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REVIEW ARTICLE

History, Prevalence and Assessment of Limited Joint Mobility, from Stiff Hand Syndrome to Diabetic Foot Ulcer Prevention: A Narrative Review of the Literature

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Abstract: ***Background*:** Limited Joint Mobility (LJM) is a dreaded complication of Diabetes Mellitus (DM). During the last half century, LJM has been studied in patients of different age because it has been considered useful for the monitoring of a patient's condition and for the prevention of vascular disease and diabetic foot.

Objectives: The main aims of this review are to describe the relationship between DM and joint mobility as well as its prevalence and assessment. We have also investigated the role of LJM in the development of diabetic foot ulcers.

***Methodology*:** An in-depth literature search was conducted to identify studies that examined the prevalence and characteristics of LJM in patients with DM of different types, age, durations and chronic complications.

***Results*:** Many factors (therapy improvements, population characteristics and different evaluation methods) concur to hinder an exact assessment of the prevalence of LJM. However, it has been confirmed that LJM is widespread among patients with DM and may affect more than two-thirds of them in addition to being a major risk factor for foot ulcer. Its role in the monitoring of a patient's condition is also important for the definition of risk thresholds such as in patients with diabetic foot. The efficacy of exercise therapy for the treatment of LJM, also in patients at risk of foot ulcer, has not been discussed.

***Conclusion*:** Difficulties encountered in the definition of the prevalence of LJM may hinder its study and the establishment of preventive interventions. However, LJM plays a key role in the monitoring of patients, especially those at risk for ulcer.

Keywords: Limited joint mobility, history, prevalence, assessment, prevention, diabetic foot ulcers.

1. INTRODUCTION

Diabetes Mellitus (DM) is a metabolic disorder representing one of the main global public health problems. It is estimated that by 2035 almost 600 million people will be affected by the disease due to the progressive increase in its incidence [1, 2]. DM patients may develop different complications during their lifetime, of which Limited Joint Mobility (LJM) is one of the most ominous [3].

In this article LJM is defined as the reduction of joint Range of Motion (ROM), usually associated with stiffness, which can affect the joints of the whole body in DM patients of all ages [4-7].

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Many authors, especially over the last 40 years, have investigated LJM from several perspectives and underlined the importance of considering this functional deficit in the management of patients with diabetes [3, 6-9].

It has been known for a long time that diabetes can lead to the development of connective tissue disorders. Several early studies on LJM focused on the relationship between LJM and other chronic complications. In particular, the relationship between changes in joint mobility and micro- and macrovascular disease (retinopathy, nephropathy), skin and lung changes were investigated [3, 10-12]. After the recognition of such a relationship, it has been suggested that assessment of LJM could be used to monitor the diabetic patient's general condition [3, 7, 9, 13, 14].

Diabetes can directly affect periarticular tissues, inducing stiffness and then LJM [3, 15-18]. Joint abnormalities and LJM are problems that can arise at disease onset, and pro-

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gressively worsen together [3, 4, 7, 19]. As a result, deficits of joint mobility should be considered among the factors that first trigger the complex vicious cycle leading to joint deficit, the development of abnormal postures, hand/foot deformity, in addition to being one of the major causal factors of diabetic foot ulcer [7- 9, 18, 20, 21].

Today attention is focused on the causal role of LJM in the development of diabetic foot ulcers due to the recognized progressive increase and severity of patients' foot complications. Diabetic foot is a huge problem with an yearly incidence of 1-4% in developed countries, leading to many hospital admissions and contributing to patients' morbidity and mortality, which can be higher in developing countries [2, 7, 22-28]. 85% of all amputations are preceded by a diabetic foot ulcer and there is an amputation every 20 seconds somewhere in the world due to diabetes [2, 24].

Identifying the role of LJM in the development of diabetic foot ulcer, providing a clear definition of its prevalence, explaining the progression of this problem and its effects on diabetes, could help to define better preventive treatments [29, 30].

The main aim of this review is to describe the relationship between DM and joint mobility and to explain its role in the development of diabetic foot ulcers in an effort to define preventive treatments.

2. HISTORY OF LIMITED JOINT MOBILITY (LJM)

The earliest observations of the presence of joint deficits in diabetic patients date back to the middle of the last century [31]. In this period, advances in DM patient therapy and, above all, the discovery of insulin (1923), radically changed routine medical practice [30]. In the middle of the last century, awareness of a progressive increase in chronic complications of severe diabetes became widespread [30]. In this same period K. Lundbeack reported the presence of a typical "Hand Syndrome" as a long-term diabetic alteration [31]. The author reported that the hands of the five patients investigated presented a dry, stiff, hard palm with a thickening of the fascia palmaris. Palpation showed a marked increase in the tone and decrease in the elasticity of the subcutaneous tissue. Hand functionality in opening and closing was adversely affected by connective tissue alterations, causing discomfort. These alterations were mostly localized to the hands and especially to the palmar surface, even if they could also affect the back and distal part of the forearms (Table **1**) [31].

Table 1. The milestone studies on LJM in diabetic patients.

Year	Author	Major Findings
1957	Lundbeak K. [31]	Although it is not possible to prove that "hand syndrome" is a true long-term manifestation of diabetic angiopathy, this disorder does not seem to occur in patients with diabetes of short duration
1971	Jung Y. *et al.* [37]	When atrophy of the hand muscles and flexion deformities of the fingers are present, transmission of the median nerve impulse from the wrist to the fingers is frequently delayed. It is our impression that when the digital flexion deformity is present, atrophy of the intrinsic hand muscles is more severe
1974	Rosenbloom AL. *et al.* [53]	Three unrelated patients have stable insulin-dependent diabetes mellitus, short stature and joint stiffness beginning 8 to 13 years after onset of diabetes.
1975	Hamlin C.R. *et al.* [35]	Juvenile diabetics have experimentally-determined ages which are significantly greater than their actual ages. This raises the possibility of a relationship between diabetes mellitus, changes in connective tissue and accelerated aging
1976	Grgic A. *et al.* [16]	Finger-joint contracture can be present in young insulin-dependent patients. In two- thirds of affected children only the fifth finger was involved. Stiff resistance to passive finger manipulation and thickened adherent skin over the dorsum of the hands were additional features
1981	Rosenbloom AL. *et al.* [42]	LJM characterizes a population exceptionally at risk for the development of early microvascular complications
1985	Delbridge L. *et al.* [57]	Neuropathic ulceration of the foot in diabetics is primarily due to the interaction of three factors: peripheral neuropathy, mechanical forces, and changes in the connective tissue. This effect is thought to explain a number of the clinical features of diabetes such as LJM
1987	Shinabarger N.I. [56]	Physical therapists should be aware of the need to address LJM when treating patients with DM by instructing them to perform routine range-of-motion exercises as prophylaxis.
1988	Delbridge L. *et al.* [58]	LJM may predispose to ulceration in susceptible neuropathic feet. These patients often have stiff "rigid" feet in association with skin ulcers
1989	Mueller M.J. *et al.* [15]	It is hypothesized that patients with insensitivity and dorsiflexion of less than 5 degrees, and subtalar joint ROM of less than 30 degrees are at greater risk for developing a plantar ulcer. The side of the most serious LJM matched the side of the ulcer in 79% of patients
1991	Fernando D.J.S. *et al.* [25]	LJM may be a major factor in causing abnormally high plantar foot pressures and contributes to foot ulceration in the susceptible neuropathic foot
2000	Dijs H.M. *et al.* [62]	Physical therapy may significantly, although only temporarily, improve the mobility of the ankle and foot joints in diabetic patients with LJM and neuropathy
2001	Infante J.R. *et al.* [36]	There was a decrease in overall prevalence of LJM from the period 1976-78 to 1998 (31% vs 7%).
2002	Goldsmith J.R. *et al.* [63]	An unsupervised range-of-motion exercise program can significantly reduce peak plantar pressures in diabetic subjects within a relatively short period of time
2004	Zimny S. *et al.* [9]	There was a strong inverse correlation between the ankle, first metatarsophalangeal JM and the pressure-time integrals in diabetic patients

