Mucopolysaccharidosis IVA in Antioquia, Colombia: A Referral-Based Case Series of Phenotype, Imaging, and Interventions

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Valeria Torres-Yepes[1,4], Samuel Rodas García[2], Andrea Jaramillo-Cerezo[1], Isabela Franco Sánchez[1], Lucelly López López[1], Carolina Baquero-Montoya[2,3], Gustavo Giraldo[1,2,3,4]

Abstract

Mucopolysaccharidosis IVA (MPS IVA; Morquio A syndrome) results from N-acetylgalactosamine-6-sulfatase deficiency, causing keratan sulfate accumulation and progressive multisystem disease. Clinical, radiographic, genetic, and functional phenotyping data from Colombia remain scarce. We characterized the phenotype, imaging findings, complications, and interventions among patients with MPS IVA followed at two specialized referral centers in Antioquia, Colombia. Clinical records available through 2021 were retrospectively reviewed, and longitudinal six-minute walk test (6MWT) data were analyzed using linear mixed-effects models indexed by age and follow-up time. Thirty-one patients were included (median age, 21 years [IQR, 12–29]; 54.8% female). Frequent findings included pectus carinatum (93.5%), hearing impairment (71.0%), valvular disease (54.8%), corneal clouding (55.2%), restrictive pulmonary physiology (63.2%), and cervical canal narrowing (81.0%). Enzyme replacement therapy was documented in 93.5% of patients. The age-based model estimated a decline of 6.18 m/year (95% CI, −9.86 to −2.49; P=0.0017), whereas the follow-up-indexed model showed no significant change (−0.94 m/year; 95% CI, −8.01 to 6.14; P=0.792), reflecting heterogeneous within-patient trajectories. Findings should be interpreted in light of the retrospective design, incomplete clinical documentation, and unavailable patient-specific enzyme replacement therapy initiation dates.

Keywords

Morquio A, mucopolysaccharidosis IVA, GALNS, phenotype, Colombia.

Background

Mucopolysaccharidosis IVA (Morquio A) results from N-acetylgalactosamine-6-sulfatase deficiency with accumulation of keratan sulfate and chondroitin-6-sulfate, driving abnormal endochondral ossification and multisystem disease [1–2]. Core skeletal features—dysostosis multiplex, thoracic cage deformity, odontoid hypoplasia, genu valgum—coexist with airway, pulmonary, cardiac, ophthalmologic, and auditory involvement [3–5].

Global epidemiology is heterogeneous [6]. Colombia reports meaningful burdens of mucopolysaccharidoses, with clusters in Antioquia and neighboring regions [7–8]. Natural-history and genotype data for Antioquia are limited. Regional series in Colombia and Chile highlight enrichment of p.Gly301Cys in GALNS, with suggested associations with severe phenotype and a putative Andean founder effect [9–11].

Enzyme replacement therapy with elosulfase alfa can improve endurance and some respiratory measures, yet skeletal pathology responds poorly due to avascular cartilage and rapid enzyme clearance [2,12–13]. Given these realities, granular

[1] Universidad Pontificia Bolivariana, Medellín, Colombia.
[2] Universidad EIA, Envigado, Colombia.
[3] Hospital Pablo Tobón Uribe, Medellín, Colombia.
[4] Clínica Universitaria Bolivariana, Medellín, Colombia.

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Corresponding Author:
Gustavo Giraldo, e-mail: tavog87@gmail.com

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regional phenotyping remains essential to plan surveillance and multidisciplinary care [5,14].

We describe the phenotype, imaging findings, complications, and interventions among patients with Morquio A followed in Antioquia, presenting denominators and 95% CIs and making explicit the missingness and constraints of the retrospective source.

Methods

Design, setting, and participants

Referral-based retrospective case series from two Medellín specialized centers, Hospital Pablo Tobón Uribe and Clínica Universitaria Bolivariana. Clinical records were available through 2021. Dated 6MWT records in the analytic file spanned 2010–2022 and were analyzed separately as longitudinal functional data. Patients with confirmed or clinically documented MPS IVA who had linkable clinical records in the source workbook were included. The final analytic denominator was 31 patients after excluding non-informative or non-linkable rows. Because screening logs, recruitment start dates, and complete exclusion reasons were not available, we do not claim population census capture or consecutive ascertainment.

