



Increased Risk of Tendon Injury Following Structured Care in Patients With Type 2 Diabetes: Post Hoc Analysis of a Large Randomized Controlled Trial With 19 Years of Follow-up

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Diabetes Care 2024;47:e57–e58 | <https://doi.org/10.2337/dc24-0330>

Tendon rupture and tendinopathy can arise from sudden occurrences and repetitive overuse and can result in a permanently reduced physical activity level (1,2). Tendon injuries are prevalent in both physically active and sedentary individuals, but the risk increases with age and with type 2 diabetes (1,3). The latter is likely due to the long-standing glycation and metabolic impact of diabetes on tendon tissue, impairing tendon structure and function, thereby increasing brittleness (2,3). We recently demonstrated that individuals with elevated glycated hemoglobin, even in the prediabetes range ($HbA_{1c} >5.7\%$, >39.8 mmol/L), had three-times-higher odds of developing tendon injury in the lower extremities compared with individuals with normal levels (4). Additionally, hypercholesterolemia (total cholesterol >5 mmol/L) was associated with 1.5-times-higher odds of tendon injury in the upper extremities, and individuals with metabolic syndrome had 2.5-times-higher odds of tendon injury in both upper and lower extremities (4). Hence, it is reasonable to assume that modern type 2 diabetes care, which serves to lower HbA_{1c} and regulate dyslipidemia, would lower the risk of tendon

injuries, although it remains to be established.

In the Diabetes Care in General Practice (DCGP) trial by Olivarius et al. (5), a total of 484 general practitioners were randomized to provide structured care (247 general practitioners, 761 patients) or routine care (237 general practitioners, 602 patients) to their patients with newly diagnosed type 2 diabetes at a time when the disease was seldom treated. The patients were enrolled in the trial between 1989 and 1991 and remained in their respective groups for 6 years. The structured care comprised follow-up visits every 3 months that included glycemic and blood pressure control and lifestyle advice, such as smoking cessation, weight loss, and increased physical activity (5). The general practitioners providing structured care attended an annual seminar to stay updated on clinical guidelines and set more optimistic goals for their patients (5). Olivarius et al. (5) found that the structured care reduced plasma glucose, HbA_{1c} , cholesterol, blood pressure, and the incidence of myocardial infarction and diabetes complications. The DCGP trial findings introduced a new paradigm on how to treat diabetes that quickly became standard care in Danish

general practice. However, the risk of musculoskeletal disorders was not evaluated.

We estimated the risk of tendon injury in the intervention period and 13-year legacy period with structured care. The outcome data were obtained from the Danish National Patient Registry as hospital contacts (International Classification of Diseases 8/10 codes for tendon injury diagnoses/surgeries). We used the definition of metabolic syndrome provided by the International Diabetes Foundation, which requires at least two of the following criteria to be met: 1) $BMI \geq 30$ kg/m², 2) fasting triglycerides ≥ 2 mmol/L, 3) hypertension, and 4) fasting plasma glucose ≥ 6 mmol/L. Only patients with measures of HbA_{1c} , fasting glucose, and total cholesterol from the DCGP database (1) were included in our analyses.

Incidences of tendon injury were compared using hazard ratios from multivariable Cox regression with corresponding 95% CI; the latter were calculated using a robust sandwich estimator to adjust for clustering of patients within practices. The intervention period and the legacy period were analyzed separately. Effects of the randomization were presented as unadjusted and adjusted for the following

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Received 15 February 2024 and accepted 3 May 2024

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Table 1—Between-group risk of tendon injury

