Emergency diabetické neropatie

Milan Kvapil

Emergency diabetické neuropatie

Milan Kvapil

Diabetická neuropatie: definice

- **Diabetická neuropatie (DN) je chronickou komplikací diabetu. Na základě mezinárodního konsenzu lze diabetickou neuropatii definovat jako nezánětlivé poškození funkce a struktury periferních somatických nebo autonomních nervů na podkladě metabolicko-vaskulární patofyziologie.**

www.diab.cz/standardy

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- **Onemocnění je značně heterogenní. Postihuje různé části nervového systému, a proto se prezentuje různými klinickými projevy. Podle závažnosti onemocnění jsou přítomné subjektivní a/nebo objektivní příznaky poruchy funkce nervu**

www.diab.cz/standardy

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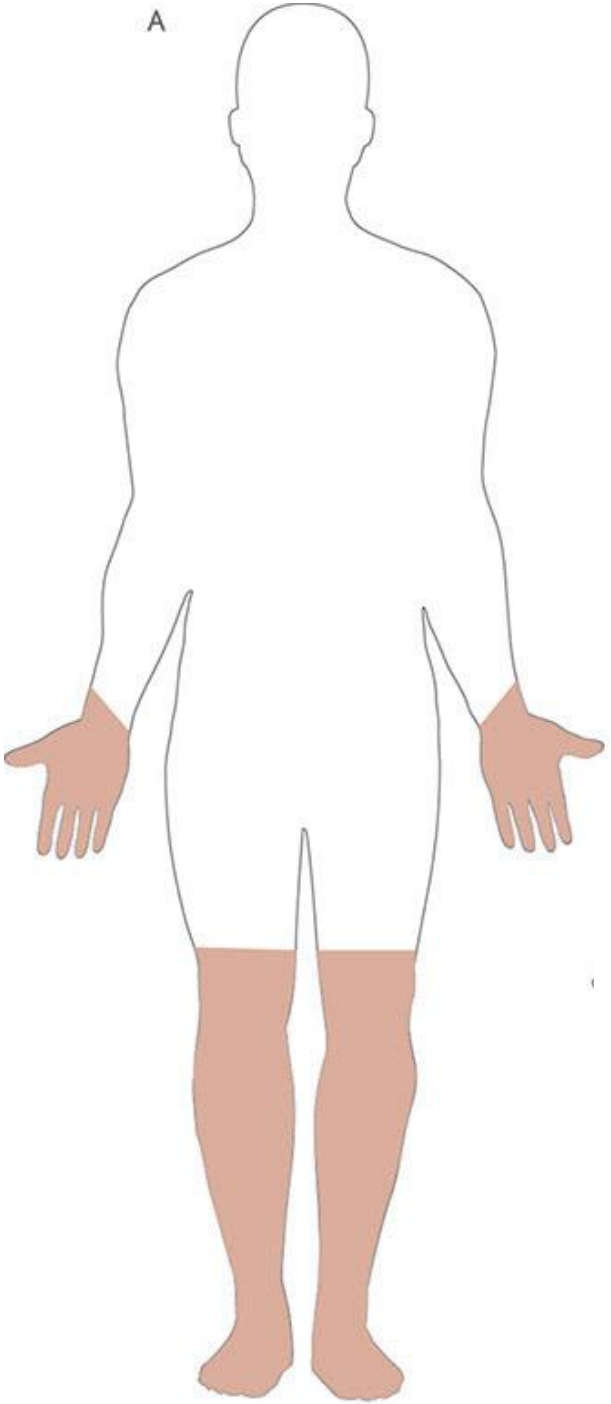
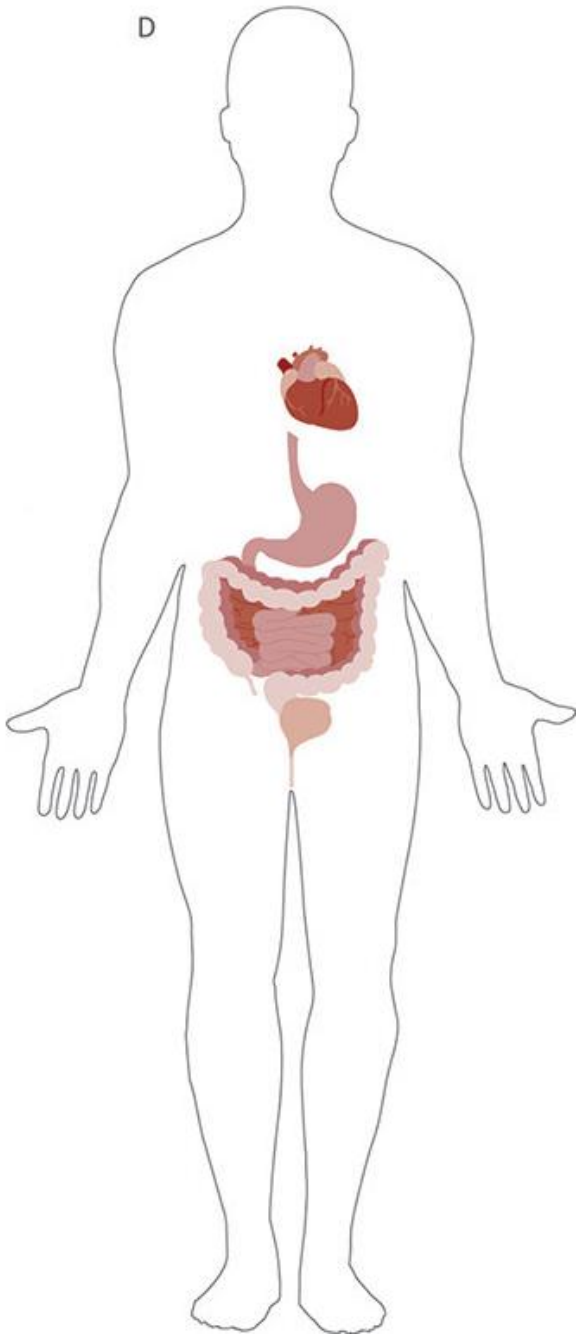
- Vždy je nutné vyloučit jinou příčinu vzniku než diabetes.

www.diab.cz/standardy

Diabetic sensorimotor polyneuropathy,
small fiber neuropathy,
or treatment induced neuropathy.
Small fiber neuropathy
has the same pattern as
diabetic sensorimotor
polyneuropathy but
neurologic examination and
electrodiagnostic studies
are different, which can
make the diagnosis difficult



BMJ 2014;348:g1799



Autonomic neuropathy (the most commonly affected organs are shown) including treatment induced neuropathy.

