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ORIGINAL ARTICLE

Discordant pattern of peripheral fractures in diabetes: a meta-analysis on the risk of wrist and ankle fractures

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Abstract

Summary To clarify if the peripheral microarchitectural abnormalities described in diabetics have clinical consequences, we evaluated the risk of wrist and ankle fractures. The meta-analysis resulted in an increase in the risk of ankle fractures and a decrease in wrist fractures risk, suggesting that microarchitecture may not be the major fracture determinant.

Introduction There is evidence for an increase in the risk of hip fractures in diabetes (both in type 1 and 2), but the risk is not established for other skeletal sites. Microarchitecture evaluations have reported a decrease in volumetric bone mineral density and an increase in cortical porosity at the radius and tibia. To investigate if there is a clinical consequence for these microarchitectural abnormalities, we performed a systematic review and meta-analysis on the risk of ankle and wrist fractures in diabetes.

Methods Medline and Embase were searched using the terms 'diabetes mellitus', 'fracture', 'ankle', 'radius' and 'wrist'. Relative risks and 95% confidence intervals were calculated using random effects model.

Results For ankle fractures, six studies were selected including 2,137,223 participants and 15,395 fractures. For wrist fractures, 10 studies were eligible with 2,773,222 subjects and 39,738 fractures. The studies included men and women, ages 20 to 109 years for the wrist and 27 to 109 years for the ankle. The vast majority of subjects had type 2 diabetes.

Diabetes was associated with an increase in the risk of ankle fractures (RR 1.30 95%CI 1.15–1.48) and a decrease in wrist fractures (RR 0.85 95%CI 0.77-0.95). In the studies that reported body mass index (BMI), the mean values were 10% higher in the diabetic groups than controls.

Conclusion The risk of fractures is increased in diabetes at the ankle and decreased at the wrist. The same pattern is observed in obesity. Although bone microarchitectural features are different in obesity and diabetes, the epidemiology of peripheral fractures is similar in both diseases suggesting that microarchitecture may not be the major determinant of peripheral fractures in these populations.

Keywords Ankle fractures · Bone · Diabetes · Wrist fractures

Introduction

There is an increase in the risk of hip fractures in diabetes, but the risk is less well described for other skeletal sites [1, 2]. A number of cohorts have reported an increase in the risk of fractures in several sites in diabetes [3–5]. The Women's Health Initiative study showed an increased risk of any fracture and all the different fracture sites evaluated, except lower arm/wrist/hand in postmenopausal women [3]. The majority of the participants were white, but other ethnic groups such as black, Hispanic and minorities were also included [3]. In elderly men, the risk of non-vertebral fracture is increased in models adjusted for age, race, clinic site and total hip BMD. However, in the further adjusted model, the risk remained increased only in insulin users [4]. Diabetic men have higher BMD but lower bone strength and lower resistance to fractures [6]. Conversely, a biracial cohort of diabetic elderly men and women reported a 64% increase in incident clinical fractures after adjustments for BMD and body composition features such as lean and fat mass, but no additional risk was associated with insulin use [5]. Several small studies have reported different findings, but meta-analyses have agreed that there is an increase in the risk of hip fracture, in type 1(T1D) and in type 2 diabetes (T2D) [1,

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2, 7–9]. Results are less consistent at other skeletal sites. The risk of any fracture is increased in T1D [9] and T2D [1, 2]. Shah et al. reported an increase in the risk of vertebral fractures in T1D [9], but there was no significant increase in T2D [1, 2, 8]. Previous evaluation of specific sites such as the distal forearm, ankle and proximal humerus in T2D showed significant increase only at the foot [2]. More data are required to establish the site-specific risk of fractures in this population.

