Multiple sclerosis
Zwanikken, Cornelis Petrus

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
1997

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):
Summary

Multiple Sclerosis (MS) is a chronic disease of the brain and the spinal cord. The cause of MS is unknown. MS usually starts in young adulthood. In the course of the disease progression of neurological handicap and increase of impairments in daily life is common.

In this study there were two aims. Firstly, the prevalence of MS was studied. All patients with MS were neurologically examined. Secondly, the Quality of Life (QoL) of all patients with MS was studied and related to their neurological condition.

In chapter 2 MS as a disease is reviewed. In the white matter of the brain and the spinal cord two kinds of processes can occur. On the one hand, there is inflammation. On the other hand there is demyelination. In the process of demyelination the isolating layer around the nerves gets lost. Demyelination develops more slowly than inflammation.

The signs and symptoms of MS are highly variable and depend on the extent and localisation of the disease process in the central nervous system. From MRI studies it is known that in MS new lesions occur in a continuous way. New lesions do not always lead to new signs and symptoms.

The course of the disease differs from patient to patient. In one and the same patient, the course in time is also highly variable. Roughly spoken two forms of the disease can be discerned that are clearly different from each other. In Relapsing Remitting MS (RR-MS) there are periods of acute deterioration (exacerbations) based upon inflammatory signs in the brain and the spinal cord. In between exacerbations the condition of the patient is stable. Patients with Primary Progressive MS (PP-MS) deteriorate in a slow way over many years. The third form of the disease is Relapsing Progressive MS, also called Secondary Progressive MS (RP/SP-MS). This third form of MS has characteristics of both other forms of MS. After a start of MS with exacerbations as in RR-MS the disease progresses steadily as in PP-MS.

In diagnosing MS the course of the disease in time is important. The diagnosis of MS may be supported by the results of ancillary investigations (MRI scanning, cerebrospinal fluid, evoked potentials). According to the Poser criteria MS is "definite" or "probable".

MS cannot be cured. Symptomatic therapy is possible for a number of complaints due to MS. Recently, β-interferon was introduced for the treatment of RR-MS. The average number of exacerbations is reduced by this drug.

In chapter 2 the concept of QoL is reviewed shortly. Different aspects that can be discerned in QoL are physical health, mental health, social functioning, role functioning and the evaluation of ones own health. A great number of scales exist to measure QoL. Some of these are intended to be used in specific diseases. Others are more generally applicable. The Minimal Record of Disability (MRD) was developed in the eighties and is intended for MS. The instrument contains data from the neurological examination that result in a score on the Expanded Disability Status Scale (EDSS) or the Disability Status Scale (DSS). The MRD also contains data about social and financial functioning.
Epidemiology of MS is discussed in chapter 3. In Europe, the prevalence of MS varies from $20/10^5$ to $40/10^5$ for the Mediterranean to up to $150/10^5$ for the northern parts of the United Kingdom. In the Netherlands only data about the prevalence of MS in the province of Groningen are available. The prevalence of MS in the province of Groningen was $56/10^5$ in 1959, $56.3/10^5$ in 1982 and $61.1/10^5$ in 1986.

Psychosocial aspects of MS are discussed in chapter 4. It is well known in MS that the handicap of patients in daily life can be very different while their neurological condition seems similar. Adaptation is thought to be an important factor to explain these differences. With better adaptation to the disease the well-being of the patient at a certain level of neurological impairment is better.

Psychosocial problems of patients with MS are numerous as shown in studies using questionnaires. Financial problems, problems of housing, and problems of transportation are important. Another important area of problems is that of relations: with the partner, with the children. Also, the relationship with the treating physician can be problematic.

Studies of the effect of rehabilitation and studies of the need of help from other persons showed that an EDSS score of '5.0' is an important milestone. Beyond this level the need of help from other persons increases. The costs relating to MS increase. MS causes problems in the ability to work. Factors that relate to having payed employment are age, sex, education and EDSS score. Disturbances of cerebral functioning (memory, power of concentration, ability to perform different tasks at the same time) have an influence that is independent of the EDSS score.

In chapter 5 the methods of this study are presented. Within the borders of the province of Groningen and with the assistance of neurologists, general practitioners and doctors in nursing homes, all patients with definite or probable MS were searched for. The period of patient inclusion was from 1991 to 1993.