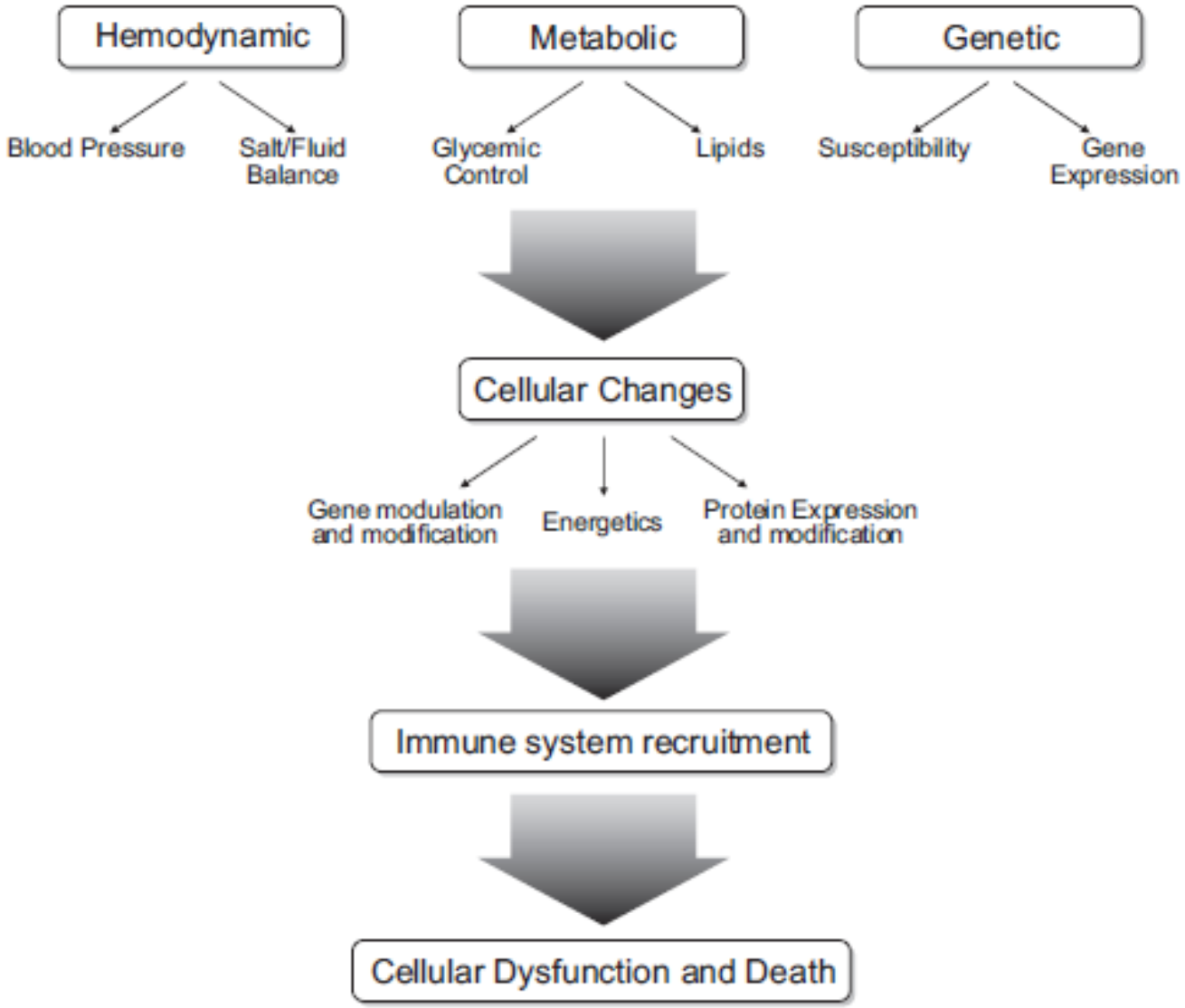
BMJ 2014;348:g1799

Diabetická neuropatie: prevalence

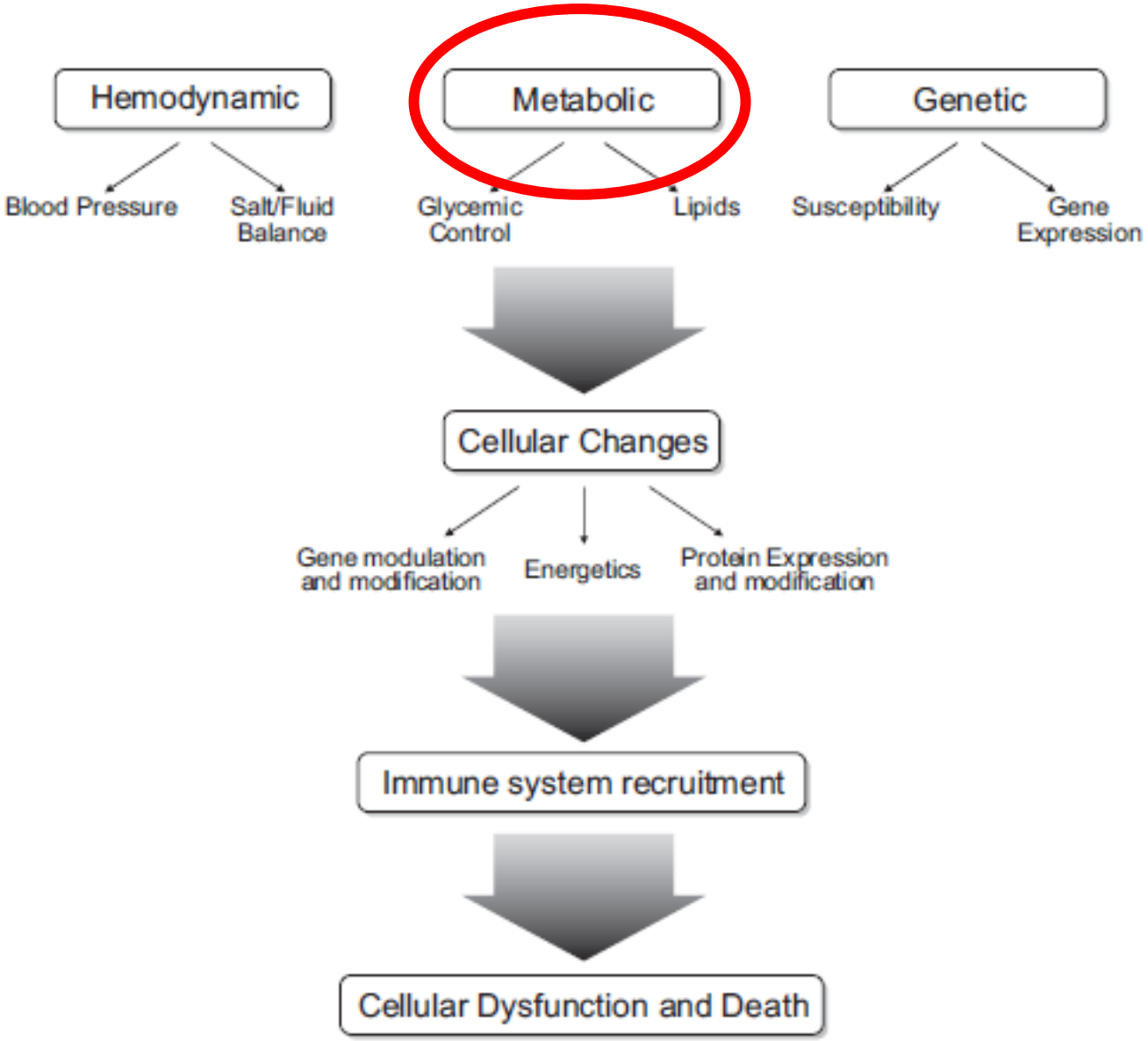
Diabetická neuropatie: prevalence

25 – 90% pacientů s diabetem

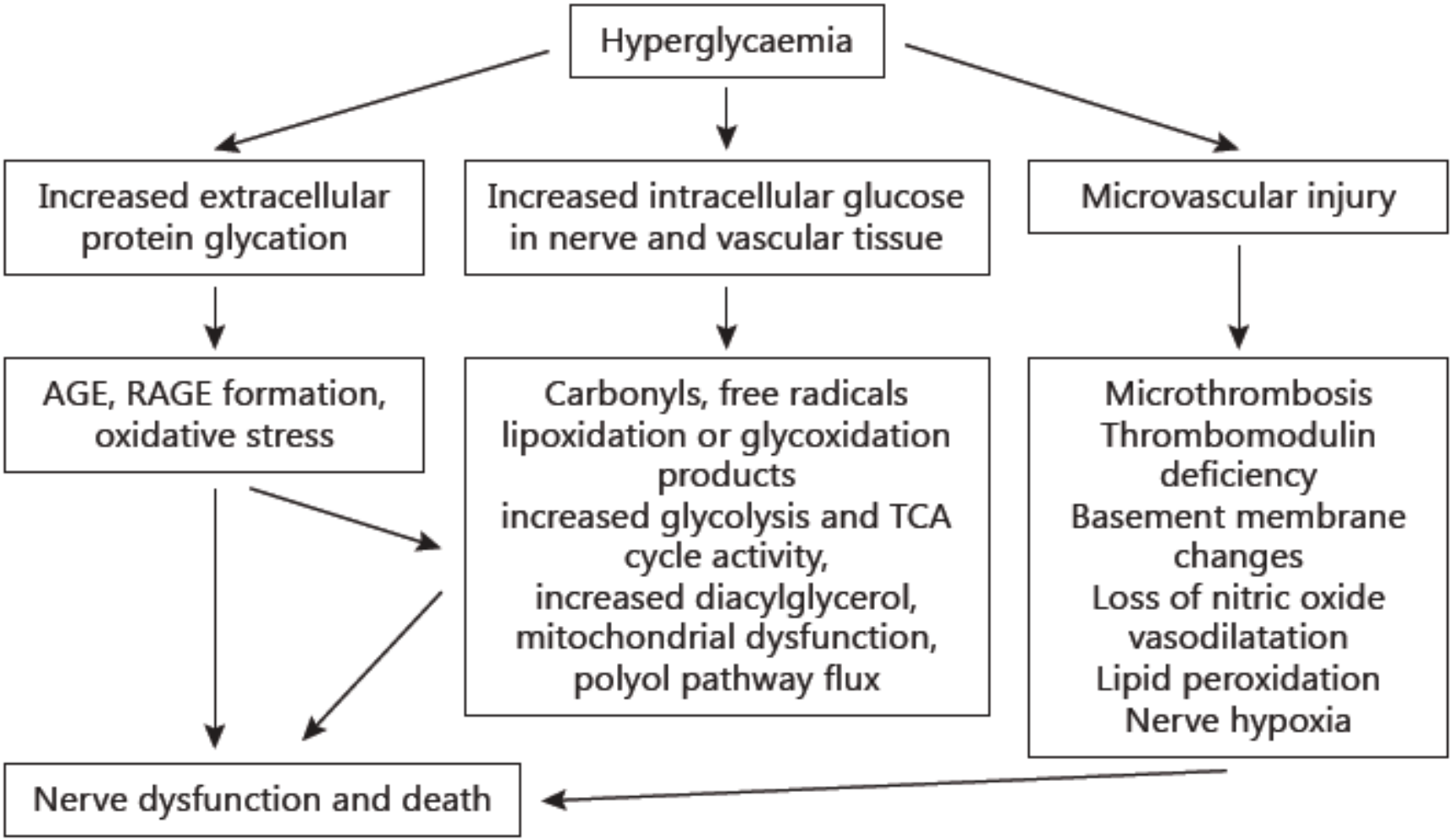
DOPORUČENÝ POSTUP DIAGNOSTIKY
A LÉČBY DIABETICKÉ NEUROPATIE (2016)
DOPORUČENI ČESKE DIABETOLOGICKE SPOLEČNOSTI ČLS JEP
DATUM REVIZE 23. 2. 2016