Variables and sources

From medical records we abstracted age, sex, place of birth, consanguinity, age at diagnosis, diagnostic methods, current manifestations by system, radiographic and cervical MRI findings, complications, functional testing, enzyme replacement therapy (ERT), and surgery. Hearing impairment was abstracted as documented in the medical record and could reflect audiometry, specialist assessment, screening history, or clinical notation; a uniform audiologic protocol was not available across centers. Operational definitions for valvular disease, restrictive or obstructive physiology, corneal clouding, and radiographic findings reflected routine clinical documentation and were not harmonized retrospectively.

ERT exposure was abstracted as documented treatment history and reported duration. The source records did not provide patient-specific initiation dates, treatment interruptions, adherence information, or active treatment status at each 6MWT assessment. Surgical history was abstracted as documented procedures, but dated surgical timelines suitable for longitudinal modeling were not consistently available.

Statistical analysis

Descriptive statistics were reported as medians with interquartile ranges for continuous variables and as counts, percentages, and exact Clopper–Pearson 95% confidence intervals for categorical variables. Denominators reflect available information for each variable. Exploratory missingness summaries compared age and sex distributions between patients with and without available data in selected domains, including pulmonary testing, cervical MRI, and molecular testing; these comparisons were used as screening summaries because the sample size limited subgroup inference.

Six-minute walk test (6MWT) records were analyzed when test dates, patient age at testing, and walking distance were available. The primary longitudinal model estimated the association between age at testing and 6MWT distance using a Gaussian linear mixed-effects model with patient-level random intercepts. A secondary descriptive model indexed time as years since each patient's first dated 6MWT to summarize within-patient change during observed follow-up. The exploratory ERT-duration model was not treated as a treatment-effect model because patient-specific ERT initiation dates, treatment interruptions, adherence data, and dated surgical timelines were unavailable. Analyses were performed in Jamovi 2.6.44 and R 4.5.2 [15–16].

Ethical considerations

The study was approved by the Research Ethics Committee of Universidad Pontificia Bolivariana. Given its observational nature and the use of anonymized clinical data, the research was classified as minimal risk in accordance with Colombian regulations and the principles of the Declaration of Helsinki [17–18]. Consequently, the requirement for informed consent was waived.

Results

Cohort profile

Thirty-one patients were included. Seventeen were female (17/31, 54.8%; 95% CI 36.0–72.7), and the median age was 21 years (IQR 12–29). Parental consanguinity was documented in 5/25 patients (20.0%; 95% CI 6.8–40.7). Place of birth was available for 28 patients: Medellín metropolitan area in 14/28 (50.0%), other municipalities in Antioquia in 12/28 (42.9%), and other Colombian departments in 2/28 (7.1%) (Table 1).

Diagnostic information

The median age at diagnosis was 4 years (IQR, 2–9). Diagnostic ascertainment was supported by clinical evaluation in 30/31 patients (96.8%). Enzyme activity was measured in 25/31 (80.6%), with a median value of 0.1 nmol/mg protein/h (IQR, 0–0.2). Urinary or blood glycosaminoglycans were measured in 15/28 patients with available data (53.6%). Molecular testing was performed in 14/31 patients (45.1%; 95% CI, 27.3–64.0). The source workbook did not reliably classify patients into mutually exclusive diagnostic-certainty categories combining enzymatic and molecular confirmation. Among molecularly tested patients, 13/14 (92.9%; 95% CI, 66.1–99.8) were homozygous for p.Gly301Cys (c.901G>T).

Table 1. Baseline sociodemographic characteristics (N=31).

Characteristic	n/N	%	95% CI
Female sex	17/31	54.8	36.0–72.7
Age, years	—	21 (12–29)	—
Parental consanguinity	5/25	20.0	6.8–40.7
Place of birth – Medellín metro	14/28	50.0	30.6–69.3
Place of birth – other Antioquia	12/28	42.9	24.5–62.8
Place of birth – other departments	2/28	7.1	0.9–23.5

Data are shown as n/N (%) with exact Clopper–Pearson 95% confidence intervals (CIs), or as median (interquartile range, IQR) for continuous variables. "N" equals the number with available information for each variable. Percentages and CIs are rounded. Missing data: consanguinity (n=6); place of birth (n=3).

