RESPONSE TO COMMENT ON WEBER ET AL.

Type 1 Diabetes Is Associated With an Increased Risk of Fracture Across the Life Span: A Population-Based Cohort Study Using The Health Improvement Network (THIN). Diabetes Care 2015;38:1913–1920

David R. Weber,[1] Kevin Haynes,[2] Mary B. Leonard,[3] Steven M. Willi,[2,4] and Michelle R. Denburg[2,4]

Diabetes Care 2015;38:e205–e206 | DOI: 10.2337/dci15-0019

A key finding of our study is that children with type 1 diabetes were at increased risk of fracture compared with age-, sex-, and practice-matched participants without diabetes (1). In his commentary (2), Dr. Shah questions the clinical significance of childhood fractures and the contribution of type 1 diabetes to fracture risk in children. To clarify, in participants with type 1 diabetes and participants without diabetes, we found that fracture incidence was highest in the 10–20-year age-group for males only; the highest incidence in females occurred in those aged 80–90 years.

From a statistical standpoint, the large sample size of our data set would be expected to reduce the risk of committing a type 2 error (failing to detect a true association between type 1 diabetes and fracture) but not to increase the risk of committing a type 1 error (identifying an association that does not exist), which was set at the standard $\alpha = 0.05$. We defined fracture at any skeletal site as the primary outcome in order to more completely investigate the effect of type 1 diabetes on fracture risk. Fragility fractures are uncommon in children and young adults; limiting the analysis to sites associated with fragility fracture in older adults (spine, hip) would likely underestimate the burden of fracture in type 1 diabetes. All fractures, fragility or otherwise, can negatively impact quality of life through physical/emotional pain, missed work/school, physical activity restriction, and increased health care expenditure (3). In children, there is also the potential for deleterious effects on bone growth should the fracture involve the growth plate (4). Dr. Shah points out that childhood fractures are usually sustained during physical activity. It is unlikely that the increased fracture risk we observed in children with type 1 diabetes was because of higher activity, as there is evidence that children with type 1 diabetes are less likely to participate in activities such as organized sports (5). Further studies are needed to determine the relationships between activity and fracture in type 1 diabetes.

Our ability to explore the possible link between hypoglycemia and fracture was limited. Hemoglobin A_{1c} (HbA_{1c}) was the only marker of glycemic control available for analysis. We found a positive association between HbA_{1c} and fracture, suggesting that sustained exposure to hyperglycemia was an important contributor to skeletal fragility. This finding argues against a major role for chronic hypoglycemia in skeletal fragility (where a negative association between fracture risk and HbA_{1c} would have been expected) but cannot rule out the contribution of acute hypoglycemic episodes. Given the increased availability of continuous glucose monitoring, we anticipate that future studies will allow for more robust assessments of the contribution of acute and chronic glycemic status to diabetes-related fracture. In summary, we found that both adults and children with type 1 diabetes were at increased risk of fracture. These findings more completely define the population with type 1 diabetes at risk for fracture and will hopefully raise awareness of this complication. We echo Dr. Shah's call for further research to identify the mechanisms of skeletal fragility in type 1 diabetes.

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

References

1. Weber DR, Haynes K, Leonard MB, Willi SM, Denburg MR. Type 1 diabetes is associated with an increased risk of fracture across the life span: a population-based cohort study using The Health Improvement Network (THIN). Diabetes Care 2015;38:1913–1920
2. Shah VN. Comment on Weber et al. Type 1 diabetes is associated with an increased risk of fracture across the life span: a population-based cohort study using The Health Improvement Network (THIN). Diabetes Care 2015;38:1913–1920 (Letter). Diabetes Care 2015;38:e204. DOI: 10.2337/dc15-1751

[1]*Golisano Children's Hospital, University of Rochester School of Medicine and Dentistry, Rochester, NY*
[2]*Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA*
[3]*Stanford University School of Medicine, Stanford, CA*
[4]*Children's Hospital of Philadelphia, Philadelphia, PA*

Corresponding author: David R. Weber, david_weber@urmc.rochester.edu.

3. Ding R, McCarthy ML, Houseknecht E, et al.; CHAT Study Group. The health-related quality of life of children with an extremity fracture: a one-year follow-up study. J Pediatr Orthop 2006;26:157–163

4. Spiegel PG, Cooperman DR, Laros GS. Epiphyseal fractures of the distal ends of the tibia and fibula. A retrospective study of two hundred and thirty-seven cases in children. J Bone Joint Surg Am 1978;60:1046–1050

5. Valerio G, Spagnuolo MI, Lombardi F, Spadaro R, Siano M, Franzese A. Physical activity and sports participation in children and adolescents with type 1 diabetes mellitus. Nutr Metab Cardiovasc Dis 2007;17:376–382