The increase in the risk of fractures in diabetes is not directly associated with bone mineral density (BMD) [1]. The risk of fractures is increased in T1D and T2D, but BMD is decreased in T1D, and increased in T2D [1, 10, 11]. The increased risk of fractures in T1D is greater than would be expected for the decrease in BMD, suggesting that other features (such as bone quality, increased fall risk or altered biomechanics) might play a role. Despite increased BMD in T2D, BMD is still able to predict fracture risk, but for a given T-score, people with diabetes have a higher risk of fractures than people without the disease [12]. Conversely, for a similar fracture risk, women and men with diabetes have a higher BMD than people without the disease [4, 12]. Therefore, BMD does not fully reflect bone fragility in diabetes.

Diabetes and osteoporosis are both major public health concerns. In 2015, the global prevalence of diabetes was 8.8%, and estimates suggest that it will reach 10.4% in 2040 [13]. T2D is the most common form of the disease, accounting for 90% of the cases. Osteoporosis is estimated to cause nine million fractures annually worldwide, resulting in significant disability [14]. Both diseases affect mainly the elderly, their prevalence is increasing worldwide, and both are associated with significant morbidity and mortality [13, 14]. As life expectancy is increasing, the prevalence of both diabetes and osteoporosis is expected to rise, increasing the burden for health care systems.

Although hip fracture risk is increased in patients with diabetes, the mechanisms associated with bone fragility in this population are not established. Investigations so far suggest that accumulation of advanced glycation end-products (AGEs) and low bone turnover may impair bone material quality [15]. Microarchitectural assessments have identified structural abnormalities [15]. High-resolution peripheral computed tomography (HR-pQCT) was used to evaluate microarchitecture at the ankle and the wrist. Several studies reported a decrease in volumetric bone mineral density (vBMD) and an increase of cortical porosity [16–20]. To evaluate if there is a clinical consequence for these microarchitectural abnormalities, we performed a systematic review and meta-analysis on the risk of ankle and wrist fractures in diabetes.

Methods

PRISMA-P was used to develop the protocol, and PRISMA statement was used as a guidance [21]. One reviewer searched databases like Medline, EMBASE and LILACS in March 2017. ‘Diabetes mellitus’, ‘fracture’, ‘ankle’, ‘wrist’, ‘radius’ and ‘forearm’ were used in the research. There were no limits in regard to languages or date of publication. In order to capture all the available information, studies that reported the risk of fractures in adults (> 18 years) with diabetes (type 1 and type 2) compared with healthy controls were included.

Additionally, we reviewed references from relevant published papers. Studies were excluded if they included children, had unclear diabetes diagnosis criteria, did not have a comparison group without diabetes or if it was not possible to extract or calculate the relative risk for fractures.

We extracted the data using a piloted questionnaire in Google Forms. For each study, data on the first author’s name, country, year of publication, study design and name, source of funding, source and age of population, numbers of exposed and unexposed subjects, numbers of events in each group, follow-up period (in cohorts), type of diabetes, gender, risk estimates and corresponding confidence intervals, possible confounders, and factors controlled for by multivariable analysis were extracted. If the relative risk was not reported, but there were enough data for adequate calculations, the risk was calculated using standard formulas.

The Newcastle-Ottawa quality assessment tool was used [22]. Specific questionnaires were applied for cohorts and case-control studies. We used funnel plots to evaluate publication bias.

The studies were grouped in meta-analyses, using the random effects model. Adjusted relative risks controlling for potential confounders such as age, gender and race were combined using Stata version 14 (Stata corporation, College Station, Texas). As just a few studies adjusted the risk for weight or body mass index (BMI) and BMD, which were potentially important confounders, these adjustments were excluded. The Chi2 test with $p < 0.1$ and the I^2 were used to evaluate heterogeneity.

Results

The research process is summarised in Fig. 1. Initial electronic searches resulted in 755 citations. After the evaluation of inclusion and exclusion criteria, 11 articles were selected, six with data about ankle fractures (distal tibia and fibula) and 10 about wrist fractures (distal radius and ulna). Data were described as relative risk in cohorts and odds ratio in case-control studies. As the frequency of fractures is low, odds ratio and relative risk can be assumed as reporting similar risk estimates [23].

