COMMENTS AND RESPONSES

Development of a Type 2 Diabetes Risk Model From a Panel of Serum Biomarkers From the Inter99 Cohort

Response to Kolberg et al.

Kolberg et al. (1) report from the Inter99 cohort that a risk score incorporating six biomarkers (adiponectin, C-reactive protein, ferritin, interleukin-2 receptor A, glucose, and insulin) is useful in the prediction of type 2 diabetes and could be recommended as a tool for identification of high-risk individuals. So far, however, there is little evidence that a procedure based partly on nonroutinely measured biomarkers is superior to risk scores based on personally known variables or on routinely measured clinical data.

An area under the receiver operating characteristic curve (AROC) of 0.76 is reported by the investigators, indicating a rather moderate diagnostic accuracy of the model (1). The investigators do not report sensitivities and specificities for different score cut points for their model, but the AROC suggests that about 40% of noncases would be falsely screened positive at a sensitivity of 80%. The presentation of the diabetes risk score (DRS) also ignores that the majority of future cases do not lay within the upper 10% of the DRS. Other risk scores based on noninvasive measures such as the German DRS (AROC 0.84) (2) or scores relying on personal as well as on routinely available clinical data such as the Framingham diabetes point score (AROC 0.85) (3) perform considerably better than the suggested biomarker model. Even for the Cambridge DRS, which only includes simple routinely collected nonbiochemical parameters, an AROC value of 0.75 was reported (4). Surprisingly, the investigators select alternative models for comparison mostly composed of one single parameter instead of comparing their model with models incorporating several routinely accessible parameters. The noninvasive clinical model given by the investigators for means of comparison does not even include sex, hypertension, or smoking status and has relatively poor performance in comparison with other noninvasive models (2,4).

Furthermore, the investigators argue that the AROC value of their risk score hardly improves when some parameters of noninvasive models are additionally incorporated in their model. However, this does not furnish evidence that biomarkers have more predictive power than routine data. In fact, it reflects that the risk factors of type 2 diabetes are highly correlated, and it would be interesting to see how large the effect on the accuracy indexes would be if it was the other way around and biomarkers would be added to models relying on personal or clinical routine data. We have previously reported that glucose, A1C, lipids, and liver enzymes improve prediction by the German DRS (AROC 0.90) but not C-reactive protein and adiponectin (5).

Analyses of the power of biomarkers to identify high-risk individuals are worthwhile. However, measurement of some of the suggested biomarkers is costly, and therefore, efforts toward a careful comparison and appraisal of different methods to predict diabetes risk have to be made. Also, diabetes risk screening is still hampered by a large number of false-positive screening results at acceptable sensitivities and consequently by large numbers needed to treat with lifestyle interventions. Thus, new prediction models should aim to optimize discrimination rather than to replace existing models.

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