Period and injury type	Group based on type of care	n	Risk time	IR (95% CI) per 1,000 person-years	HR (95% CI)	P value	Adjusted HR (95% CI)*	Adjusted P value*
Intervention								
Upper extremity	Routine	6	2,995	2.00 (0.72; 4.39)	Reference		Reference	
	Structured	7	3,602	1.94 (0.77; 4.03)	0.97 (0.33; 2.81)	0.951	0.65 (0.18; 2.36)	0.515
Lower extremity	Routine	5	3,011	1.66 (0.52; 3.91)	Reference		Reference	
	Structured	2	3,633	0.55 (0.05; 2.02)	0.34 (0.07; 1.74)	0.195	0.32 (0.04; 2.37)	0.267
Overall	Routine	11	2,946	3.73 (1.85; 6.70)	Reference		Reference	
	Structured	9	3,577	2.52 (1.14; 4.80)	0.68 (0.29; 1.60)	0.375	0.54 (0.20; 1.44)	0.220
Legacy								
Upper extremity	Routine	23	3,825	6.01 (3.81; 9.04)	Reference		Reference	
	Structured	46	4,819	9.55 (6.99; 12.74)	1.66 (0.97; 2.83)	0.064	1.33 (0.68; 2.58)	0.403
Lower extremity	Routine	4	3,928	1.02 (0.26; 2.63)	Reference		Reference	
	Structured	18	5,056	3.56 (2.11; 5.64)	3.51 (1.18; 10.46)	0.025	8.97 (1.27; 63.20)	0.028
Overall	Routine	26	3,686	7.05 (4.60; 10.35)	Reference		Reference	
	Structured	57	4,720	12.08 (9.14; 15.65)	1.78 (1.09; 2.92)	0.022	1.65 (0.87; 3.11)	0.123

*Adjusted for sex, age, diabetes duration, cohabitation status, educational level, Charlson's comorbidity index, BMI, smoking habits, physical activity, glycemic control, acute myocardial infarction, stroke, hypertension, total cholesterol, triglycerides, urinary albumin, retinopathy, peripheral neuropathy, diabetes medication, hypertension medication, and lipid-lowering medication.

covariates obtained from the Danish National Prescription Registry: sex, age, diabetes duration, cohabitation status, educational level, Charlson's comorbidity index, BMI, smoking habits, physical activity, glycemic control, acute myocardial infarction, stroke, hypertension, total cholesterol, triglycerides, urinary albumin, retinopathy, peripheral neuropathy, diabetes medication, hypertension medication, and lipid-lowering medication.

A total of 103 tendon injuries were registered, 37 in the routine care group and 66 in the structured care group. In the legacy period, there was a significantly higher risk of injury in the lower extremity in the structured care group according to both the unadjusted and adjusted analyses (incidence rate 3.6 vs. 1.0 per 1,000 person-years, adjusted hazard ratio 9.0, $P = 0.0276$) (Table 1).

In summary, the introduction of structured care improved outcomes in type 2 diabetes but markedly increased the risk of lower-extremity tendon injury. The specific variable(s) contributing to the increased risk, other than the care modality (the randomization), remains unknown. However, we speculate that elements of present-day management of the disease, including

weight loss attempts, pharmacotherapy, and increased physical activity (higher load imposed on vulnerable tendons), may increase the risk of tendon injury, suggesting that the progression of exercise intensity should be considered when prescribing physical activity. Therefore, tendon injuries should be reported in future studies of diabetes interventions.

Funding. This study was supported by RegionH, Bispebjerg Hospital, Center for Healthy Aging (Nordea Foundation), University of Copenhagen, and the Danish Medical Research Council.

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

Author Contributions. V.S., R.K.-R., and C.C. conceptualized the study. M.B.S. and C.C. collected the data for analyses (diagnosis and surgery codes). V.S. and A.W. conducted the analyses. All authors interpreted the results. Subsequently, M.B.S. and C.C. wrote the first version of the manuscript and finalized it based on substantial comments by all authors, especially by V.S. All authors reviewed and approved the final version of the manuscript prior to submission. V.S. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Prior Presentation. The study was presented in oral form in the Capital Region of Denmark at the Symposium for Physio- and Occupational Therapists at Hvidovre Hospital on 26 October 2023 and subsequently at the Lassen Day Conference at Bispebjerg Hospital on 7 December 2023.

Handling Editors. The journal editors responsible for overseeing the review of the manuscript were John B. Buse and Vanita R. Aroda.

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