Current manifestations

Pectus carinatum was documented in 29/31 patients (93.5%; 95% CI 78.6–99.2), short neck in 21/31 (67.7%; 95% CI 48.6–83.3), kyphoscoliosis in 13/31 (41.9%; 95% CI 24.6–60.9), and pes planus in 12/31 (38.7%; 95% CI 21.9–57.8). Hearing impairment was recorded in 22/31 (71.0%; 95% CI 52.0–85.8), corneal clouding in 16/29 (55.2%; 95% CI 35.7–73.6), and valvular disease in 17/31 (54.8%; 95% CI 36.0–72.7). Restrictive pulmonary physiology was present in 12/19 patients with available testing (63.2%; 95% CI 38.4–83.7), and obstructive physiology in 7/20 (35.0%; 95% CI 15.4–59.2). Hepatomegaly was uncommon, documented in 2/30 patients with available information (6.7%; 95% CI, 0.8–22.1).

Imaging

Radiographic findings included genu valgum in 15/23 patients (65.2%; 95% CI, 42.7–83.6), odontoid hypoplasia in 8/20 (40.0%; 95% CI, 19.1–64.0), kyphosis in 8/22 (36.4%; 95% CI, 17.2–59.3), and radiographic coxa valga in 2/21 (9.5%; 95% CI, 1.2–30.4). Cervical MRI was available for 21/31 patients. Among those with MRI data, any abnormality was recorded in 19/21 (90.5%; 95% CI, 69.6–98.8), cervical canal narrowing in 17/21 (81.0%; 95% CI, 58.1–94.6), atlanto-occipital hypoplasia in 7/21 (33.3%; 95% CI, 14.6–57.0), atlanto-occipital subluxation in 4/21 (19.0%; 95% CI, 5.4–41.9), and platyspondyly in 19/21 (90.5%; 95% CI, 69.6–98.8). These MRI percentages use the scanned subgroup as the denominator.

Complications and interventions

Cervical compression was documented in 20/29 patients (69.0%; 95% CI 49.2–84.7), respiratory compromise in 21/31 (67.7%; 95% CI 48.6–83.3), mobility limitation in 14/29 (48.3%; 95% CI 29.5–67.5), tracheal obstruction in 2/28 (7.1%; 95% CI 0.9–23.5), and surgical complications in 2/29 (6.9%; 95% CI 0.8–22.8). ERT exposure was recorded in 29/31 patients (93.5%; 95% CI 78.6–99.2), with a median duration of 6 years (IQR 4–8). Walking aids were documented in 5/24 patients (20.8%; 95% CI 7.1–42.2). Surgeries included cervical fixation in 16/29 (55.2%; 95% CI 35.7–73.6), knee surgery in 13/29 (44.8%; 95% CI 26.5–64.3), adenoidectomy in 8/31 (25.8%; 95% CI 11.9–44.6), tonsillectomy in 5/31 (16.1%; 95% CI 5.4–33.7), tympanostomy tubes in 3/31 (9.7%; 95% CI 2.0–25.8), and inguinal or umbilical herniorrhaphy in 4/31 (12.9%; 95% CI 3.6–29.8) (Table 2).

Functional endurance

Dated 6MWT records were available for 26/31 patients (83.9%); 22/31 (71.0%) had at least two dated assessments. The primary mixed-effects model included 76 observations from 22 patients and estimated lower mean walking distance at older ages (−6.18 m/year; 95% CI, −9.86 to −2.49; P=0.0017; ICC=0.68) (Table 3; Figure 1). This age-based estimate describes the association between testing age and distance in the observed records, not a uniform trajectory for every patient. In pediatric and adolescent patients, lower-than-expected walking distance at older ages may reflect failure to gain functional capacity with growth as well as true loss of function; no age-, sex-, or height-adjusted reference correction was available for this series. In the secondary follow-up-indexed analysis, which used years since each patient's first dated 6MWT, the estimated mean within-patient change was −0.94 m/year (95% CI, −8.01 to 6.14; P=0.792) (Table 3; Figure 2). Individual trajectories showed heterogeneous patterns, including stable, increasing, and decreasing values. Documented ERT exposure should not be interpreted as active treatment at each assessment, and treatment-effect analyses were not performed because ERT initiation dates, treatment interruptions, adherence data, and dated surgical timelines were unavailable.

Paired FEV1 and 6MWT data were available for only three patients, precluding analysis of functional-pulmonary coupling.