The Newcastle-Ottawa toll was used to evaluate the studies’ quality. The studies had good quality and an average score of 6.7 (from 6 to 8). Funnel plot evaluation revealed no publication bias.

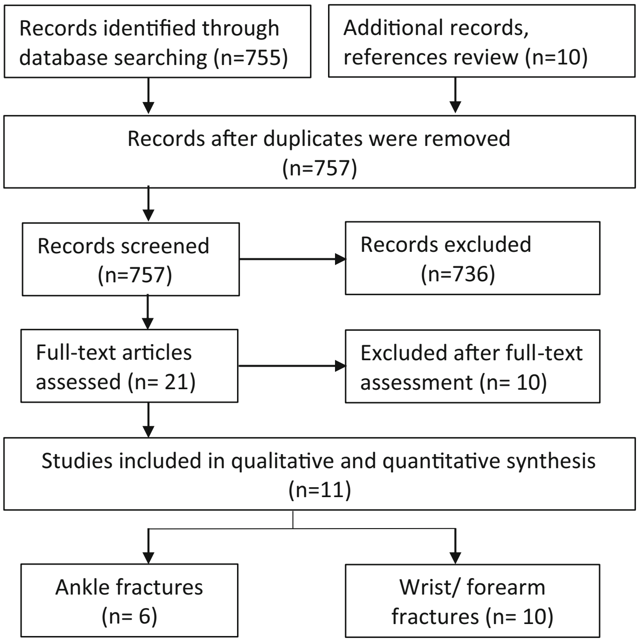


Fig. 1 Selection flow chart (adapted from PRISMA diagram)

Ankle fractures

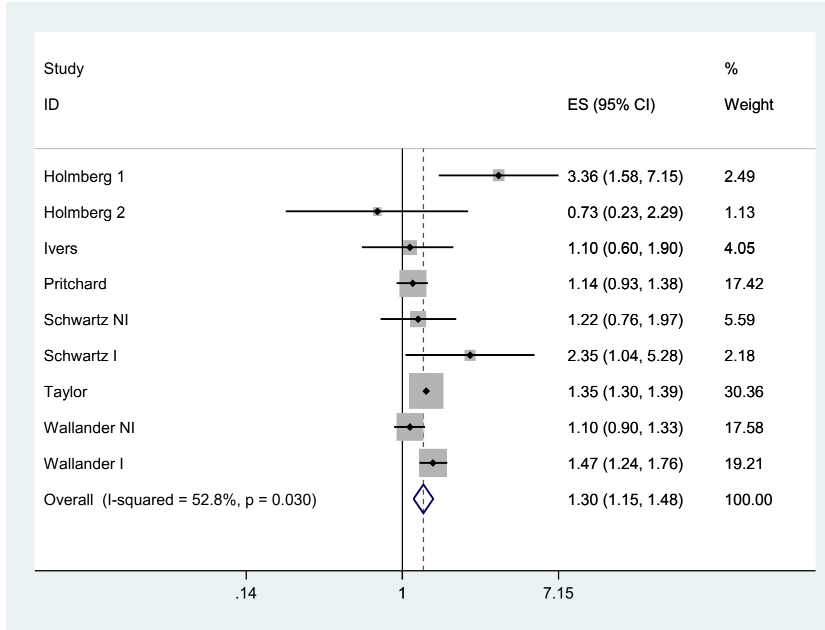
For ankle fractures, six studies were selected: five cohorts [24–27, 29] and one case-control study [28]. In the cohorts, the mean follow-up was 7.4 years (range 1.3 to 25 years). In the case-control study, for each case, three controls were selected [28]. The age range was from 27 to 109 years. One study recruited participants from 27 to 61 years [26], another one from 49 to 97 years [24]. Pritchard et al. evaluated registry data from people older than 50 years [28]. The remaining three studies report data from people older than 65 years [25, 27, 29]. Two studies reported data from the USA [25, 27], one from Canada [28], two from Sweden [26, 29] and one from Australia [24]. Most of the studies reported data from white populations [24, 26, 28, 29]. Where other ethnicities were included, less than 10% were black people and 2% were other ethnicities [25, 27]. Three studies reported data from a registry [27–29] and three recruited participants [24–26]. Two studies reported data specifically from T2D [25, 29], while the others did not state the disease type [24, 26–28]. Three studies excluded fractures associated with high-energy/trauma [25, 26, 28], while the three others (registry based), did not report the energy associated with the fractures [24, 27, 29]. Two studies reported data just from women [25, 28], two reported the risk specifically for men and women [26, 29] and the two others did not report gender-specific risk [24, 27]. In the three studies which reported BMI, it was on average 10% higher in the group with diabetes [25, 28, 29]. In three studies, there was a significant increase in the risk of ankle fractures in diabetes [RR 1.28 (CI 1.12–1.47) [29]; RR 1.34 (CI 1.30–1.39) [27]; RR 3.36 (1.58–7.15) for women [26]]. In the other three studies, the increase in the risk of ankle fractures in diabetes was not statistically significant [RR1.1 (CI 0.6–1.9) [24]; RR 1.14 (0.93–1.38) [28]; RR 1.22 (0.76–1.97) [25]. Two studies reported a higher risk in the insulin user group RR 2.35 (1.04–5.28) [25] and RR 1.47 (1.24–1.76) [29].

