

## OBSERVATIONS

## Correspondence Between the International Diabetes Federation Criteria for Metabolic Syndrome and Insulin Resistance in a Cohort of Italian Nondiabetic Caucasians

The GISIR database

In 2005, the International Diabetes Federation (IDF) released a consensus definition of the metabolic syndrome. The definition, intended to provide a feasible predictor of cardiovascular disease and type 2 diabetes, includes elevated waist circumference plus two of the following factors: reduced HDL cholesterol or raised blood pressure, triglycerides, or fasting glucose (1). Insulin resistance is a major pathogenic factor for the metabolic syndrome and may independently contribute to the risk of cardiovascular disease and type 2 diabetes (2). We assessed the diagnostic accuracy of the IDF definition of metabolic syndrome in identifying subjects with insulin resistance, defined as being in the lower quartile of insulin-stimulated glucose disposal ( $M_{\text{clamp}}$ ) determined by a standardized hyperinsulinemic-euglycemic clamp (40 mU/min per  $\text{m}^2$  body surface area), in a sample of 531 nondiabetic Caucasians from the GISIR (Group of Italian Scientists of Insulin Resistance) database; 28.2% of subjects met the IDF criteria. All components of the metabolic syndrome correlated significantly with  $M_{\text{clamp}}$  with the closest association being with waist circumference ( $r = -0.63$ ,  $P < 0.0001$ ) and the weakest with fasting glucose ( $r = -0.28$ ,  $P < 0.0001$ ) and

blood pressure ( $r = -0.23$ ,  $P < 0.0001$ ). Stepwise regression analysis in a model, including the components of the metabolic syndrome, sex, and age, revealed that only three variables were independently associated with  $M_{\text{clamp}}$ : waist circumference accounted for 38.4% of its variation, triglycerides accounted for 2.3% of the variation, and HDL cholesterol accounted for 1.0% of the variation. In a logistic regression analysis with adjustment for age and sex, the risk of IDF-defined metabolic syndrome increased according to the  $M_{\text{clamp}}$  quartile, with the most insulin-resistant subjects having 15.6-fold higher risk (95% CI 7.7–33.8) than the most insulin-sensitive subjects. Sensitivity of the IDF criteria to identify insulin resistance was low (54.5%), but specificity was high (80.5%). Among the components of the metabolic syndrome, waist circumference showed high sensitivity (90.9%) but low specificity (42.6%), and fasting glucose and triglycerides showed low sensitivity (25.0 and 34.8%, respectively) and relatively high specificity (85.0 and 79.7%), whereas blood pressure and HDL cholesterol showed both low sensitivity (53.0 and 56.1%, respectively) and low specificity (64.9 and 65.9%). The poor sensitivity of IDF criteria in identifying subjects with insulin resistance suggests that a significant number of subjects are insulin resistant, possibly at risk for cardiovascular disease and type 2 diabetes, but are not labeled as having metabolic syndrome. Indeed, 60 of 381 (15.7%) subjects who did not meet IDF criteria were insulin resistant (lowest  $M_{\text{clamp}}$  quartile). Compared with the subgroup of insulin-sensitive subjects ( $M_{\text{clamp}}$  quartiles 2–4) who did not meet IDF criteria, these insulin-resistant subjects had a significantly worse cardiometabolic risk profile, including higher BMI, waist circumference, fasting glucose, triglycerides, and blood pressure. These results suggest that the IDF criteria have good specificity but low sensitivity in identifying insulin resistance in nondiabetic subjects but fail to recognize a significant number of insulin-resistant subjects who have an unfavourable cardiometabolic risk profile.

GIORGIO SESTI, MD<sup>1</sup>  
BRUNELLA CAPALDO, MD<sup>2</sup>  
PAOLO CAVALLO PERIN, MD<sup>3</sup>  
STEFANO DEL PRATO, MD<sup>4</sup>  
LUCIA FRITTITTA, MD<sup>5</sup>  
SIMONA FRONTONI, MD<sup>6</sup>  
MARTA LETIZIA HRIBAL, PHD<sup>1</sup>  
GIULIO MARCHESINI, MD<sup>7</sup>  
GIUSEPPE PAOLISSO, MD<sup>8</sup>  
PIER MARCO PIATTI, MD<sup>9</sup>  
ANNA SOLINI, MD<sup>4</sup>  
ENZO BONORA, MD<sup>10</sup>

ON BEHALF OF THE GROUP OF ITALIAN  
SCIENTISTS OF INSULIN RESISTANCE (GISIR)\*

From the <sup>1</sup>University of Catanzaro, Catanzaro, Italy; the <sup>2</sup>University of Naples-Federico II, Naples, Italy; the <sup>3</sup>University of Turin, Turin, Italy; the <sup>4</sup>University of Pisa, Pisa, Italy; the <sup>5</sup>University of Catania, Catania, Italy; the <sup>6</sup>University of Rome-Tor Vergata, Rome, Italy; the <sup>7</sup>University of Bologna, Bologna, Italy; the <sup>8</sup>University of Naples II, Naples, Italy; the <sup>9</sup>University of Milan-Vita e Salute, Milan, Italy; and the <sup>10</sup>University of Verona, Verona, Italy.

Address correspondence to Giorgio Sesti, MD, Medicina Sperimentale e Clinica, Policlinico, Universitario Mater Domini, Viale Europa, Campus Germaneto, 88100, Catanzaro, Italy. E-mail: sestigi@unicz.it.

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**APPENDIX** — \*Other GISIR investigators: University of Catania: Roberto Baratta and Salvatore Graci; University of Catanzaro: Arturo Pujia and Francesco Andreozzi; University of Milan-Vita e Salute: Livio Luzi, Lucilla Monti, and Emanuela Setola; University of Padua: Saula Vigili de Kreutzenberg and Roberto Vettor; University of Pisa: Eleuterio Ferrannini and Andrea Natali; University of Rome-La Sapienza: Giancarlo De Mattia and Frida Leonetti; University of Rome-Tor Vergata: Daniela Bracaglia and Maria Adelaide Marini; and University of Verona: Riccardo Bonadonna.

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