Discussion

This referral-based series from Antioquia shows the expected multisystem pattern of Morquio A, including frequent skeletal, cervical, cardiac, pulmonary, ocular, and auditory involvement, paralleling international registry and natural-history descriptions [3,4,19]. Valvular disease was documented in approximately

Table 2. Clinical features, diagnostics, imaging, complications, and interventions.

Variable	n/N	%	95% CI
Diagnostic approach			
Clinical evaluation supportive of diagnosis	30/31	96.8	83.3–99.9
Urinary/blood glycosaminoglycans measured	15/28	53.6	33.8–72.5
Enzyme activity measured	25/31	80.6	62.5–92.6
Enzyme activity, nmol/mg protein/h	—	0.1 (0–0.2)	—
Age at diagnosis, years	—	4 (2–9)	—
Molecular Studies			
Molecular testing performed	14/31	45.1	27.3–64.0
Homozygous p.Gly301Cys (among tested)	13/14	92.9	66.1–99.8 †
Compound heterozygous (among tested)	1/14	7.1	0.2–33.9 †
Current manifestations			
Pectus carinatum	29/31	93.5	78.6–99.2
Short neck	21/31	67.7	48.6–83.3
Kyphoscoliosis	13/31	41.9	24.6–60.9
Pes planus	12/31	38.7	21.9–57.8
Clinical coxa valga	2/31	6.5	0.8–21.4
Hearing impairment	22/31	71.0	52.0–85.8
Corneal clouding	16/29	55.2	35.7–73.6
Valvular disease	17/31	54.8	36.0–72.7
Restrictive pulmonary physiology	12/19	63.2	38.4–83.7
Obstructive pulmonary physiology	7/20	35.0	15.4–59.2
Hepatomegaly	2/30	6.7	0.8–22.1
Radiography (skeletal)			
Kyphosis	8/22	36.4	17.2–59.3
Radiographic coxa valga	2/21	9.5	1.2–30.4
Odontoid hypoplasia	8/20	40.0	19.1–64.0
Genu valgum	15/23	65.2	42.7–83.6
Cervical MRI (n=21 with studies)			
Any abnormality	19/21	90.5	69.6–98.8
Cervical canal narrowing	17/21	81.0	58.1–94.6
Atlanto-occipital hypoplasia	7/21	33.3	14.6–57.0
Atlanto-occipital subluxation	4/21	19.0	5.4–41.9
Platyspondyly	19/21	90.5	69.6–98.8
Complications and functional status			
Cervical compression	20/29	69.0	49.2–84.7
Respiratory compromise	21/31	67.7	48.6–83.3
Mobility limitation	14/29	48.3	29.5–67.5

Table 2. Cont.

Variable	n/N	%	95% CI
Tracheal obstruction	2/28	7.1	0.9–23.5
Surgical complications	2/29	6.9	0.8–22.8
Walking aids required	5/24	20.8	7.1–42.2
Interventions			
Enzyme replacement therapy (ERT)	29/31	93.5	78.6–99.2
ERT duration, years	—	6 (4–8)	—
Cervical fixation	16/29	55.2	35.7–73.6
Knee surgery	13/29	44.8	26.5–64.3
Adenoidectomy	8/31	25.8	11.9–44.6
Tonsillectomy	5/31	16.1	5.4–33.7
Tympanostomy tubes	3/31	9.7	2.0–25.8
Inguinal/umbilical herniorrhaphy	4/31	12.9	3.6–29.8

Exact Clopper–Pearson 95% CIs are provided for all proportions. "N" equals the number with available information for each row. Continuous variables are reported as median (interquartile range, IQR). Definitions, including valvular disease, restrictive or obstructive pulmonary physiology, and radiographic criteria, reflect clinical documentation and were not standardized across services. Missing data were most frequent for pulmonary testing, selected radiographic items, cervical MRI, and walking-aid documentation. † Among patients with molecular testing.