Data were summarised in a meta-analysis. Two studies are reported as unadjusted data [28, 29], the remaining data were adjusted for age [25, 26], age and gender [24], gender, race, age, calendar year, urban/rural area, geographic region and median income [27].When the data were pooled together, we found an increased risk of ankle fractures in people with diabetes (RR 1.30 95%CI 1.15–1.48) (Fig. 2). Subgroup analysis found a higher risk in people with diabetes who used insulin (RR 1.56 95%CI 1.15–2.12) than the risk in non-insulin users (1.24 95%CI 1.07–1.45). The meta-analysis summarises data from 2,137,223 participants and 15,395 fractures.

Wrist fracture

Of the 10 wrist fracture studies selected, nine were cohorts, six prospective [24–26, 29–31] and three retrospective [27, 32, 33], and one study was a case-control study [34]. The follow-up ranged from 1.3 to 25 years, and the mean was 7.6 years in the cohorts. Four studies reported data from the USA [25, 27, 33, 34], three from Sweden [26, 29, 30], one from the Netherlands [31], one from Canada [32] and one from Australia [24]. Most studies reported data from white populations [24, 26, 29–31] while the North American ones included other ethnicities. One study included Canadian indigenous people [32], and two others included around 10% of black people [25, 27]. In one study, 20% were Asiatic, 15% black and 10% Hispanic [34]. In another, 66% were non-white [33], although it was not specified which ethnicities were included, due to non-availability of the data in the registry. In six studies, participants were recruited [24–26, 30, 31, 34] and in four studies, data came from a registry [27, 29, 32, 33]. The age of the participants varied from 20 to 109 years. Two studies reported data from young people, one from people older than 20 years [32] and the other from 27 to 61 years [26]. Two studies reported data from the fifth decade, one study observed people older than 45 years [34] and another older than 49 years [24]. One study reported data from people older than 55 years [31] and another one older than 60 years [33]. Four studies reported data from elderly people, three from 65 years [25, 27, 29] and one from people older than 75 years [30]. Three studies reported the risk for men and women [26, 29, 31], two reported data just from women [25, 30] and the other five did not state gender-specific risks [24, 27, 32–34]. The majority of the studies did not specify the type of diabetes, although three reported data specifically from T2D [25, 29, 31]. Two studies reported the specific risk in insulin users [25, 29]. In two studies, high-energy fractures were excluded from the analyses [25, 26], while the others made no distinction. Two studies

