

PREVALENCE AND RISK OF DUPUYTRÈN DISEASE IN PATIENTS WITH DIABETES VERSUS NON-DIABETIC PATIENTS

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Abstract

Objectives: The aim of the study was to calculate the prevalence rates and risk of appearance of Dupuytrèn disease in diabetic patients with both type-1 (T1DM) and type-2 diabetes (T2DM). **Material and Method:** 384 patients were analysed, of which 47 had T1DM, 140 had T2DM and 197 were non-diabetic controls. Diabetic patients were followed at the Clinical Center for Diabetes, Nutrition and Metabolic Disease of the Emergency Clinical County Hospital and Department of Dermatology in Oradea, all of them having a diabetes duration of at least 5 years. **Results and Conclusions:** The risk of Dupuytrèn's disease is over 4.5 times greater in patients with type-2 diabetes. The risk of Dupuytrèn's disease is 3-6 times greater in patients with micro-vascular complications.

key words: Dupuytrèn's disease, diabetes, prevalence

Background

There is no clear definition of Dupuytrèn disease in the literature. It could be defined as a condition of uncertain etiology, localized at conjunctive tissue level in the palm of the hand and in fingers, which determines the progressive and irreversible retraction of the palmar aponeurosis, of its expansion and surrounding conjunctive tissue, which will eventually lead to various degrees of finger deformity and flexion [1].

The etiology of this disease is unknown, and a number of important observations addressed the disease's pathogenesis. There is data suggesting genetic predisposition as an

etiological factor, and also a higher incidence of the disease in epileptic patients, patients with liver diseases and patients with diabetes.

The prevalence of Dupuytrèn's disease in the general adult population is around 2-6% [2], but it may approach 20% or more in diabetic patients [3].

Other authors reported that the prevalence of the disease in diabetics varies from 1.6 to 63%, but it is probably around 40%. Approximately 10-15% of patients with Dupuytrèn's disease appear to be suffering from diabetes [4].

The disease appears to manifest most common in white, European patients, with a 6/1 Male-to-Female ratio.

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Kischer discovered micro-vascular changes in the nodular and perinodular lesions of Dupuytrèn's disease similar with those found in some diabetic micro-vascular complications, like retinopathy and nephropathy [5]. Also, Dupuytrèn's disease demonstrated that it is directly linked to micro-vascular changes in diabetic patients (retinopathy, nephropathy).

An increase in the quantity of type-III collagen was identified in the palmar fascia and especially in the nodular tissue. The increase in type-III collagen proportion, surrounded by type-I collagen is typical for embryonal collagen, and the increase in sulfated glycosaminoglycans present in Dupuytrèn's disease is characteristic to immature tendon structures [6].

As no hard data were reported previously in Romania, the aim of our study was to calculate the prevalence rates and risk of appearance of Dupuytrèn's disease in a group of patients with both type 1 (T1DM) and type 2 (T2DM) diabetes.

Material and Method

A prospective and observational study was performed, developed over a period of 4

years. 384 patients were analyzed, of which 47 had T1DM, 140 had T2DM and 197 were non-diabetic controls. Patients were followed at the Clinical Center for Diabetes, Nutrition and Metabolic Disease of the Emergency Clinical County Hospital and Department of Dermatology in Oradea, Romania, all of them having a diabetes duration of at least 5 years, while the non-diabetic patients were followed, in parallel, in the Internal Medicine Department of the same hospital.

The statistical analysis was undertaken using the application EpiInfo version 6.0, program belonging to the Center of Disease Control and Prevention in Atlanta, adapted for medical statistics. Significance was tested by χ^2 method. A p value < 0.05 was considered significant.

We also calculate the relative risk (RR) - the ratio of the chance of developing Dupuytrèn's disease among members of a group exposed (diabetics, respectively T1DM) related to a group not exposed (non-diabetics, respectively T2DM).

Demographic characteristics of the study group are given in [Table 1](#).

Table 1. Study group characteristics.

Parameters	Diabetics	T1DM	T2DM	Non-diabetics
Females (%)	50.27	48.94	50.71	50.76
Average Age (years)	52.46±13.56	45.96±15.60	54.64±12.62	51.19±16.21
Average duration of DM (years)	14.56±3.14	11.61±3.85	15.14±4.22	-

Both in diabetics and non-diabetics, the Male-to-Female ratio was 1/1 (50.27% versus 49.73%, respectively 50.76% versus 49.24%). Average age in diabetic patients was 52.46 years and in non-diabetic patients 51.19 years,

with no significant statistical differences (p>0.05) between the groups in this respect.