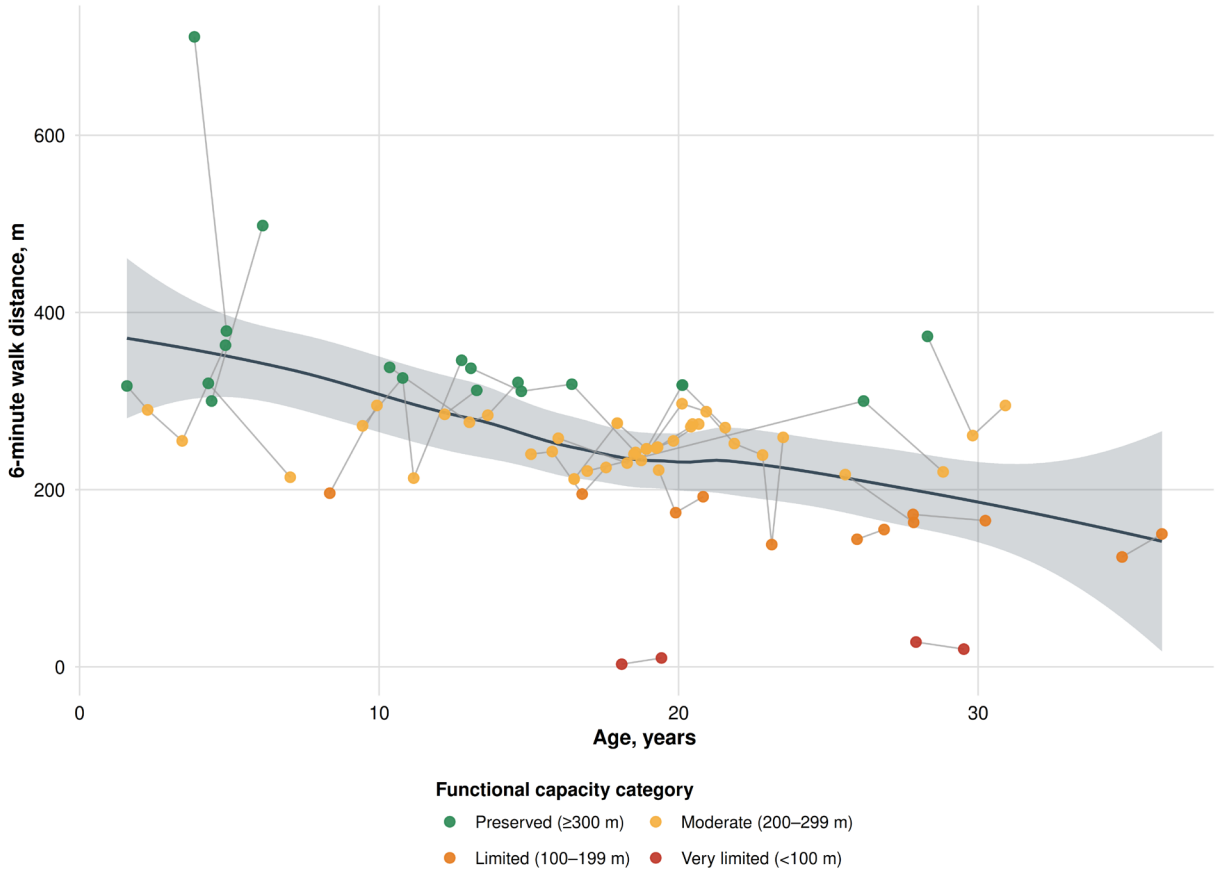


Figure 1. Six-minute walk distance by age in patients with MPS IVA.
Individual dated 6-minute walk test (6MWT) observations are plotted against age at testing. Points are color-coded by functional capacity category: preserved (≥300 m), moderate (200–299 m), limited (100–199 m), and very limited (<100 m). Gray lines connect repeated observations from the same patient. The fitted LOESS curve and 95% confidence band summarize the descriptive age-related pattern and are not intended to estimate treatment effect or individual prognosis. Functional categories are descriptive and were not modeled as predictors.

Table 3. Summary of six-minute walk test (6MWT) assessments and longitudinal modeling.

Metric	Value
Patients with ≥1 dated 6MWT record, n/N (%)	26/31 (83.9)
Patients with ≥2 dated 6MWT records, n/N (%)	22/31 (71.0)
Dated 6MWT observations with finite distance, n	80
Observations included in the primary mixed-effects model, n	76
Calendar years of testing	2010–2022
Age at testing, years, median	18.5
6MWT distance, m, median	255.0
Primary mixed-effects slope, m/year	–6.18
95% CI for primary slope, m/year	–9.86 to –2.49
p value for primary slope	0.0017
Follow-up-indexed slope, m/year since first dated 6MWT	–0.94
95% CI for follow-up-indexed slope, m/year	–8.01 to 6.14
p value for follow-up-indexed slope	0.792
Intraclass correlation coefficient	0.68
Marginal / conditional R^2	0.20 / 0.74
Exploratory non-causal model	
Exploratory ERT-duration coefficient, m/year	4.68
95% CI for ERT-duration coefficient, m/year	–13.46 to 22.81
p value for ERT-duration coefficient	0.592

