



Prof Rodica Pop-Busui

Chairperson at EASD; Professor of Metabolism, Endocrinology and Diabetes, University of Michigan, Ann Arbor, Michigan, USA

Q1

Why is diabetic neuropathy such a prevalent complication in the USA?

Diabetic neuropathy is arguably the most prevalent chronic complication, not only in USA, but throughout the Western world. In addition, emerging data demonstrate very high prevalence rates worldwide. Although all reasons are still not well understood, many of us are actively working to unveil and understand what drives this high risk. An important point is the broad spectrum of diabetic neuropathy clinical manifestations, including peripheral and autonomic forms. In addition, the plethora of risk factors besides hyperglycaemia that contribute to nerve fibre damage and loss include other important players such as the underlying chronic inflammation in diabetes and prediabetes, obesity, insulin resistance, ageing, and lifestyle, as well as several recently described socioeconomic factors.

Q2

You have served as principal investigator on a number of landmark diabetes trials to study the mechanisms of diabetic complications, including diabetic cardiovascular autonomic and peripheral neuropathy. Have you ever experienced a particularly unusual or surprising case? What results did you find?

Indeed, I have had the privilege of leading several neuropathy evaluations and studies in a number of large cohorts of Type 1 and Type 2 diabetes mellitus. Several examples come to mind and I will enumerate just few: firstly, we have conclusively demonstrated in the >10,000 patients with Type 2 diabetes mellitus participating in the ACCORD trial that cardiovascular autonomic neuropathy at baseline independently predicted all-cause and cardiovascular mortality during the trial, doubling the mortality risk. Secondly, with my younger colleague and mentee Dr Kara Mizokami-Stout, by phenotyping the

large Type 1 diabetes mellitus Exchange cohort (a contemporary cohort of patients with Type 1 diabetes mellitus reflecting the current standard of care practice in the entire USA and including >25,000 patients), we found that socioeconomic factors are driving a high risk for neuropathy, which has not been demonstrated before; our findings were published earlier this year (2020) and were then confirmed by our colleagues in Scotland, UK with the Scottish Type 1 Register. Thirdly, the differences in the risk-factor profiles between peripheral and autonomic neuropathy that we were able to unveil with complex analyses in the fully phenotyped Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) cohort. This study was published earlier this year as well with my colleague Dr Barbara Braffett and the rest of the neuropathy team.

Q3

The coronavirus 2019 (COVID-19) pandemic has been extremely pressurising for healthcare professionals and you recently co-authored an article titled “COVID-19 and Diabetes: A Collision and Collusion of Two Diseases”. What makes patients with diabetes highly susceptible to COVID-19 and how has the pandemic complicated the treatment of patients with diabetes this year? What were the take-home messages of this article?

Overall, there is a consensus from clinical studies and meta-analyses that diabetes is a risk factor for serious COVID-19 infection and mortality. Although research is ongoing, several common risk factors are contributing and include the fact that patients with diabetes frequently suffer from comorbidities such as obesity, hypertension, cardiovascular disease, and chronic kidney disease, and dyslipidaemia, which predispose them to poorer COVID-19 outcomes. In addition,

the low-grade inflammation and degree of glucose control and hyperglycaemia at infection time all promote more severe forms of infection and a higher release of inflammatory mediators.

Q4 You are set to present several sessions at the EASD Virtual Meeting 2020. How widespread has the knowledge of diabetic neuropathy become since the start of your career?

I was honoured to present a plenary lecture on the epidemiology of diabetic neuropathies and share all recent data on this important complication. It is our role to disseminate the knowledge on the actual magnitude of this complication, its risk factors, and the characteristics of patients who are more likely to develop the disease, as well as to provide guidance on the best way to screen, diagnose, and manage patients.

Q5 As co-director of the Neuropathy Centre at the University of Michigan, what are some of the projects that your research team work on?

We have several exciting projects, including a Phase II/III clinical trial designed to test a potential new disease-modifying treatment for diabetic neuropathy, which is funded by the National Institutes of Health (NIH). I am also involved in a couple of novel and complex phenotyping studies in patients with both Type 1 and Type 2 diabetes mellitus, which are funded by the NIH and the Juvenile Diabetes Research Foundation (JDRF). Additionally, we are very excited that we have received funding from the NIH to study longer-term effects of COVID-19 in patients with diabetes.

Q6 What was the long-term goal you set out to achieve when you began your career? Do you still regularly set yourself goals to achieve in your personal or academic development?

I have dedicated my entire career to research and clinical care, targeting new therapies and new technologies to fight against diabetes and its complications, including implementing optimal management of hyperglycaemia and

all risk factors in these patients, and advocating for access to optimal care for all patients with diabetes. I am very fortunate to have succeeded in my career thus far, as I am a Professor with Tenure of Internal Medicine, Metabolism, Endocrinology ,and Diabetes, Vice Chair of clinical research for the entire department of Internal Medicine with a faculty of approximately 900 and I am also honoured with an endowed professorship by the University of Michigan. I have achieved national and international recognition, including chairing the American Diabetes Association (ADA) Position Statement on Diabetic Neuropathy. At this stage, my goals are to help our younger and early-career colleagues to succeed as well.

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