

Age at Onset and Therapeutic Efficacy of Primidone in Essential Tremor

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Objective: To study the therapeutic response to primidone in essential tremor (ET) patients, based on age at onset.

Background: Age at onset in ET shows a bimodal distribution, with an early peak in the 20's and another of late onset in the 60's. Differences in clinical features, rate of progression, pathophysiology, co-morbidities, and mortality have been reported in early as compared to late onset ET. Therapeutic response to medications is also highly variable. Here, we sought to examine differences in therapeutic response to primidone with respect to age.

Methods: We examined the medical records of 1074 ET patients who were evaluated by movement disorders specialists in the US Veterans Affairs Parkinson's Disease Research, Education and Clinical Center (PADRECC), in Houston, Texas, between 2001 and 2018. Age groups were classified based on the MDS Task Force on Tremor classification of age at onset.¹ Response to primidone was classified as none, mild, moderate, or significant based on subjective feedback. Mild response was graded as improvement in tremor without change in functional abilities, moderate response was improvement in tremor and functional abilities but consistent use of adaptive strategies, whereas a significant response was improvement in tremor with minimal use of adaptive strategies.

Results: Age at onset for the entire ET cohort showed the expected bimodal distribution (Fig. 1). 321 ET subjects had a documented therapeutic response to primidone. Of these, 9% had adolescent, 23% early adult, 31% middle adult, and 37% elderly age at onset. In the adolescent group (age at onset 1–20 years, n = 30), 33% reported no, 30% mild, 27% moderate and 10% excellent response. 10% of the early adulthood group (age 21–45 years, n = 72) reported no response, whereas mild, moderate, and excellent responses were reported in 35%, 47% and 8%, respectively. The middle age group (age 46–60 years, n = 100) had response rates of none (23%), mild (19%), moderate (49%) and excellent (9%). In the elderly age group (age ≥ 61, n = 119) responses were none (20%), mild (23%), moderate (50%) and excellent (7%).

