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MS and cardiovascular comorbidities

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Multiple Sclerosis Sessions
at ECTRIMS 2019

MS and cardiovascular comorbidities: who is at risk and how should we manage these patients?

Cardiovascular (CV) comorbidities are common among people with multiple sclerosis (pwMS).[1] In this article, we look at data presented at ECTRIMS 2019 that add to our understanding of this subject.

Prevalence of CV comorbidities in people with MS

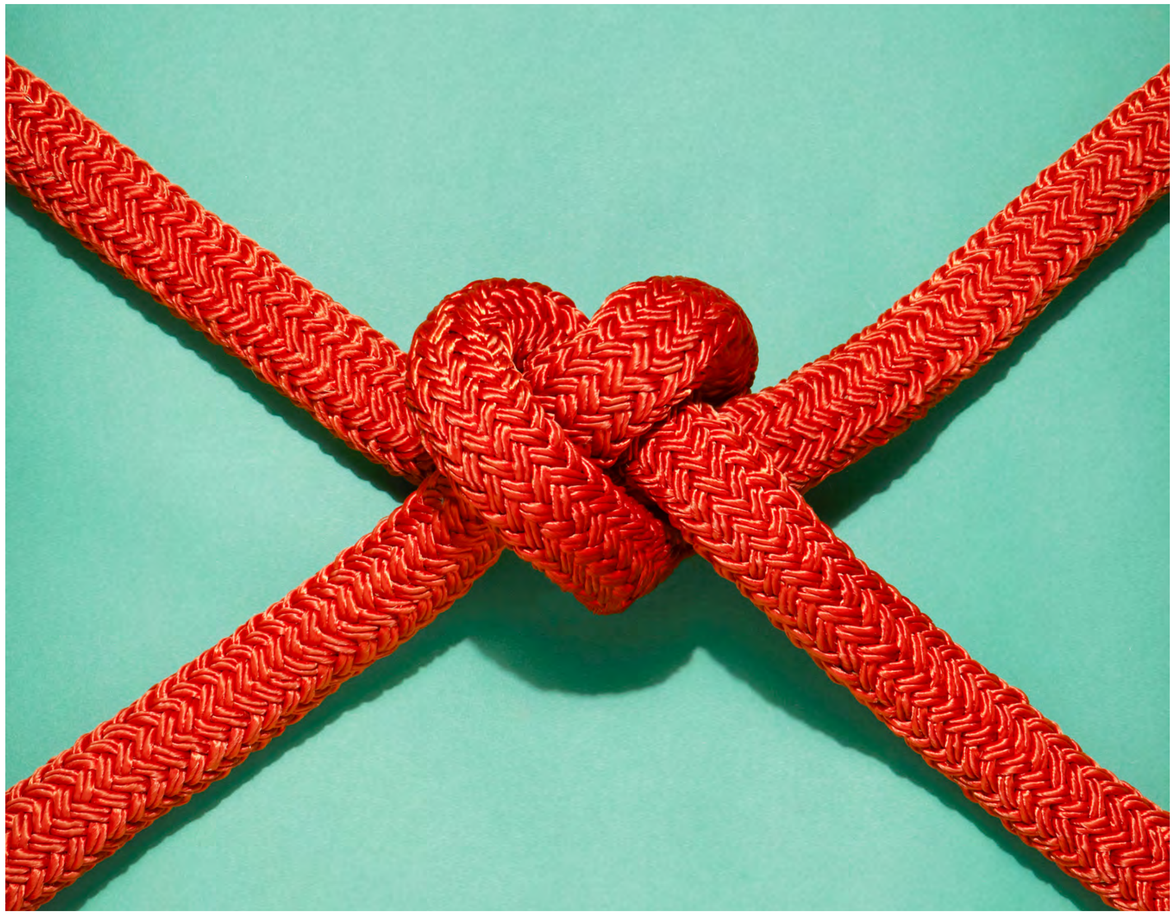
CV disease is the leading cause of mortality globally (accounting for 40% of deaths) and the second most common cause in high-income countries (23% of deaths) after cancer. Authors of a systematic review calculated estimated prevalence rates using available population-based studies, and, according to this measure, 10.9% of pwMS had hyperlipidaemia, 18.6% had hypertension, 2.5% had ischaemic heart disease and 3.3% had cerebrovascular disease. These prevalence rates were greater than in the general population.[1,2]

Data presented at this year's ECTRIMS confirm a high burden of CV comorbidities among pwMS. For example, among 231 pwMS treated in Greece, hypertension was present in 8.2%, hyperlipidaemia in 6% and diabetes in 3.9%. In a retrospective cohort study of 6602 pwMS and 61,828 people without MS in Sweden, there was a higher frequency of stroke, transient ischaemic attack (TIA) and peripheral vascular disease among pwMS 10 years before MS diagnosis. After diagnosis of MS, pwMS had an increased incidence of major adverse cardiac events, TIA and heart failure.[3,4]

