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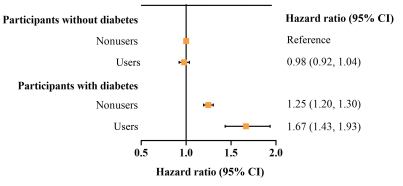
Diabetes Care®

In This Issue of *Diabetes Care*

By Max Bingham, PhD

Calcium Supplementation Is Linked to Raised Cardiovascular Risk in Diabetes

Calcium supplement use is associated with higher risk for cardiovascular disease outcomes and all-cause mortality in individuals with diabetes but not in individuals without diabetes, according to Qiu et al. (**p. 199**). The authors warn that individuals with diabetes might want to be cautious with longer-term use of calcium supplements and instead focus on natural ways of sourcing calcium via a good diet. They also stress that there is a continued need to balance any adverse effects of supplementation with potential benefits, particularly in terms of bone health. The findings come from further analysis of the UK Biobank and included just under 434,400 individuals to look at potential associations between habitual calcium supplementation and cardiovascular disease events and mortality according to diabetes status. The authors identified 26,374 incident cardiovascular disease events over a follow-up of 8 years and 20,526 deaths over a follow-up of 11 years (of which just over 4,000 were cardiovascular disease deaths). After adjusting for multiple factors, they found that calcium supplement use was significantly associated with higher risk for cardiovascular disease incidence and mortality and all-cause mortality, but this was true only in those with diabetes. In addition to general cardiovascular risk, the authors identified significant associations between calcium supplementation and higher risks for cerebrovascular disease, ischemic heart disease, and heart failure, but again only in those with diabetes. The same additive interactions also existed with the cardiovascular subtypes. In terms of mechanisms, the authors note several possible explanations for the association. However, they highlight the instantaneous spike in serum calcium levels following supplementation (that does not occur with dietary calcium) and how it might contribute to vascular calcification on top of the increased risks involved in diabetes anyway.



Cardiovascular disease incidence according to diabetes status and use or nonuse of calcium supplementation.

Qiu et al. Associations of habitual calcium supplementation with risk of cardiovascular disease and mortality in individuals with and without diabetes. Diabetes Care 2024;47:199–207

Postdischarge Care Can Mitigate Cognitive Impairment–Linked Risk for Readmission of Patients With DKA or Severe Hyperglycemia

Cognitive impairment appears to be associated with elevated readmission risk for patients who were hospitalized for severe hyperglycemia or diabetic ketoacidosis, according to Wang et al. (**p. 225**). Notably, however, postdischarge care can potentially mitigate the risk for readmission for such patients, although other factors also appear to influence readmission risk. Based on the findings, the authors highlight the potential benefits of postdischarge care but note that further research is needed to enhance sensitivity for cognitive impairments and types of postdischarge care not captured in the original data sets they used. The findings come from an analysis of the Nationwide Readmission Database, aimed at identifying individuals who were hospitalized for either severe hyperglycemia or diabetic ketoacidosis in the years 2016–2018. The authors then compared 30-day all-cause readmission risk in individuals with and without cognitive impairment and the effect of postdischarge care on risk. The authors identified just under 24,000 patients with severe hyperglycemia and just over 140,000 patients with diabetic ketoacidosis who were admitted. Approximately 11% of patients with hyperglycemia and 1% of those with diabetic ketoacidosis had cognitive impairment of some sort when initially hospitalized. Once adjusted for a series of covariates, the authors found that cognitive impairment in those with severe hyperglycemia increased readmission risk by 23% when no postdischarge care was provided. In diabetic ketoacidosis, the increased risk was 35%. In both cases, the readmission risk was almost completely mitigated when patients received postdischarge care. "Our findings underscore the critical need to enhance postdischarge outcomes for this vulnerable subpopulation with diabetes with cognitive function decline," said author Hui Shao. "It is a call to action for the health care community to intensify focus and care for this unique population, ensuring that they receive the targeted support they need following hospital discharge. This research paves the way for more personalized and effective strategies in managing the health of patients with diabetes who have cognitive impairments."