The diagnosis of Dupuytrèn's disease was made through clinical examination.

Results

At the beginning of the study Dupuytr n's disease had a 15.51% prevalence in diabetics and 5.58% in non-diabetics ($p < 0.001$) as shown in [Table 2](#), resulting in a risk over 2.5 times higher in diabetics (with an average duration of diabetes of 14.56 years) than non-

diabetics ($RR = 2.777$). Baseline (Initial) data presents information regarding patients already diagnosed with Dupuytr n's disease. The final data (at the end of the study) presents information including the cases that have been added following active diagnosis during the study.

Table 2. Prevalence of Dupuytr n's disease.

	Diabetics		T1DM		T2DM		Non-diabetics	
	Nr.	%	Nr.	%	Nr.	%	Nr.	%
Initial								
Men	9	9.68	3	12.50	6	8.70	4	4.12
Women	20	21.28	5	21.74	15	21.13	7	7.00
Total	29	15.51	8	17.02	21	15.00	11	5.58
Final								
Men	19	20.43	4	16.67	15	21.74	11	11.34
Women	35	37.23	7	30.43	28	39.44	18	18.00
Total	54	28.88	11	23.40	43	30.71	29	14.72

Table 3. Cumulative incidence of Dupuytr n's disease.

	Diabetics		T1DM		T2DM		Non-diabetics	
	Nr.	%	Nr.	%	Nr.	%	Nr.	%
Male	10	10.75	1	4.17	9	13.04	7	7.22
Female	15	15.96	2	8.70	13	18.31	11	11.00
Total	25	13.37	3	6.38	22	15.71	18	9.14

At the end of the study, the prevalence of Dupuytr n's disease has risen significantly in both diabetics (from 15.51% to 28.88%, $p = 0.003$) and non-diabetics (from 5.58% to 14.72%, $p = 0.010$), phenomenon explained by the active identification of cases during the study. The prevalence of Dupuytr n's disease remains significantly higher in diabetics than non-diabetics at the end of four years of study (28.88% versus 14.72%) ($p < 0.001$).

Initially the prevalence of Dupuytr n's disease in T1DM was not significantly higher than in T2DM (17.02% versus 15.00%) ($p = 0.572$) while at the end of the study the prevalence of Dupuytr n's disease was not significantly higher in T2DM compared with

T1DM (30.71% versus 23.40%) ($p = 0.113$) as shown in [Table 2](#). The prevalence of Dupuytr n's disease in T1DM increased non-significantly by the end of the study, from 17.02% to 23.40% ($p = 0.132$), while in T2DM it increased significantly, from 15.00% to 30.71% ($p < 0.001$).

We also calculated the number of new cases of Dupuytr n's disease identified in our study groups during the 4 years of the study (cumulative incidence).

Cumulative incidence of Dupuytr n's disease was higher in diabetics than non-diabetics (13.37% versus 9.14%, $p = 0.041$) and in T2DM than T1DM (15.71% versus 6.38%, $p < 0.001$).

Cumulative incidence of Dupuytrèn's disease was higher in females than males, in both diabetics and non-diabetics (15.96% versus 10.75%, $p=0.042$, and 11.00% versus 7.22%, $p=0.037$), as well as in T1DM and T2DM (8.70% versus 4.17%, $p=0.002$, respectively 18.31% versus 13.04%, $p=0.051$).

During the period studied (4 years), the risk of Dupuytrèn's disease (newly identified cases) is almost 1.5 times higher in diabetics than non-diabetics, regardless of sex (RR=1.490 in men and RR=1.451 in women).

In T2DM, the risk of Dupuytrèn's disease is 2.5 times higher than type-1 diabetes (RR=2.462), larger in men (RR=3.130) and smaller in women (RR=2.106).

The prevalence of Dupuytrèn's disease in diabetics increases with ageing, the highest prevalence being found in ages over 65 (26.67%). There were no cases of Dupuytrèn's disease in individuals under the age of 25 (Figure 1).