Passing from these first observations to the study of joint mobility at the foot level required many more years of research. In the late '60s and early '70s it has been reported that some connective tissue properties throughout the body can be affected by both diabetes and aging [31-34], anticipating the current knowledge that processes leading to the development of LJM are similarly affected by both these elements, even if the pathogenetic factors of such reduced joint mobility are not fully understood [4, 35, 36].

Since the 1970s many studies have reported on the role of LJM as a marker of longstanding diabetes complications. The relationship between LJM and the presence or severity of neuropathy [25, 37-39], macrovascular disease [10, 40], and especially microvascular complications [5, 8, 41, 42] in patients with type 1 and 2 DM at different ages has been investigated [43-47]. Researchers were looking for a common cause for both impairments associated with alterations in structural macromolecules of the connective tissue extracellular matrix. It has been found that modifications of large vessels and microcirculation in addition to endothelial dysfunction and inflammation may cause ischemia and then induce connective tissue fibrosis [3, 48-50]. LJM has been considered a separate diabetes-induced complication which is independently associated with other chronic microvascular complications [13, 51, 52].

Other important publications on the history of joint mobility changes in diabetic patients emerged from the University of Florida in the mid- '70s [16, 31, 53]. In 1974, Rosenbloom *et al*. reported that joint stiffness induced limited extension and flexion of the interphalangeal, metacarpophalangeal, toes, wrist and ankle in three teenagers with Type 1 Diabetes Mellitus (T1DM). They also described the possible presence of some limitations in patients' elbows, knees, hips, trunk and neck. The presence of deformity or pain in addition to the progression of joint mobility over time has also been considered (Table **1**) [53].

In 1974, Grgic *et al*. increased the sample size of young patients investigated by evaluating 229 campers and a control population of schoolchildren. Contractures of one or more fingers were detected in 28.4% of the young patients investigated, while fewer than 1% of the healthy controls were affected. The authors also suggested the possible role of increased cross-linking in the development of periarticular and skin thickening in addition to early rigidity that young diabetic patients may show (Tables **1** and **2**) [16].

Table 2. Prevalence of LJM.

References	General Purpose	Sample Size	Study Population/ Location	Equipment and Methods	LJM Prevalence
Grgic A. (1976) [16]	To verify that joint contractures are a common manifestation of childhood diabetes mellitus.	229 patients, 210 controls	7 to 18-year old insulin-dependent patients (USA)	LJM of the hands was evaluated using Tabletop test. The examiner confirmed the limitation by passive extension of the patient's fingers	28.4% of patients with DM had contractures of one or more fingers. 20.5% were Stage I; 7.9% were Stage II
Rosenbloom AL (1981) [42]	To substantiate the relationship between LJM and the early development of microvascular complications.	309	1- to 28-year old subjects with DM (USA)	LJM of the hands was evaluated using Prayer sign. The examiner confirmed the limitation by passive extension of the patient's fingers	29.8% of patients with DM had LJM of small and large joints. 83% were at risk for microvascular complications after 16 years of diabetes if joint limitation was present, but only 25% at risk if joint limitation was absent
Brice J.E.H. (1982) [86]	To study LJM in the hands of children, their families, and unrelated non-diabetic children	112 patients	2- to 16-year old children with DM (U.K.)	LJM of the hands was evaluated using prayer sign and tabletop test.	42% of children with DM had LJM, with 14% having more severe involvement
Kennedy L. (1982) [41]	To investigate the prevalence of LJM in the hands of patients with childhood onset Type I diabetes and the correlation with severe proliferative retinopathy	115 patients	5- to 57-year old type I DM patients (U.K.)	LJM of the hands was evaluated using tabletop test.	36.5% of subjects with DM had LJM. Proliferative retinopathy was detected in 70.0% of patients with LJM compared to 15.0% with normal joint mobility
Starkman H. (1982) [69]	To define the prevalence of LJM of the hand in patients with type 1 diabetes mellitus	100	3- to 22-year old type I patients with diabetes (USA)	LJM of the hands was evaluated using prayer sign and tabletop test	32% of patients had LJM of the hand