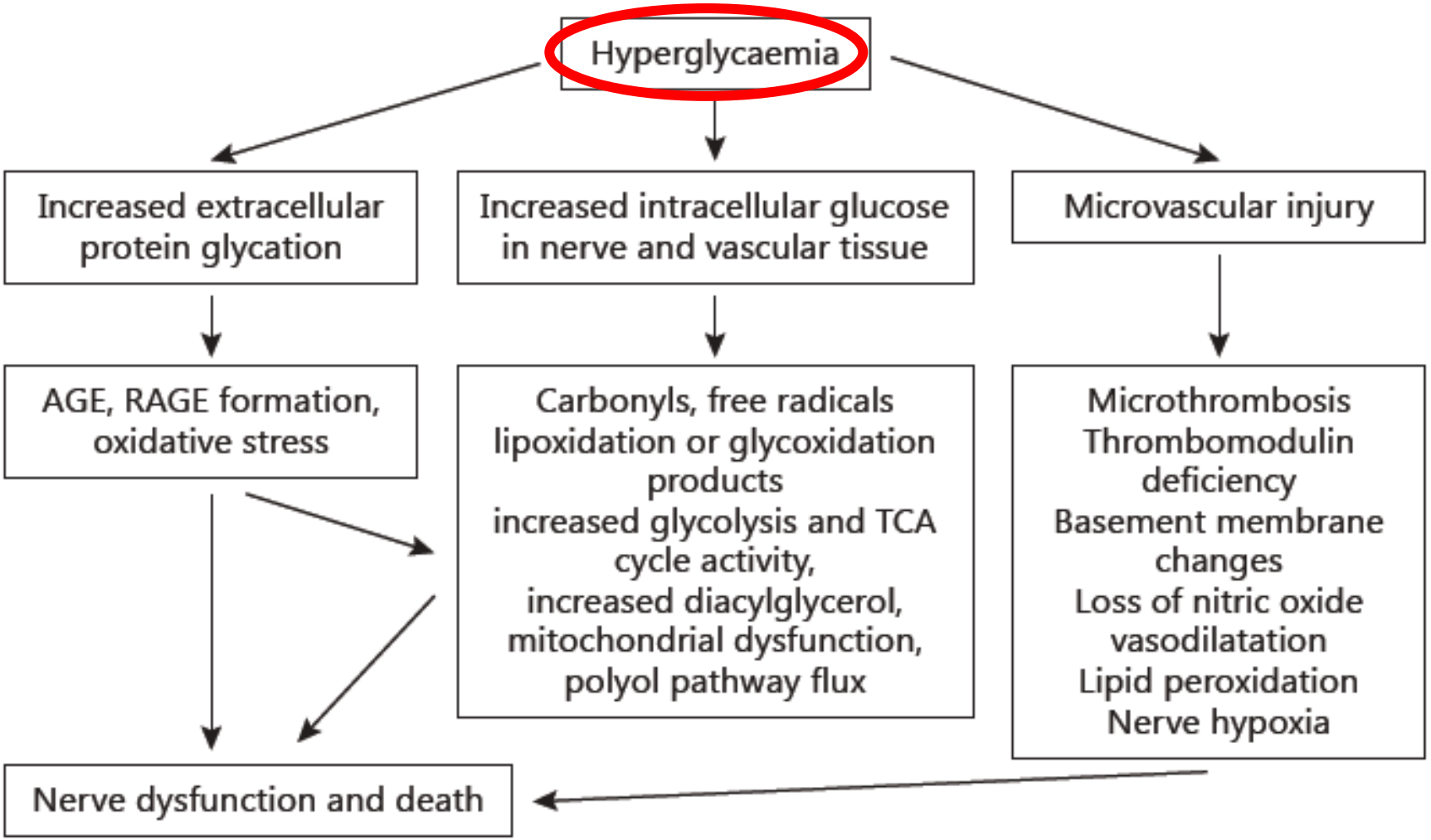
Physiol Rev. 2013 Jan;93(1):137-88



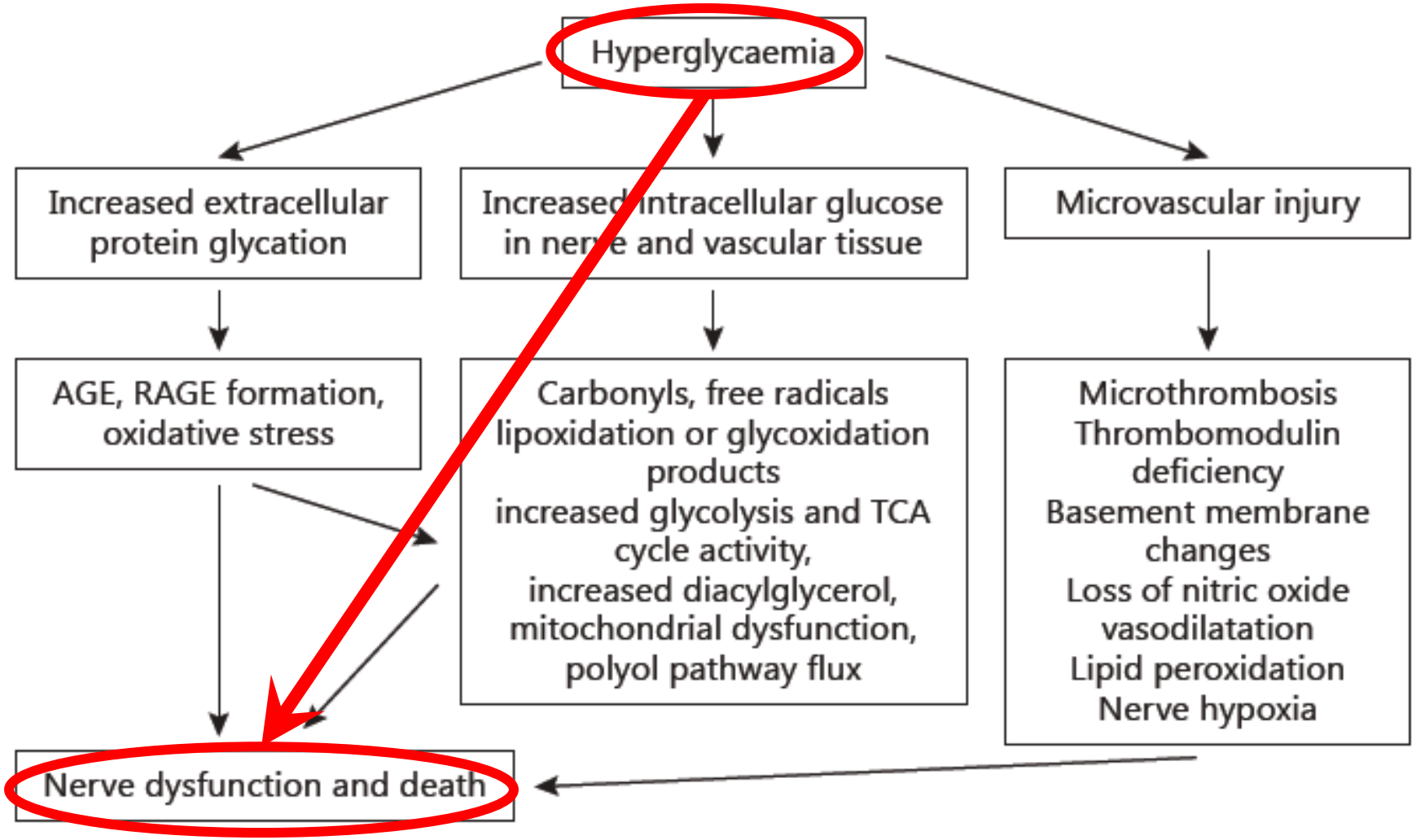
Physiol Rev. 2013 Jan;93(1):137-88



Neuroendocrinology 2013;98:267–280



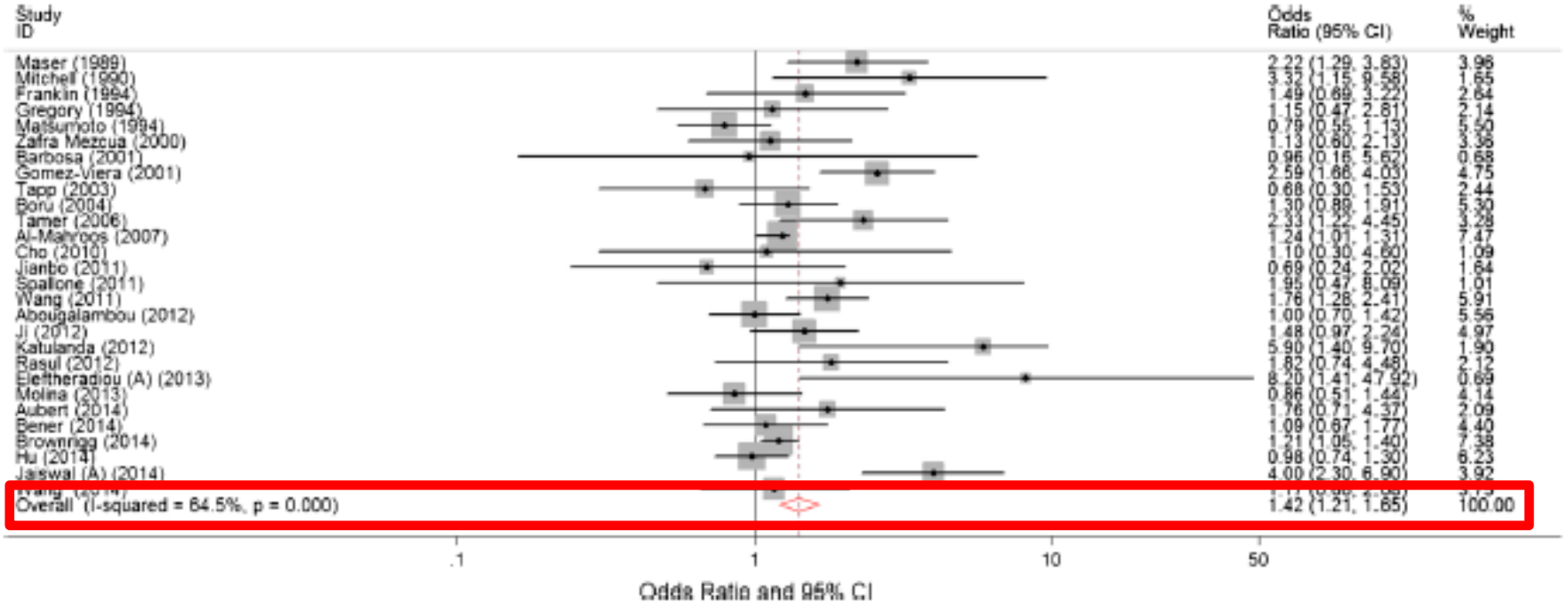
Neuroendocrinology 2013;98:267–280



Neuroendocrinology 2013;98:267–280

The Effect of Cigarette Smoking on Diabetic Peripheral Neuropathy: A Systematic Review and Meta-Analysis

Carole Clair, MD MSc[1], Marya J. Cohen, MD MPH[2], Florian Eichler, MD[3], Kevin J. Selby, MD[1], and Nancy A. Rigotti, MD[4]



Kouření zvyšuje riziko DN o 42%!!!

J Gen Intern Med 30(8):1193–203

www.dm2t.cz

www.cukrovka.cz

Diagnostika
autonomní diabetické neuropatie

SYSTÉM	DIAGNOSTICKÉ MOŽNOSTI
Kardiovaskulární	Kardiovaskulární testy (Ewing, spektrální analýza) Radionuklidové metody (123 I MIBG) Stanovení hladiny katecholaminů
Gastrointestinální	Scintigrafické metody (Tc99, I111, dechový test-k. octanová), sonografie, Paracetamolový test, manometrické metody
Urogenitální	Test na i.cavernózní aplikace prostaglandinu PG E1 Urodynamometry Kontrola residua v močovém měchýři
Sudomotorický	Termoregulační potní testy, Neuropad Testy kožních otisků
Oči	Pupilometrie

Diagnostika autonomní diabetické neuropatie

SYSTÉM	DIAGNOSTICKÉ MOŽNOSTI
Kardiovaskulární	916 BRITISH MEDICAL JOURNAL VOLUME 285 2 OCTOBER 1982 *Regular Review* **Diagnosis and management of diabetic autonomic neuropathy** D J EWING, B F CLARKE
Gastrointestinální	Scintigrafické metody (Tc99, I111, dechový test-k. octanová), sonografie, Paracetamolový test, manometrické metody
Urogenitální	Test na i.cavernózní aplikace prostaglandinu PG E1 Urodynamometry Kontrola residua v močovém měchýři
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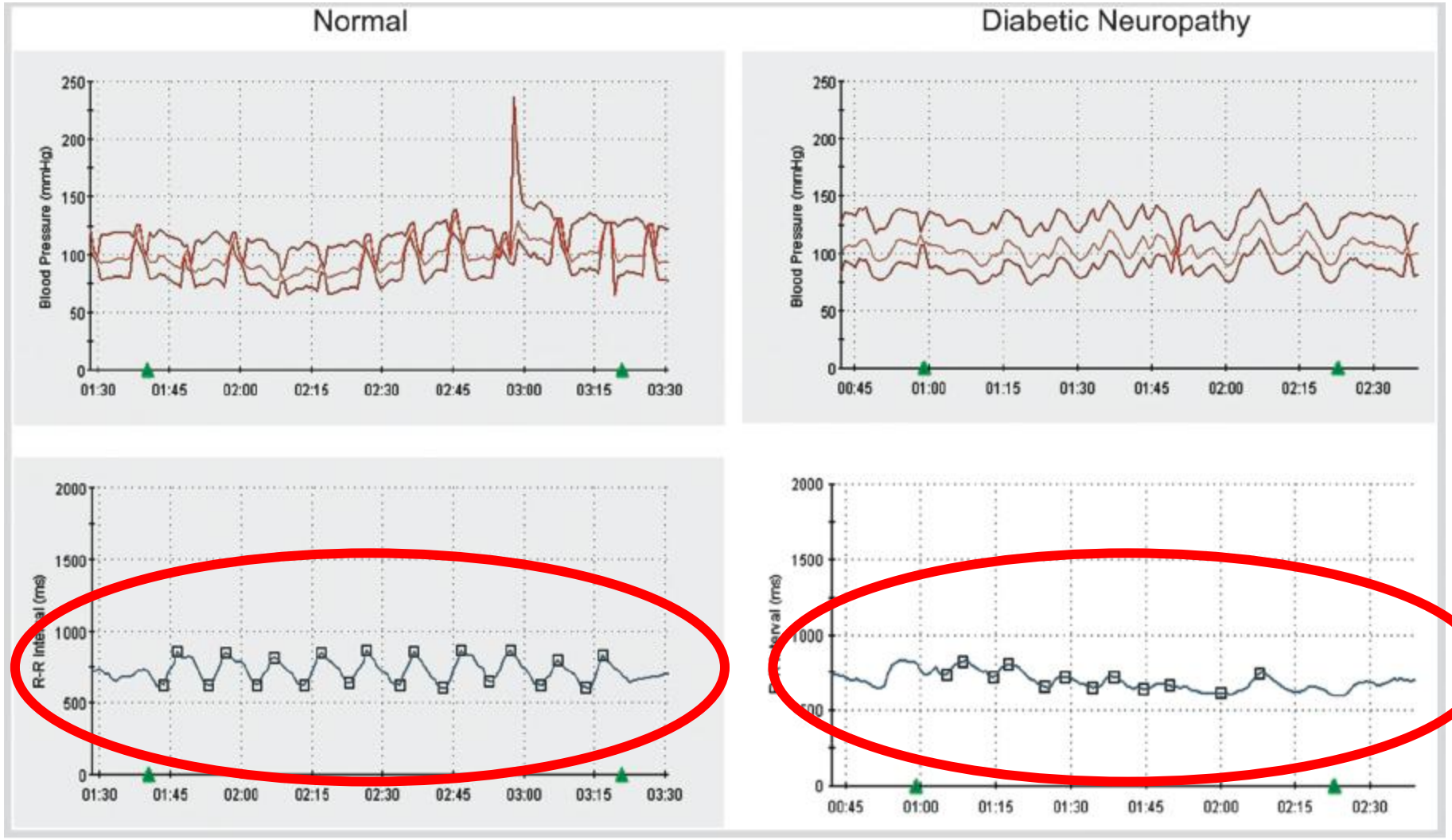


Continuum (Minneap Minn) 2014;20(5):1226–1240.

