CO105

Characterizing age at loss of ambulation among patients with Friedreich Ataxia: A retrospective study using health administrative claims data in the United States

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1. Background & Objectives:

- Friedreich Ataxia (FA) is a progressive and degenerative neuromuscular disorder, characterized by worsening ataxia, scoliosis, and loss of ambulation (LOA).[1]
- LOA is associated with a spectrum of symptoms, starting with early declines in balance and gait instability and culminating with the inability to stand unassisted. The rate of progression is variable, but most patients are fully wheelchair bound as a result of their disease within 10 to 20 years of symptom onset.[1]
- Currently, there is only one treatment that has been licensed specifically for FA (omaveloxolone; approved in 2023 by the FDA). However, its indication in the United States (US) is restricted to patients with FA who are aged 16 years and older.
- FA management focuses on treatment of symptoms, secondary complications due to FA, and comorbidities, through pharmacotherapy, supportive aids, surgery, and physical therapy.[2,3]

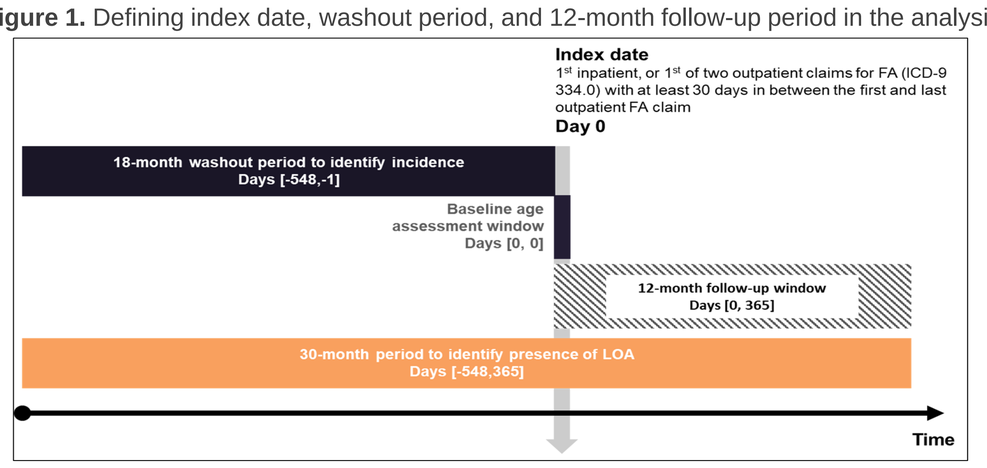
This study aimed to characterize the age at LOA among a cohort of patients with FA, using retrospective US claims data.

2. Methods:

- Data source: US Merative MarketScan Commercial database (Aug 2010 to Sept 2020).
- Inclusion criteria: Children and adults with ≥12 months of follow-up and ≥1 inpatient, or ≥2 outpatient visits separated by ≥30 days, with primary or secondary diagnosis of FA (ICD-9 334.0) prior to Oct 2015.* Index visit was defined as 1st inpatient or 2nd outpatient visit with diagnosis of FA.
- All incident patients with FA (ICD-9 334.0) prior to Oct 2015 were identified.
- Incidence was defined with an 18-month washout period with no FA diagnostic codes. Included patients were followed up for 12 months (**Figure 1**).
- This 30-month period was used to observe LOA by age at FA diagnosis.
- For this study, LOA is defined by the presence of ≥1 diagnosis for difficulty of walking or claim for mobility aids including manual wheelchairs, walkers, motorized wheelchairs, scooters, or power-assisted wheelchairs. This corresponds with the initial declines in balance and gait instability observed in FA patients.
- Age at index date was used as a proxy for age at FA diagnosis. Results were stratified into two categories: <16 years; 16-24 years at FA diagnosis.