During a stable phase of MS neurological examination was done including the MRD. Within two weeks the patient was visited at home by an interviewer. The MRD contains the Functional Systems (FS) and the EDSS score to assess the neurological condition. The other parts of the MRD are the Incapacity Status Scale (ISS) and the Environmental Status Scale (ESS). The EDSS score ranges from '0' (no neurological abnormalities) to '9.5' (completely restricted to bed with severe problems in communication and swallowing). The ISS with 16 items measures especially activities of daily living. The ESS has seven items and measures social consequences of MS.

The interview at home included the Groningen Activity Restriction Scale (GARS), the Subjective Definition of MS (SDMS), the Overall Evaluation of Health (OEH), the Nottingham Health Profile (NHP, sections "Physical Mobility", "Energy", and "Pain"), the 28 item version of the General Health Questionnaire (GHQ-28), and the Self Esteem scale.

The GARS measures Activities of Daily Life (ADL) in 11 items and Instrumental Activities of Daily Life (IADL) in seven items. The opinion of the patient as to MS is measured with the
Summary

SDMS which consists of six items. The OEH is a one-item visual analogue scale to measure the opinion of the patient's own health. The NHP measures the opinion of the patient in different domains: "Physical Mobility" (eight items), "Energy" (three items), and "Pain" (eight items). The GHQ-28 gives an impression of mental health. The scale consists of four sections of seven items each: "Somatic complaints", "Anxiety & Insomnia", "Social dysfunctioning", and "Depression". Finally Self Esteem measures the self appreciation in ten items.

During the study, 423 patients with definite or probable MS were identified (chapter 6). There were 133 males and 290 females. The mean age was 47 years. MS existed for 16 years. The EDSS score was '4.6'. In comparison with patients with RR-MS, patients with RP/SP-MS and PP-MS were older and were having MS for a longer period of time. Their EDSS score was higher. While the average age and EDSS score of patients with RP/SP-MS were very similar to that of patients with PP-MS, patients with RP/SP-MS were longer suffering from MS.

The prevalence of MS in the province of Groningen was 76.2/10^5. From 1960 to 1992 the number of people with first signs and symptoms of MS increased each year with a maximum in 1985 of 3.7/10^5. After 1985 the number of people with first signs and symptoms of MS goes down. This phenomenon probably relates to the long period of time that is sometimes needed to diagnose MS.

Of all 423 patients, 244 were interviewed. In RR-MS there were no differences between the interviewed and the non-interviewed patients. In RP/SP-MS and PP-MS non-interviewed patients were older in comparison to the interviewed patients. They were longer suffering from MS. The EDSS score was higher. Differences between the interviewed patients and the non-interviewed patients occurred from a EDSS score of '8.0' and higher. The main reason was the fact that patients residing in nursing homes were excluded from the interview.

The interviewed patients with RR-MS (99) generally were having few signs and symptoms, the most important being bladder and bowel problems. Patients with progressive MS (PROG-MS, 80 patients with RP/SP-MS and 65 patients with PP-MS) scored worse for all items of the FS. The only difference between RP/SP-MS and PP-MS was the "Visual Functions" score: worse for patients with RP/SP-MS. The mean EDSS score of the patients with RP/SP-MS was '5.8', of the patients with PP-MS '5.7'. The ISS showed the same differences between patients with RR-MS and patients with PROG-MS. Again, patients with RP/SP-MS were having worse scores for "Vision" than patients with PP-MS. The ESS gave similar results: the better scores for patients with RR-MS and the worse scores for patients with PROG-MS. Less than half of the patients with RR-MS indicated that they were having no problems with "Work" or "Social Activity". For all items of the ESS and almost all items of the ISS (exceptions "Medical Problems", Mood&Thought","Mentation") there was a clear correlation with the EDSS score with the worse scores occurring at higher (worse) scores of the EDSS.

The ADL and IADL as measured by the Groningen Activity Restriction Scale (GARS) of the 244 patients that were interviewed are discussed in chapter 7. There were few problems in patients with RR-MS. The items that caused most problems were "heavy cleaning" (46% of the
interviewees at least 'some difficulty') and "shopping" (33% of the interviewees at least 'some
difficulty'). No differences were shown between patients with RP/SP-MS and PP-MS. Patients
with PROG-MS were having significantly more problems with ADL and IADL than patients
with RR-MS. Some activities of the GARS were relatively easy for patients with PROG-MS
("feeding oneself" 74% 'no difficulty', "washing face/hands" 73% 'no difficulty', "using toilet"
51% 'no difficulty'). The most difficult items of ADL in the GARS were "walking stairs",
"walking outdoors", "cutting nails". In IADL, the most difficult items were "heavy cleaning" and
"making beds", followed by "shopping" and "washing/ironing". In patients with RR-MS and
even more in patients with PROG-MS there was a clear correlation between ADL/IADL and the
EDSS score.