QT interval, corrected for heart rate, is associated with HbA_{1c} concentration and autonomic function in diabetes

K. Stern[1], Y. H. Cho[2,3], P. Benitez-Aguirre[2,3], A. J. Jenkir
A. C. Keech[4,8] and K. C. Donaghue[2,3]

[1]Sydney Medical School, University of Sydney, [2]Children's Hospital at Westmead, Institute of End
Health, University of Sydney, [4]National Health and Medical Research Council, Clinical Trials Centre
[6]Centre for Vision Research, Westmead Millennium Institute, [7]Department of Ophthalmology, Uni
Alfred Hospital, Sydney, Australia

Accepted 25 January 2016

- This is the first study to show significant associations between abnormal pupillometry, cardiac autonomic dysfunction and longer QTc interval in adolescents with Type 1 diabetes.
- A threshold of QTc > 409 ms in adolescents with Type 1 diabetes differentiates those most at risk of autonomic dysfunction, in addition to being female, having higher HbA_{1c}, BMI and total cholesterol.

Abstract

Aims To examine QT intervals corrected for heart rate (QTc) in adolescents with Type 1 diabetes compared with control subjects, and to determine associations with metabolic control and autonomic function.

Methods Resting electrocardiogram recordings of 142 adolescents with Type 1 diabetes [mean (SD) age 15.3 (2.0) years, diabetes duration 9.0 (3.5) years, HbA_{1c} 71 (17) mmol/mol or 8.7 (1.6)%] and 125 control subjects [mean (SD) age 15.7 (2.5) years] were used to calculate QTc duration and derive mean heart rate and heart rate variability (HRV) values. Linear and logistic regression models were used to examine the associations between QTc, metabolic control and autonomic function (HRV and pupillary function).

Results QTc duration was not significantly different between subjects with Type 1 diabetes and control subjects (mean duration 392 vs 391 ms; $P = 0.65$). In the Type 1 diabetes group, QTc was positively associated with HbA_{1c} [β = 4 (95% CI 2, 6); $P < 0.001$] and inversely associated with severe hypoglycaemic events [β = -10 (95% CI -20,-2); $P = 0.01$], less insulin/kg [β = -12 (95% CI -22, -2); $P = 0.024$] and less HRV. In the Type 1 diabetes group, QTc in the highest quintile (≥409 ms) vs quintiles 1–4 had more pupillary abnormalities (83 vs 56%; $P = 0.03$), lower pupillary maximum constriction velocity (4.8 vs 5.3 mm/s; $P = 0.04$), higher heart rate (78 vs 72 beats per min; $P = 0.02$) and lower HRV (standard deviation of mean NN intervals 4.0 vs 4.3 ms, $P = 0.004$ and root-mean-square difference of successive NN intervals 3.7 vs 4.1 ms; $P = 0.004$).

Conclusions Although there are concerns about hypoglycaemia in general in people with Type 1 diabetes, chronic hyperglycaemia, rather than intermittent hypoglycaemia, appears to be more deleterious to autonomic cardiac function, even in adolescence. Longer QTc was associated with higher HbA_{1c} concentration, lower risk of hypoglycaemia and autonomic dysfunction. Longitudinal studies are warranted.

Diabet. Med. 33, 1415–1421 (2016)

Klinické konsekvence diabetické neuropatie

DIABETIC AMYOTROPHY*

BY

HUGH GARLAND, T.D., M.D., F.R.C.P.

Physician-in-Charge, Department of Neurology, General Infirmary at Leeds

Although neurological complications of diabetes have been recognized for almost a hundred years, they have not received the detailed attention usually given to neurological disorders, nor the attention they deserve. That they are common is beyond doubt. Joslin *et al.* (1952) saw 913 diabetics with neurological syndromes in one hospital during a five-year period; this list included a number of disorders of the nervous system which were probably coincidental, but 519 consisted of syndromes of areflexia, paraesthesiae, pain, weakness, and wasting, most of which were almost certainly by-products of diabetes. More recently Matthews (1955) has found evidence of "neuropathy" in 37% of 545 unselected diabetics. Since the total number of diabetics in the world is said to be about twenty million it would seem that "diabetic neuropathy" may include millions of victims. The term "neuropathy" is used rather loosely, sometimes referring to disturbances of peripheral nerves only (in the previous sense of "neuritis") and sometimes more widely to include motor and sensory disorders resulting from lesions of the spinal cord,

Br Med J. 1955 Nov 26;2(4951):1287-90

Summary

Twelve patients are described, showing a syndrome which includes weakness and wasting of muscles with tendon areflexia, all associated with frank diabetes or at least with impaired glucose tolerance.

There is evidence that some of these cases result from a myelopathy and that changes may occur at any cord level, though they are most commonly seen in the lumbar region.

Pain of a similar distribution to the amyotrophy is a frequent though not constant feature.

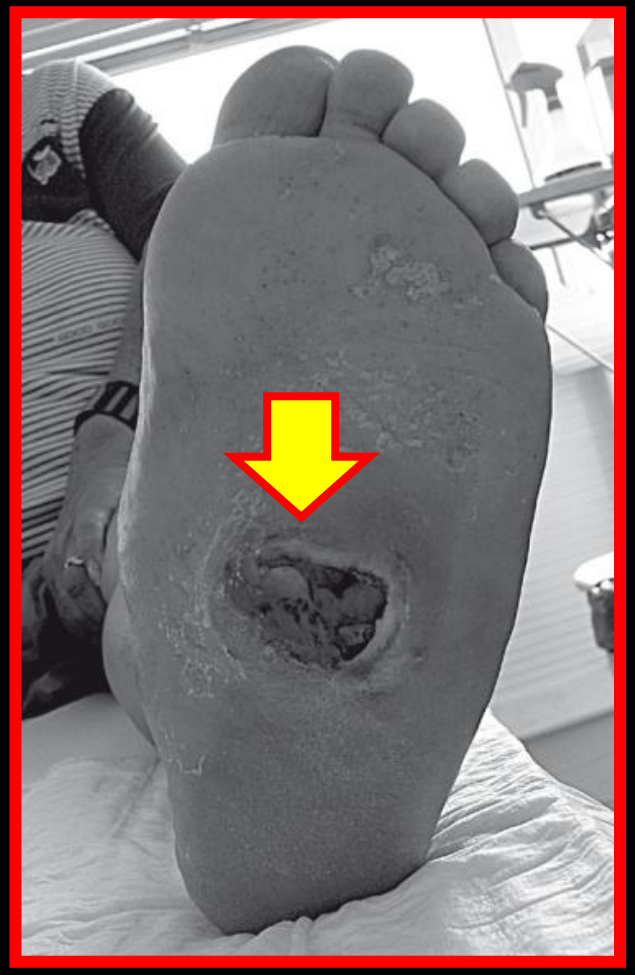
The protein content of the C.S.F. may be normal or raised.

Affected muscles always show electromyographic changes, though of varying character.

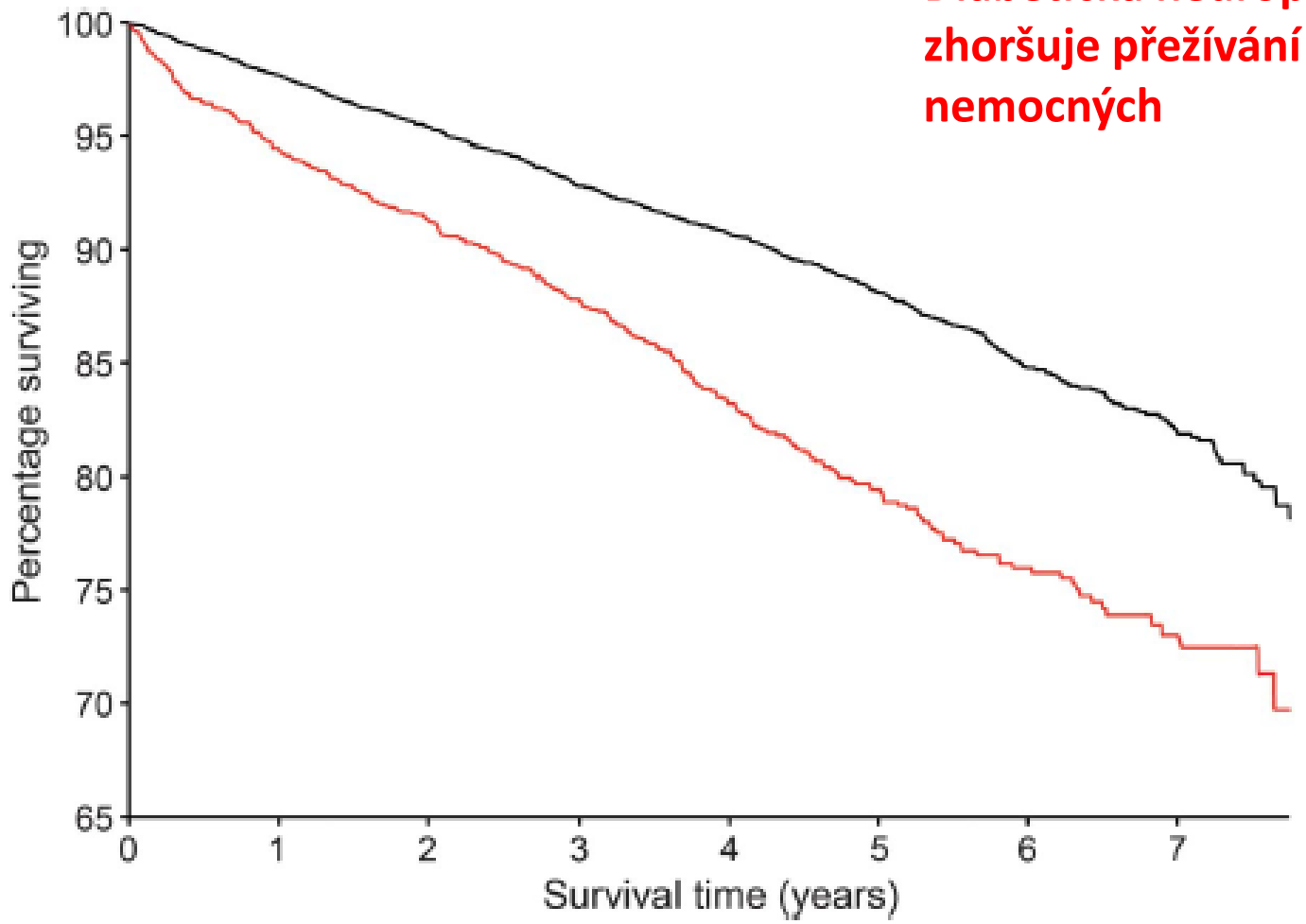
At the present time "diabetic amyotrophy" would appear to be the best term to apply to the syndrome.

Diabetic amyotrophy is the result of uncontrolled diabetes and is probably always reversible by full diabetic control.