Data include patients with dated six-minute walk test (6MWT) records. Percentages use the full analytic cohort as the denominator (N=31). Among patients with at least one dated 6MWT, 22/26 (84.6%) had two or more dated assessments. The primary mixed-effects model included 76 observations from 22 patients with finite age-at-test and distance values and modeled 6MWT distance as a function of age in decimal years, with patient-level random intercepts. The follow-up-indexed model used years since each patient's first dated 6MWT to describe within-patient change during observed follow-up; it should not be interpreted as a treatment-effect model. Marginal and conditional R^2 values summarize variance partition for the primary Gaussian mixed-effects model. The enzyme replacement therapy (ERT) duration model was exploratory and used clinician-reported ERT duration; it does not estimate a pre/post ERT effect because patient-specific treatment initiation dates were unavailable. Surgery-timing effects were not estimable because dated surgical events were unavailable.

55% of patients, restrictive physiology in 63% of those tested, and corneal clouding in 55% of patients with available data. These findings support surveillance of heart valves, pulmonary function, airway, and corneas [4,5,12,20]. Hearing impairment was documented in 71% of patients, higher than the 37% reported in a recent scoping review [21]. This difference should be interpreted as an ascertainment and documentation issue rather than a direct prevalence contrast. In this series, hearing impairment was abstracted from routine clinical records and could reflect audiometry, specialist assessment, screening history, or clinical notation. The exact source for each documented case was not consistently coded, and a uniform audiologic protocol was not available across centers.

The dated 6MWT records provide two complementary views of functional endurance. The age-based mixed model estimated lower walking distance at older testing ages, averaging about 6 meters per additional year of age. In a series that includes children and adolescents, this estimate should not be read only as annual functional loss. In healthy children, walking distance generally increases with growth and maturation into adolescence; patients with MPS IVA may fail to gain the expected functional reserve even before overt decline is apparent. Because age-, sex-, and height-adjusted reference values were not available for this analysis, the −6.18 m/year estimate is best interpreted as an age-associated functional pattern in clinical records rather than a pure deterioration rate.

The follow-up-indexed analysis addresses a different question: how each patient's recorded 6MWT changed after the first available test. When elapsed time was measured from the first dated 6MWT, the average within-patient slope was close to zero, and the confidence interval included both modest decline and modest improvement. This pattern is compatible