This high level of comorbidities translates into an increase in mortality: data recently presented at EAN 2019 showed that pwMS were at increased risk of CV-related death compared with people without MS (incidence rate per 10,000 person-years, 16.8 vs 11.6).[5]

Interaction of CV comorbidities with MS

CV disease interacts with MS and may contribute to disability progression: in a study of 8983 patients, the risk of early gait disability increased by 51% for each CV condition and the median



time from diagnosis to the need for ambulatory assistance was decreased by 6 years in pwMS with CV comorbidities vs those without. Among pwMS, hypertension and heart disease are independently associated with decreased grey matter and cortical volume. Furthermore, low-density lipoprotein cholesterol and total cholesterol levels are associated with MRI measures of inflammatory activity.[6–8]

Data presented at ECTRIMS 2019 provide further evidence of this link. A network of 10 MS centres showed that patients with elevated serum neurofilament light chain (NfL) had poorer neurologic function than those with normal levels, and patients with diabetes (a well-known CV risk factor) had over two-fold higher odds than those without diabetes to have elevated NfL. Furthermore, Nikolaidis et al. showed there was a significant correlation between the number of comorbidities and expanded disability status score (EDSS).[3,9]

Who is at risk?

The overall risk of comorbidities increases with age in pwMS, just as in the general population. While pwMS are at increased risk of comorbidities compared with the general population, the gap between the two groups is particularly marked in younger patients compared with older patients: the risk for an additional disease diagnosis among 25,476 pwMS in Sweden was x2 that in the general population (n=25,117) up to age 35, and this decreased with age to x1.3 in patients aged > 80 years.[10,11]

The risk of comorbidities also varies according to stage of MS. In data from the Argentinean RelevarEM registry (n=1588), the Charlson comorbidities index was 3.9% in patients with clinically isolated syndrome, 13.5% in RRMS, 28.7% in SPMS and 17.4% in PPMS.[10]

Results from a post-mortem study presented at ECTRIMS 2019 provides further information on CV risk in MS. Among pwMS who died at a young age, an MS-related arteriopathy was observed, even in those who did not have a high burden of CV disease. In patients who did have a high burden of CV disease, pwMS were more susceptible to develop cerebral small vessel disease than people without MS.[12]

Management of patients with CV comorbidities

CV comorbidities can influence treatment decisions regarding disease-modifying treatments (DMTs). For example, neurologists frequently delay DMT initiation in pwMS with ischaemic heart disease. This highlights that some DMTs may not be suitable in the presence of CV comorbidities, because either the DMTs are associated with side effects that are particularly deleterious in these patients (e.g. hypertension) or because these patients are susceptible to certain side effects (e.g. macular oedema).[13,14]

Ruth Ann Marrie recommends that pwMS and CV conditions be empowered to adopt positive health behaviours (including smoking cessation, weight loss and increasing physical exercise), and that MS care teams implement policies to identify patients at risk and provide appropriate treatment (including antihypertensive therapy, lipid-lowering and blood glucose control). These treatments may have a positive impact on MS: blood glucose

treatment in pwMS and metabolic syndrome is associated with reduction in MRI lesion load vs no treatment. Also, preliminary data suggest that statin therapy reduces brain atrophy vs placebo in patients with progressive MS.[14-16]

Conclusion

Given the high prevalence of CV comorbidities among pwMS and the potential impact of these conditions on disability progression, it is important that the MS care team identify those at risk and ensure appropriate risk factor modification.

References

1. Marrie RA, Reider N, Cohen J, et al. A systematic review of the incidence and prevalence of cardiac, cerebrovascular, and peripheral vascular disease in multiple sclerosis. *Mult Scler J* 2015; 21: 318–31.

2. Dagenais GR, Leong DP, Rangarajan S, et al. Variations in common diseases, hospital admissions, and deaths in middle-aged adults in 21 countries from five continents (PURE): a prospective cohort study. *Lancet* 2019; 0. DOI:10.1016/S0140-6736(19)32007-0.

3. Nikolaidis I, Bakirtzis C, Boziki M, et al. Comorbidities in multiple sclerosis patients in a Greek tertiary MS Center. In: ECTRIMS. 2019: P1197.

4. Piehl F, Castelo-Branco A, Chiesa F, et al. Cardiovascular disease in patients with multiple sclerosis: a nationwide cohort study in Sweden. In: ECTRIMS. 2019: 148.

5. Persson R, Lee S, Minton N, et al. Cause and Age of Mortality in Patients Diagnosed with Multiple Sclerosis. In: EAN. 2019: O1206.

6. Kappus N, Weinstock-Guttman B, Hagemeier J, et al. Cardiovascular risk factors are associated with increased lesion burden and brain atrophy in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2016; 87: 181–7.

7. Marrie RA, Rudick R, Horwitz R, et al. Vascular comorbidity is associated with more rapid disability progression in multiple sclerosis. *Neurology* 2010; 74: 1041–7.

8. Weinstock-Guttman B, Zivadinov R, Horakova D, et al. Lipid profiles are associated with lesion formation over 24 months in interferon-β treated patients following the first demyelinating event. *J Neurol Neurosurg Psychiatry* 2013; 84: 1186–91.