Fig. 2 Forest plot risk of ankle fractures in diabetes

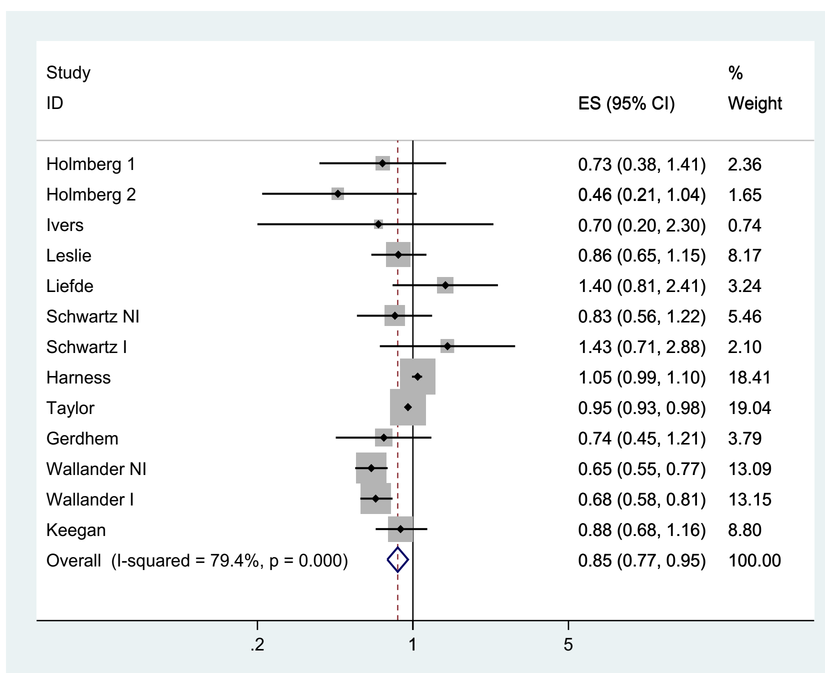


Holmberg 1 women; Holmberg 2 men; NI non-insulin users; I insulin users;

reported a significant decrease in the risk of wrist fractures: Taylor et al. reported RR 0.95 (95%CI 0.93–0.98) [27] and Wallander et al. reported RR 0.67 (95%CI 0.59–0.76) [29]. In all the other studies, the association was not significant: RR 0.73 (95%CI 0.38–1.41) for women and RR 0.46 (95%CI 0.21–1.04) for men [26]; RR 0.70 (95%CI 0.20–2.30) [24]; RR 0.86 (95%CI 0.65–1.15) [32]; RR 1.40 (95%CI 0.81–2.41) [31], RR 0.83 (95%CI 0.56–1.22) for non-insulin users and RR 1.43 (95%CI 0.71–2.88) for insulin users [25]; RR 1.05 (95%CI 0.99–1.10) [33]; RR 0.74 (95%CI 0.45–1.21) [30]; and OR 0.88 (0.68–1.16) [34].

All the studies were pooled in a meta-analysis. We found a significant decrease in the risk of wrist fractures [RR 0.85 (95%CI 0.77-0.95)] (Fig. 3). The risk was not decreased in insulin users [RR 0.91 (95%CI 0.45–1.85)]. The analysis included data adjusted for age [25, 26, 31], age and gender [24], gender, race, age, calendar year, urban/rural area, geographic region, median income [27], age, gender and ethnicity [34]

Fig. 3 Forest plot risk of wrist fractures in diabetes



Holmberg 1 women; Holmberg 2 men; NI non-insulin users; I insulin users;

and unadjusted data [29, 30, 32, 33]. However, sensitivity analysis of adjusted and unadjusted data showed similar patterns. This meta-analysis reports data from 2,773,222 subjects and 39,738 fractures. The studies included men and women, from 20 to 109 years, the vast majority with T2D.