Br Med J. 1955 Nov 26;2(4951):1287-90



Diabetická neuropatie zhoršuje přežívání nemocných



Conclusions: Polyneuropathies have notable neurologic impairments beyond their identified multiple comorbidities. Life expectancy is shortened. Diabetic polyneuropathy is underidentified. The quantified extent of the disease burden and refined comorbidity associations emphasize that greater research efforts and health care initiatives are needed. ***Neurology*® 2015;84:1644–1651**

Neurology 2015;84: 1644–1651

The influence of cardiovascular autonomic neuropathy on mortality in type 1 diabetic patients; 10-year follow-up

Silvie Lacigova, Jitka Brozova, Daniela Cechurova, Jitka Tomesova, Michal Krcma, Zdenek Rusavy

Aim. The aim of our retrospective study was to answer the question if the presence of cardiovascular autonomic neuropathy (CAN) affects mortality in type 1 diabetic patients during a 10-year follow-up.
Methods. Patients with type 1 diabetes mellitus examined for CAN in 2003 were enrolled in this retrospective study. A total of 278 patients were included and divided into two groups according to the presence or absence of CAN (111 CAN+, 167 CAN-). The group characteristics and outcomes were compared at baseline and after ten years (in 2013).
Results. In the follow-up period, a total of 18 patients died; CAN+ (14/111; 12.6%) and CAN- (4/167; 2.4%) ($P < 0.001$). At baseline, the CAN+ patients were older (47 vs. 33 years; $P < 0.001$), had longer duration of diabetes (20 vs. 12 years; $P < 0.05$), had worse glycemic control assessed by HbA1c (73 vs. 68 mmol/mol; $P < 0.05$), higher systolic (130 vs. 120 mmHg; $P < 0.001$) and diastolic (80 vs. 70 mmHg; $P < 0.01$) blood pressure and had more diabetic complications. In our analysis we found the strongest predictor of mortality to be the presence of CAN ($P < 0.01$) and the blood pressure value at baseline ($P < 0.05$). Other baseline characteristics, including the duration of diabetes, age and the presence of micro- and macrovascular complications were not significant. The statistical analysis was performed using logistic regression step-wise analysis.
Conclusions. During the 10-year follow-up, CAN+ patients had a 5-fold higher mortality rate than CAN- patients. The strongest predictor of mortality was the presence of CAN.

Biomed Pap Med Fac UP 2016 Mar; 160(1):111-117.

Důsledky neuropatie

- **Náhlá smrt – kratší život**
- **Amputace nohy**
- **Závažné trávicí potíže (zácpa, průjem)**
- **Nehojící se rány**
- **Otoky, kolapsové stavy,**
- **Pomalá reakce zornice na osvit - oslnění**
- **Inkontinence, infekce močových cest**
- **Erektilní dysfunkce**

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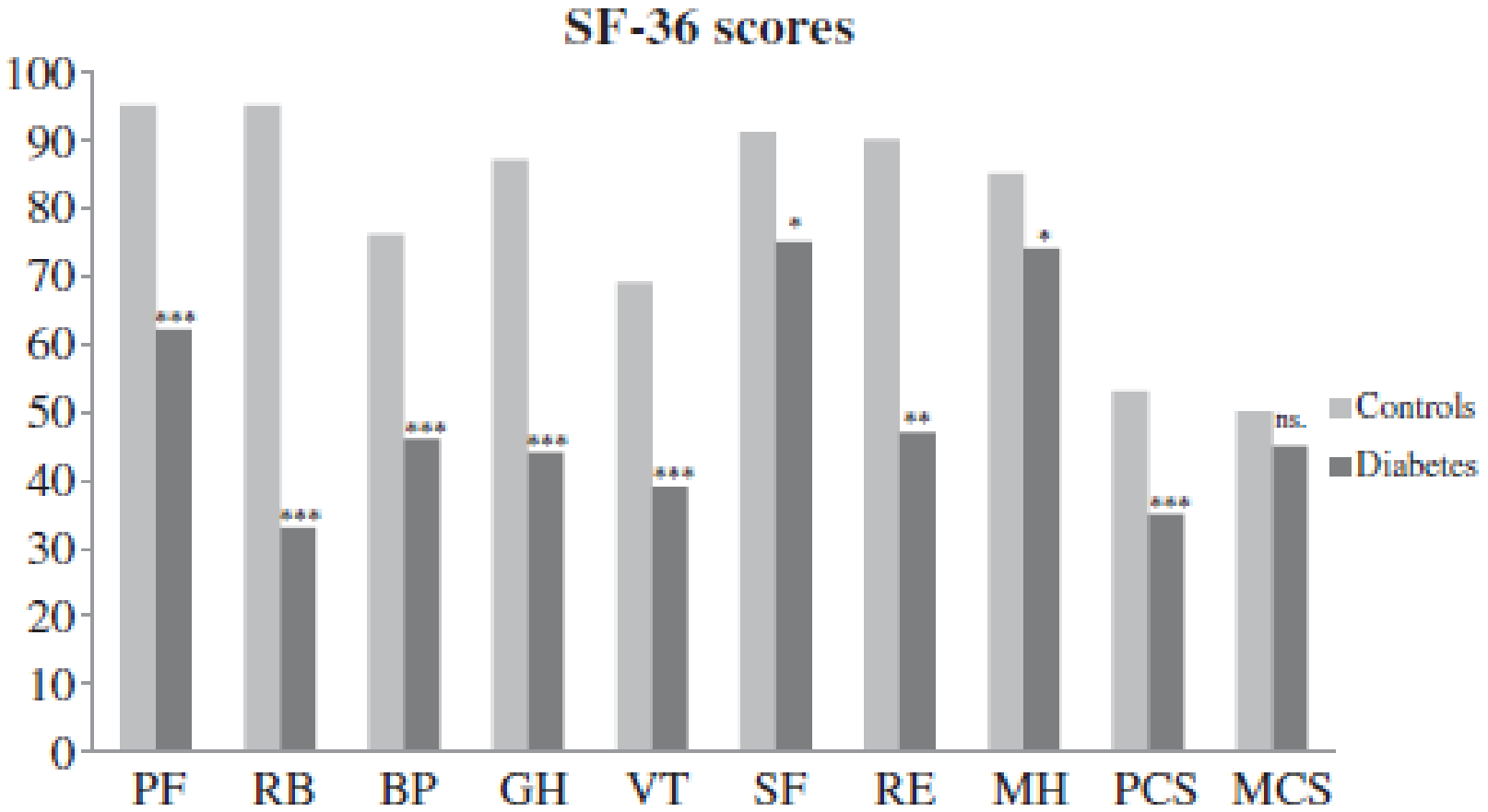
- **Erektilní dysfunkce**
- **Prostě špatně se žije**

Contents lists available at ScienceDirect

Journal of Diabetes and Its Complications

journal homepage: WWW.JDCJOURNAL.COM

Association between visceral, cardiac and sensorimotor polyneuropathies in diabetes mellitus☆



Journal of Diabetes and Its Complications 28 (2014) 370–377

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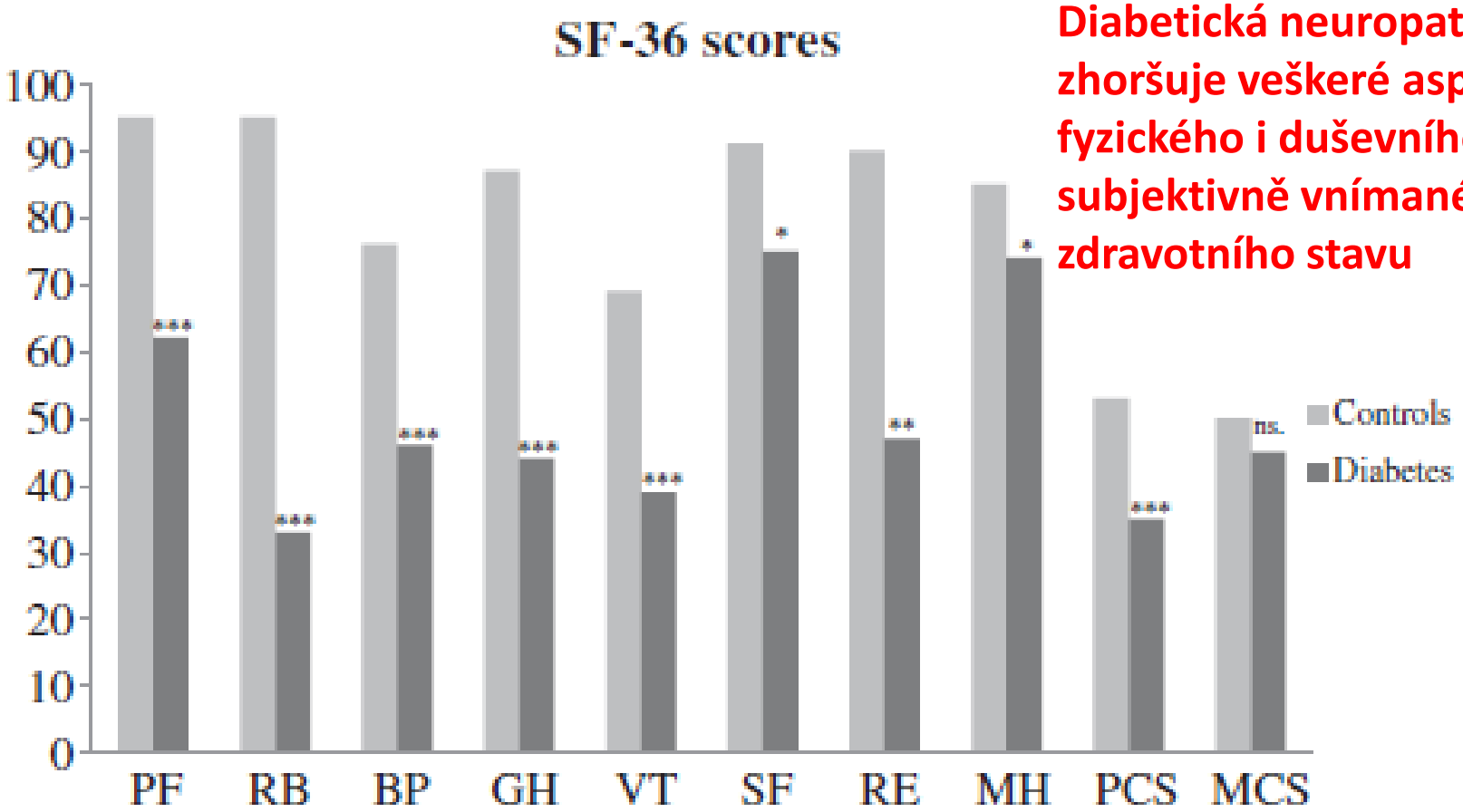
Association between visceral, cardiac and sensorimotor polyneuropathies in diabetes mellitus☆



Diabetická neuropatie zhoršuje veškeré aspekty fyzického i duševního subjektivně vnímaného zdravotního stavu

Journal of Diabetes and Its Complications 28 (2014) 370–377

Je jiná u DM 1 a DM 2?

Diabetic Neuropathy: One disease or two?