9. Fitzgerald K, Sotirchos E, Smith M, et al. Serum neurofilament light chain is associated with MS outcomes and comorbidity in a large population of people with multiple sclerosis. In: ECTRIMS. 2019: A23.

10. Alonso-Serena M, Rojas J., Silveira F, et al.. Comorbidities in multiple sclerosis in Argentina: baseline data from the Argentinean MS Registry (RelevarEM). In: ECTRIMS. 2019: P1195.

11. Smith K., Burkill S, Hiyoshi A, et al.. Burden of comorbid diseases among MS patients in Sweden. In: ECTRIMS. 2019: P1194.

12. Geraldes R, Esiri M, Palace J, et al. Vascular disease in Multiple Sclerosis: a whole body approach. In: ECTRIMS. 2019: 146.

13. Zhang T, Tremlett H, Leung S, et al. Examining the effects of comorbidities on disease-modifying therapy use in multiple sclerosis. *Neurology* 2016; 86: 1287–95.

14. Marrie RA. Comorbidity in multiple sclerosis: Implications for patient care. Nat. Rev. Neurol. 2017. DOI:10.1038/nrneurol.2017.33.

15. Chataway J, Schuerer N, Alsanousi A, et al. Effect of high-dose simvastatin on brain atrophy and disability in secondary progressive multiple sclerosis (MS-STAT): a randomised, placebo-controlled, phase 2 trial. *Lancet* 2014; 383: 2213–21.

16. Negrotto L, Farez MF, Correale J. Immunologic Effects of Metformin and Pioglitazone Treatment on Metabolic Syndrome and Multiple Sclerosis. *JAMA Neurol* 2016; 73: 520–8.

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Making the patients' voice heard in the future of MS disease assessment

PROMs are part of a triad of outcome measures, with the others being rater-based tests and objective tests. Rater-based tools include Expanded Disability Status Scale (EDSS) and Multiple Sclerosis Functional Composite (MSFC); however, the widely used EDSS has repeatedly been shown to have psychometric limitations, meaning that more responsive measures are needed. Sensitive measures are becoming increasingly important as growing numbers of patients with low disease activity are being treated, and so smaller differences need to be measured.[1] PROMs can be used alongside biological and physical methods to measure treatment efficacy and disease course from the

patients' perspective.[1,2] Examples of two classic PROMs used in clinical trials are the 29-item Multiple Sclerosis Impact scale (MSIS-29) and the 12-item MS Walking Scale (MSWS-12). The importance and scope of use of these measures is highlighted by their being translated into more than 75 languages.[3] These and other PROMs can help to achieve high-quality patient-centred care; however, questions still remain regarding their accuracy and the context in which they should be used.[2,4–6]
In this article, we present data from ECTRIMS 2019 on why PROMs are important and how PROMs research has progressed.

Why are patient reported outcome measures important?

PROMs are well established in MS clinical research, and expanding the use of PROMs into routine clinical care may facilitate uncovering aspects of MS that would otherwise go unrecognised. They may also allow clinicians to discover their patients' priorities (particularly in terms of treatment goals), improve communication with their patients and implement shared decision-making.[6]
During a Hot Topics session at ECTRIMS 2019, data from a narrative review showed that there is a growing body of evidence that using patient-centred care models improve satisfaction with care and overall health outcomes. PROMs were seen to be central in this patient-centred approach as, despite the challenges around time limitations6 and interpretations, they provide valuable information on symptoms, treatment experiences, care preferences and daily living needs and values in a structured and consistent way over time.[2,7] When patients were asked what they were looking for in a healthcare provider, one said:

"Open to your concerns, as opposed to trying to be a dictator telling you what you should be doing"

– Patient with MS discussing what they want from their MS care

Furthermore, Geremakis and colleagues reported on the impact of a patient-centred specialty model of care on PROMs. From these preliminary data collected via web-based PROMs, the group concluded that increasing patient access to care and quality of care at a MS patient-centred specialty practice improves patient experience with providers and their staff.[7]

> "I believe there is a strong justification for advancing many of the patient-reported outcome instruments that we have
>
> Prof. Jeremy Hobart

Moving towards novel PROMs in MS

A study presented at ECTRIMS 2019 used the UK MS Registry (UKMSR), the largest repository of PROMs in the UK, to generate a new MS disability PROM. The UKMSR works with more than 40 NHS neurology clinics to collect and validate PROM data from patients with MS. In this study, 83 patients were assessed by EDSS and then by two PROMs: MSIS-29 v2 and the MSWS-12. When using multivariate linear regression the team was able to account for 94% of EDSS variance, meaning that these two PROMS were able to accurately predict EDSS outcomes in these patients with MS.[8]

