Temporal Changes of Diagnostic Accuracy for Multiple System Atrophy: A 15-Year Analysis from 2008 to 2022

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ABSTRACT

OBJECTIVE: To determine if the rate of accurately diagnosing multiple system atrophy (MSA) has increased over the past 15 years.

BACKGROUND: Diagnostic accuracy of MSA is suboptimal. The second consensus diagnostic criteria have been used since 2008; however, the International Parkinson and Movement Disorder Society (MDS) recently proposed revised criteria. To understand how these revised criteria will improve current diagnostic rates, it is necessary to first know the updated diagnostic accuracy before the revised criteria become regularly implemented.

METHODS: We identified 425 consecutive patients with clinically diagnosed MSA whose brains were sent to our brain bank from 2008 to 2022. After excluding 104 cases with inadequate clinical information, this study included 321 cases (136 women and 185 men). To ensure an approximately equal distribution in numbers, we divided them into two groups: 172 cases in 2008-2017 and 149 cases in 2018-2022. Diagnostic accuracy was compared between these groups and also in clinical subtypes (the parkinsonian type (MSA-P) and cerebellar type (MSA-C)).

RESULTS: Among 321 patients, 225 patients were pathologically MSA and the overall diagnostic accuracy was 70%. The remaining 30% had alternative pathological diagnoses including Lewy body disease (18%), progressive supranuclear palsy (3.7%), cerebrovascular disease (1.2%), corticobasal degeneration (0.9%), and others (5.9%). Diagnostic accuracy in 2018-2022 was significantly higher compared to that in 2008-2017 (78% vs. 63%, P=0.005). Brain MRI scans were significantly more frequently performed in 2018-2022 compared to 2008-2017 (91% vs. 79%, P=0.0031. Diagnostic accuracy for MSA-C was similar in both groups (87% in 2008-2017 and 93% in 2018-2022), while that for MSA-P was significantly higher in 2018-2022 compared to that in 2008-2017 (72% vs. 59%, P=0.04).

CONCLUSIONS: This study demonstrates that diagnostic accuracy of MSA in recent years has improved over time. The increased use of brain MRI might have contributed to the improved diagnosis accuracy.

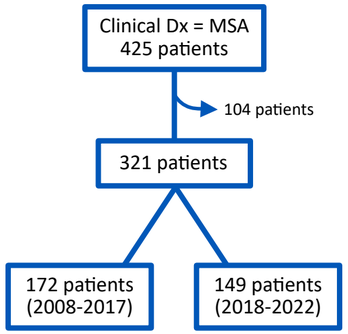
OBJECTIVES

- To understand the current status of diagnostic accuracy for MSA
- To compare diagnostic accuracy between 2008-2017 and 2018-2022 and between clinical subtypes (MSA-P and MSA-C)

METHODS

- From 2008 to 2022, 425 consecutive patients with clinical diagnosis of MSA and whose brains were examined at Mayo Clinic brain bank were identified.
- After excluding 104 cases without adequate clinical information, 321 cases were examined.
- Clinical information was systematically collected from medical charts.
- Cases were divided into 172 in 2008-2017 and 149 in 2018-2022 to ensure an approximately even distribution of numbers; diagnostic accuracy was compared between these two groups.

Figure 1 Study design



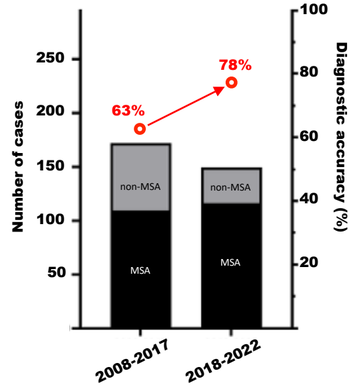
RESULTS

- Among 321 patients with clinical diagnosis of MSA, 225 were pathologically diagnosed as MSA. The overall diagnostic accuracy was 70% from 2008 to 2022.
- The remaining 30% had alternative pathological diagnoses including Lewy body disease (18%), progressive supranuclear palsy (4%), corticobasal degeneration (1%), and cerebral small vessel disease (1%).
- Regarding clinical subtypes, MSA-P and MSA-C accounted for 75% and 23%, respectively.
- Diagnostic accuracy of MSA-P over 15 years was significantly lower compared to that of MSA-C (64%vs. 91%, $p < 0.0001$).
- Among 58 Lewy body disease cases, 56 (97%) had autonomic dysfunction (6 had urinary symptoms, 18 had orthostatic hypotension, and 32 had both), 18 (31%) exhibited cerebellar symptoms, and 34 (59%) had at least one supportive features for MSA from the MDS criteria[1]. Regarding autonomic dysfunction, 37 (64%) met the more stringent requirements for clinically established MSA by the MDS criteria.
- Among 12 PSP cases, 9 (75%) had autonomic dysfunction, 8 (67%) had cerebellar symptoms, and 7 (58%) had at least one of the supportive features.
- Diagnostic accuracy was 63% in 2008-2017, and significantly improved to 78% in 2018-2022 ($p = 0.005$).
- For the two time periods, diagnostic accuracy for MSA-P was significantly higher in 2018-2022 compared to that in 2008-2017 (72% vs. 59%, $p = 0.04$). Diagnostic accuracy for MSA-C was 87% in 2008-2017 and 93% in 2018-2022, which was similar in both terms ($p = 0.44$).
- To understand the reason for the improved diagnostic accuracy, we investigated the availability of MRI in each time periods. Brain MRI scans were more frequently performed in 2018-2022 compared to 2008-2017 (91% vs. 80%, $p = 0.012$).

Table 1 Patient characteristics

Features	N = 321
Female sex	42% (136)
Age at onset (years, mean±SD)	60 ± 9
Age at death (years, mean±SD)	68 ± 9
Duration (years, mean±SD)	8 ± 4
Clinical subtypes	
MSA-P	75% (242)
MSA-C	23% (74)
MSA-A	2% (6)
Pathological diagnosis	
MSA	70% (225)
Lewy body disease	18% (58)
Progressive supranuclear palsy	4% (12)
Corticobasal degeneration	1% (3)
Cerebral small vascular disease	1% (3)
Others	6% (19)

Figure 2 Diagnostic accuracy in two time periods



DISCUSSION

- New criteria for MSA diagnosis were proposed in 2022 after the second consensus criteria in 2008[2].
- While recent retrospective autopsy studies have shown that the new MDS criteria are more diagnostically accurate than the second consensus criteria[3,4], prospective analysis is warranted.
- The present study demonstrated that the overall diagnostic accuracy of MSA over the last 15 years was 70%, and that it increased from 63% in the first 10 years to 78% in the most recent 5 years.
- The increased availability of brain MRI may have contributed to the improvement in diagnostic accuracy.
- While MSA-C showed consistently high diagnostic accuracy in both time periods, MSA-P, despite improvements, remained suboptimal.

CONCLUSIONS

- Clinical diagnostic accuracy of MSA was 70% from 2008 to 2022, improving to 78% in the most recent five years.
- This study provides baseline data for future studies examining how diagnostic accuracy of MSA changes with the new criteria.

REFERENCES

1. Wenning GK, et al. *Mov Disord.* 2022
2. Gilman S, et al. *Neurology* 2008
3. Virameteekul S, et al. *Mov Disord.* 2023
4. Sekiya H, et al. *Neurology* 2023