

Dystonia in untreated Early Onset Parkinson's disease

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Introduction: Dystonia may represent the initial sign in Parkinson's disease (PD), especially in patients with age at onset (AAO) lower than 50 years (early-onset PD, EOPD) [1,2]. Pathophysiological mechanisms underlying such peculiar PD presentation are still unknown; likewise, it is unclear if dystonia at onset might identify a distinct clinical PD subtype.

Objective: To outline main clinical and genetic features of *de novo* EOPD patients presenting with dystonia by a single-center retrospective longitudinal cohort study.

Methods: Clinical charts of 170 *de novo* (newly diagnosed and untreated) EOPD patients prospectively followed-up were screened, selecting patients presenting with dystonia (EOPDdyst). Demographics, genetics, motor and non-motor features, therapies, complications, rate of change in Hoehn and Yahr score and levodopa equivalent daily dose (LEDD) were analysed in EOPDdyst cohort in comparison to EOPD *de novo* patients without dystonia.

Results: Dystonia had a prevalence of 14.1%. EOPDdyst patients had lower AAO than the non-dystonic (41.5 ± 6.1 vs 44.2 ± 5.2 , $p=0.03$). Pathogenic genetic variants were more frequent in EOPDdyst (29.2% vs 9.6%, $p=0.001$), mostly in autosomal recessive genes (57.1%). PRKN variants were the most common in the EOPDdyst group (42.9%), GBA variants in the non-dystonic group (50%). EOPDdyst patients had symmetrical motor presentation (16.7% vs 2.7%, $p=0.004$) and suffered with earlier levodopa induced dyskinesias (LIDs) (1.00 ± 0.91 years vs 2.79 ± 2.55 years, $p=0.049$). Adjusting the analysis for the genetic origin, the two groups did not show significant differences in any item.

Conclusions: Main clinical milestones seem to not differ in EOPDdyst patients. However, dystonia in EOPD mostly imply a genetic origin, especially of recessive forms, which accounts for earlier onset and probably a wider motor network impairment.

References:

- [1] A.S. Shetty, K.P. Bhatia, A.E. Lang, Dystonia and Parkinson's disease: What is the relationship?, *Neurobiol Dis.* (2019). <https://doi.org/10.1016/j.nbd.2019.05.001>.
- [2] R. Mehanna, Age Cutoff for Early-Onset Parkinson's Disease: Recommendations from the International Parkinson and Movement Disorder Society Task Force on Early Onset Parkinson's Disease, *Movement Disorders Clinical Practice.* (2022). <https://doi.org/10.1002/mdc3.13523>.