In literature results of the GARS are reported in rheumatoid arthritis, different kinds of
neoplasms, persons over 56 years of age that who consult their physician, and healthy persons.
Largely due to the patients with PROG-MS, results of the patients with MS were worse in
comparison with all these groups.

The Subjective Definition of MS (SDMS) of the 244 interviewed patients is discussed in
chapter 8. Almost three-quarter of all patients thought of MS as a serious disease, patients with
PROG-MS more so than patients with RR-MS. Patients with PROG-MS thought more often than
patients with RR-MS that MS gives cause to dependence from other persons. Only for four
items of the SDMS there was a weak correlation with the EDSS score. Based upon the results of
the SDMS patients with MS probably think of MS as a serious disease right from the start. As
progression of neurological handicap occurs, some patients value their disease as even more
serious. Adaptation to MS than becomes more difficult. The SDMS was no unequivocal scale. It
was not possible to reduce the answers to the seven items to one sum score. The SDMS is
useful at a single item-level.

The Overall Evaluation of Health (OEH, chapter 9) resulted in a value of '7.1' (possible
range '0' to '10') for patients with RR-MS and '5.1' for patients with PROG-MS. No
differences were shown between patients with RP/SP-MS and patients with PP-MS. These values
compare with values of healthy people for a reasonable to good health ('6.5' to '8.1') and a poor
to moderate health ('4.2' to '5.8'). Appreciation of health became worse with higher EDSS
scores.

Appreciation of physical health as to "Physical Mobility", "Pain", and "Energy" was
measured with the Nottingham Health Profile (NHP, chapter 10). In RR-MS, there were few
problems. Most problems occurred in "Energy" (62% of all patients with RR-MS). Again no
differences were observed between patients with RP/SP-MS and PP-MS. Both in "Physical
Mobility" and "Pain" and "Energy" patients with PROG-MS performed worse than patients with
RR-MS. Some items of the NHP having to do with being able to walk were difficult to answer
by part of the respondents. The median EDSS score of these respondents was '7.5' - '8.0'. All
parts of the NHP correlated strongly with the EDSS score, "Physical Mobility" most of them.

Results of patients with PROG-MS on the NHP were comparable with those of people with
Summary

arthritus. Comparatively, healthy elderly people (over 65 years of age), rescue workers, women with a full-term pregnancy, and people who consulted their physician had better scores. Results of patients with RR-MS were in between scores of women with a full-term pregnancy and healthy elderly people.

In chapter 11 results of the General Health Questionnaire (GHQ-28) are presented. Patients with MS valued their subjective mental health somewhere in between mental health of healthy people and people who visited an outpatient department of Psychiatry. Compared with a random sample from the general population results of patients with MS were worse for "Social dysfunctioning" and "Depression". Results of patients with RR-MS, RP/SP-MS, and PP-MS were nearly the same. Patients with PROG-MS had slightly worse scores for "Depression" in comparison to patients with RR-MS. Only for "Depression" there was a correlation with the EDSS score in the sense of more depressive complaints with higher EDSS scores. It was concluded that there is only a minor connection of subjective mental health of patients with MS to their neurological handicap.

Finally, in chapter 12 results of Self Esteem are shown. Again, there were no differences between patients with RP/SP-MS and PP-MS. Patients with PROG-MS had less Self Esteem than patients with RR-MS. With higher (worse) DSS scores Self Esteem became less.

In chapter 13 it is discussed how QoL of patients with MS can be described with the instruments of this study. First, specific aspects of QoL are depicted with the appropriate scales, for example "Physical Function" by using the FS scores and the EDSS score, items of the ISS and the ESS, the GARS, and "Physical Mobility" of the NHP. Than, a more global impression of the general well-being of the respondent is described with for example the OEH score. Almost every item of the instruments in this study correlated in some way with the OEH score ranging from 0.17 (SDMS item) tot 0.47 ("Energy" of NHP). Linear regression analysis showed that the OEH score can only be partly predicted from the results of the other scales. The only factors of importance for the OEH score were "Mentation" from the ISS and "Pain" from the NHP. This could imply that disturbances of cognitive functioning as they occur in MS are essential for QoL just like "Pain". On the other hand, it can be concluded that the OEH gives only limited information about QoL.