Brian C. Callaghan[1], **Junguk Hur**[1], and **Eva L. Feldman**[1,*]

[1]Department of Neurology, University of Michigan, Ann Arbor, MI, USA

Abstract

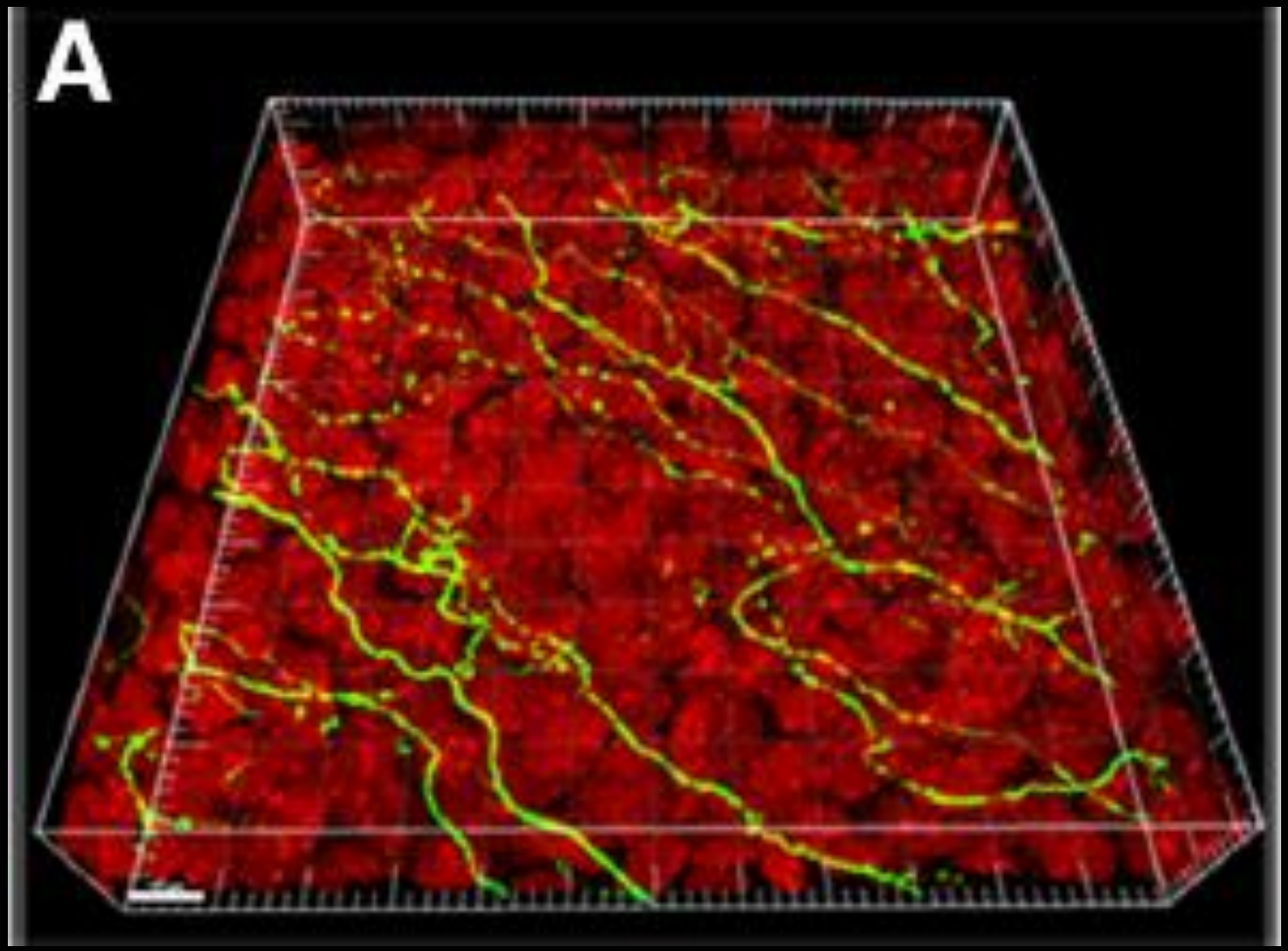
Purpose of review—To compare and contrast the evidence for the effect of glucose control on the prevention of neuropathy in type 1 (T1DM) and type 2 (T2DM) diabetes mellitus.

Recent findings—In T1DM, multiple clinical trials have demonstrated a large benefit from enhanced glucose control, whereas the benefit in T2DM is much more modest. Epidemiologic and laboratory evidence exists to support factors other than hyperglycemia in the development of neuropathy including obesity, hypertension, dyslipidemia, inflammation, and insulin resistance.

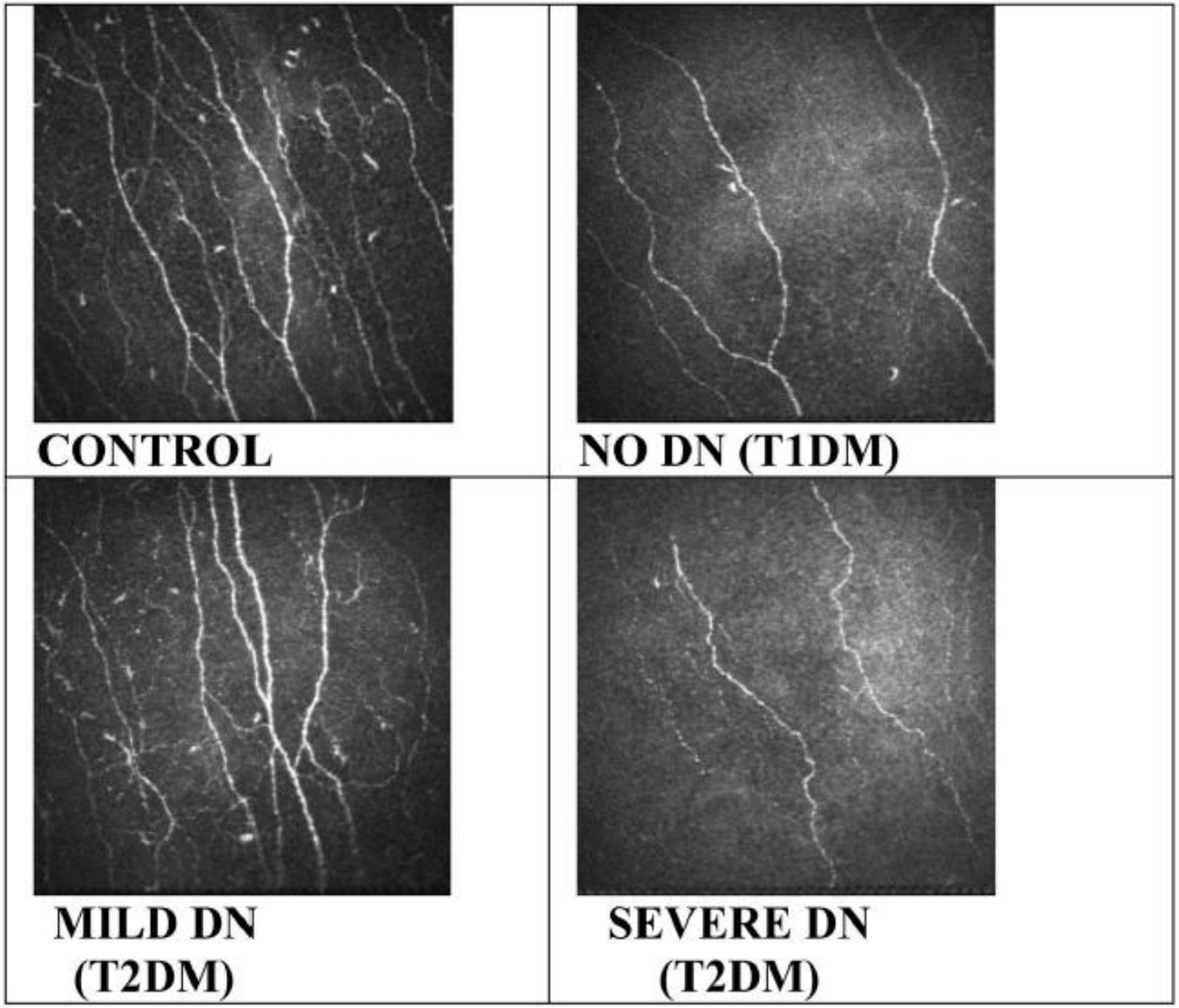
Summary—T1DM neuropathy and T2DM neuropathy are fundamentally different. In T1DM, glucose control has a large effect on the prevention of neuropathy; therefore future efforts should continue to concentrate on this avenue of treatment. In contrast, in T2DM, glucose control has a small effect on the prevention of neuropathy; as a result, more research is needed to define the underlying mechanisms for the development of neuropathy. Understanding these mechanisms may lead to novel therapeutic approaches to prevent or treat diabetic neuropathy.

Curr Opin Neurol. 2012 October ; 25(5): 536–541.

Můžeme zobrazit diabetickou neuropatii?



Am J Pathol 2014, 184: 2662e2670;



J Diabetes Complications. 2014 ; 28(5): 658–661.

Můžeme léčit diabetickou neuropatii?

Nejlepší je prevence!!!!

Cochrane Database Syst Rev. 2014 Feb 14;2:CD009122.

DM 1. typu

Under intensive glucose control,
the risk of developing microvascular complications
was reduced compared to conventional treatment
for
Neuropathy: 29/586 (4.9%) versus 86/617 (13.9%);
RR 0.35 (95% CI 0.23 to 0.53);
P< 0.00001;
1203 participants; 3 trials;
high quality evidence.

Cochrane Library

Cochrane Database of Systematic Reviews

Intensive glucose control versus conventional glucose control for type 1 diabetes mellitus (Review)

Fullerton B, Jeitler K, Seitz M, Horvath K, Berghold A, Siebenhofer A

Cochrane Database Syst Rev. 2014 Feb 14;2:CD009122.

DM 2. typu

Four studies that reported the primary outcome, involving 6669 participants with type 2 diabetes, the annualized RD of developing clinical neuropathy was -0.58% (95% CI 0.01 to - 1.17)

In type 2 diabetes mellitus, enhanced glucose control reduces the incidence of clinical neuropathy, although this was not formally statistically significant P = 0.06).

However, enhanced glucose control does significantly reduce nerve conduction and vibration threshold abnormalities.

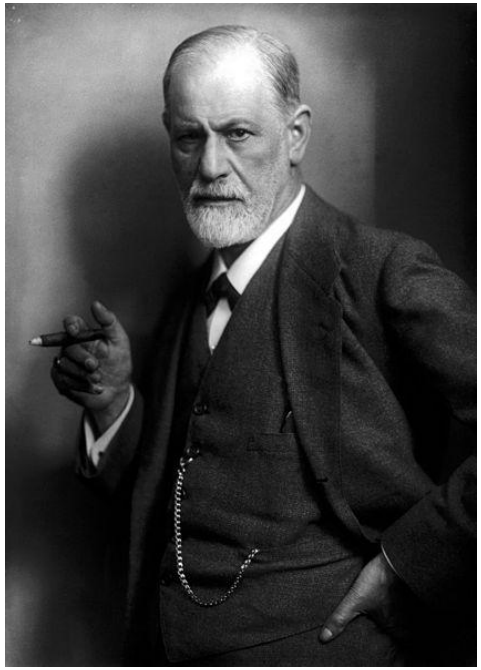
Cochrane Database Syst Rev. 2012 Jun 13;6:CD007543.

Jak můžeme léčit diabetickou neuropatii?