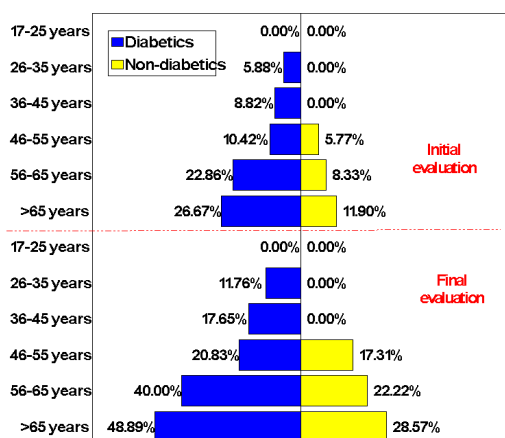


Fig. 1. Prevalence of Dupuytrèn's disease according to age groups, comparatively in diabetics/non-diabetics

In both T1DM and T2DM, the prevalence of Dupuytrèn's disease is peaking in people aged over 65, (42.86% and 23.68% respectively). There were significant

differences between the prevalence of Dupuytrèn's disease in T1DM vs. T2DM in age groups over 45 years ($p<0.001$).

In the studied period, the cumulative incidence of Dupuytrèn's disease had an increasing trend in both diabetics and non-diabetics (from 5.88% in ages between 26-35 to 22.22% in ages over 65, and from 11.54% in ages between 46-55 to 16.67% in ages over 65) as shown in Figure 2. We noticed that the rate of increase from an age group to another in diabetics is between 1.5-3% in under 55 years old and 5-7% in those over 55 years old, while in non-diabetics the rate of increase is almost constant at 2.5-2.8%. There are significant differences between the cumulative incidence of Dupuytrèn's disease in diabetics vs. non-diabetics in different age groups, especially in ages over 55 years old ($p<0.001$).

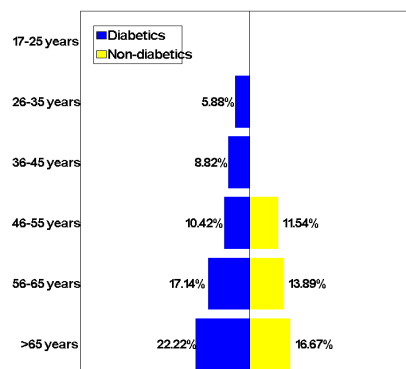


Fig. 2. Cumulative incidence of Dupuytrèn's disease in regards to age groups, compared between diabetics and non-diabetics.

In T1DM, the cumulative incidence of Dupuytrèn's disease was highest between 56-65 years (16.67%), followed by a slightly convex curve of incidence, while in T2DM, the maximum cumulative incidence was encountered after the age of 65 years (23.68%) as shown in Figure 3, with the incidence taking the shape of a concave curve, with a

minimum cumulative incidence for ages between 46-55 years.

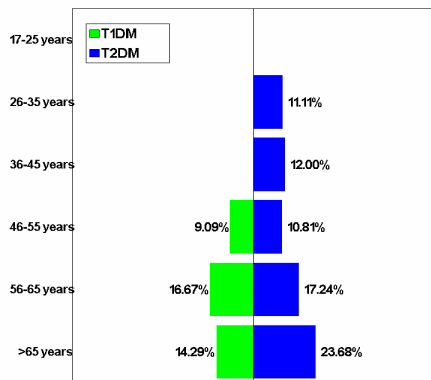


Fig. 3. Cumulative incidence of Dupuytrèn's disease in regards to age groups, compared between T1DM and T2DM.

There were significant differences between the cumulative incidence of Dupuytrèn's disease in T1DM and T2DM in different age groups, especially at ages below 45 ($p < 0.001$) and over 65 years ($p = 0.027$).

The cumulative incidence of Dupuytrèn's disease increased proportionally with the duration of diabetes, from 6.90% in patients with less than 10 years diabetes duration to 23.40% in those with more than 20 years disease evolution ($p < 0.001$) as shown in [Figure 4](#).

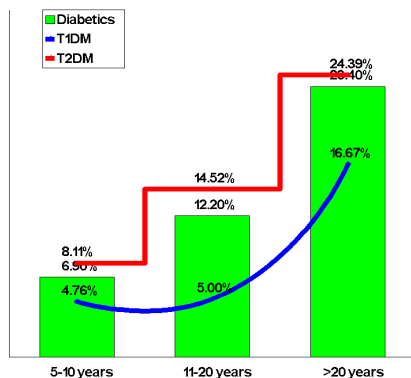


Fig. 4. Cumulative incidence of Dupuytrèn's disease related to the evolution time of diabetes.