(Table 2) Contd…

References	General Purpose	Sample Size	Study Population/ Location	Equipment and Methods	LJM Prevalence
Chapple M. (1983) [81]	To define the prevalence of finger joint contractures in 2 groups of DM patients with and without retinopathy	211 patients, 106 controls	105 patients with DM and retinopathy (*49.4 ±14.7 yrs); 106 without retinopathy (*48.6± 12.2 yrs). 106 age-matched controls (UK)	To demonstrate the presence of finger joint contractures the subjects laid both painted hands palmar surfaces down onto a sheet of paper and pressed with his/her weight firmly onto the distal metacarpal heads and fingers	25.2% of patients with DM had finger joint contracture compared to 7.5% of the control group. The prevalence of contractures was similar in those diabetics with and without retinopathy (29.5% *vs.* 20.8%)
Rosenbloom A.L. (1983) [18]	To determine whether there is a genetic component to the development of LJM	204 patients, 336 first-degree relatives, and 90 controls	7- to 23-year old patients with IDDM. First-degree relatives and controls had different age (USA)	LJM of the hands was evaluated using prayer sign. The examiner confirmed the limitation by passive extension of the patient's fingers	21% of children and youths with IDDM had LJM. Among nondiabetic parents, 3% had joint limitation. Only 1 of normal controls had joint stiffness
Fitzcharles M.A. (1984) [44]	To determine the prevalence of LJM in adult NIDD patients, and to investigate its association with the presence of complications of diabetes.	80 patients, 47 controls	Elderly subjects with NIDD, age and sex-matched controls (CANADA).	LJM of the hands was evaluated using the prayer sign. The examiner confirmed the limitation by passive extension of the patient's fingers	45% of patients with NIDD and 14.9% of controls had LJM NIDD patients with impaired joint mobility had a significantly increased frequency of microvascular disease, as shown by retinopathy and/or nephropathy (42% *versus* 22%)
Beacom R. (1985) [132]	This study extends our observations on the relationship of LJM with retinopathy in type I diabetes and the possible pathogenesis of LJM in diabetes.	204	7- to 71-year old patients with insulin-dependent diabetes (U.K.)	LJM was assessed by tabletop test (as Grgic *et al*. 1976)	43% of patients had LJM. Retinopathy was detected in 70.5% of patients with LJM *versus* 30.2% with normal joints
Starkman H. (1986) [73]	To assess the prevalence of LJM, its relationship to age, age of onset (or diagnosis), duration of diabetes, and to certain chronic complications such as retinopathy, neuropathy, and nephropathy	361 patients, 45 controls	11- to 83-year old patients with DM and 19- to 69-year old non-diabetic controls without evidence of arthritis (USA)	LJM of the hands was evaluated using prayer sign and tabletop test	58% of patients and 4% of controls had LJM. In particular, 55% of patients with insulin-dependent diabetes mellitus and 76% with non-insulin-dependent diabetes mellitus had LJM. Symptomatic neuropathy was documented in 23.3% of diabetic population of whom 70.2% showed LJM. Retinopathy was detected in 74.6% of diabetic population of whom 61.4% showed LJM.
Garg S.K. (1992) [12]	To evaluate the relationship of LJM with early diabetic renal and retinal damage	357	Diabetic patients of at least 14 years old who are insulin-dependent with at least 5 years of disease (USA)	LJM of the hands was evaluated using prayer sign	26% of patients had LJM. 19% had stage 1 and 7% had stage 2 involvement of their interphalangeal joints. Subjects with LJM had more advanced diabetic retinopathy as compared with subjects without LJM
Arkkila P.E.T. (1997) [75]	To evaluate the relationship of LJM with the control of diabetes, atherosclerotic vascular disease, and other diabetic complications in NIDDM	139	Elderly patients (*61.3±12.3 yrs) with NIDDM (FINLAND)	LJM of the hands was evaluated using prayer sign. The examiner confirmed the limitation by passive extension of the patient's fingers.	60% of patients had LJM. 23% of patients were classified as having mild, 32% moderate, and 4% severe LJM. 27% had peripheral vascular disease

(Table 2) Contd…

References	General Purpose	Sample Size	Study Population/ Location	Equipment and Methods	LJM Prevalence
Frost D. (2001) [10]	To study the relationship of LJM in type 1 diabetic patients with microvascular complications, hypertension, and early atherosclerosis and to determine whether sex has an influence on possible associations.	335	14- to 40-year old type 1 diabetes patients (GERMANY)	LJM of the hands was evaluated using prayer sign. The examiner confirms the limitation by passive extension of the patient's fingers	33.7% of patients had LJM (29.8% in women and 38.9% in men). Men with LJM had significantly more frequent cases of hypertension (28.6 *vs*. 12.5%), proteinuria (25.5 *vs*. 10.2%), and retinopathy (48.2 *vs*. 14.8%) than men without LJM.
Lindsay J.R. (2005) [76]	To evaluate if the prevalence of LJM may have decreased during the past two decades	204	4- to 79-year old type 1 diabetic patients (U.K.)	LJM was assessed in both the 1981-1982 and 2002 series by the method of Grgic *et al.* 1976 (Tabletop test). The examiner confirmed the limitation by passive extension of the patient's fingers	The prevalence of LJM has fallen across two decades from 43 to 23% between the 1980s and 2002
Amin R. (2005) [11]	To determine risk factors for development of microalbuminuria in relation to detection of LJM of the interphalangeal joints in a longitudinal cohort of type 1 diabetic subjects	479	Patients with T1DM diagnosed at the age of <16 years were followed from diagnosis of diabetes with annual assessments (U.K.)	LJM of the hands was evaluated using prayer sign. The examiner confirmed the limitation by passive extension of the patient's fingers. LJM was diagnosed only if present for 2 or more years	37.2% of patients had LJM after a median of six observations per subject. After a median follow up of 10.9 years, 35.1% developed LJM at a median age 13.0 years and duration 5.2 years
Al-Matubsi H.Y. (2011) [70]	To evaluate the prevalence of these changes and their association to diabetes duration. and its complications in DHS using electrophysiological measurements	187	17- to 75-year old type 1/2 diabetes patients (JORDAN)	LJM of the hands was evaluated using prayer sign	29.4% of patients had LJM. 20.0% of type 1 DM patients and 32.4% of type 2 DM subjects had LJM
Pandey A. (2013)72	To investigate the prevalence of hand disorders in diabetic patients, and to study the relationship of these hand disorders with microvascular complications	200 patients, 200 controls	19- to 65-year old type 2 DM patients (*51.8±11.5 yrs) and age- and sex-matched non-diabetic controls (INDIA)	LJM of the hands was evaluated using prayer sign and flattening sign	40.5% of patients and 8.5% of controls had LJM. LJM was the most common hand disorder and more common in patients who had microvascular complications
Mustafa K.N. (2016) [68]	To assess the prevalence of musculoskeletal disorders of the hand in adult patients with T2DM and their relationship to disease duration, glycemic control and microvascular complications	1,000 patients	23- to 88-year old (*57.8± 9.5 yrs) T2DM patients (JORDAN)	LJM of the hands was evaluated using prayer sign	63.1% of patients had LJM (58.8% male, 67.0% female)
Mineoka Y. (2017) [71]	To determine the relationship between LJM of the hand and diabetic foot risk classified using the criteria of the IWGDF	528 patients	Elderly patients with type 2 diabetes (JAPAN)	LJM of the hands was evaluated using prayer sign or tabletop test	19.9% of patients had LJM

DM: Diabetes Mellitus; ROM: Range of Motion; LJM: Limited Joint Mobility; PN: Peripheral Neuropathy; 1st MTPJ: First Metatarsophalangeal Joint; IDDM Insulin-dependent Diabetic; (NIDD): Non Insulin-dependent; International Working Group on the Diabetic Foot. diabetic (NIDD)
*= mean age.

In 1971, Jung *et al*. reported that the presence of finger contractures ("Diabetic hand syndrome") was positively correlated with the duration of disease and peripheral nerve dysfunction [37]. This study drove the next research to investigate the role played by LJM and peripheral neuropathy in the development of diabetic foot ulcer [9, 25, 44, 45].

Until the mid - '80s [31], the fact that LJM was detected in the majority of diabetic patients aroused little interest in clinicians, and some patients felt disappointed due to functional impairments affecting their normal daily living [54]. However, it was suggested to include LJM assessment in the physical examinations routinely carried out in T1DM patients in order to detect the presence of significant functional limitations [8, 13, 55]. In 1987, Shinabarger *et al*. reported that specialists should assess joint mobility in diabetic patients and suggest physical therapy to maintain ROM, minimize pain, and improve the patient's functional independence [56].