With factor analysis it was tried to reduce the results of all items in the different scales to a limited number of data. The FS fell apart into two factors relating respectively to the spinal cord and to the higher parts of the central nervous system.

The ISS and the ESS were also examined with factor analysis. The ISS broke up into three factors that were called "Spinal cord", "Brain stem" and "Brain". For "Spinal cord" and "Brain stem", patients with PROG-MS clearly had worse results than patients with RR-MS. There were no differences for the factor "Brain" according to the course of MS. The EDSS score correlated strongly with the score on "Spinal cord" and somewhat less strongly with "Brain stem". There was no correlation between the EDSS score and the score on "Brain". The ESS contained only one underlying dimension which was called "Social". Again, there were significant differences
between patients with RR-MS on the one hand and patients with PROG-MS on the other hand with also a strong correlation with the EDSS score. This implies that the EDSS score gives a reasonable indication of the need of help of the patient with MS.

Then, the GARS, SDMS, OEH, NHP, GHQ-28, ISS and ESS together were examined by factor analysis. This resulted in three factors that were called "Physical functioning", "Mental functioning", and "Opinion of MS". There were clear differences between patients with RR-MS and patients with PROG-MS for "Physical functioning" and for "Opinion of MS". The EDSS score correlated significantly with these factors. No differences were discovered between RR-MS and PROG-MS for "Mental functioning". The EDSS score correlated only weakly with the score on "Mental functioning".

In this study, the EDSS score apparently depended strongly on motor disturbances at the level of the spinal cord. The strong correlation between the EDSS score and a number of instruments as used in this study makes it plausible that self-reporting by the patient leads to a reasonably reliable EDSS score. With the exception of visual function the course and severity of complaints of patients with RP/SP-MS were comparable to those of patients with PP-MS.

"Mental functioning" correlated only weakly with the EDSS score. Therefore, it is advisable to use specific instruments for mental well-being when studying QoL of patients with MS.

Usually, the EDSS score of a patient cannot be changed. The factors "Mental functioning" and "Opinion of MS" could be changed. Attention to these two factors is useful to improve QoL of patients with MS.
**Lijst van gebruikte afkortingen:**

<table>
<thead>
<tr>
<th>Acroniem</th>
<th>Explanatie</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADL</td>
<td>Aktiviteiten van het Dagelijks Leven</td>
</tr>
<tr>
<td>CPI</td>
<td>California Psychological Inventory</td>
</tr>
<tr>
<td>DSS</td>
<td>Disability Status Scale</td>
</tr>
<tr>
<td>EDSS</td>
<td>Expanded Disability Status Scale</td>
</tr>
<tr>
<td>ESS</td>
<td>Environmental Status Scale</td>
</tr>
<tr>
<td>FS</td>
<td>Functional Systems</td>
</tr>
<tr>
<td>GARS</td>
<td>Groningen Activity Restriction Scale</td>
</tr>
<tr>
<td>GHQ-28</td>
<td>General Health Questionnaire, 28 vragen-versie</td>
</tr>
<tr>
<td>HLA</td>
<td>Human Leukocyte Antigen</td>
</tr>
<tr>
<td>IADL</td>
<td>Instrumentele Aktiviteiten van het Dagelijks Leven</td>
</tr>
<tr>
<td>ISS</td>
<td>Incapacity Status Scale</td>
</tr>
<tr>
<td>MRD</td>
<td>Minimal Record of Disability</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>MS</td>
<td>Multiple Sclerose</td>
</tr>
<tr>
<td>n.s.</td>
<td>niet significant</td>
</tr>
<tr>
<td>NHP</td>
<td>Nottingham Health Profile</td>
</tr>
<tr>
<td>OEH</td>
<td>Overall Evaluation of Health</td>
</tr>
<tr>
<td>PP-MS</td>
<td>Primair Progressieve Multiple Sclerose</td>
</tr>
<tr>
<td>PROG-MS</td>
<td>Progressief verlopende MS (RP/SP-MS en PP-MS tezamen)</td>
</tr>
<tr>
<td>QoL</td>
<td>Quality of Life</td>
</tr>
<tr>
<td>RR-MS</td>
<td>Relapsing Remitting Multiple Sclerose</td>
</tr>
<tr>
<td>RP/SP-MS</td>
<td>Relapsing Progressive/Secundair Progressieve Multiple Sclerose</td>
</tr>
<tr>
<td>SD</td>
<td>Standaard Deviatie</td>
</tr>
<tr>
<td>SDMS</td>
<td>Subjectieve Definitie Multiple Sclerose</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>