Discussion

There is an increase in the risk of ankle fractures, and a decrease in the risk of wrist fractures in diabetes. Ankle and wrist fractures have distinct epidemiological patterns. Ankle fractures are not considered typical osteoporotic fractures [35, 36]. Having an ankle fracture is a predictor of a future fracture at other sites [36]. However, the risk of an ankle fracture is not associated with low axial BMD, but with increased weight and BMI [35, 36]. Overweight and obesity are highly prevalent in T2D, the main group evaluated in this study [13]. Interestingly, microarchitectural abnormalities without decreased BMD were previously associated with ankle fractures [37]. Stein et al. reported disrupted microarchitecture but no BMD abnormalities in postmenopausal women with ankle fractures [37]. Microarchitectural abnormalities were observed mainly in the trabecular compartment. They were more pronounced at the tibia, but also observed at the wrist. The authors argue that this finding could highlight underlying bone fragility despite relatively normal BMD. Cortical porosity was not associated with ankle fractures in this study [37].

Conversely, wrist fractures are a major osteoporotic fracture. They account for up to 18% of all fractures in people older than 65 years, and can be the first clinical indicator of osteoporosis [38]. Bone density, geometry, microstructure and strength are all determinants of wrist fractures [39]. Melton et al. reported microarchitectural abnormalities in a wrist fracture population, and the deficit in trabecular bone was relatively greater than in cortical bone. Cortical porosity was similar in cases and controls and some analyses suggested that Colles' fractures are associated with disruptions of trabecular architecture [39]. Some evidence suggests that obesity decreases the risk of wrist fractures [40].

The discordant pattern observed in this study might reflect the weight excess in the population observed. Although obesity is generally considered protective against fracture, the effect on fracture risk is site dependent [15, 40]. Several studies reported a decrease in the risk for femoral and wrist fractures and an increase for ankle and upper arm fractures [40]. Obese adults have greater BMD than normal weight controls [41]. Evans et al. reported favourable microarchitecture features such as increased cortical and trabecular BMD in obese people when compared to normal-weight adults [41]. Non-bone features also play an important role. The thick soft tissue has a protective effect in absorbing the impact in hip fractures [40]. Obese people tend to fall backwards or sideways, which might favour the occurrence of upper arm fractures over wrist fractures [40]. On

Table 1 Studies and population baseline characteristics for ankle fractures

First author	Year	Country of study	Setting—name of the study/cohort	Study design	Follow-up (cohort) y	Number of participants	Source of population	Age y (mean ± SD)	RR (95%CI)	DM diagnosis	Fracture diagnosis	DM type
Ivers [24]	2001	Australia	The Blue Mountains Eye Study	Cohort study	5 years	DM 216 Non-DM 3438	Recruitment	49–97 (66)	1.1 (0.6–1.9)	Self-report	Self-report confirmed by radiology report	NR
Schwartz [25]	2001	USA	Study of Osteoporotic Fractures (SOF)	Cohort study	9.4 y (mean)	T2D 657 Non-DM 8997	Recruitment	> 65 (71 ± 5)	NI 1.22 (0.76–1.97) I 2.35 (1.04–5.28)	Self-report	Self-report confirmed by radiology report	T2D
Holmberg [26]	2006	Sweden	Malmo Preventive Project	Cohort study	M (7–25) 19y W (7–22) 15y	DM 381 Non-DM 32,738	Recruitment	27–61 (M 44 W 48)	M 0.73 (0.23–2.29) W 3.36 (1.58–7.15)	Self-report	Registry	NR
Taylor [27]	2011	USA	Random 5% sample of Medicare beneficiaries from 2000 to 2005	Cohort study	4.2	Total pop 1,694,051 (DM non-reported)	Registry	> 65 y	1.35 (1.30–1.39)	Registry	Registry	NR
Pritchard [28]	2011	Canada	Manitoba Bone Density Program	Case-control	Case-control[#] 3 controls/each case	DM 3054 Non-DM 9151	Registry	> 50 y 68(± 9)	1.14 (0.93–1.38)	Medical records	Registry	NR
Wallander [29]	2017	Sweden	FRAILCO	Cohort study	1.3 y (mean)	T1D 2883 T2D 79,159 Non-DM 343,603	Registry	> 65 y (80.2 ± 8.2)	NI 1.10 (0.9–1.33) I 1.47 (1.24–1.76)	Registry	Registry	T1D and T2D