Životospráva zlepšuje kompenzaci

Životospráva zlepšuje kompenzaci

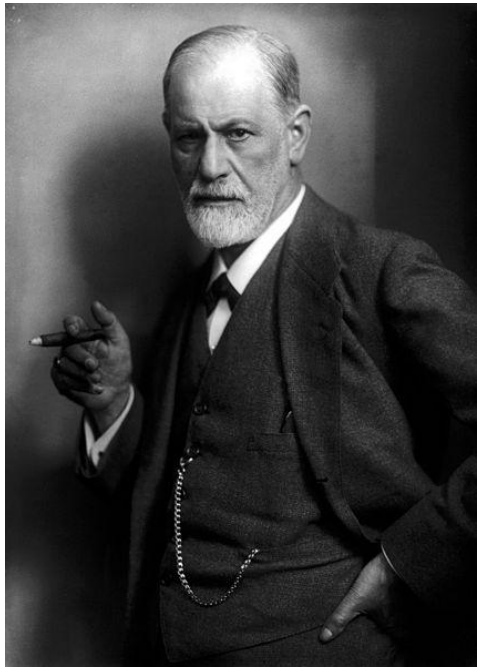
Těsná kompenzace diabetu
je nejlepší terapie



Sigmund Freud

6. 5. 1856 – 23. 9. 1939

„Vzdáte-li se kouření, pití a milování, nebudete ve skutečnosti žít déle,



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6. 5. 1856 – 23. 9. 1939

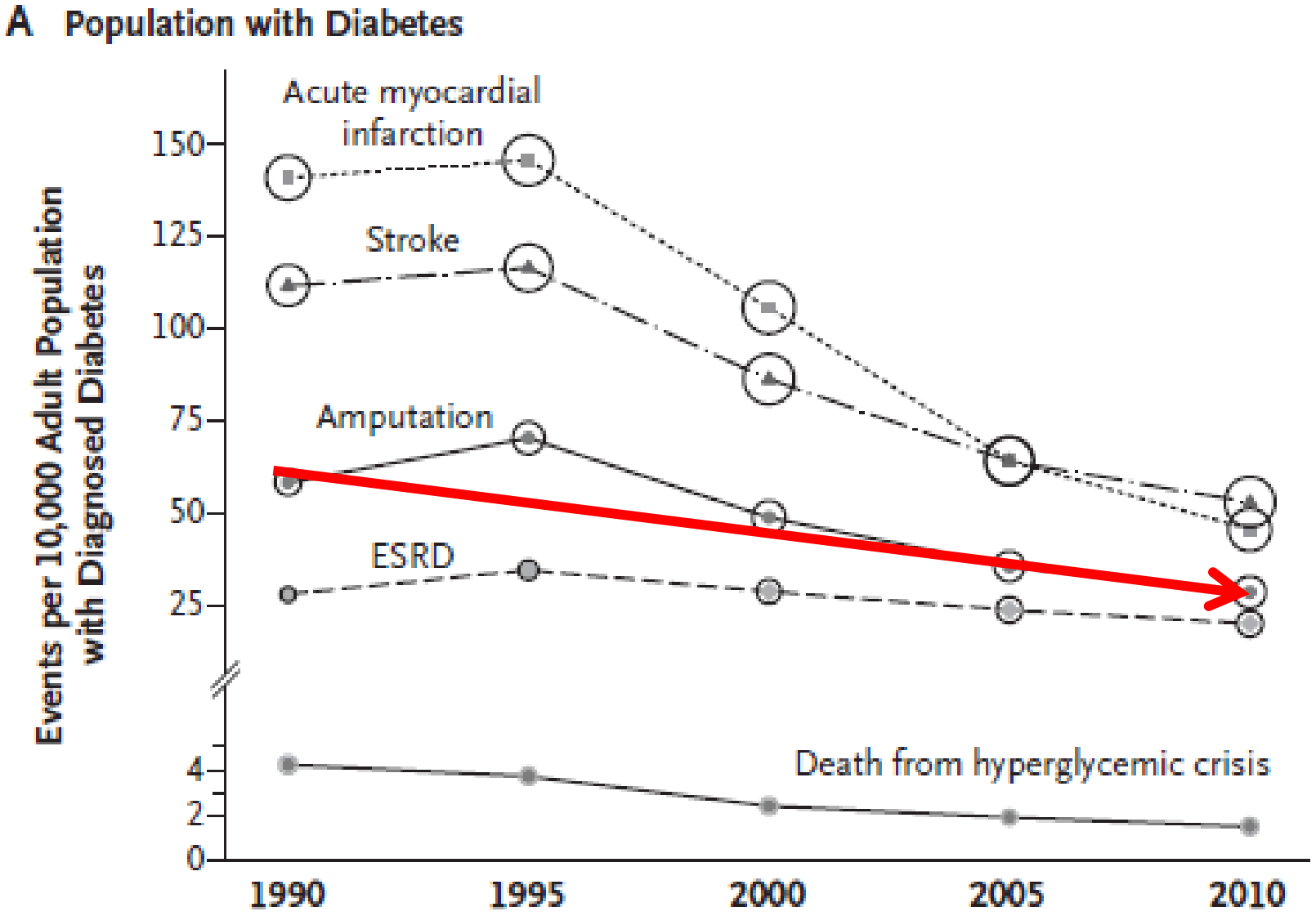
„Vzdáte-li se kouření, pití a milování, nebudete ve skutečnosti žít déle,

ale jen vám to tak bude připadat.“

Nezbývá, než intenzivní farmakologická terapie hyperglykémie

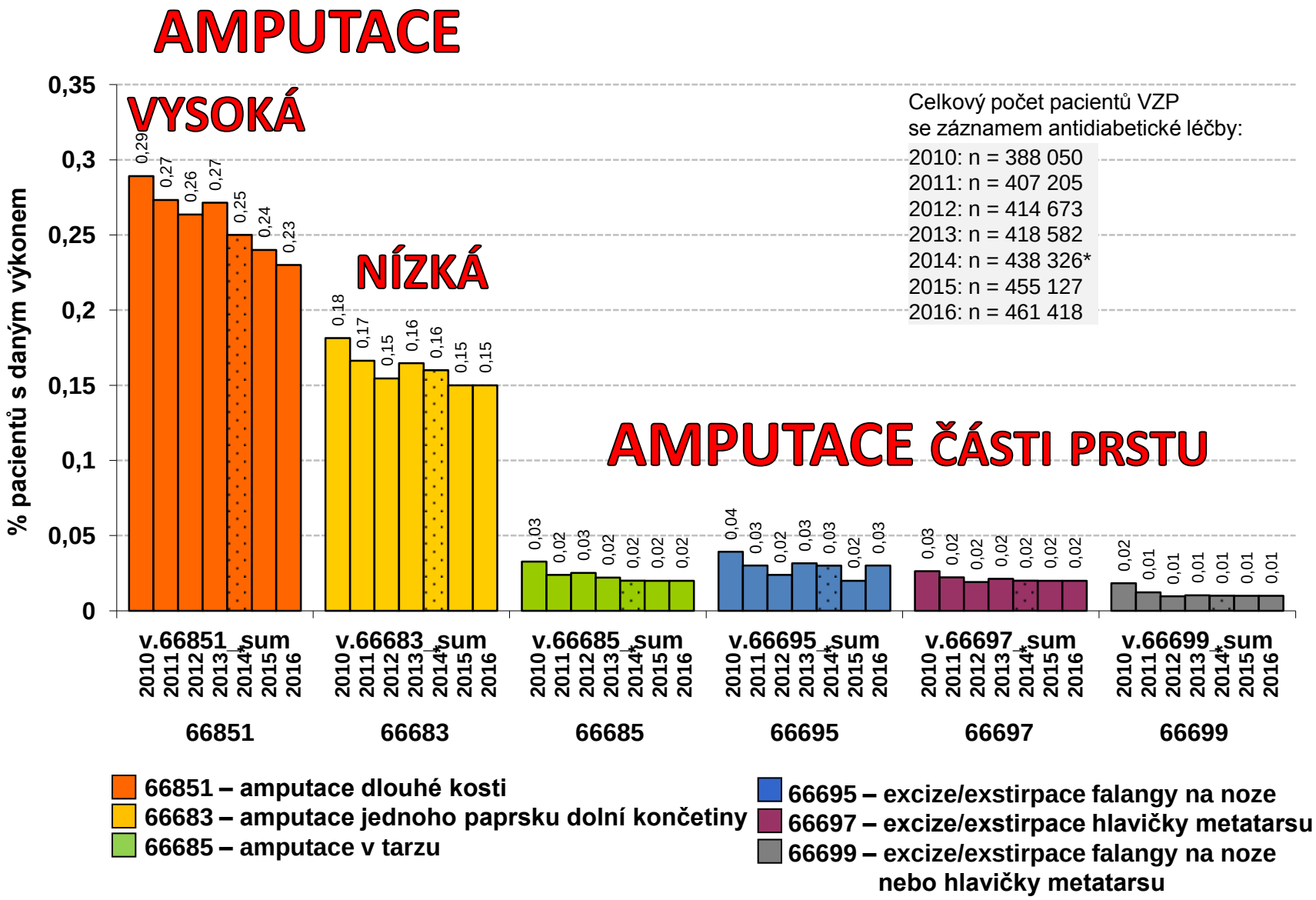
Nezbývá, než intenzivní farmakologická terapie hyperglykémie

K čemu jsou průchodné arterie, když pacient může zemřít na komplikace diabetické polyneuropatie?



N Engl J Med 2014;370:1514-23.

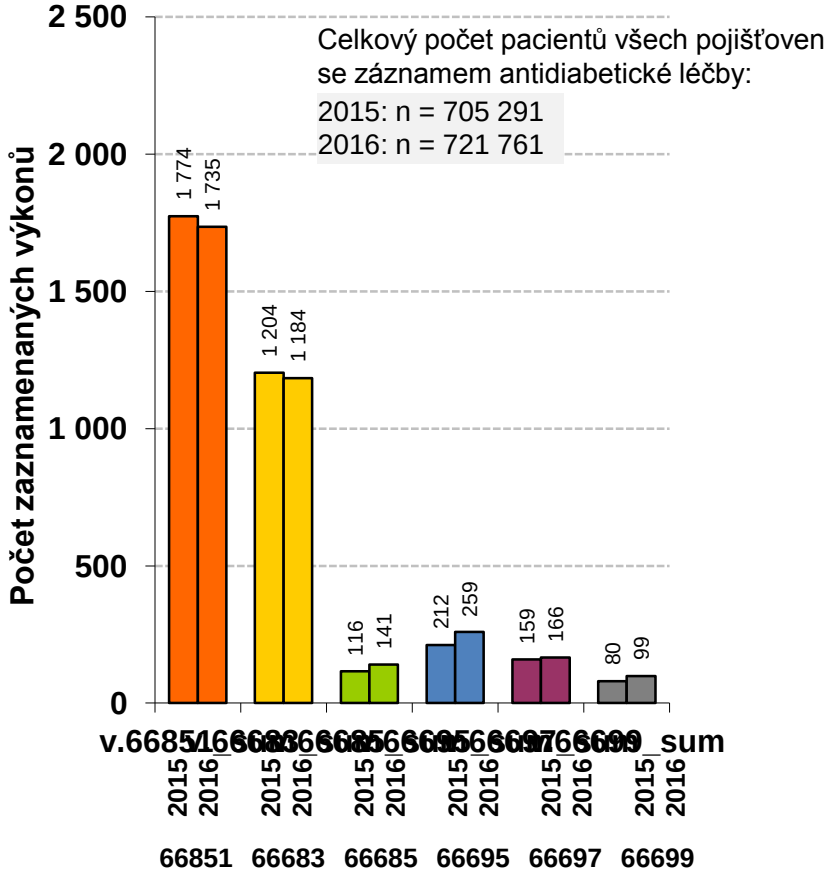
Provedené výkony na diabetické noze u pacientů se záznamem antidiabetické léčby v datech VZP v letech 2010–2016