For PROMs to be effectively used in clinical trials they must prove that they measure clearly defined concepts in specific clinical contexts. Further PROMs research presented at ECTRIMS aimed to develop a walking PROM that satisfied scientific and regulatory requirements for MS clinical trials. Using qualitative interviews of 59 patients with a variety of MS types and expert opinion, a conceptual framework of four primary domains around walking with MS was created. The group focused on activities related to walking and, using mixed methods, produced a 32-item PROM. In an independent cohort of 611 patients with MS, this novel PROM, named the MSWS-32, showed excellent performance characteristics and was conceptually and empirically superior to the currently used MSWS-12. Theoretically MSWS-32 represents a better primary endpoint measure for relapsing MS, secondary progressive MS and progressive MS in clinical trials.[5]

Conclusions

Currently, PROMs are being refined in clinical trials, but their use in clinical practice is in its relative infancy. Here we have highlighted some of the important reasons for PROMs to be used more extensively in clinical practice. Further research is needed to validate them and ensure their clinical utility. To this end, Prof. Hobart recommends a closer look at identifying concepts of interest, e.g. functions or symptoms and defining the context of use for each patient-focused outcome measure when creating PROMS, while Prof. Solari highlighted the need for these measures to be acceptable for use and meaningful for the patient and healthcare provider.[3,6]

References

1. Schäffler N, Schönberg P, Stephan J, Stellmann JP, Gold SM, Heesen C. Comparison of patient-reported outcome measures in multiple sclerosis. *Acta Neurol Scand* 2013; 128: 114–21.

2. Finlayson M. PROMS: supporting patient-centred care. In: ECTRIMS. 2019: Hot Topic 9. 194.

3. J. Hobart. 20 years of MSIS-29 - importance of an MS specific QoL scale. In: ECTRIMS. 2019: Hot Topic 9. 193.

4. Nelson EC, Eftimovska E, Lind C, Hager A, Wasson JH, Lindblad S. Patient reported outcome measures in practice. *BMJ* 2015; 350: 1–3.

5. J. Hobart LB. Advancing walking measurement in multiple sclerosis clinical trials: a new patient-reported outcome measure. In: ECTRIMS. 2019: Scientific session 9. 216.

6. A. Solari. PROMs in standardized MS care. In: ECTRIMS. 2019: Hot Topic 9. 195.

7. C. Geremakis, D. Campagnolo, S. Stuart, A. Ahmad, N. Hu CT. The Impact an MS patient-centered specialty practice has on patient-reported outcomes related to their care team experience. In: ECTRIMS. 2019: P1184.

8. W. Rodgers, R. Middleton, H. Downing-Wood, K. Tuite-Dalton1, D.V. Ford RN. Towards a clinically validated PRO measurement of disability in people with MS. In: ECTRIMS. 2019: P451.

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ECTRIMS 2019 Highlights

The international ECTRIMS conference, which takes place every year, is dedicated to basic and clinical research in the field of MS. Here is a summary of presented data that we found interesting at the September 2019 meeting in Stockholm, Sweden.

Changes in diagnosis of MS

The MS community is continuing to evaluate the impact of the 2017 revisions to the McDonald criteria for the diagnosis of MS. At ECTRIMS 2019, Stawiarz and colleagues presented promising data showing that, in Sweden, adoption of the new criteria led to a shortening in the time to MS diagnosis: with the first McDonald criteria, 50% of patients received a diagnosis within 1.4 years and with the second, this duration was reduced to 4 months. Moreover, with the revised criteria, almost 90% of patients received a diagnosis within a year of onset of symptoms. [1,2]

Changes in the diagnostic criteria have played an important role in altering the long-term prognosis of MS, as shown in a study by the Cemcat group in Barcelona that was presented at ECTRIMS 2019: the investigators found that from 1994 to 2017, there was

a 70% reduction in the risk of reaching EDSS 3.0 among people with MS (pwMS). They looked at factors that could have contributed to this change and found that simply changing the diagnostic criteria from the Poser criteria (used 1994–2000) to McDonald 2017 reduced the risk of EDSS 3.0 by 32%. This meant that the group of patients considered as having MS is now 'enriched' with patients with milder disease than before. In addition to this phenomenon, the investigators also found that mean time from CIS diagnosis to starting a DMT was reduced by 85% and concluded that this reduction, as well as changes in environment and healthcare standards, could have contributed to the improvement in prognosis.[3]

In the highlights session, Aksel Siva observed that MS misdiagnosis is a universal problem and, in the future, increased use of PET, the MRI central vein sign and paramagnetic phase rims / iron rings may help to reduce misdiagnosis.[4]

Retinal biomarkers in MS

Optic nerve pathology and abnormal retinal ganglion cell loss is evident in almost all pwMS. Therefore, retinal parameters are potentially useful to quantify and track neurodegeneration in MS. Optical coherence tomography (OCT) parameters are among the most promising biomarkers, as highlighted by a scientific session at this year's ECTRIMS that summarised data from several ECTRIMS abstracts. Notably, Bsteh and colleagues presented data showing that serum neurofilament light (sNfL) predicts retinal thinning in patients with RRMS – further evidence to strengthen the value of sNfL as a biomarker of neuroaxonal damage and prognosis. However, only 15–20% of annual peripapillary retinal nerve fibre layer (pRNFL) variance could be predicted from annual sNfL levels.[5] During this session, the presenters discussed how to combine biomarkers to generate a network of information to overcome shortcomings that each biomarker has in isolation and allow for a more comprehensive overview of the disease state.[6]

