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HbA$_{1c}$ Levels, Body Weight Change, and Risk of Pancreatic Cancer Among Patients With Long-Standing Diabetes Mellitus: A Case-Control Study

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Introduction: Screening for sporadic pancreatic cancer (PaC) needs the upfront characterization of high-risk groups. New-onset diabetes mellitus and weight loss represent two important criteria for identifying people at increased risk of PaC in the general population.

Aims: To assess whether similar criteria (i.e., HbA$_{1c}$ levels and body weight change) may render it possible to identify patients at high risk of PaC within the long-standing diabetes mellitus population.

Methods: Using data from the UK-based Clinical Practice Research Datalink, we conducted a matched (1:10) case-control study. Cases were patients, aged 30 to 89 years, with an incident diagnosis of PaC (index date) and preceding diabetes mellitus present for >2 years at the index date. We matched the cases with controls, i.e., patients without a diagnosis of PaC, by various variables including diabetes duration. We categorized HbA$_{1c}$ levels according to different time intervals before the index date, each divided into quartiles. Weight change specified the relative change from baseline (i.e., >3 years before the index date) until the index date. Applying multivariable conditional logistic regression, we compared HbA$_{1c}$ levels as well as weight change between cases and controls.

Results: We found 476 cases and 4724 controls. Compared with HbA$_{1c}$ levels ≤47.5 mmol/mol, HbA$_{1c}$ levels ≥64.0 mmol/mol were associated with odds ratios (ORs) for PaC of 4.94 (95% CI 3.52-6.94) and 2.66 (95% CI 2.00-3.54) within 6 months and >1-2 years before the index date, respectively. Weight loss ≥15.0% was associated with an OR of 15.40 (95% CI 10.65-22.26) compared with no weight change. 14.7% of cases and 0.5% of controls showed both weight loss ≥15.0% and an HbA$_{1c}$ level ≥64.0 mmol/mol (within 2 years before the index date). The OR for PaC associated with presence of both characteristics was 60.97 (95% CI 35.87-103.65), when compared with patients showing none of them.

Conclusions: High HbA$_{1c}$ levels and weight loss appeared to be helpful criteria for identifying patients at high risk for PaC among patients with long-standing diabetes mellitus. Studies on the exact course of worsening in glycemic control and weight loss at a patient level are needed. Efforts to define high-risk groups should focus on both patients with new-onset diabetes mellitus and patients with long-standing diabetes mellitus.

Keywords: pancreatic cancer, diabetes, weight loss, HbA$_{1c}$, CPRD.
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