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Letter to the Editor

Reply to the Letter to the Editor of Tomoyuki Kawada concerning "Self-reported urinary impairment identifies 'fast progressors' in terms of neuronal loss in multiple system atrophy"

Sirs:

We thank Dr. Kawada for his interesting comment regarding our recent article on patients with multiple system atrophy (MSA) and brain volume loss.

For disease-modifying trial, one challenge is to find biomarkers that accurately identify aggressive MSA early in the disease course. In previous studies using clinical scores alone, a faster disease progression in MSA measured on the Unified Parkinson's Disease Rating Scale III (UPDRSIII) was linked to lower baseline scores in Hoehn and Yahr and UPDRS III (Seppi et al., 2005). This faster motor progression associated with mild disease severity at baseline was also seen during the validation of Unified Multiple System Atrophy Rating Scale (Geser et al., 2006). These studies may suggest that researchers should identify aggressive MSA cases in those with mild disease severity at baseline which can be a controversy in itself. To date, clinical scales assessing a range of symptoms and signs in MSA have largely been used to measure disease progression in therapeutic trials. However, a number of inherent limitations make them insufficient for tracking the disease progression. Thus clinical trials in MSA are still hampered by the lack of surrogate endpoints.

The objective of our study was to assess the performance of MRI-derived measures to track disease progression in term of neuronal loss in MSA: with the exception of urinary score, baseline demographics and clinical factors did not influence whole-brain atrophy rates in MSA. Dr. Kawada and our manuscript highlight clinical studies that suggest that baseline urinary impairment has an association with poor prognosis. These studies may support a meaningful association between brain atrophy rates and urinary symptoms affecting our MSA patients.

However, the performance of clinical and MRI-derived measures to predict the speed of clinical deterioration and brain tissue loss in MSA is an initial approach, and certainly our work shows just a weak association between brain volume loss and a self-reported urinary impairment. We have the same concerns that Dr. Kawada that the reported association and its value would have certainly been increased with a bigger sample so the measurements should be interpreted in light of this caveat. A bigger sample of MSA patients would also help to stratify these studies according to clinical variants of MSA.

Future research should use quantitative approaches for estimation of the urinary function such as cistometry. Increased samples and quantitative biomarkers may highlight stronger and clinical meaningful association between brain atrophy and autonomic dysfunction of the urinary bladder.

Declaration of Competing Interest

Carlos Guevara reports no disclosures.

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Carlos Guevara*

Facultad de Medicina, Universidad de Chile, Santos Dummont 999, Santiago, Chile

E-mail address: cguevara@hcuch.cl.

* Amapolas 1475, Providencia, Santiago, Chile

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