Two abstracts at ECTRIMS presented conflicting data on the association of OCT measures and cognitive performance in pwMS. In the first abstract, Dreyer-Alster and colleagues reported that, among 896 pwMS, neither retinal nerve fibre layer (RNFL) thickness nor ganglion cell thickness had a significant association with

> "There was a dramatic shortening of time from MS onset to MS diagnosis in Sweden, in recent decades
>
> Prof. Leszek Stawiarz

global cognitive score, which included assessment of memory, executive function, visual–spatial measures, attention, information processing speed, motor skills and verbal function. They concluded that OCT was not a useful tool to assess CNS neurodegeneration associated with cognitive performance. In the second abstract, 51 pwMS had five different retinal parameters measured: pRNFL, macular RFNL, macular ganglion cell-inner plexiform layer, inner retinal layer and inner nuclear layer. The authors found a correlation between cognitive function as measured using the Brief International Cognitive Assessment for MS (BICAMS) and some parameters, particularly pRNFL and inner nuclear layer. The group concluded that OCT is a valuable tool for alerting the clinician to potential cognitive impairment in MS. Variation in these results could be partially be explained by the variation in the retinal layers analysed and the cognitive assessment tools used.[7,8]

Further to OCT parameters, visual evoked potentials can be used as predictive tools. An abstract at ECTRIMS showed that, among 112 patients with optic neuritis (ON), multifocal visual evoked potentials (mfVEP) in the unaffected eye have predictive value in determining whether patients with ON will develop MS.[9]

Epigenetics in MS: a novel look at MS pathogenesis

Dysregulation in epigenetics, the ability of the cell to adapt gene expression depending on environmental pressures, has been implicated in the pathophysiology of MS. At this year's ECTRIMS, Kular and colleagues aimed to profile DNA methylation changes in the post-mortem brain tissue of pwMS compared with healthy controls. They identified methylation changes in, and therefore dysregulation of, genes involved in CREB signalling, axonal guidance and synaptic activity. These variations are novel potential contributors to MS disease pathophysiology. A further study highlighted the ability of a synthetic version of vitamin D3, calcitriol, to produce CD14+ cells that have different DNA methylation and expression profiles. This could partly explain the beneficial effect of vitamin D in preventing MS and the latitudinal variation in MS prevalence. [10-12]

In another study presented at ECTRIMS, Olsen and colleagues found a characteristic signature of demethylated myelin oligodendrocyte glycoprotein circulating free DNA in the sera of patients with active RRMS compared with patients with inactive disease and with healthy controls. This epigenetic biomarker, using methylation-specific probes, represents a minimally invasive measure of oligodendrocyte cell death that may be useful for monitoring disease progression in the future.[13]

Overview of the highlights session

ECTRIMS 2019 concluded with the highlights session, where Prof. Young and Prof. Siva presented their pick of new and interesting data from this year's conference. Prof. Young started by presenting new data on MS and pregnancy and some of her take-home messages were:

- MS in the mother is associated with a small increase in neonatal risk, apart from any drug exposure
- Pregnancy delays clinically isolated syndrome and RRMS onset
- Pregnancy in active MS increases risk of disease progression

Prof. Young went on to highlight that elevated serum neurofilament levels are associated with worse neurological function and certain comorbidities, e.g. diabetes. Also, age, EDSS, and MRI at onset and at 2 years may allow predict risk of converting to SPMS.[14]

During Prof. Siva's presentation he mentioned that radiologically isolated syndrome (RIS) may now allow clinicians to make a pre-clinical diagnosis of MS at a very early stage, and while it is clear that not all individuals with RIS develop MS, sNfL may allow prediction of clinical conversion to MS. Prof. Siva concluded his presentation with some treatment-related take-home messages, including:

- B-cell therapies have been shown to reduce IgG, IgM and IgA levels, and this is also a side effect of other immunosuppressive MS therapies. It is suggested that IgG monitoring should be performed in pwMS using these therapies
- Discontinuation of disease-modifying therapies in pwMS over 60 years of age may not influence clinical outcome in terms of relapse risk or risk of confirmed disability progression4

"Some patients are risk takers, and some are not, so it's up to us to take a personalised approach"

– Prof. Emmanuelle Waubant

Conclusions

This year's ECTRIMS in Stockholm contained interesting insights in diagnosis of MS, retinal biomarkers, epigenetics, pregnancy in pwMS and disease-modifying therapy. Many of these data promise to change clinical practice in the coming years.

For more information on data presented at ECTRIMS, you can see all the abstracts at http://www.professionalabstracts.com/ectrims2019/iplanner/#/grid/1568332800 and ECTRIMS attendees and members can view selected presentations and posters at https://onlinelibrary.ectrims-congress.eu/ectrims/.