At the end of 1980s, an increasing number of authors began to study the relationship between LJM and diabetic foot ulcer with a growing interest in considering LJM as one of the major risk factors in the development of foot ulcers [25, 57, 58, 59]. This pathway led to the identification of patients at risk and ulcerative risk thresholds: both useful markers for monitoring diabetic patients and defining their treatment (Table **3**) [3, 15, 60, 61].

Since the beginning of the current century, specific studies have investigated the effects of different types of exercise training programs on LJM--showing that a few weeks of physical activity can significantly increase joint ROM at the foot and ankle level (Table **1** and **3**) [62- 66].

3. LJM PREVALENCE

It has been difficult to define the precise prevalence of LJM in the diabetic population, and over the years, the aims, methods and characteristics of populations to be investigated have changed [54, 67-69]. Several studies have evaluated different joints without a precise definition of the prevalence, because some joints, such as those of the distal limbs, seem to be particularly affected by diabetes even though it affects the whole body [8, 54]. Researchers have used different methods and devices to assess LJM [42, 46, 58, 67], but varying onsets and population characteristics (*i.e.* comorbidities, disease duration, mean age) found in type 1 and type 2 DM may limit the definition of its prevalence (Table **2**) [4, 68, 70-72].

Table 3. LJM and diabetic foot: a complex relationship.

Study (Year)	General Purpose	Sample Size	Equipment and Duration	Major Findings
Larsen K. (1987) [116]	To evaluate the role of abnormal extension of the big toe as a cause of ulceration in diabetic feet	18 patients with diabetes and ulcer on the tip of the big toe	Clinical examination of the foot: joints, muscles, walking and PN	In diabetic patients, the extension of the big toe is probably related to the presence of PN. The phenomenon is easily overlooked unless observation of barefoot walking is included in the clinical examination
Birke J.A. (1988) [117]	To determine the relationship between the MTPJ extension and big toe ulceration in subjects with feet lacking sensitivity	40 patients with a history of plantar ulceration of the big toe, or on the plantar surface of the foot excluding the big toe, and 20 normal controls	MTPJ extension was measured by a "rabbit ear". Torque range of motion was obtained using an electrogoniometer strain gauge, and microcomputer	There is a significant relationship between limitation of big toe MTPJ extension and the presence of plantar big toe ulceration. The presence of hallux limitus in a patient with an insensitive foot should alert the physical therapist and other clinicians to anticipate and prevent ulceration under the big toe
Delbridge L. (1988) [58]	To examine the incidence of LJM in the diabetic foot and its association with neuropathic ulceration	18 patients with DM and history of neuropathic ulceration; 24 without history of foot disorders; 20 control patients	Joint mobility in the foot was assessed in the subtalar-joint and in the hallux. A number of comparative measurements were made on the hands of each patient	The subtalar ROM for the patients with diabetic neuropathic ulcers was significantly different from both the control patients and the diabetic patients without ulcers. There was a significant association between subtalar and hallux joint ROM. LJM in the diabetic foot may contribute to the development of tissue breakdown preceding ulceration by increasing shear forces at susceptible sites
Mueller M.J. (1989) [15]	To determine whether differences in sensation and joint mobility exist between DM patients with and without a history of plantar ulcer and nondiabetic controls	46 patients with and without a history of plantar foot ulcer and 24 nondiabetic controls	Ankle dorsiflexion and subtalar joint motion were measured with a plastic goniometer	There was a significant difference between ankle dorsiflexion and subtalar JM in patients with a history of ulcer and the control group. Insensitivity appears to be the additional factor that must be coupled with LJM of foot deformity to produce a plantar ulcer
Fernando D.J.S. (1991) [25]	To examine the relationship between LJM, foot pressures and foot ulceration in patients with DM	64 patients divided into 5 groups by the presence of diabetes, LJM and neuropathy	Joint mobility was assessed at subtalar and MTPJs; plantar foot pressures were assessed by pedobarography	A strong association between LJM and elevated plantar foot pressures in patients with diabetes has been documented. LJM may be a major factor in causing abnormally high plantar foot pressures and contributes to foot ulceration in the susceptible neuropathic foot

(Table 3) Contd…

Study (Year)	General Purpose	Sample Size	Equipment and Duration	Major Findings
Mueller M.J. (1995) [14]	The primary purpose was to determine the relationship of plantar-flexor peak torque and dorsiflexion ROM to peak ankle moments and power during the late stance phase of walking	9 subjects with DM and associated PNs; 10 without DM	A standard plastic goniometer was used to measure ankle dorsiflexion. Plantar-flexor peak torque was measured by the Lido Active isokinetic table. Force platform, foot switches and an EV system were used for gait testing	Although dorsiflexion ROM did not contribute to the ankle moment or power during walking, the hierarchical multiple regression analysis showed there was a strong correlation between PFPT and dorsiflexion ROM. There also was a strong correlation between dorsiflexion ROM and ankle power. Ankle dorsiflexion ROM appears to allow the necessary moment arm to produce an ankle plantar-flexion moment during walking
Dijs H.M. (2000) [62]	To determine whether any improvement of LJM in the diabetic foot could be achieved by means of specific physical therapy techniques	11 patients with DM, LJM and neuropathy; 17 normal controls, 11 controls with DM; 9 patients with DM and neuropathy but a negative prayer sign	JM was measured at the ankle, subtalar, and 1st MTPJ in addition to first ray. Measurements were taken at baseline, after 10 and 20 sessions of passive joint mobilization at a rate of two sessions per week. Measurements were repeated at 3, 6, 9 and 12 months after completion of therapy	Physical therapy may significantly, although temporarily, improve the mobility of the ankle and foot joints in patients with LJM and neuropathy. After 10 sessions a significant improvement in mobility was observed in all joints considered. Further therapy (20 sessions) resulted in a small additional improvement. The ROM obtained after 20 sessions was not significantly different from that observed in the normal controls except for the 1st MTPJ. Nine months after treatment, only the subtalar joint still showed a significant improvement in joint mobility
Zimny S. (2004) [9]	To assess the role of LJM in causing abnormal high plantar pressures in the forefoot of patients with an at-risk foot	70 patients with DM (35 with neuropathy and without history of ulcer; 35 without neuropathy) and 30 nondiabetic control subjects	Joint mobility was assessed at the ankle and 1st MTPJ. Pressure-time integrals as dynamic variables were measured in each foot	The ankle and 1st MTPJ was significantly reduced in the foot of the at-risk group. LMJ showed a better sensitivity and specificity for detecting an impaired forefoot plantar load compared with the vibration perception threshold in diabetic patients with an at-risk foot. Ankle JM reduced to an angle of 20–25° appears to be an ideal cut-off value that indicates elevated time-dependent pressure on the forefoot in diabetic patients with an at-risk foot
Rao S. (2006) [38]	To examine the relationship between ankle dorsiflexion ROM, ankle stiffness and plantar loading during gait in individuals with and without DM and neuropathy	10 subjects with DM and 10 age- and gender- matched non-diabetic control subjects	Passive ankle dorsiflexion ROM and stiffness were measured. Kinematic, kinetic and plantar pressure data were collected as subjects walked at 0.89 m/s (2 mph)	In spite of differences in passive ankle dorsiflexion ROM and stiffness, subjects with DM demonstrated gait-related ankle motion, stiffness and plantar pressures similar to control subjects. Subjects with DM and neuropathy utilized strategies such as shortening their stride length and reducing the power of push-off to modulate plantar loading
Turner D.E. (2007) [39]	To investigate the relationship between LJM and plantar pressure	53 patients with PN, with and without ulceration, 25 patients without ulceration or PN, and 25 control subjects	Movements of the ankle joint complex and 1st MTPJ were recorded together with plantar pressures	Ankle joint complex ROM measured in the gait is not different from that in normal subjects, even in patients with PN and history of ulceration. Lacking a correlation between passive and gait ROM at the ankle joint complex may limit the utility of current clinical techniques to detect LJM