Figure 1. Age at onset of ET symptoms.²

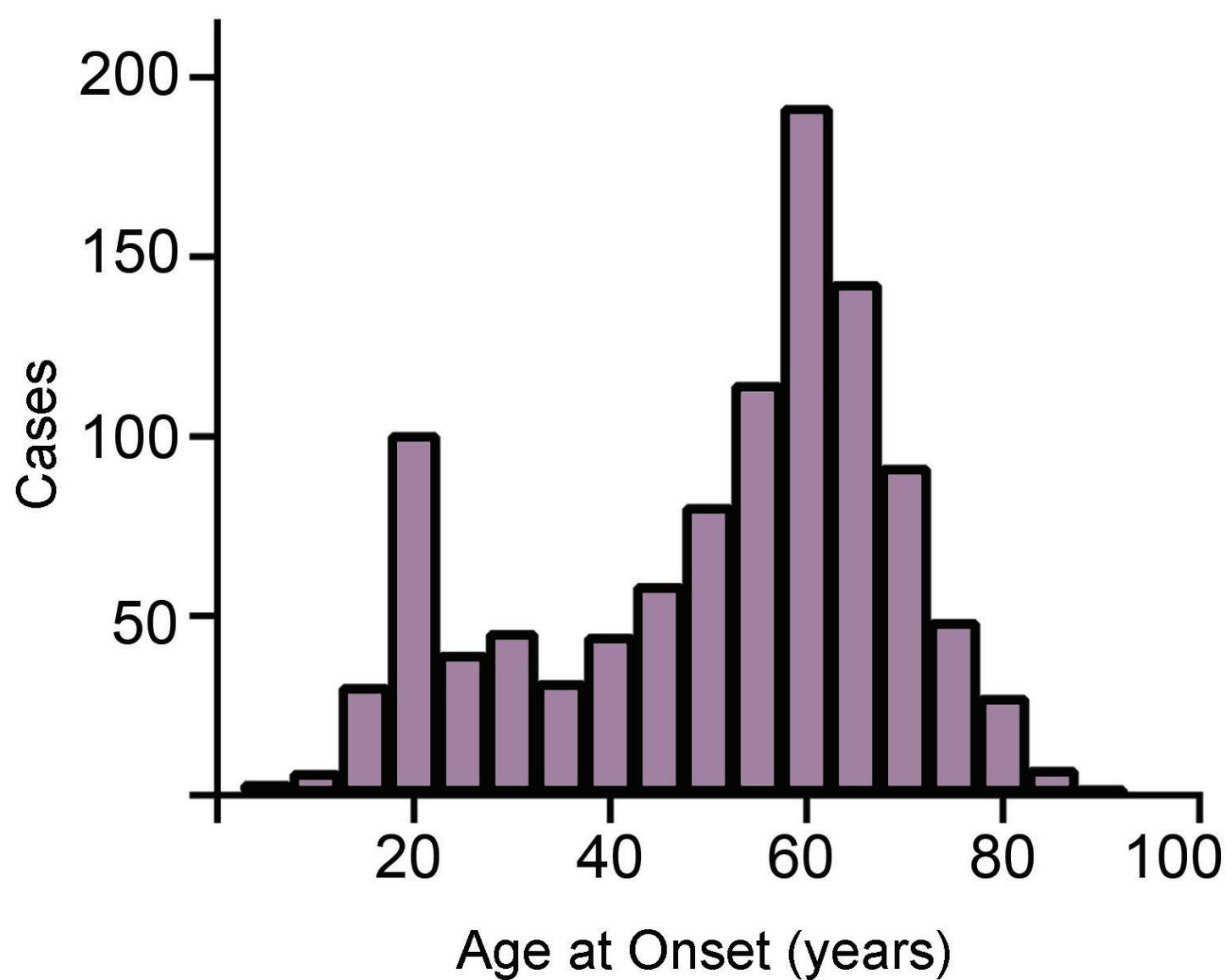
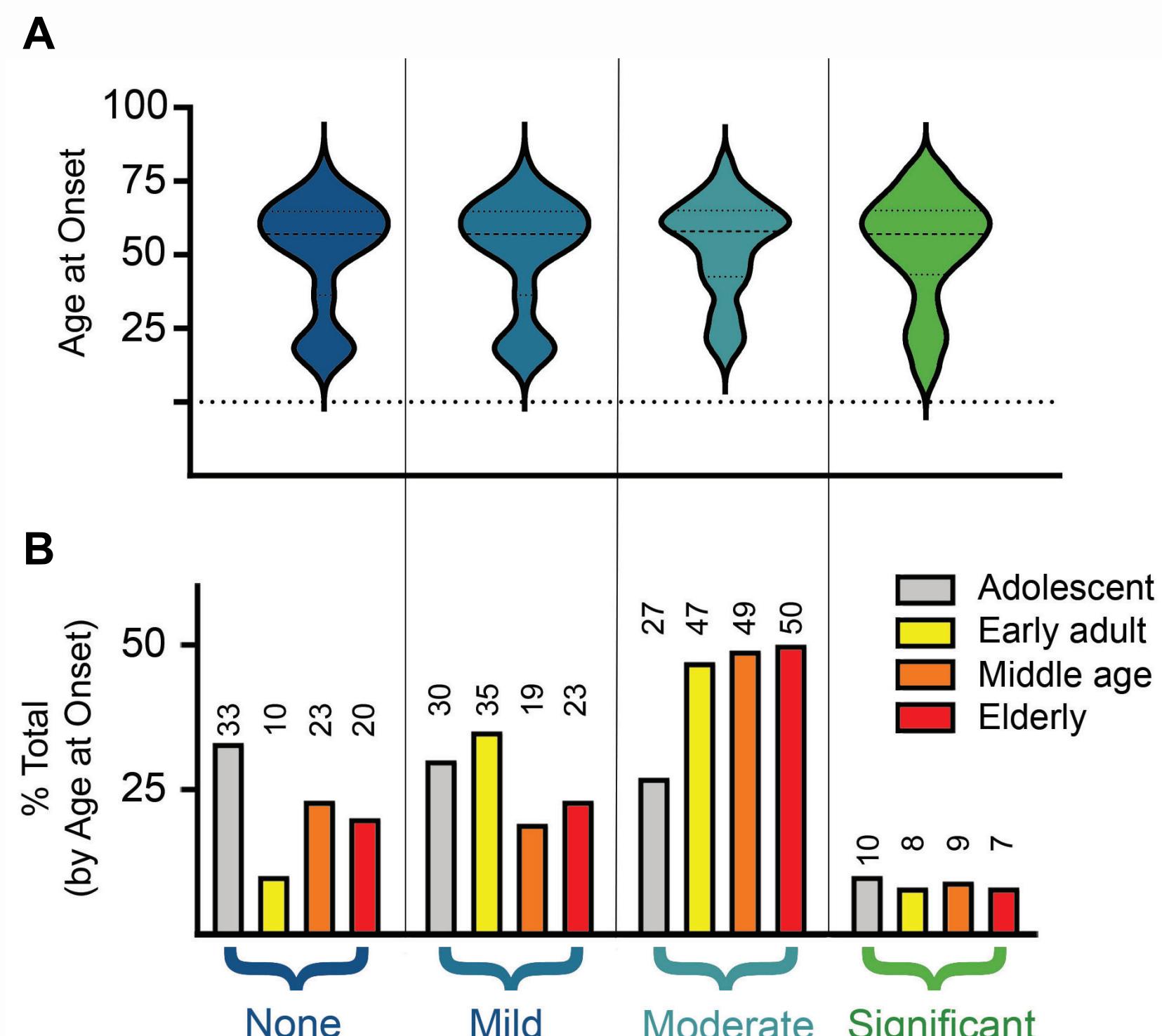


Figure 2. Therapeutic response to primidone in ET based on age at onset:
A) Violin plot; B) Histogram.



Conclusion: In this retrospective chart review, the least favorable response was noted in adolescents. Moderate was the most common therapeutic response in all age groups except adolescent age. It is intriguing to speculate that primidone resistance is an endophenotype for young onset ET that could be useful in future genetic dissection of the syndrome.

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