References

1. Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol* 2018; 17: 162–73.

2. Stawiarz L, Hagel E, Hillert J et al. Introduction of new diagnostic criteria for multiple sclerosis and time interval between disease onset and MS diagnosis. In: ECTRIMS. 2019: P99.

3. Tintore M, Arrambide G, Otero-Romero S et al. Long term outcomes. Changes in MS prognosis through the CIS Barcelona cohort: a 25-year tale. In: ECTRIMS. 2019

4. Siva A. ECTRIMS clinical highlights part 2. In: ECTRIMS. 2019.

5. G. Bsteh, K. Berek, H. Hegen, et al. Serum neurofilament light chain levels correlate with peripapillary retinal nerve fibre layer-thinning as measured by optical coherence tomography in multiple sclerosis. In: ECTRIMS. 2019: Scientific Session 13. 285.

6. Calabresi P. OCT as a prognostic marker. In: ECTRIMS. 2019: Scientific Session 13. 283.

7. S.J. Baetge, M. Dietrich, M. Filser, et al. Optical coherence tomography (OCT) in multiple sclerosis: Is cognitive performance associated with retinal layer thickness? In: ECTRIMS. 2019: P568.

8. S. Dreyer-Alster, A. Gal AA. Retinal nerve fiber layer and ganglion cell thickness analysis using optical coherence tomography are not useful as predictors for cognitive impairment in MS. In: ECTRIMS. 2019: P1303.

9. G. Pihl-Jensen JF. Predictive value of optical coherence tomography, multifocal visual evoked potentials and full-field visual evoked potentials of the fellow, non-symptomatic for multiple sclerosis development in patients with acute optic neuritis. In: ECTRIMS. 2019: P1304.

10. Ntranos A. Epigenetics as a therapeutic/environmental mediator in MS. In: ECTRIMS. 2019: Hot Topic 10. 253.

11. L. Kular, M. Needhamsen, M. Zeitelhofer-Adzemovic, et al. DNA methylation changes in brains from Multiple Sclerosis patients. In: ECTRIMS. 2019: P481.

12. L. Ong, G. Parnell, G. Stewart DB. Can the effects of Vitamin D on MS risk be explained by its impact on DNA methylation? In: ECTRIMS. 2019: P487.

13. J. Olsen, L. Afinowicz, R. Tipon, et al. Non-invasive blood epigenetic biomarkers of CNS cell loss. In: ECTRIMS. 2019: Hot Topic 10. 254.

14. Young C. ECTRIMS clinical highlights part 1. In: ECTRIMS. 2019.

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Family planning for male patients with MS, an interview with Dr Marja-Liisa Sumelahti

Marja-Liisa Sumelahti, Tampere University, Finland, discusses the often-neglected topic of considerations for patients with MS who are planning to start a family. You can watch the full video here.

Please find the transcript of the video below:

When male patients with MS come to talk about starting a family the biggest concern they usually bring up is the question about heritability of MS, and we have an easy answer for that because MS in big picture is not a heritable disease and it is a rare disease in the population because the risk in general population is 1 per 330, and if you have a first degree relative with MS the risk increases and it's 1 to 48, and if there is a second degree relative it's a 1 to 110. So, there is a certain risk, but we don't talk about a heritable disease. So, there is an easy answer to my patients.

Of course men are, as women are, concerned about their ability to bring up the children. If the disease progresses, or if severe relapses occur, these are of course problems related to active MS. And, in cases of highly active MS, the problem we have to face concerns certain medications because some highly active drugs are not good in a situation where a female is pregnant, and even if a male partner uses these drugs he has to withdraw from these drugs. So, this is an important question to consider, of course. But, considering all the drugs we have in MS today this problem concerns only a few drugs. So, it's not a huge problem. If a male MS patient is using the new highly active, or some of the new highly active drugs, he has to withdraw but usually it's not a problem because the treatment episode is very short. And, it's only a year and then they have to wait for 6 months after that. So it's not a real withdrawal. It's just that we have to postpone the family planning to a safer period when using the new drugs.

The main barriers among men with MS when we discuss starting a family, they bring up mostly problems in sexual dysfunction – that's the main problem. In some cases I've run into question that a young man is wondering if he's even, you know, if it's even possible for him to start a relationship, and start family planning when he has received the MS diagnosis.

The main unanswered questions concerning male fertility in MS are epidemiological. It would be interesting to know if their family size is equal to men in the same age group. What's the age distribution when they start their families. And one important question is how does disability affect family planning? When general neurologists meet a man with MS who starts to talk about family planning, the most important question is to consider the medication – the situation has to be safe. He has to be withdrawn from the highly active medications that are teratogenic – that's the most important thing. And, I think that general neurologists should be ready to discuss all the matters that concern family planning in general – all the views: the social view, individual view of the patient, because this is a huge commitment in MS patients' life. It's a lifelong commitment. Disease is lifelong. So, this is a very important decision for both patients and for the doctor as well. Usually, what a general neurologist could do, I think, they could reassure the patient that it's okay for them to start a family.