DM, diabetes mellitus, type not specified; T1D, type 1 diabetes; T2D, type 2 diabetes; M, men; W, women; NI, non-insulin users; I, insulin users; NR, non-reported

[#] Case-control study: for each case, three controls were selected

Table 2 Studies and population baseline characteristics for wrist fractures

First author	Year	Country of study	Setting—name of the study/cohort	Study design	Follow-up (cohort) y (years)	Number of participants	Source of population	Age y (mean)	RR (95%CI)	DM diagnosis	Fracture diagnosis	DM type
Schwartz [25]	2001	USA	Study of Osteoporotic Fractures (SOF)	Cohort study	9.4 y (mean)	T2D 657 Non-DM 8997	Recruitment	> 65 (71 ± 5)	NI 0.83 (0.56–1.22) I 1.43 (0.71–2.88)	Self-report	Self-report confirmed by radiology report	T2D
Ivers [24]	2001	Australia	The Blue Mountains Eye Study	Cohort study	5 y	DM 216 Non-DM 3438	Recruitment	49–97 (66)	0.7 (0.2–2.3)	Self-report	Self-report confirmed by radiology report	NR
Keegan [34]	2002	USA	Kaiser Permanent Northern California	Case-control		Cases: 1000 Controls: 1913 Number of DM not reported	Recruitment	> 45 y	0.88 (0.68–1.16)	Self-report	Registry	NR
Leslie [32]	2005	Canada	The First Nation Cohort	Retrospective cohort study	12 y	DM 3699 Non-DM 107,578	Registry	> 50 y (68 ± 9)	0.86 (0.65–1.15)	Medical records	Registry	NR
De Liefde [31]	2005	Netherlands	The Rotterdam study	Cohort study	6.8 y	T2D 792 Non-T2D 7191	Recruitment	> 65	1.4 (0.81–2.41)	Test result	Registry	T2D
Gerdhem [30]	2005	Sweden	Osteoporotic Prospective risk assessment (OPRA)	Cohort study	3–6.5 (4.6) y	DM 67 Non-DM 961	Recruitment	> 75 y	0.74 (0.45–1.21)	Self-report	Self-report + registry	NR
Holmberg [26]	2006	Sweden	Malmo Preventive Project	Cohort study	M (7–25) 19 y W (7–22) 15 y	DM 381 Non-DM 32,738	Recruitment	27–61 (M 44 W 48)	M 0.46 (0.21–1.04) W 0.73 (0.38–1.41)	Self-report	Registry	NR
Taylor [27]	2011	USA	Random 5% sample of Medicare beneficiaries from 2000 to 2005	Cohort study	4.2	Non-DM pop 1,694,051 (DM pop not reported)	Registry	> 65 y	0.95 (0.93–0.98)	Registry	Registry	NR
Harness [33]	2012	USA	Kaiser Permanent South California	Retrospective cohort study	6 y	DM120,796 Non-DM 403,816	Registry	> 60 y	1.05 (0.99–1.1)	Registry	Registry	NR
Wallander [29]	2017	Sweden	FRAILCO	Cohort study	1.3 y (mean)	T1D 2883 T2D 79,159 Non-DM 343,603	Registry	> 65 y (80.2 ± 8.2)	NI 0.65 (0.55–0.77) I 0.68 (0.58–0.81)	Registry	Registry	T1D and T2D

DM, diabetes mellitus, type not specified; T1D, type 1 diabetes; T2D, type 2 diabetes; M, men; W, women; NR, non-reported; NI, non-insulin user; I, insulin user the other hand, an increase in the mechanical strain at the ankle has been reported [35].