(Table 3) Contd…

Study (Year)	General Purpose	Sample Size	Equipment and Duration	Major Findings
Allet L. (2010) [107]	To evaluate the effect of a specific training program on gait and balance of patients with DM	71 patients with clinically diagnosed neuropathy were enrolled: intervention group (35) - control group (36)	Gait, balance, fear of falls, muscle strength and joint mobility of ankle, hip and knee were measured at baseline, after intervention and at 6-month follow-up. Patients were enrolled in training sessions (2 times a week for 12 weeks)	A specific training program can improve gait speed and balance, and increase both muscle strength and joint mobility of patients with a vibration perception threshold ≤4 with a Rydel–Seiffer tuning fork. Increased hip and ankle strength as well as ankle mobility may explain the progress in gait velocity and both static and dynamic balance. Ankle dorsal, Flexor strength and ankle dorsiflexion mobility values further decreased at 6 months, possibly explaining the regression of gait and balance measurements
Francia P. (2015) [7]	To evaluate how ankle joint mobility can be useful in the identification of patients with diabetes at risk of foot ulcer	87 patients with and without history of foot ulcer, and 35 healthy control subjects	Ankle JM was evaluated using an inclinometer. Patients with diabetes were followed up for diagnosis of foot ulcer over the next 8 years	Diabetes and aging reduced ankle JM although diabetes seemed to reduce plantar flexion to a more specific extent. Reduced ankle JM was mostly associated with a previous history of foot ulcer. Groups showed similar results as to Δ– right–left ankle difference. Seventeen out of 22 of our cases (77.27%) with a history of ulceration and who had a subsequent foot ulcer, had the first episode in the same foot with lower ankle JM. The evaluation of ankle JM is a valid and reliable ulcer risk scale that indicates which foot is at higher risk of ulcer
Francia P. (2015) [64]	To design an experimental protocol of exercise therapy for subjects with long-term DM	26 patients with diabetes and 17 healthy controls	Ankle JM and strength were measured before and after exercise therapy. Patients participated in a 12-week training program on 3 non-consecutive days a week	12-weeks of exercise therapy significantly improved joint mobility, muscular performance and walking speed in patients. After exercise therapy muscular strength and gait speed achieved a value similar to that of controls
Cerrahoglu L. (2016) [108]	To investigate whether a home-based exercise program could improve ROM for foot joints and plantar pressure distribution during walking in patients with DM	Patients were divided into two groups: 40 subjects with neuropathy and 40 without. Both of these groups were randomized into exercise (20) and control (20)	Ankle and 1st MTPJ ROM were measured. Pedobarography was used to measure plantar pressure. Home self-care program consisted of ROM, stretching and strengthening exercises	Exercises applied to the foot and ankle joints may increase ROM in patients with DM and improve plantar pressure distribution independent of the presence of neuropathy.
Kanchanasamut W. (2017) [129]	To investigate the effects of a mini-trampoline exercise program on foot mobility, plantar pressure, and sensation perception of patients with DM and PN	Twenty-one patients with PN received foot-care education. Among these, 11 received a further 8-weeks of home-based exercise	1st MTPJ ROM and plantar pressure values were measured	Patients with PN had lower peak plantar pressure at the medial forefoot and higher peak plantar pressure at the lateral forefoot after completing the 8-week mini-trampoline exercise program. These results might be related to an increase in the 1st MTPJ ROM

DM: Diabetes Mellitus; ROM: Range of Motion; LJM: Limited Joint Mobility; PN: Peripheral Neuropathy: 1st MTPJ: First Metatarsophalangeal Joint.

It is known that T2DM patients may have glucose intolerance or mild type 2 diabetes mellitus for some years prior to being diagnosed, and LJM can occur in early clinical stages [4, 17]. In particular, LJM in T2DM patients is usually added to the possible negative effects on joint mobility induced by aging [4, 7, 17]. T1DM has an abrupt onset, normally followed by timely diagnosis and treatment. This means that in patients who develop LJM, the functional deficit usually occurs after some years of disease, even though it has been reported that young patients with T1DM may also have significantly reduced joint mobility within a few months of onset [3, 11]. These factors explain, at least in part, the marked variability in the LJM prevalence reported over the years, from 9 to 76% [42, 68, 71, 73-75].

In the last decade, 20 years of follow-up studies have reported that hand LJM prevalence in T1DM populations has

decreased, probably due to improved treatments for diabetic patients (Tables **1** and **2**) [36, 76]. These and other studies have reported that young subjects with T1DM show a significant decrease of joint mobility in the first years of their disease which then is maintained or decreases slowly in adulthood [7, 53]. However, a peak prevalence of LJM has been found in about 65% of DM patients with over 30 years of disease [76]. Curiously, the first advances in diabetic patients' care have led to a growing consideration of LJM as an impairment [31]. Additional therapeutic advances achieved since the end of the last century seem to have reduced the problem, at least in young patients with T1DM [37, 77].

Although several studies report that LJM prevalence increases with diabetes duration [10, 16, 42, 55, 78] and reduces metabolic control [12, 70, 78, 79], not all studies confirm the relationship between reduced joint mobility and glycemic control in young and adult patients with T1DM [18, 44, 64, 73, 80, 81] or T2DM [82]. In this sense, it has been reported that mathematical models can, at least in young patients with diabetes, describe the relationship between metabolic control maintained over the years and ankle joint mobility [83].

However, it is conceivable that joint mobility progressively deteriorates in patients with long-term disease, and it is known that DM patients of different ages, sex or type have less joint mobility of the foot and ankle than healthy controls [6, 7, 9, 64, 84]. Therefore, it has been noted that joint mobility in the diabetic population continues to decrease while the risk of foot ulcers increases and this deficit is significantly higher in patients with neuropathy or a history of ulceration (Table **2**) [2, 25, 58, 84].