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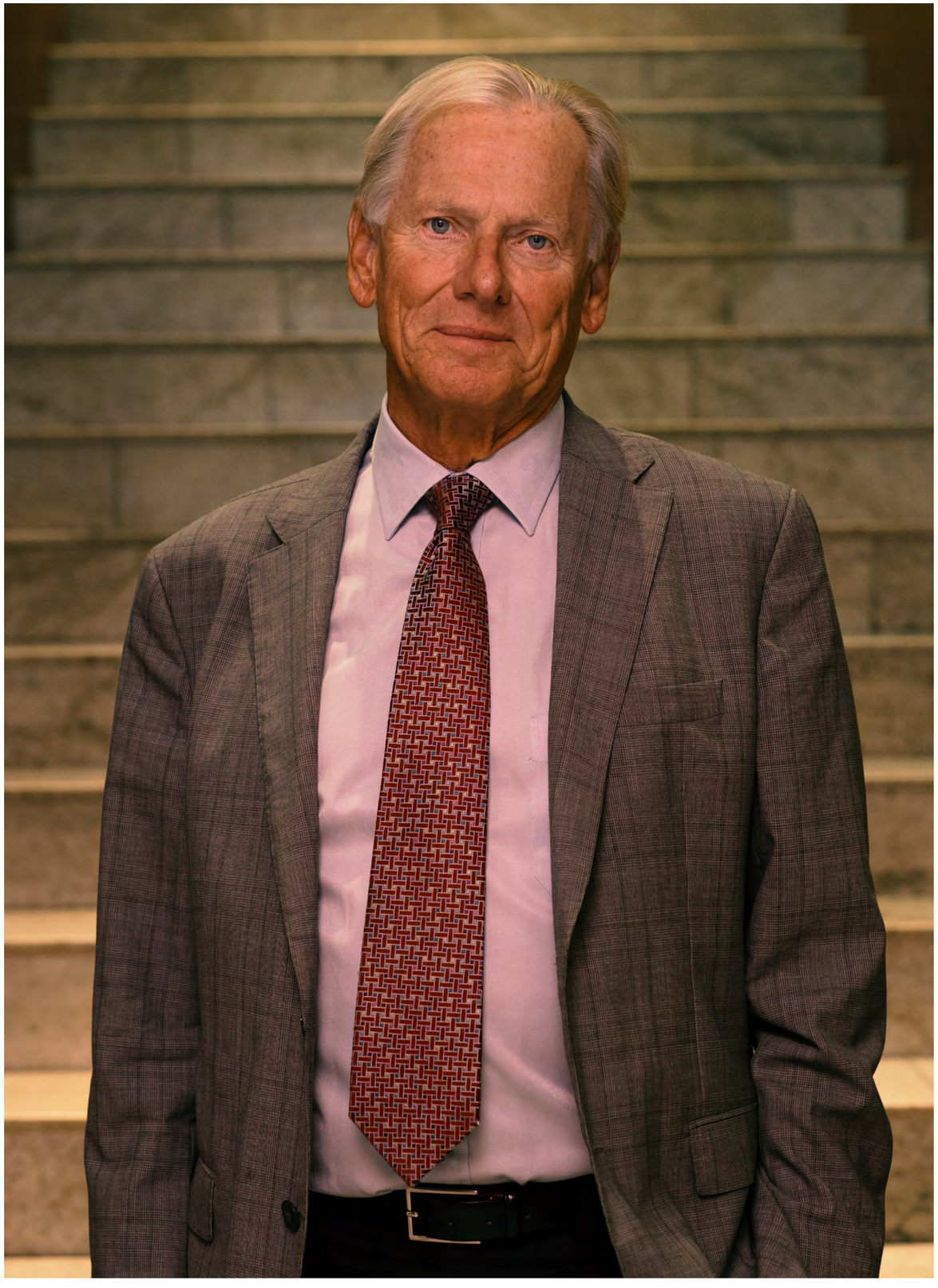
The MS Care Unit, an interview with Professor Soelberg Sørensen

Per Soelberg Sørensen, Professor of Neurology at the University of Copenhagen, discusses the optimization and potential beneficial impacts of the MS care unit on patient management. You can watch the full video here.



Please find the transcript of the video below:

We know that the MS care differs a lot between various countries but in fact we don't know how much, so the first thing we are going to look at is do a worldwide survey to see how the MS care is in various countries. And, of course we know that some countries already have what we call the MS care unit, which basically is a number of neurologists working together with other disciplines. And so, you could say you have the whole care in one place.

We know that not all MS patients can be seen in multidisciplinary MS care units, but we want to make it possible for any patients, when there is a demand for it, to be referred to a multidisciplinary unit. So, it's not a place where all patients should stay but if there are problems with the monitoring, problems with treatment decisions, you could refer the patients to this unit and there should be MS specialists, both MS neurologist and MS nurses, and this unit should be able to provide any disease modifying drug that the patient needs.