In T1DM, the cumulative incidence of Dupuytrèn's disease is approximately the same at an evolution time of diabetes under 20 years (4.76% at 5-10 years and 5% at 11-20 years), with triple values being found after 20 years (16.67%) ($p < 0.001$).

In T2DM, the cumulative incidence of Dupuytrèn's disease increases constantly with the increase in the time of diabetes evolution, from 8.11% in 5-10 years to 14.52% in 11-20 years ($p = 0.043$) and 24.39% over 20 years ($p = 0.030$).

Cumulative incidence of Dupuytrèn's disease in patients with complications is significantly higher compared to patients without complications (17.29% versus 3.70%) ($p < 0.001$) as shown in [Figure 5](#).

In T1DM the cumulative incidence was 8.33% in persons with complications, while persons without complications did not present any single case of Dupuytrèn's disease.

In T2DM the cumulative incidence was 20.62% in patients with complications and 4.65% in patients without complications ($p < 0.001$).

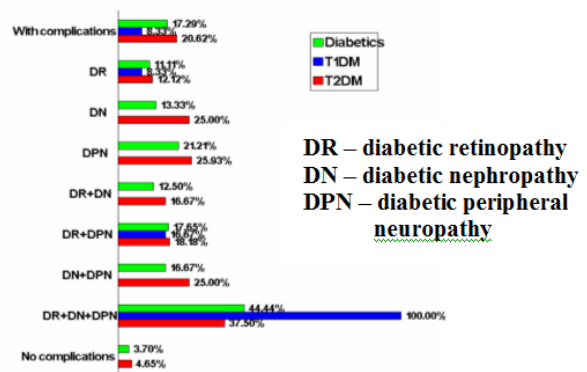


Fig. 5. Cumulative incidence of Dupuytrèn's disease according to the presence of micro-vascular complications.

The risk of Dupuytrèn's disease is over 4.5 times greater in patients with

complications than in patients without complications (RR=4.669), while in T2DM patients the risk was 4.5 times greater risk in the same situation (RR=4.433).

The greatest cumulative incidence was encountered in subjects with all three complications: DR+DN+DPN (44.44% of diabetics, 100% in T1DM and 37.50% in T2DM). The cumulative incidence of Dupuytr en’s disease increased in parallel with the number of associated complications (Figure 5).

There are two instances of risk increase of Dupuytr en’s disease: from patients without complications to those with at least one complication (RR=4.065) and from those with 1-2 complications to patients with 3 complications (RR=2.756).

We also analyzed the cumulative incidence of Dupuytr en’s disease according to the presence of each individual diabetic microvascular complication. Because of the small number of cases of Dupuytr en’s disease in T1DM, the analysis was made on the whole dataset of diabetic patients.

The cumulative incidence of Dupuytr en’s disease was significantly higher in patients with retinopathy, associated or not with other complications, than in patients without complications ($p<0.001$) as shown in Figure 6.

In comparison with patients without complications, the risk of Dupuytr en’s disease is 3 times higher in patients with retinopathy without other complications (RR=3.000) and over 6 times higher in patients with retinopathy associated to other complications (RR=6.353).

Associating other complications to retinopathy increases the risk of Dupuytr en’s disease over two times (RR=2.118).

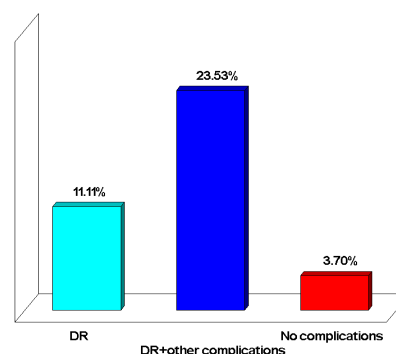


Fig. 6. Cumulative incidence of Dupuytr en’s disease in patients with retinopathy.

Cumulative incidence of Dupuytr en’s disease was significantly higher in patients with nephropathy, associated or not with other complications, than in patients without complications ($p<0.001$) as shown in Figure 7.

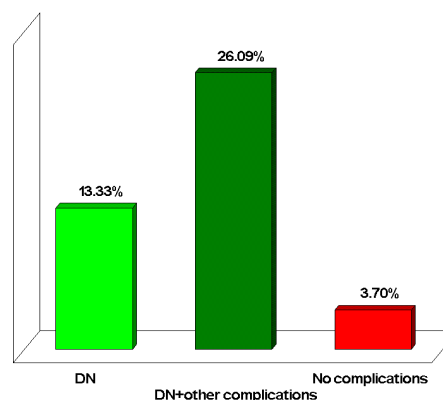


Fig. 7. Cumulative incidence of Dupuytr en’s disease in patients with nephropathy.