*334.0 was replaced by a non-specific ICD-10 code in September 2015

Figure 1. Defining index date, washout period, and 12-month follow-up period in the analysis

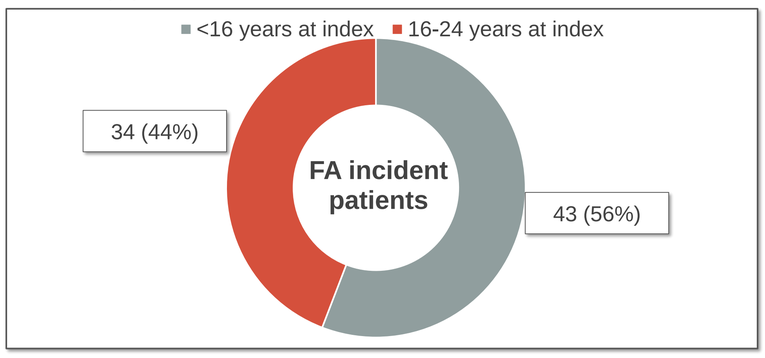


Abbreviations: FA = Friedreich ataxia; ICD = International Classification of Diseases

3. Results:

- A total of 77 incident patients with FA were diagnosed before 24 years of age; 43 (56%) diagnosed <16 years and 34 (44%) between 16-24 years (**Figure 2**). Mean (SD) age at diagnosis for the two groups was 10.9 (4.0) years for those diagnosed <16 years and 20.2 (2.7) years for those diagnosed between 16-24 years (**Table 1**).
- Of 77 patients, 42 (55%) had LOA captured within this 30-month period (**Table 1**). Of those with LOA, the majority (74%) experienced this during the 18-month pre-index washout period.
- Among those diagnosed with FA <16 years (n=43):
  - 19 (44%) had observed LOA over the 30-month period with a mean (SD) of 10.3 (4.3) years at the time of observed LOA.
- Among those diagnosed with FA between 16-24 years (n=34):
  - 23 (68%) had observed LOA with a mean (SD) of 18.9 (3.0) years at the time of observed LOA.
  - The distribution of patients by age at LOA, overall and by age at diagnosis is summarized in **Figure 3**.
- 83% of these LOA cases were identified through their use of manual wheelchair; among older patients, this proportion was even higher (96%, **Table 1**).
- Older patients also often used manual wheelchairs along with other types of aids.
- Uses of other aids were lower among younger patients.

Figure 2. Distribution of age at FA diagnosis for incident patients with FA in the MarketScan commercial dataset, n (%)



Abbreviations: FA = Friedreich ataxia; LOA = loss of ambulation

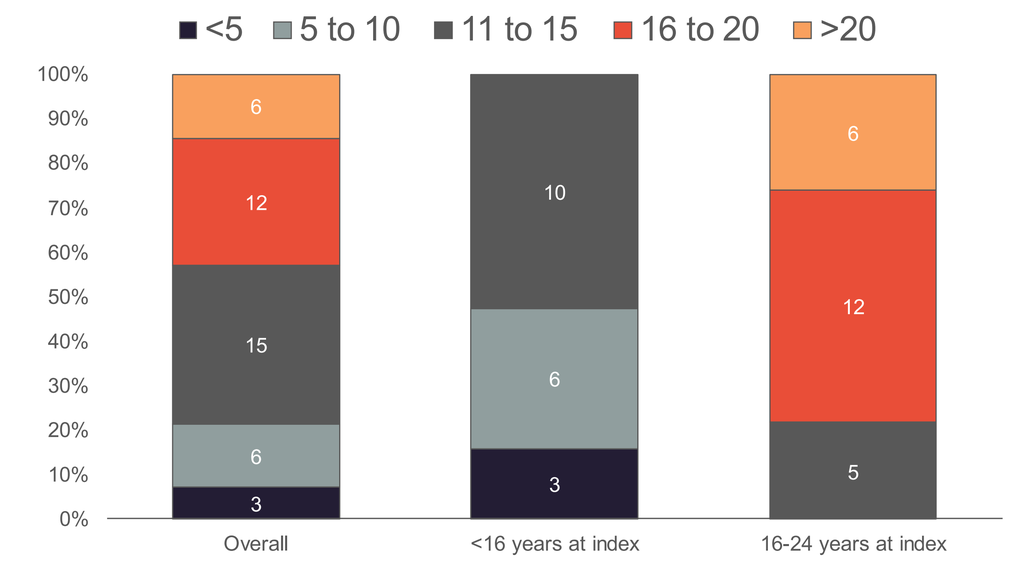
3. Results cont'd:

Table 1. Results summary of LOA among incident patients with FA in the MarketScan commercial dataset