The core of the MS unit is the MS neurologist and the MS expert nurses. And then you can build on that and to call it an MS care unit, you would at least need to have a physiotherapist and MS psychologist and preferably a psychologist. And then if you have the fully developed MS unit, then you have a number of specialists that work within the unit, MS urologists, rehabilitation persons and so forth. Whereas in the small unit you would have to collaborate with external experts.

There are always challenges and, of course, we know that there might be one fully developed MS care unit in each region of a country. And, of course, most patients will still be seen by either non-academic MS centres or by a practicing neurologist and in some countries even the general practitioner. And the challenge is, of course, to help get the collaboration with these so that they will refer those patients to the MS care units that need to go there and also there will be a collaboration in treatment between those so patients can go back when there has been treatment been initiated.

In most places the nurse will have the key role because there is a shortage of MS neurologists, which means that some of the tasks that maybe today is done by an MS neurologist will have to be done about by MS nurse or a physiotherapist – scoring patients on different scales and giving advice about medicine and adverse effects and so forth. This will be collected by the MS nurse.

And then if there's a need the patients will be seen by the MS neurologist.

We are now moving from looking at relapses, now looking at the whole spectrum of activity or including MRI and maybe some biomarkers and what we are aiming at today is to see if we can provide what we call no evidence of disease activity or NEDA; knowing that this goal cannot be achieved in all patients. But this is what we thrive at. And so there is definite change in the goal of the treatment to a more effective treatment and to get real stable disease.

This is of course one of the things that we are going to measure – what is being achieved by the MS care unit and, of course, we hope that the goal is to prevent the disability, the long term disability, and treat patients to the target – meaning that we would delay or even prevent patients going from the relapsing phase into the progressive phase. So, the goal is to prevent disability in the long term.

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at ECTRIMS 2019

Lifestyle Management in MS, an interview with Dr Andrew Chan

Professor Andrew Chan, from the University of Bern in Switzerland, discusses his recommendations for lifestyle management for patients with MS. You can watch the full video here.

Please find the transcript of the video below:

Whenever I discuss lifestyle management with my patients, I try to differentiate whether he wants to know or she wants to know because he wants to drop, or not start, the disease modifying treatment, or whether the patient really wants to do something on top. These are entirely different situations and one has to discuss that, because the first situation really indicates that something like adherence could be too low, or that there's still something, some unsolved questions about potential disease modifying treatments or about the disease which needs to be discussed. When it comes to the second sort of situation, the patient wants to know "is there anything, Doctor, which I can do on top of my medication?" I tell him, mostly, you know, you should behave like before and try to have a healthy lifestyle.

What do you recommend to your patients when they ask about their diet?

We see a lot of data where specifics like alcohol consumption, environmental factors, smoking, negatively affect MS, or we have been talking about sodium chloride. Some aspects, of course, deal with the microbiome and whether by specific diets we can somehow alter the bacteria in the gut in order to somehow modify also the MS treatment. However, I think it's not there yet that we can really recommend a specific procedure or a specific diet in order to modify these aspects. In general, what I recommend is like what I would recommend to you or my children, a healthy diet which is generally described as the Mediterranean diet. What we've recently learned is that prognosis in MS is improving, so we will see a lot of elderly patients with MS hopefully well controlled, but they are probably at higher risk also for cardiovascular disease and it appears that especially in these patients preventing other secondary diseases, or diseases which can ensue in later life like strokes or myocardial infarctions, would really have a big impact and diets like Mediterranean diet would play a major role in this.

What do you recommend to your patients when they ask about smoking and alcohol?

I would recommend to my patients to stop smoking. However for many patients who are severely disabled that is like a lifestyle, something that is really quality of life. The one cigarette after dinner, or something, I try to find a balance there. When it comes to alcohol, I'm a bit less strict. However, I would try to recommend to my patients to avoid an exaggerated intake of alcohol. Alcohol, the effect on MS is controversially discussed, one has to say, but then in the end what we see regularly is that like these issues you have, the patient has an increase of liver function tests and we just don't know what it comes from, either from the disease modifying treatment or from intake of alcohol or something, so also to limit the alcohol intake would be the other dietary suggestion.

There is good data around that in general, the prognosis of MS is negatively affected by smoking and then additionally, certain specific functions such as cognition or motor function may also be negatively affected. However, if you put that into a larger context because smoking very often does not come alone but maybe you know these people have other rather vascular risk factors like increased body mass index, high sugar intake, lack of fruit and vegetables in their diet, stuff like that then you can observe that these sort of aspects could for example be associated with brain atrophy. So, the more sort of these risk factors you have it appears that the stronger the brain atrophy is, that is data from the groups in the States right now.

What do you recommend to your patients when they ask about exercise?

So structured and formalised exercise is certainly important but mainly in order to show the efficacy to, for example, payers or people who don't believe in these kinds of interventions. In daily clinical routine I tried to have the threshold that the patient takes up physical exercise as low as possible. If I tell him you need to do this and that, at least for this or that times or so, and have it controlled by someone or by a wearable that raises the threshold and the likelihood the patient will not do anything. So I'm very happy with whatever the patient does.

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