4. LJM ASSESSMENT

Since the earliest studies regarding the relationship between diabetes and JM, researchers have investigated both axial and appendicular joints, including those of the lower limb [53, 79, 82, 85]. To better understand the evaluation methods applied to this field, it should be considered that LJM was first investigated in children and young people with T1DM [16, 42, 86], then in adults and elderly subjects with type 1 or type 2 DM [41, 43, 44, 81, 87] and lastly in patients with peripheral neuropathy or a history of diabetic foot ulcer [9, 15, 25, 58]. The differences in the populations investigated, study aims, and clinical needs determined the assessment used.

For many years, attention has mainly been focused on hand assessment, and during the '70s and early '80s, many authors investigated the deficits of hand joint movement and posture, especially in young and adult patients with T1DM. At this time, a variety of terms such as "diabetic hand syndrome" [88, 89], joint stiffness [88, 90], juvenile diabetic cheiroarthropathy [87, 89] and LJM [5, 53] were added to the first definition of "stiff hand syndrome" [31]. These studies investigated the inability of diabetic patients to fully extend the metacarpophalangeal and interphalangeal joints in the absence of overt musculoskeletal or neurological disease [18, 42]. It has been described that hand LJM develops starting from the fifth finger and moves forward in a lateral direction to progressively affect the other fingers. The interphalangeal joints, metacarpophalangeal and large joints of the hand are progressively affected [54] with a distal/proximal trend resulting in the typical hand deformity that diabetic patients may exhibit. In the early 1980s LJM was defined as a "bilateral painless limitation of the finger joints often associated to thick, tight, and waxy skin" [42, 87].

Grgic *et al*., one of the first authors to investigate LJM, introduced the "Tabletop" sign test to evaluate the presence of LJM in diabetic patients. The test requires the patient to put his/her hands on the top of a table with the palm down and fingers fanned. Patients are classified on the basis of the contact that his/her fingers and palm have with the plane surface [16, 91]. A similar test, the "Pryer" sign, was introduced later [42]. This test consists of trying to bring the palms and palmar surfaces of the proximal and distal interphalangeal joints of both hands together tightly, with the fingers fanned. The patient's inability to completely close the gaps between the palms and fingers when pressing his/her hands together demonstrates the presence of limited joint extension. In case of incomplete contact, the examiner confirms these limitations by passively extending the patient's fingers (Table **1**) [16, 42]. These tests were considered useful screenings for LJM in the clinic [67, 92], but they only provide a first indication of problems associated with joint stiffness, postural abnormalities, or hand deformities in diabetic patients [8, 46, 81, 82, 86, 93].

The increasing interest in evaluation of LJM has led to more objective assessment methods. Firstly, it was suggested to use a sheet of paper on which to leave an imprint when running the Tabletop sign test [81], then hand joint ROM was assessed using a goniometer [46, 58, 82], which provided a quantitative assessment, evaluating also initial subclinical limitations (Tables **2** and **3**) [46, 56, 85].

In the following years, a more extensive interpretation of LJM in diabetes was made by considering it as a whole body problem [8, 58, 79, 89]. At the end of 1980s, the goniometer was used to investigate the relationship between foot/ankle LJM and diabetic foot ulcer [15, 58]. Since assessment of joint mobility at the foot and ankle level using a goniometer may present pitfalls and take time [94-96], some studies introduced new methods of evaluation, and verified the reliability of the different ankle and foot joint mobility assessments [38, 94, 97]. Other simple devices such as the inclinometer [7, 64, 66, 98] or more complex ones such as the mechanical goniometer, electrogoniometer, electromagnetic tracker sensor, and tailored equipment [38, 95, 99-101] such as the equinometer [102] were used to evaluate flexibility and joint mobility, especially at the ankle level [7, 98, 99]. In particular, it has been underlined that, by using friendly-user devices such as the inclinometer, it was possible to create a simple and fast method to introduce ankle joint mobility evaluation into clinical practice [7, 64].

It is important to consider that patients evaluated by all these methods are in non-weight-bearing conditions [15, 38, 103]. It has been hypothesized that this could be a limiting factor if the results achieved are compared with the foot plantar pressure evaluated in standing or in dynamic conditions [38, 39]. Therefore, later studies assessed joint mobility during walking because it could provide important information on the causes of DFU (plantar pressure distribution) and LJM progression [38, 39, 104-106].

It is also important to underline that several factors may hinder full comprehension of the relationship between LJM and the risk of developing diabetic foot ulcer in adults and elderly patients. The presence of other diseases or past surgeries may induce joint mobility alterations; moreover, the patient's training status could affect the relationship between his/her risk of LJM and diabetic foot ulcer [62, 63, 64, 107, 108].

A further difficulty encountered in the assessment of the lower limb joints is due to the patient's inability to get into a comfortable baseline condition, due to muscle contracture (*e.g*. gastrocnemius and/or hamstrings muscles) [21, 109].

Although the possible role of joint mobility deficit in diabetic foot ulcer development is well documented [7, 25, 58], the presence of all these limitations indicates the need of a common methodological protocol to evaluate joint mobility.

5. LJM AND DIABETIC FOOT: HISTORY OF A YOUNG RELATIONSHIP

5.1. Early History

The genesis and development of the relationship between LJM and diabetic foot has been influenced by the long-held opinion that gait is the only cause of abnormal foot plantar pressures and one of the major causes of diabetic foot ulcer [110].

Oakley *et al*. in 1956, in addition to focusing attention on the relationship between peripheral neuropathy and foot ulcers, explained that the presence of stiff and deformed toes together with the lack of normal heel and toe movement during walking, results in abnormal thrust of the metatarsal heads. This can result in calluses and the formation of painless ulcers in the underlying neuropathic skin [111]. Other specialists have focused their attention on the effects of gait in the development of foot deformities and calluses as important risk factors for ulcers [110, 112, 113]. Only later was LJM considered as a factor causing gait abnormalities and affecting orthostatic and dynamic posture [21, 107, 114]. It is currently conceivable that foot and ankle LJM may also be the result of a subject's gait anomalies.

In 1985 Delbridge *et al*. published an article suggesting that neuropathic ulcer of the soles in diabetic patients was due to the interaction of peripheral neuropathy, abnormal mechanical forces (partly due to the neuropathy) and connective tissue alterations. In addition to confirming that a load transfer from the toes to the metatarsal heads can occur in these patients, maybe due to the paresis of the foot's muscle, they explain that the glycosylation of skin proteins and subcutaneous tissues of the foot soles (*i.e*. collagen and keratin) could stiffen tissues, and then increase the tensile strength. These changes could contribute to the development of neuropathic ulceration and poor wound healing [57].

A few years ago the same group of researchers published one of the first studies on the alterations in vertical force exerted on the foot sole during walking on a load-sensitive surface by diabetic patients with and without neuropathic ulcers. Cterenko *et al*. in addition to suggesting that all plantar ulcers occur on the side of maximum loading, reported that the vertical force through the toes was reduced in diabetic patients compared to healthy subjects with a median shift of the same forces [115].