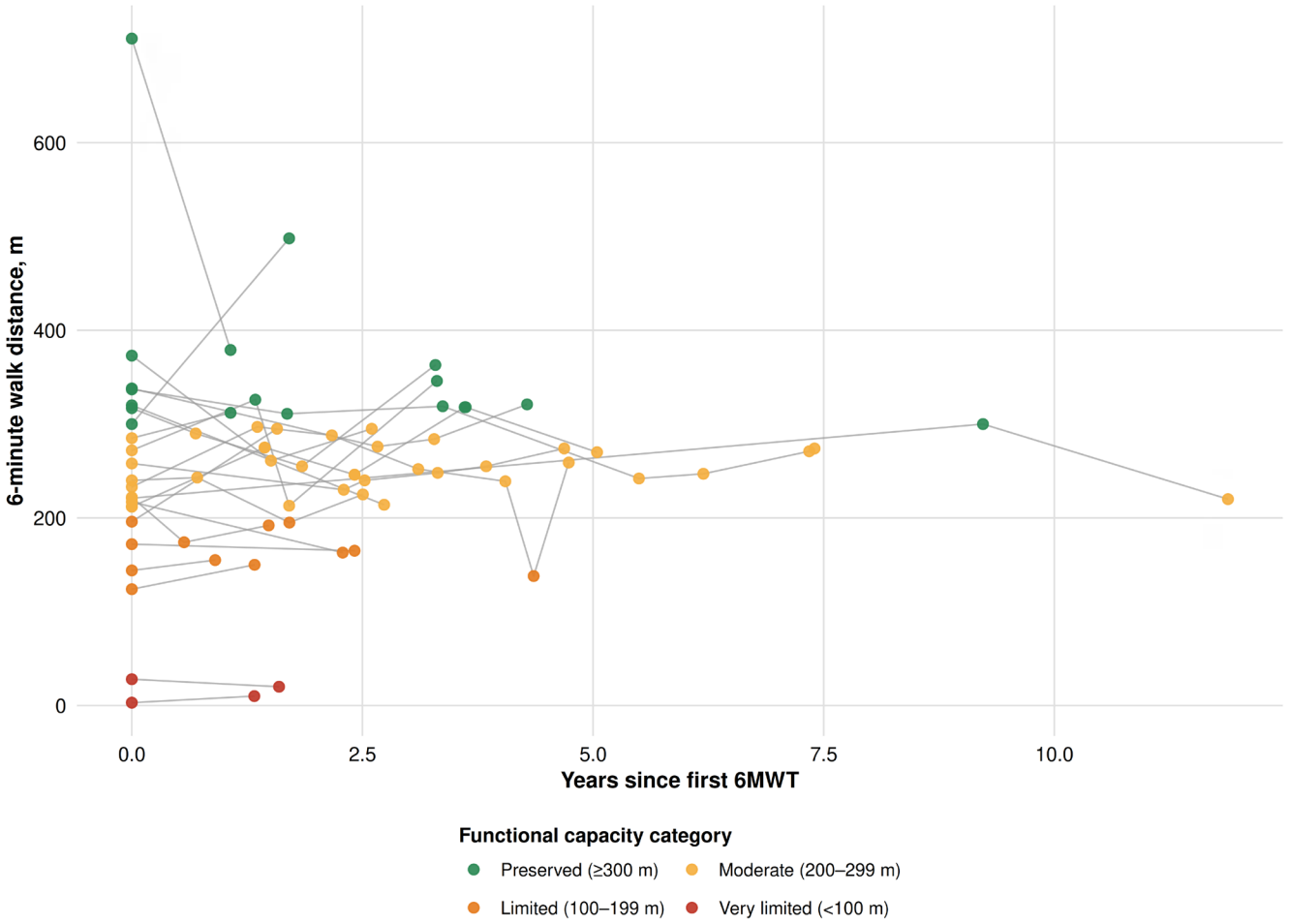


Figure 2. Individual 6MWT trajectories indexed to each patient's first dated test.
Repeated dated 6-minute walk test (6MWT) observations are displayed as years since each patient's first dated 6MWT. Gray lines connect observations from the same patient, and points are color-coded by functional capacity category. This figure is descriptive and is intended to show within-patient heterogeneity during observed follow-up; no regression curve, LOESS smoother, or confidence band is displayed. The figure should not be interpreted as evidence of treatment effect or causal stabilization.

with heterogeneous follow-up trajectories, including relative stability in several patients. It does not negate the age-based association, because the two analyses answer different questions: one compares walking distance across testing ages, while the other describes change after each patient enters the available 6MWT record.

Among molecularly tested patients, homozygous p.Gly301Cys was frequent (13/14), consistent with previous Colombian and Chilean reports [9–11]. This finding supports a hypothesis-generating regional founder-effect interpretation, but it applies only to the tested subgroup. The broadly distributed skeletal involvement observed in this series is compatible with prior descriptions of severe GALNS-associated disease, although incomplete molecular testing and limited genetic heterogeneity precluded formal genotype–phenotype correlation analyses.

The combination of approximately 69% cervical compression, 81% cervical canal narrowing among patients with MRI data, and 55% cervical fixation is consistent with specialized referral practice, where decompression and stabilization are used to prevent or treat cervical myelopathy [4,14]. This estimate may overstate cervical canal narrowing in the full series if MRI was obtained preferentially in patients with neurologic signs, clinical suspicion, or surgical planning needs. Airway and sleep pathology are frequent in Morquio A and are reflected in ENT procedures in this series and in prior work on sleep-disordered breathing [22].

Documented ERT exposure was recorded in 29/31 patients, with median reported duration of 6 years. This variable should not be read as active treatment status at every 6MWT assessment. Published studies report improvement or stabilization in

endurance and selected respiratory measures after ERT, while established skeletal disease often persists [2,12–13]. In this dataset, patient-specific ERT start dates, interruptions, adherence information, and dated surgical timelines were unavailable. The analysis therefore cannot estimate pre/post ERT change, treatment-related stabilization, treatment failure, or perioperative effects on walking distance.

Pulmonary function data remained too sparse for modeling functional-pulmonary coupling. Only three patients had usable FEV1–6MWT paired data, so these results are best treated as an audit of data availability rather than evidence of association. Future prospective cohorts should collect spirometry and 6MWT on synchronized dates to evaluate whether restrictive or obstructive physiology predicts endurance.

