 MHz following shear rate reductions from 500 s⁻¹ to residual shears of 0 (stasis), 1, 2, 10, 50, 100, and 200 s⁻¹. The increase in EA was determined with the integrated backscatter coefficient as a function of time and shear rate.

RESULTS — The time required to form aggregates was shorter in diabetic patients at shear rates below 200 s⁻¹ (P < 0.01). Erythrocytes formed larger aggregates in diabetic patients than in control subjects (P < 0.05 at 2 to 100 s⁻¹).

CONCLUSIONS — Ultrasound can potentially noninvasively demonstrate, in vivo and in situ, the impact of local abnormal EA on arteriovenous flow disorders in diabetes.

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Figure 1—A: Raising slopes from 2 to 8 s of the IBSC as a function of the shear rate applied to blood samples (means ± SD). B: IBSC at the plateau of RBC aggregation as a function of the shear rate. The power of 0 dB corresponds to that of a perfect flat stainless steel reflector. Two-way analyses of variance (Tukey method for multiple comparisons) confirmed impact of shear rate (P < 0.001) and population (P < 0.001) on IBSC slopes and IBSC at plateaus. The P values shown on the figure correspond to multiple comparisons between populations. IBSC slopes at 2 s⁻¹ were correlated with physiological variables (Pearson coefficient r = 0.39, P = 0.02 for A1C; r = 0.53, P = 0.03 for fibrinogen; r = 0.54, P = 0.02 for immunoglobin G; and r = 0.72, P = 0.001 for haptoglobin). Forward-stepwise regressions explained IBSC kinetic slopes at 2 s⁻¹ by the following model (r = 0.94): IBSC kinetic = -1.02 (P = 0.009) + 0.67 haptoglobin (P < 0.001) + 0.11 immunoglobin G (P = 0.003) + 5.60 A1C (P = 0.048). Only immunoglobin G was positively correlated with the plateau of IBSC at 2 s⁻¹ (Pearson coefficient r = 0.49, P = 0.046).

CONCLUSIONS — Statistically significant differences in Fig. 1 were noted for shears between 2 and 100 s⁻¹, which correspond to normal flow at center streams and pathological flow stasis in recirculation zones of large systemic veins and arteries. Accordingly, EA in diabetes can be related to lower-limb artery ischemic events, microangiopathy in foot extremities, and retinopathy. Inflammation is involved in pathogenesis of type 2 diabetes and RBC aggregation, which agrees with our results (legend of Fig. 1). Subacute inflammatory state promoting RBC aggregation is also associated with obesity (8) and metabolic syndrome (9). Thus, reducing inflammation (and indirectly aggregation) with statins and A1C with antidiabetic medication and/or diet are indicated because both have known benefits to cardiovascular consequences of diabetes. We reported measurements from a laboratory instrument, but a short-term objective is sizing RBC aggregates in vivo with ultrasound (10). At 32 MHz, superficial (5–6 mm depth) vessels can be scanned. The proposed noninvasive method should be...
investigated further because it may have potential benefit for diagnosis and follow-up of diabetic foot complications and for monitoring therapy.

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