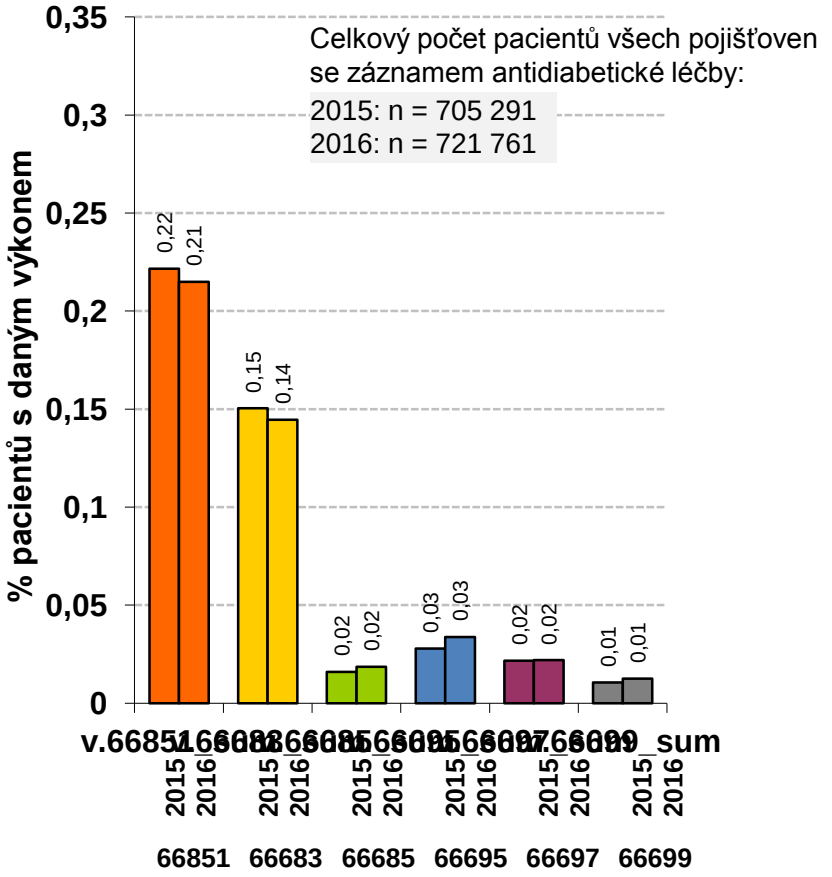


Zdroj: 2010–2013 data VZP, 2015–2016 data VZP v NRHZS;
*hodnoty pro rok 2014 byly aproximovány, jelikož příslušná data jsou aktuálně nedostupná

Provedené výkony na diabetické noze u pacientů se záznamem antidiabetické léčby v datech NRHZS v letech 2015–2016

Počet zaznamenaných výkonů a % diabetiků s daným výkonem v letech 2015–2016





66851 – amputace dlouhé kosti
66683 – amputace jednoho paprsku dolní končetiny
66685 – amputace v tarzu
66695 – excize/exstirpace falangy na noze
66697 – excize/exstirpace hlavičky metatarsu
66699 – excize/exstirpace falangy na noze nebo hlavičky metatarsu

Zdroj: 2015–2016 data NRHZS

Farmakologická léčba

Lék	Kontraindikace	Hlavní nežádoucí účinky	Vedlejší pozitivní účinky	NNT	NNH	NNMH
Tricyklická antidepresiva (např. amytriptylin)	stav po infarktu myokardu, arytmie	přírůstek hmotnosti, sedace, orlostatická hypotenze, anticholinergní efekt	antidepresivní efekt, terapie nespavosti	1.3–2.4	2.7–6.0	15–18
SNRI (inhibitory zpětného vychytávání serotoninu a norepinefrinu – např. venlafaxine, duloxetine)	dysfunkce jater a ledvin, kardiální onemocnění, alkoholismus	nausea, spavost a zácpa	antidepresivní účinek	3.1.– 6	9.6	17–21
Gabapentin	renální insuficience	sedace, vertigo, periferní otoky	antiepileptikum	3.3–5.8	2.7–3.7	11–20
Pregabalin	renální insuficience	sedace, vertigo, periferní otoky	antiepileptikum, snížení úzkosti a nespavosti	2.9–5	3.7	11–23
Opioidy	závislost na opiátech nebo jiných látkách, současné užívání SNRI nebo tricyklických antidepresiv (serotoninový syndrom), řízení, riziko sebevraždy	nevolnosti až zvracení, zácpa, ospalost, motání hlavy	rychlý nástup analgetického účinku	2.4–4.3	3.6	7.8

Podle:
Neuroendocrinology 2013;98:267–280

Počet Pac. léčených na jeden NÚ

Počet Pac. léčených na jeden závažný NÚ

Treatment of symptomatic diabetic polyneuropathy with the antioxidant α-lipoic acid: a meta-analysis

D. Ziegler, H. Nowak*, P. Kemplert†, P. Varghat† and P. A. Low§

Abstract

Aims To determine the efficacy and safety of 600 mg of α-lipoic acid given intravenously over 3 weeks in diabetic patients with symptomatic polyneuropathy.

Methods We searched the database of VIATRIS GmbH, Frankfurt, Germany, for clinical trials of α-lipoic acid according to the following prerequisites: randomized, double-masked, placebo-controlled, parallel-group trial using α-lipoic acid infusions of 600 mg i.v. per day for 3 weeks, except for weekends, in diabetic patients with positive sensory symptoms of polyneuropathy which were scored by the Total Symptom Score (TSS) in the feet on a daily basis. Four trials (ALADIN I, ALADIN III, SYDNEY, NATHAN II) comprised $n = 1258$ patients (α-lipoic acid $n = 716$; placebo $n = 542$) met these eligibility criteria and were included in a meta-analysis based on the intention-to-treat principle. Primary analysis involved a comparison of the differences in TSS from baseline to the end of i.v. Treatment between the groups treated with α-lipoic acid or placebo. Secondary analyses included daily changes in TSS, responder rates (≥ 50% improvement in TSS), individual TSS components, Neuropathy Impairment Score (NIS), NIS of the lower limbs (NIS-LL), individual NIS-LL components, and the rates of adverse events.

Results After 3 weeks the relative difference in favour of α-lipoic acid vs. placebo was 24.1% (13.5, 33.4) (geometric mean with 95% confidence interval) for TSS and 16.0 % (5.7, 25.2) for NIS-LL. The responder rates were 52.7% in patients treated with α-lipoic acid and 36.9% in those on placebo ($P < 0.05$). On a daily basis there was a continuous increase in the magnitude of TSS improvement in favour of α-lipoic acid vs. placebo which was noted first after 8 days of treatment. Among the individual components of the TSS, pain, burning, and numbness decreased in favour of α-lipoic acid compared with placebo, while among the NIS-LL components pin-prick and touch-pressure sensation as well as ankle reflexes were improved in favour of α-lipoic acid after 3 weeks. The rates of adverse events did not differ between the groups.

Conclusions The results of this meta-analysis provide evidence that treatment with α-lipoic acid (600 mg/day i.v.) over 3 weeks is safe and significantly improves both positive neuropathic symptoms and neuropathic deficits to a clinically meaningful degree in diabetic patients with symptomatic polyneuropathy.

Diabetic Medicine, 21, 114–121

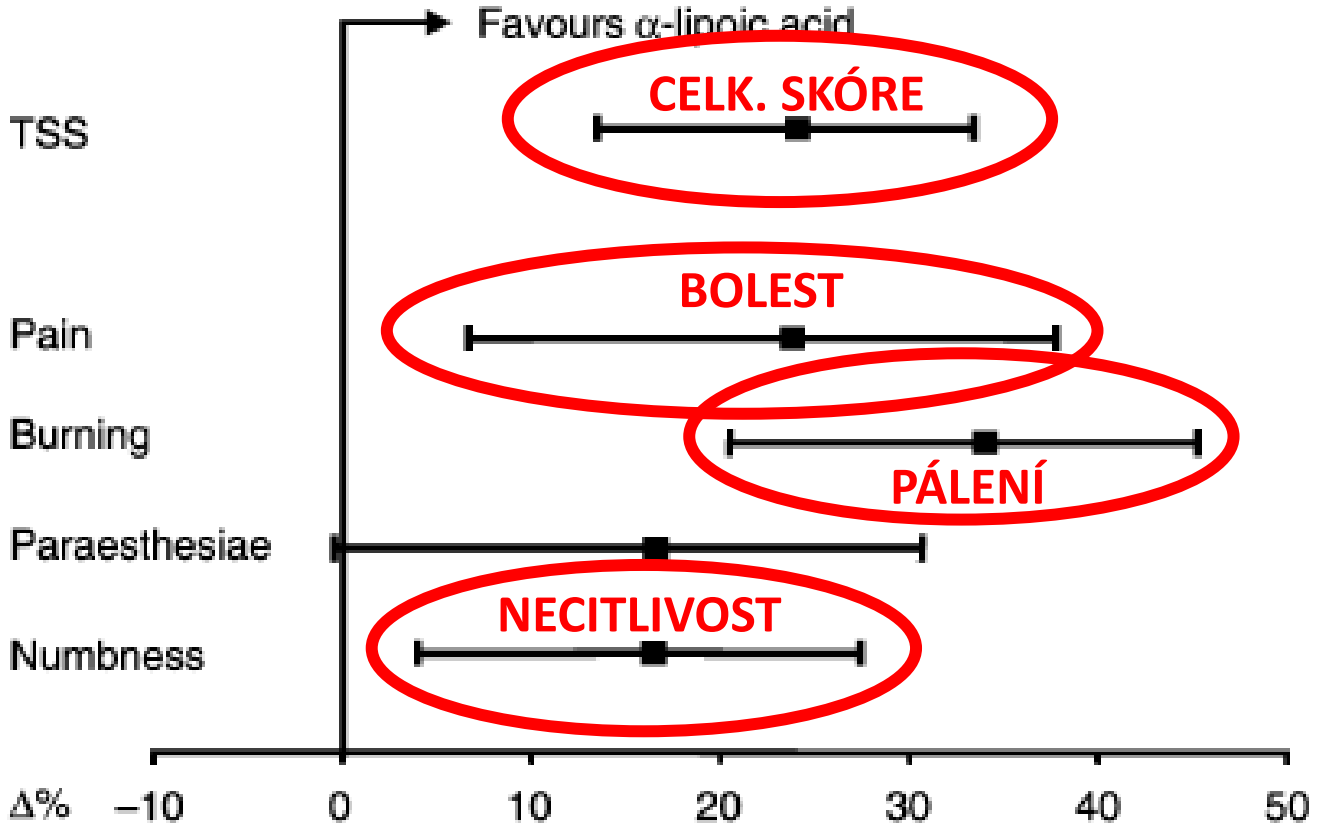


Figure 4 Relative differences between α-lipoic acid and placebo at 3 weeks vs. baseline in the Total Symptom Score (TSS) and the four individual neuropathic symptoms in the pooled groups. Displayed are point estimates for Δ% = (1 − ratio of the geometric means) × 100 with 95% confidence interval (CI); CI > 0 favours α-lipoic acid.

Diabetic Medicine, 21, 114–121

Parestezie

- Brnění
- Mravenčení
- Pálení
- Pocit studených nohou
- Řezání
- „divný pocit“
- Bolest spíše vzácně


CACTUS CLUB CAFE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CACTUS CLUB CAFE

- **Pocit studených nohou**

Poruchy senzitivity:

- **Parestezie**
- **Dysestezie**
- **Hypestezie**
- **Anestezie**

Poruchy senzitivity:

- **Parestezie**
- **Dysestezie**
- **Hypestezie**
- **Anestezie**

- **Zkušenost je nepřenositelná: jak vysvětlit pacientovi, který necítí, že necítí?**

Souhrn

- **Diabetická neuropatie je závažnou komplikací diabetu**

Shrnutí

- Diabetická neuropatie je závažnou komplikací diabetu
- **Příznaky diabetické neuropatie *nejsou* alarmující, což vede k jejich podcenění….**

Shrnutí

- Diabetická neuropatie je závažnou komplikací diabetu
- Příznaky diabetické neuropatie nejsou alarmující, což vede k jejich podcenění….
- **..ale důsledky diabetické neuropatie jsou velmi závažné, invalidizující a fatální**

Shrnutí

- Diabetická neuropatie je závažnou komplikací diabetu
- Příznaky diabetické neuropatie nejsou alarmující, což vede k jejich podcenění….
- ..ale důsledky diabetické neuropatie jsou velmi závažné, invalidizující a fatální
- **Nejúčinnější prevence je intenzivní terapie diabetu**

Děkuji za pozornost