Variable-specific denominators were reported because several clinical domains had incomplete documentation. Age, sex, ERT exposure, and several core manifestations were available for nearly all patients, whereas pulmonary testing, cervical MRI, molecular testing, audiology source, walking-aid documentation, treatment timing, adherence, and dated surgical events were incomplete or nonuniformly captured. This pattern affects interpretation: estimates based on tested subgroups, such as pulmonary physiology and cervical MRI findings, should not be treated as population-level prevalence estimates.

Limitations are typical of retrospective referral-center series. Definitions for valvular disease, restrictive or obstructive physiology, corneal involvement, hearing impairment, and radiologic criteria were not standardized across services. Exploratory complete-versus-missing comparisons did not identify statistically detectable differences in age or sex distributions for selected domains, but the small sample limits power to detect imbalance. Dated longitudinal information was usable mainly for the 6MWT. Patient-specific ERT initiation dates, active treatment status, adherence data, treatment interruptions, dated surgical events, and perioperative recovery intervals were unavailable. Referral-center sampling may overestimate complication rates relative to community prevalence, limiting generalizability beyond similar tertiary settings.

Prospective natural-history work with standardized protocols, dated assessments, harmonized definitions, and age-, sex-, and height-adjusted functional references would allow more precise modeling of endurance, respiratory function, cervical disease, treatment exposure, and surgical trajectories. Population-genetic studies could evaluate the founder-effect hypothesis for p.Gly301Cys and inform targeted carrier or newborn screening strategies [1,11]. Pragmatic effectiveness studies in Colombian health systems—accounting for access, adherence, treatment interruptions, and timing—could define real-world ERT outcomes. The therapeutic horizon includes improved enzyme targeting, chaperones, and gene therapy/editing approaches [13], but multidisciplinary care remains the backbone of management today [5,14].

Conclusions

In this referral-center case series from Antioquia, MPS IVA presented with frequent skeletal disease and cervical, respiratory, cardiac, ocular, and auditory involvement. Most patients had documented ERT exposure, but cervical fixation and lower-limb orthopedic surgery remained common. Findings based on tested subgroups, including pulmonary physiology and cervical MRI, should be interpreted with their denominators and referral-based ascertainment in mind.

Dated 6MWT records showed lower walking distance at older testing ages, with marked between-patient variability. In pediatric and adolescent patients, this pattern may reflect failure to gain the walking capacity expected with growth as well as loss of function. Follow-up-indexed trajectories were heterogeneous, and the available data do not support causal claims about ERT effectiveness, treatment failure, surgical effects, or treatment-related stabilization. Future studies should collect synchronized 6MWT, pulmonary function, echocardiography, cervical MRI, treatment dates, adherence, interruptions, surgical timelines, and perioperative recovery intervals using harmonized definitions.

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Ethics Approval and Consent to Participate

The study was approved by the Research Ethics Committee of Universidad Pontificia Bolivariana. Given its observational nature and the use of anonymized clinical data, the research was classified as minimal risk in accordance with Colombian regulations and the principles of the Declaration of Helsinki. Consequently, the requirement for informed consent was waived.

Authors' Contributions

VT-Y, GG Conceptualization. SR-G, AJ-C, IF-S, LL-L, and CB-M Data curation. VT-Y, GG, SR-G, AJ-C, IF-S, LL-L, and CB-M Formal analysis. VT-Y, GG, SR-G, AJ-C, IF-S, LL-L, and CB-M Methodology. VT-Y, GG Validation. VT-Y, GG, SR-G, AJ-C, IF-S, LL-L, and CB-M Writing - original draft. VT-Y, GG, SR-G, AJ-C, IF-S, LL-L, and CB-M Writing - review & editing.

Declaration of Conflicting Interests

The authors declare that the scientific content, data interpretation, and conclusions were developed independently. BioMarin Pharmaceutical Inc. provided support for editorial language and style review and covered the article processing charge. BioMarin did not participate in study design, data extraction, statistical analysis, interpretation of findings, or drafting of the scientific conclusions. BioMarin did not have access to patient-level datasets or analysis scripts.

Data Availability

The dataset analyzed in this study is not publicly available due to institutional and legal restrictions but may be made available upon reasonable request to the corresponding author.

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