In the years immediately following, Larsen and Birke confirmed that the abnormal extension of the big toe (hallux limitus) and lack of sensitivity in the foot may cause ulcers on the tip and under the great toe in diabetic patients [116, 117]. Larsen specified that the presence of abnormal big toe postures can be diagnosed by observing the patient while walking barefoot since the big toe is markedly extended during the whole walking cycle [116]. Birke *et al*. suggested that physical therapists and other clinicians should evaluate how to treat patients with this problem in order to prevent ulceration under the big toe [30, 117, 118]. Therefore, even in these years, the study of the relationship between diabetes and foot ulcers, while considering the role of gait and stiffness of some foot joints, did not consider, as a whole, the role of limited joint mobility.

5.2. Confirmation of the First Studies

One important advance in the study of the relationship between LJM and diabetic foot was made in 1988 by Delbridge *et al*. [58], in which joint mobility of the hand and big toe was evaluated by goniometer in 42 diabetic patients with and without a history of neuropathic ulcer and 20 healthy controls. The authors also evaluated the subtalar joint because of its important role in foot biomechanics. Their focus--first on the quality of foot movement and then on the whole body in patients at risk--was a key step forward in the treatment of diabetic foot. They confirmed the association between LJM and neuropathic ulceration in patients with a history of this syndrome, and also reported that LJM usually occurs in foot and hand joints, indicating it is a widespread phenomenon that may stiffen the foot, especially at the subtalar joint [56, 58].

A year later, Mueller *et al*. discussed the possible role of ankle LJM as a risk factor for ulcers. Their study in diabetic patients with and without a history of plantar ulcer and healthy controls confirmed the hypothesis that LJM may also increase local pressure on the insensitive foot, leading to ulceration [15]. In agreement with Delbridge *et al*., Mueller *et al*. suggested that limited ankle dorsiflexion, and subtalar joint mobility may reduce the foot's ability to absorb shock; the transverse rotation and accommodation of the increased weight may contribute to the development of tissue breakdown that can precede ulceration in patients without foot sensitivity. The foot's limited dorsiflexion could result in increased pressure on the forefoot, particularly during the late walking phase, thus increasing the risk of developing ulcers in that area [9, 15]. Although all these first studies aimed to investigate the relationship between LJM (ankle, subtalar, and first metatarsophalangeal joints) and diabetic foot ulcer, the authors did not directly measure foot plantar pressure [9, 15].

At the end of the 1980s Masson *et al*. underlined that it is the presence of sensory neuropathy that makes LJM a major risk factor for ulcers by leading to dangerous alterations in the foot plantar pressure [59, 119].

In 1991 the same group of researchers published a study aimed at confirming the relationship, only hypothesized before, between LJM, abnormal dynamic plantar foot pressures and foot ulceration [25]. In addition to 15 healthy controls, they investigated 49 adult patients with or without neuropathy and LJM in order to create four groups of patients. Joint mobility was measured by goniometer in four joints: interphalangeal, metacarpophalangeal, subtalar and first metatarsophalangeal. The authors demonstrated for the first time a strong association between LJM and high plantar foot pressures in the diabetic foot. They also showed that the subtalar ROM revealed a strong correlation between peak plantar foot pressure and a history of previous plantar foot ulceration [25]. The results of this study reconfirmed that no patient with LJM and normal peripheral nerve function had developed foot ulceration (Table **3**) [25, 59].

However, more recently it has been reported that abnormal muscle strength and gait--typically associated with diabetic peripheral neuropathy--can also occur in patients without peripheral neuropathy and that LJM can affect the quality of gait even in these patients [25, 58, 120-123]. This condition suggests the usefulness of evaluating the presence of LJM in all diabetic patients, with or without diabetic peripheral neuropathy, for the prevention of foot ulcers [7, 21, 120, 122].

In the early 1990s the first studies confirming the correlation between the presence of abnormal foot plantar pressure during gait [57, 58, 110], LJM and the development of plantar foot ulcers in diabetic patients, were carried out [25]. Studies by Delbridge and later by Fernando *et al*. in 1991 are among the latest ones confirming the relationship between foot and hand joint mobility [25, 58]. Consequently, since that time the study of foot and ankle joint mobility in the diabetic population has been focused on the quality of gait, plantar pressure distribution and posture.

5.3. A Broader Relationship: Effect of LJM on Foot Plantar Pressure, Posture and Quality of Gait

During the last 25 years, some studies have confirmed the direct relationship between LJM and abnormal plantar foot pressure [9, 84]. In 2004 Zimny *et al.* investigated passive ankle mobility, the first metatarsophalangeal subtalar joint by goniometer in 30 controls and 70 diabetic patients (type 1 and 2), with and without neuropathy [9]. The pressure-time integral during walking was evaluated using a pressure-sensitive insole sensor. The results of the study confirmed that both the LJM and the vibration perception threshold are significantly correlated to the forefoot pressure-time integral in these patients at risk of diabetic foot ulcer. Joint mobility showed a strong inverse correlation with the forefoot pressure-time integral. These authors concluded that LJM is a major factor in the pathogenesis of diabetic foot ulcers and specified that patients with impaired ankle and/or first metatarsophalangeal subtalar joint mobility are at risk of foot ulceration [9].

Viswanathan *et al*. also investigated dynamic plantar foot pressure in addition to subtalar and first metatarsophalangeal joint mobility by goniometer, as well as mean dynamic foot pressures while walking barefoot on a platform system in 295 diabetic patients and 50 healthy age-matched controls. Their results show that foot plantar pressure and joint mobility undergo comparative alterations [84]. As suggested by Fernando *et al.,* these studies indicate that LJM is a major causal factor of high plantar foot pressure [25].

Mueller, Rao and Tunner also investigated the relationship between foot and ankle joint mobility in static and dynamic conditions as well as plantar pressure distribution [38, 39, 106]. Their most recent studies on small samples seem to show that, despite a significant reduction in passive joint mobility evaluated with the patient in prone position, compared to healthy controls, these parameters do not seem to affect the quality of gait or the distribution of plantar pressure. A patient's gait was characterized by reduced speed and length of step [38, 39]. These results seem to suggest that, as a whole, a patient's abnormal walking activity has more effect on gait than LJM does, and that the metatarsophalangeal subtalar joint seems to be more affected, confirming a distal proximal trend (Table **3**).

5.4. Another Complex Correlation: LJM, New Monitoring Parameters, Ulcerative Risk Thresholds and Exercise Therapy

In 1989 Mueller and colleagues reported that diabetic patients with insensitivity and less than 5° of ankle dorsiflexion, and a subtalar joint ROM less than 30° are at higher risk of developing a plantar ulcer, suggesting that these values could be used as monitoring parameters [15]. In 2004 Zimny *et al*. reported that ankle joint mobility in flexion and extension, reduced from 20° to 25°, seems to be an optimal cut-off value indicating high time-dependent pressure in the forefoot of diabetic patients with a foot at risk [9].

