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Letter to the Editor

Before Myasthenia is Classified as Refractory, all Outcome Variables should be Taken into Account

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Letter to the Editor

We read with interest the article by Woo *et al*. on a retrospective population-based cohort study using the Health Insurance Review and Assessment database from South Korea to identify patients with myasthenia gravis (MG) at high risk of severe disease progression or mortality [1]. Of 458 MG patients, 361 had a history of myasthenic crisis (MC) and 319 had refractory MG [1]. Patients with a previous MC had a higher risk of mortality than patients without MC, and patients with refractory MG had an increased risk of severe disease progression [1]. The study is noteworthy, but some points require discussion.

The first point is that the diagnostic criteria for MG were not specified. Did all patients have elevated AchR, MUSK, or LRP4 antibodies? Were patients with seronegative MG also included? This is crucial, as approximately 10–15% of MG patients may be seronegative [2]. Were only patients with generalized MG included, or were patients with ocular myasthenia also included? Did all patients included meet the criteria for a diagnosis of MG [3]?

The second point is that it is not clear why only one ICD-10 code (G70.0) was used to identify MG [1]. In addition, the ICD codes G70.01 (acute myasthenic exacerbation), G73.0 (myasthenic syndrome in endocrine disorders), and T44.0X (poisoning by anticholinesterase agents) should have been included in the analysis [4]. How many patients with MG were overlooked because only a single ICD code was used?

The third point is that it is not certain that a patient with a diagnosis code for intubation and a diagnosis code for MG was ventilated due to MC. How were reasons excluded for patients requiring intubation and ventilation that were not related to MC and MG? Similarly, admission to the intensive care unit does not necessarily mean that MG was the reason.

The fourth point is that the occurrence of MC does not necessarily mean that the prognosis for MG is poor. For example, if a cholinergic crisis occurred due to an overdose by the treating physician, impaired metabolism, or medication error by the patient, this does not necessarily mean that the prognosis is poor.

The fifth point is that it is not clear why MG was classified as having a poor prognosis when corticosteroids and two non-steroidal immunosuppressants were used [1]. The switch to a second immunosuppressant may simply be due to side effects or intolerance, but does not necessarily have to be related to ineffectiveness.

The sixth point is that it is risky to define mortality as the absence of further contact with a patient within the next year [1]. A patient who no longer appears in the databases could also have taken a long vacation, had their diagnosis revised, moved abroad, or simply taken a self-prescribed break from medication. With regard to the criterion of "no further claims," there is a discrepancy between the 'results' section (within 365 days) and the "sensitivity analysis" (within the next 180 days) [1]. This discrepancy should be eliminated. Death should be confirmed by a definitive date of death.

The seventh point is that it was not defined how deaths due to causes other than MG were excluded. Particularly in patients who die outside the hospital, it can be difficult to assess whether MG was really the cause of death.

In summary, the study presented has some methodological limitations that should be considered before drawing any final conclusions. More factors than those considered may influence the course of the disease, the outcome, and the mortality of MG patients.

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