In comparison to patients without complications, the risk of Dupuytr en’s disease is 3.5 times greater in patients with nephropathy without other complications (RR=3.600) and over 7 times greater in patients with nephropathy associated to other complications (RR=7.043).

Associating other complications to nephropathy increases the risk of Dupuytr en’s disease almost 2 times (RR=1.957).

Cumulative incidence of Dupuytr n's disease was significantly higher in patients with neuropathy, associated or not with other complications, than in patients without complications ($p < 0.001$) as shown in [Figure 8](#).

In comparison to patients without complications, the risk of Dupuytr n's disease is over 5.5 times larger in patients with neuropathy without associated complications ($RR=5.727$) and over 12.5 times bigger in patients with neuropathy with associated complications ($RR=12.656$).

Associating other complications to neuropathy increases the risk of Dupuytr n's disease over two times ($RR=2.210$).

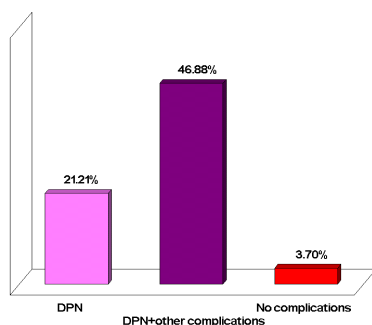


Fig. 8. Cumulative incidence of Dupuytr n's disease in patients with neuropathy.

Discussions

A prospective study spreading over 5 years analyzed the frequency of Dupuytr n's disease in patients with T1DM in Finland. The authors intended to clarify the main factors in the evolution of Dupuytr n's disease in patients with diabetes and evaluate if the presence of Dupuytr n's disease may predict the evolution of diabetes-related complications [7].

Thus, 207 patients with T1DM, aged 29 ± 9.5 years, were studied at baseline. Five years later, a follow-up study was performed, in 166 patients. The presence of Dupuytr n's

disease was examined and patients have been classified according to the following complications: history of proliferative retinopathy, peripheral symmetrical polyneuropathy and clinical nephropathy. The results showed that the prevalence of Dupuytr n's disease was of 4% (8 cases) at baseline analysis [7].

Regarding the lack of association between the metabolic control of the subjects and Dupuytr n's disease in this study group, it should be noted that the control of diabetes was the same as in the conventional therapy group of the DCCT study. So there were too few patients available and a good enough control of diabetes to determine if an adequate metabolic control could prevent the evolution of Dupuytr n's disease in these patients [7].

A preliminary study lead by Dupuytr n himself showed a correlation of the disease with the workplace [8], this fact being later confirmed by more authors [9].

Even if usually Dupuytr n's disease is more common in men, in diabetic patients the sex ratio is equal [10].

The presence of Dupuytr n's disease did not predict the evolution of retinopathy or other diabetic complications in the next 5 years, because of the small number of subjects [7]. Thus, no final conclusion regarding the predictive value of Dupuytr n's disease for the development of complications in diabetic patients can be drawn [11].

The results of another study determined that diabetic patients presented with a higher incidence of Dupuytr n's disease, as well as a limitation of articular mobility, carpal tunnel syndrome or finger flexor tenosynovitis, compared to non-diabetics [12].

In our study, Dupuytrèn's disease correlated with the micro-vascular changes in diabetic patients, the cumulative incidence of Dupuytrèn's disease being significantly higher in diabetics with micro-vascular complication (retinopathy, nephropathy, neuropathy), than in diabetics without these complications.

Conclusions

The risk of Dupuytren's disease is almost 2.8 higher in diabetic patients in comparison with non-diabetic subjects. The risk of Dupuytrèn's disease is over 4.5 times greater

in diabetic patients with complications than patients without complications (RR=4.669), and in type 2 diabetes this risk is almost 4.5 times greater (RR=4.433). The highest cumulative incidence was encountered in patients with all three complications: DR+DN+ DPN (44.44% of diabetics, 100% in T1DM and 37.50% in T2DM subjects). Associating other complications to retinopathy, nephropathy or neuropathy, increases the risk of Dupuytrèn's disease approximately two times.

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