	Overall (n=77)	<16 years at index (n=43)	16-24 years at index (n=34)
Age at FA diagnosis, years			
Mean (SD)	15.0 (5.8)	10.9 (4.0)	20.2 (2.7)
LOA, n (%)	42 (54.5%)	19 (44.2%)	23 (67.6%)
LOA identification method, n (%*)			
Manual wheelchairs	35 (83.3%)	13 (68.4%)	22 (95.7%)
Diagnosis only	19 (45.2%)	8 (42.1%)	11 (47.8%)
Walkers	8 (19.0%)	4 (21.1%)	4 (17.4%)
Motorized wheelchairs	8 (19.0%)	1 (5.3%)	7 (30.4%)
Scooters	4 (9.5%)	1 (5.3%)	3 (13.0%)
Age at LOA, years			
Mean (SD)	14.1 (5.7)	10.3 (4.3)	18.9 (3.0)
Among those with LOA in the 18-mo washout period, n (%*)	31 (73.8%)	11 (57.9%)	20 (87.0%)
Mean (SD)	13.0 (6.4)	8.7 (4.8)	18.5 (2.9)
Among those with LOA in the 12-mo washout period, n (%*)	11 (26.2%)	8 (42.1%)	3 (13.0%)
Mean (SD)	16.5 (5.2)	12.5 (2.4)	21.5 (2.7)

Abbreviations: FA = Friedreich ataxia; LOA = loss of ambulation; mo = month; SD = standard deviation
Notes: *percentage calculated out of total number of patients who had LOA

Figure 3. Distribution of patients by age at LOA in years, overall and by age at diagnosis



Abbreviations: FA = Friedreich ataxia; LOA = loss of ambulation

4. Limitations:

- This study used a large, real-world, US dataset which allowed for identification of a substantial number of patients with FA for robust analyses.
- Nevertheless, a few limitations of this study are notable, primarily:
  - Given that the data source is composed of patients on commercial insurance, patients with FA with later-onset disease may be over-represented in the cohort, as observed through the larger proportion of patients between the ages of 16-24 years at index FA diagnosis; however, limitations may exist in ascertaining incidence with a washout period of eighteen months, and therefore the representativeness of this cohort will need to be better assessed upon comparison to real-world studies with longitudinal data.
  - It is difficult to ascertain complete LOA using claims data alone; presence of claims for mobility aids may not be indicative of LOA but rather the start of LOA.
    - This is also supported through the observed large proportion of patients with LOA in the washout period
  - Due to the lack of a specific ICD-10 code for FA between September 2015 and September 2020, the results from this study are limited to a cohort of patients identified in or before 2015 and generalizability to cohorts diagnosed since then is uncertain.

5. Discussion & Conclusions:

- This study provides real-world estimates of ambulation loss, a key indicator of clinical progression among patients, and thus disease burden, for commercially insured patients with FA in the US.
- While limitations exist in ascertainment of LOA using claims data, findings suggest that those who had earlier onset of FA also had earlier start of LOA, with the majority of ambulation difficulties starting prior to FA diagnosis.
- In this cross-sectional analysis, most patients who were diagnosed with FA before 24 years of age experienced some degree of walking difficulty before the age of 16 years. Of those with LOA, the majority (57%) lost ambulation before 16 years.
- To slow progression of the disease and address early ambulation loss, initiation of disease modifying treatment at a young age is critical.

6. References:

1. Cook A & Giunti. British medical bulletin. 2017:1-12
2. de Silva et al. Orphanet journal of rare diseases. 2019;14(1):1-10.
3. Schulz et al. Nat Rev Neurol. 2009;5(4):222-234

FUNDING & DISCLOSURES: This study was funded by PTC Therapeutics. AS and IT are employees of PTC Therapeutics. CQ, LP, and KJ are employees of Broadstreet HEOR, which received funds from PTC Therapeutics for this work, and GV received consulting fees from PTC Therapeutics. Medical writing and editorial support was provided by Broadstreet HEOR and was funded by PTC Therapeutics.

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THE INTERNATIONAL SOCIETY FOR PHARMACOECONOMICS AND OUTCOMES RESEARCH (ISPOR) EUROPEAN CONFERENCE, COPENHAGEN, DENMARK, NOVEMBER 12-15, 2023