Prognostic information for people with MS – impossible or inevitable?

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Abstract

Delivering prognostic information is a challenging issue in medicine and has been largely neglected in the past. A major reason has been a suspected nocebo effect of pessimistic estimates, although this is largely unproven. Among people with multiple sclerosis (MS), there is a strong unmet need to receive long-term prognostic information. This viewpoint discusses reasons for this blind spot in physicians' attitude, foremost amongst which is the uncertainty of prognostic estimates. Possible strategies to move forward include tools to identify matching patients from large well-defined databases, to deliver an evidence-based individualized estimate of long-term prognosis, and its confidence interval, in a clinical setting.

Diagnostic disclosure of any medical condition includes information about prognosis. This is an essential requirement for an accurate informed decision on treatment and management. Patients' autonomy is the bioethical principle behind any informed choice and has recently been emphasized as one of the main principles of the Revised Declaration of Geneva.[1] However, the "curative model" of modern medicine, which increasingly focuses on diagnosis and treatment, has de-emphasized prognostication.[4] Indeed, doctors often refrain from openly discussing prognosis with patients affected by chronic, progressive and malignant diseases. Why? Firstly, the high variability of the clinical course may elicit feelings of uncertainty, adversely affecting patients' psychological well-being. Secondly, being fully aware of an unfavorable prognosis may lead the patient, their next of kin or the physician to stop the treatment or to decide not to accept any treatment (withdrawal of care bias). In line with this notion, studies in critical care medicine have shown that early "do-no-resuscitate" order may lead to earlier death.[2] Thirdly, pessimistic beliefs and expectations may result in worse outcomes (the “nocebo” effect), in the same way that optimism and overconfidence are conducive to individual advantage. This self-fulfilling prophecy concept has been used as a major argument to refrain from disclosing negative prognostic information, in keeping with the bioethical principle ‘*primum non nocere*’, but this seems to be in conflict with patients’ right to know their prognosis.

These arguments are still open to debate. While patients’ hope and optimism seem to have a relevant impact on the outcome of chronic conditions, it remains unclear to what extent communicating a possibly poor prognosis influences the patients’ perception of their condition and the disease course. As patients and physicians preferences and attitudes may substantially differ, purposely refraining from prognostication, although with the best intention, might not be appropriate.[10] Furthermore, the way information is delivered (e.g. discussing the risk of mortality instead of survival rates) might have a relevant impact on how patients perceive an unfavorable prognosis. The notion that sharing information on negative prognosis has a lasting nocebo effect is largely unproven and studies in terminally ill patients have shown that physicians are systematically too optimistic, possibly delaying effective palliative care measures. [3,4]

The ethics and practices surrounding prognostication, in conditions such as critical care, cancer and neurodegenerative disease, has been recently the subject of several studies and debates. It is now well accepted that providing prognostic information is ethically sound and welcomed by the majority of patients. For instance, among those at risk of developing Huntington’s disease, which can dramatically affect quality of life, predictive genetic testing is appreciated and positively impacts on young patients' approach to life.[5] Realistic expectations about prognosis give patients the opportunity to adjust short and long-term life goals. However, the majority of studies as well as practice guidelines(7) have so far addressed the impact of prognostication among patients affected by life-threatening conditions and end-of-life situations, while the influence of prognostication in chronic diseases has seldom been assessed.

Long-term prognosis in multiple sclerosis (MS) is a highly complex and controversial issue, as the disease clinical phenotype and evolution vary greatly.[6] At the extremes of this wide spectrum lie individuals with aggressive forms of the disease, leading to severe disability within a relatively short time, and others with milder disease who do not accumulate any substantial functional impairment despite a long disease duration. Factors associated with worse prognosis are: a primary progressive disease course, male sex, older age at clinical onset, a high lesion load on magnetic resonance imaging of the brain and cord at presentation, and frequent relapses in the first few years.(8) However, when applied to the individual patient, the validity of these prognostic factors is uncertain, and long-term disease evolution remains unpredictable.

The therapeutic approach in MS is extremely challenging. The use of more effective treatments comes at the cost of potential severe side effects, but might help to achieve a better control of disease activity, especially in people at higher risk of experiencing accumulation of severe disability. On the other hand, a watchful waiting approach without immediate treatment, or treatment with drugs of lower efficacy and toxicity, might be adequate in people with MS at low risk of progression. Access to timely and personalized prognosis information may help the shared decision-making process regarding treatment. Despite this, in a recent survey of 3,175 people with MS in the UK, around half of participants claimed to have never discussed their long-term prognosis with their physician and around half claimed to have “no idea” about their condition’s expected outcome.[7] While the overwhelming majority of people with MS would welcome more prognostic information, a substantial minority did not want to know, or were ambivalent. The study showed that the preferences of people with MS were predominantly influenced by psychological factors rather than by disease-associated features, such as disease activity or accumulation of disability.

Evidence-based medicine and shared decision-making need to be practiced alongside each other to ensure delivery of optimal care. The evidence base for long-term prognostication in MS can be improved. By using large longitudinal cohort data, analytic tools for individualized forecast estimates can be developed in order to improve prognostication. Based on 28 years of observational data from the London Ontario MS cohort, a prognostic tool has been developed and initially evaluated. This tool provides an estimate of the time to reach important disability milestones, such as the conversion to secondary progressive disease, requiring a walking cane, being bedridden and dying from MS.[8] Such a tool’s perceived usefulness was addressed by Dennison et al. (2018)[7] and it was concluded that it may be helpful for shared decision-making. Interestingly, participants preferred using the prognostic information with the support of the healthcare professional and opinion was divided on whether the tool should be publicly available online. This supports the notion that complex information might be best conveyed in a guided setting by an appropriately trained health professional (not necessarily a physician). In line with these findings a previous study showed that people with MS generally agree to be informed about their condition’s two-year outcome estimate, though the value of such short-term prognostic information was rated to be limited.[9]

The increased access to data from large registries, allowing to integrate information into algorithms matching individual demographic and clinical characteristics, with high selectivity and statistical power, makes more accurate and detailed long-term prognostic estimates feasible. Such estimates, including their confidence intervals, are urgently needed when making complex treatment decisions. Based on an individual’s expected outcome, more appropriate therapeutic approaches can be chosen. However, the optimum method of communicating prognosis and its level of certainty to people with MS needs to be studied. Finally, helping individuals to learn how to cope with uncertainties of their disease may give space for the hope of a more favorable course.

Conflict of interest

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