In our recent study, with 87 diabetic patients and 51 healthy control subjects, we reported that patients with a total mobility in both ankles (plantar flexion plus dorsiflexion) of less than 93° (right and left), as measured by goniometer, can predict an increased risk of foot ulcer over the next 8 years [7]. This ankle ROM is 30% lower than in healthy controls according to values reported in other studies that evaluated patients with diabetic peripheral neuropathy [38, 103, 106]. This study underlines that reduced dorsiflexion may result from the patient's progressively rigid posture in foot plantar flexion [15]. The evaluation of plantar flexion starting from a resting position freely assumed by the ankle, might help us to understand the relationship between LJM and plantar foot ulcer, helping to clarify the role of time spent in a standing position as a risk factor for ulcers [7, 64, 124]. In fact, it has been suggested that the upright position may play a role in the development of foot ulcers in addition to the effects of gait [124, 125].

The strength of the relationship between LJM and diabetic foot has been confirmed by retrospective and prospective studies that evaluated the ankle joint. It has been reported that the first ulceration was detected in the same foot presenting less joint mobility in 77-79% of the patients investigated [7, 15, 126].

While Shinaberger suggested evaluation and treatment of LJM with physical therapy in diabetic patients in 1987 [56], many years earlier, in 1934, Joslin suggested that exercise therapy should be included in the treatment of DM patients

with foot ulcer. In the early 1980s Brand, Birke *et al*. organized a multidisciplinary team approach to define the treatment of neuropathic ulcers through an interdisciplinary model which included physical and medical therapy, as well as rehabilitation [30, 117, 127]. In the 21st century a number of studies have focused on investigating the effect of exercise therapy in the treatment of patients with LJM, with or without diabetic peripheral neuropathy and a history of ulceration, in an attempt to prevent foot ulcers and falls [62, 63, 65, 66, 107, 128, 129]. These studies indicate that functional deficit is reversible although the effects on the patient's overall condition are not yet known, because improvements in joint mobility achieved with exercise therapy can be lost, at least partially, only a few months after the end of the training period [62, 107]. As a result, patients' attendance at physical therapy sessions that include exercises aimed to recover joint ROM, may be a confounding factor for using joint mobility evaluation as a means of patient monitoring. This result seems to suggest that the abnormal and limited use of these joints can trigger a complex vicious cycle and result in significant LJM more than tissue alterations.

6. DISCUSSION

This review discusses the important and complex history of research investigating the relationship between diabetes and LJM, its effect on different aspects in the field of diabetes research as well as the role it plays in diabetic foot ulcers.

The relationship between diabetes and joint stiffness has been observed since the 1950s but it was only in the mid-1970s that interest on the relationship between diabetes and LJM emerged [31, 53, 91]. Over the last 40 years some studies have underlined that diabetes affects the quality of all tissues in the patient's body, including connective ones, having also negative effects on joint mobility [34, 35, 49].

Study of the problems associated with LJM in recent years has been focused on people of different ages with type 1 or type 2 diabetes with and without chronic complications [43-47]. The use of different methods and devices has hindered a precise overview of the problem which is of growing interest due to the need to organize appropriate therapy [7, 18, 38, 54, 95, 99-102].

Over the years there has been a "skills transfer" in the assessment of LJM in the clinic, among young and adult-elderly patients. The first observations were made on the hands of the elderly [31], and then body and hand joints in children [18, 73, 91] were also investigated. Afterwards, foot and ankle joint mobility in the elderly was extensively investigated [9, 15, 25], and lastly, evaluations of the lower limbs were performed in young subjects [7, 8].

The effects of diabetes on foot joint mobility have been described, just as was previously done for the hand. It was first reported that diabetic patients, especially those affected by diabetic peripheral neuropathy, could show a rigidity of the toes [111, 116], and then a stiff "rigid" foot [58]. We recently reported that a patient's whole body posture can be affected by such condition, which underlines the importance of preventing and treating "diabetic rigid postures" and including them in the diabetic foot preventive protocols [21]. Diabetic patients may show a rigid posture control strategy that, in addition to restrictions imposed by their disease, can limit their daily activities [21, 114], thus triggering a vicious cycle of rigid posture, movement, and compromised lifestyle [21, 58, 114, 130].

Today it is well known that both young and elderly DM patients, when compared with age-matched controls, have less foot and ankle joint mobility [7, 9, 15]. We have learned from the 1960s studies that LJM in young diabetic patients is mostly due to the disease [16, 53], while joint mobility deficits in elderly subjects with a long history of diabetes result from both disease and aging [4, 33, 35]. However, recent studies report that the practice of some sports or exercise training program can improve joint mobility while inactivity can reduce it [21, 62, 64, 107, 130, 131].

Altogether, studies on LJM demonstrate that many factors can concur in hindering the correct interpretation of joint mobility in diabetic patients. Beyond this, the actual possibility of having reference values that alert to the presence of an ulcerative event should be carefully considered [7, 9, 15]. Total ankle joint mobility of less than about 45° seems to indicate the presence of ulcerative risk, especially in diabetic peripheral neuropathy patients. Long-term studies have reported similar values of ankle joint mobility in subjects at risk or with a history of foot ulcer, suggesting that resting foot posture can result in development of rigid plantar flexion, which is, in and of itself, a possible risk factor for the development of foot ulcers [7, 21, 38, 103]. It is conceivable that the marked reduction of joint mobility at the level of the distal lower limb and foot joints is a sign of a patient's fragility to whom even mild stresses may induce ulceration.

Recent studies have evaluated the efficacy of exercise therapy programs on ROM in LJM patients. Although the results of these studies clearly demonstrate that significant short-term improvements in ROM values can be achieved in only a few weeks, the actual effects of such protocols on the quality of posture, movement, and especially on gait are not yet known. Consequently, the preventive effect of exercise therapy on the development of deformities and, ultimately, on dreaded chronic complications such as foot ulcers is still unknown. Therefore, studies aimed at investigating these research fields are strongly needed.

7. LIMITATIONS OF THE STUDY

This article provides a narrative review of studies without following the PRISMA guidelines for a transparent and complete reporting of systematic reviews and meta-analyses [133]. Some studies on LJM in diabetic patients may not have been considered.

CONCLUSION

Limited joint mobility is a chronic complication of diabetes that arises with the onset of the disease and progresses with it. The history of research on the relationship between diabetes and LJM is very long and articulated. The complexity of this relationship has meant that many factors have hindered the identification and definition of its prevalence. LJM represents a risk factor for the development of foot ulcers but also a means of monitoring a patient's condition. The impor-

tance of this disease, as a whole, means that additional studies are needed to define, through standardized methods and devices, the prevalence of LJM in different populations and to implement prevention regimens and even more personalized treatments.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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