COMMENT ON SKUDDER-HILL ET AL.

Fat Distribution Within the Pancreas According to Diabetes Status and Insulin Traits. Diabetes 2022;71:1182–1192

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We read the recent article by Skudder-Hill et al. (1) with great interest. In that study, the authors measured the distribution of intrapancreatic fat across the regions of the pancreas by MRI in 368 adults from the general population cohort and analyzed the relationship between regional intrapancreatic fat deposition and diabetes status and insulin traits. Although the authors presented an intriguing concept, some of the statements and conclusions in their study merit further discussion.

With the growing recognition that the clinical relevance of HbA_{1c} and glucose mismatches could lead to misclassification of diabetes and prediabetes when using the HbA_{1c} test alone for diagnosis (2), both glucose and HbA_{1c} measurements are combined and used to ensure accurate diagnoses in the three American Diabetes Association–recommended criteria (fasting plasma glucose, 2-h postload glucose during 75-g oral glucose tolerance tests, and HbA_{1c}). The authors' statement of diabetes status based on fasting plasma glucose or HbA_{1c} may lead to misclassification of the included individuals.

Furthermore, the authors concluded that there were no significant differences in regional intrapancreatic fat according to diabetes status. Similar work also was pursued by Martin et al. (3), in which Mendelian randomization analysis did not show a causal role of pancreas fat in the risk of type 2 diabetes. Indeed, increased pancreas volume showed a decreased risk of type 2 diabetes (odds ratio 0.76 [95% CI 0.62, 0.94] or 24% decreased risk per 1 SD) (3). Pancreatic fat increased proportionately with aging and BMI and the pancreatic volume decreased, resulting in a proportionately higher fat content (4). Measurement of pancreatic fat content in such variable pancreas volumes may yield flawed data, and the pancreatic volume alteration may be the alternative risk factor. In addition, the relationship between intrapancreatic fat distribution in the head, tail, or body and pancreas volume needs further investigation.

Finally, we note that HOMA apportions the basal state of insulin and glucose in terms of resistance and β-cell function. It seems that considerable caution should be exercised in using HOMA of insulin resistance as an accurate measure of total body, peripheral, or hepatic insulin resistance (5). Specifically, the meaning of HOMA of insulin resistance can vary according to whether decreased insulin secretion or decreased insulin removal is the major determinant of the change in plasma insulin.

Since sometimes it is not enough to declare the limitations of the study, and considering that some of those mentioned here may change the whole pathogenesis picture, we respectfully propose that there is still no strong evidence of the causality of the pathophysiological processes of increased intrapancreatic fat deposition and that insulin resistance occurs initially in the tail and body of the pancreas.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

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