Hyperglycaemia is present in both T1D and T2D, but the pathophysiology of each type is different. T1D is characterised by insulin deficiency that often starts before the peak of bone mass accrual. On the other hand, in T2D, there is insulin resistance which starts most frequently in adulthood, although a trend for a precocious start has been observed recently. Obesity is also more frequent in T2D than T1D, although the prevalence of obesity in T1D has been rising, especially associated with intensive insulin therapy [42]. These features contribute to the BMD pattern observed in diabetes. BMD is decreased in T1D and increased in T2D [1]. In a meta-analysis that evaluated BMD in both types of diabetes, BMI was significantly associated with BMD in T2D but not in T1D [1]. How all these different features impact in the risk of fractures is still to be defined. The increase in the risk is remarkably higher in T1D, but successive meta-analyses have described a progressive lower risk: from RR = 6.94 (95%CI 3.25–14.78) by Vestergaard in 2007 to RR = 3.78 (95%CI 2.05–6.98) by Shah in 2015 [1, 9]. The absolute risk in T2D is lower than T1D but 90% of people with diabetes have T2D, and there are estimates for an increase of T2D prevalence worldwide [13]. This suggests that the majority of fractures associated with diabetes will affect the T2D population.

Several studies have described microarchitecture in T2D, and non-favourable findings are observed in the cortical compartment [16, 18, 20, 43, 44]. Two studies have reported an increase in cortical porosity at the radius [16, 18] and two others at the tibia [20, 44]. Besides, the standard ultradistal site, Nilsson et al. evaluated a more proximal section, located at 14% of the limb length (a site of mainly cortical bone) and found a decrease in cortical porosity at the radius [43]. The diabetic groups evaluated are diverse, including people of different ages, disease duration and complications. All these features could contribute to the non-consistent findings and make difficult to establish a more specific pattern for the cortical compartment findings in this population.

The fracture pattern observed in this study is similar to the pattern described in obesity, despite different microarchitectural findings in both diseases. In diabetes, the described pattern is a decrease in vBMD and an increase in cortical porosity [16–20]. In obesity, Evans et al. reported greater vBMD and lower cortical porosity [41]. These findings suggest that microarchitecture is not the main determinant of peripheral fractures in these populations.

This study has limitations. A major limitation is the combination of type 1 and type 2 diabetes in the same analysis. T1D is associated with the lack of insulin and T2D with insulin resistance, with different consequences to bone health. However, few studies addressed specifically each type of the disease, preventing this analysis. Although men, non-white and T1D participants were included, they account for the minority of the groups and this should be taken in account while evaluating the results. The majority of the participants are white postmenopausal women, a group especially susceptible to fractures. A large amount of data came from registry studies, which do not specify the population characteristics, and many potential confounders such as age, weight/BMI, type, duration and age of onset of diabetes, metabolic control, and the presence or absence of microvascular complications could not be addressed (Tables 1 and 2). Different factors were used to adjust the risk estimates in each study. Consequently, unadjusted data and data adjusted for different factors were used in this analysis. As just a few studies reported data adjusted for weight, these adjustments were excluded.

It was desirable to pool together data from studies with adjustments for weight/BMI and to compare them with the unadjusted ones to investigate the role of BMI in the association between diabetes and ankle/wrist fractures. However, this comparison was not possible as just two studies had this adjustment for the risk of ankle fractures [25, 28] and three for wrist fractures [25, 29, 31]. The evaluation of data adjusted and unadjusted for weight could help to elucidate the amount that obesity contributes to fracture risk in diabetes.

Therefore, there are still important questions to be answered for bone health in diabetes. The site-specific pattern of fractures in people with diabetes is still being established. Also, investigations of the effect of many features, such as the type, age of onset and duration of the disease, the metabolic control and diabetic complications are ongoing. More information about the pattern of fractures in diabetes and how these individual features affect the risk of fractures in this population might help to understand how diabetes affects the skeleton. This is important for management planning and adequate interventions design.

In summary, there is an increase in the risk of ankle fractures and a decrease in the risk of wrist fractures in diabetes, despite adverse microarchitectural properties at both sites. Obesity, which is considered protective against the most fractures, but increases the risk of ankle fractures may play a role in these fractures pattern in diabetes, independently from microarchitecture. More studies are needed to clarify the features associated with the increased risk of fractures in the diabetic population to guide adequate management.

Compliance with ethical standards

Conflicts of interest None.

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