Wang et al. Associations between postdischarge care and cognitive impairment–related hospital readmissions for ketoacidosis and severe hypoglycemia in adults with diabetes. Diabetes Care 2024;47:225–232

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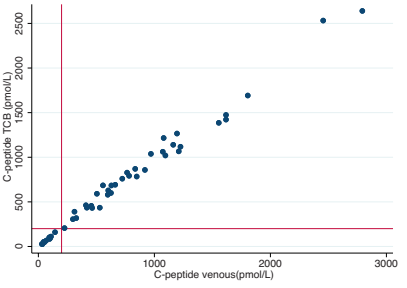
Painless Transdermal Blood Sampling Success for C-Peptide Measurements in Type 1 Diabetes

Transdermal blood collection appears to offer an alternative to venous blood sampling for measuring the biomarker C-peptide in children and adults with type 1 diabetes, according to Besser et al. (**p. 239**). The approach is only minimally invasive and much less painful than venous blood sampling, and potentially it could be administered at home. The study centers on a microsampling device called TAP, or touch-activated phlebotomy, which is designed to collect small transdermal capillary blood (TCB) samples painlessly. The system had been tested in several clinical and laboratory settings but not for C-peptide and islet autoantibodies or for its acceptability when used with children, prompting the study. The authors recruited 71 individuals with type 1 diabetes and 20 adults without diabetes to undergo sampling via the venous and TCB sampling routes to measure C-peptide and islet autoantibodies. They then used Bland-Altman plots to assess the bias and limits of agreement between the two methods. They also assessed acceptability of the methods via age-appropriate questionnaires. The authors found that the device took a mean of 2.35 min to collect a capillary sample with few complete failures or low volumes (<35 µL). C-peptide measured via TCB sampling showed good agreement with C-peptide measured via venous plasma, but detection of islet autoantibodies was much less successful, with multiple examples of divergent results from the two methods. On acceptability, TCB sampling was preferred by most, but not all, of the participants, with 63% of individuals with type 1 diabetes preferring TCB sampling. "Participants in the study preferred the transdermal device to blood sampling with a needle, and the method appeared reliable for measuring C-peptide. This has major implications," said author Rachel E.J. Besser. "The transdermal collection method has great potential for assessment of β-cell function, such as following interventions to preserve C-peptide in type 1 diabetes, where more frequent assessments could prove insightful. It also has potential for use in other pediatric settings, and this now needs testing."



Relationship between C-peptide measured in venous blood samples and via TCB sampling.

Besser et al. Transdermal blood sampling for C-peptide is a minimally invasive, reliable alternative to venous sampling in children and adults with type 1 diabetes. Diabetes Care 2024;47:239–245

Hyperosmolar Hyperglycemia State Incidence for Denmark

The incidence of the life-threatening but rare complication of diabetes called hyperosmolar hyperglycemic state, or HHS, is explored by Rosager et al. (**p. 272**). While confirming that the condition is rare, at least in Denmark, they also identify a series of characteristics of patients who are acutely admitted for the condition, noting that their observations may facilitate better treatment for patients. The findings come from a nationwide register–based cohort study that was based on data from the years 2016–2018 and aimed to identify all acutely admitted cases of HHS based on predefined criteria. Roughly 4.8 million inhabitants aged ≥18 years were initially included in the study. They found 634 cases of acutely admitted patients with HHS during the 3-year study period. Among these were 114 patients with type 1 diabetes and 277 with type 2 diabetes. In total, there were 24,196 and 251,357 individuals with type 1 or type 2 diabetes, giving incidence rates of 16.5 and 3.9 per 10,000 person-years, respectively. Notably, a third of patients with HHS had not previously received a diagnosis of diabetes. Additionally, 394 individuals had "pure" HHS, while 240 had a combination of HHS and diabetic ketoacidosis. Patients with pure HHS tended to be older and had more comorbidities, more prescription medicines, and higher levels of undiagnosed diabetes. Additional subgroups also appeared to exist in relation to acidosis and acute kidney injury. According to the authors, HHS can develop over many days and frequently occurs with precipitating factors, such as infections. Use of glucocorticoids and benzodiazepines was also common prior to hospitalization. "With this study, we bring new knowledge on the incidence and characteristics of patients with HHS that can be considered by clinicians when diagnosing these critically ill patients," said author Emilie V. Rosager. "This study builds a foundation for us to further investigate precipitating factors for HHS and the association between osmolarity and mortality in patients with hyperglycemia."

Rosager et al. Incidence and characteristics of the hyperosmolar hyperglycemic state: a Danish cohort study. Diabetes Care 2024;47:272–279

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