Quality of Life Changes in Patients with Alport Syndrome: Results from the ATHENA Study

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Introduction

Alport Syndrome (AS) is a rare genetic disorder caused by mutations in genes coding for type IV collagen (COL4) α3, α4 and α5 proteins leading to hematuria, renal failure, hearing loss and eye involvement.

CKD is associated with progressively worse quality of life (QOL) scores. The presence of a progressive genetic disease can also impact QOL. QOL has not previously been reported in patients with AS. As there is more interest in developing pharmaceutical therapies for Alport syndrome, it will be important to understand the changes in QOL that occur over time in patients with AS in order to understand the impact of any therapeutic intervention on QOL. This study reviewed results of SF-36 QOL surveys in patients with AS who participated in the ATHENA observational study.

Methods

- ATHENA was a prospective international multi-center observational cohort study designed to characterize the progression of renal dysfunction in subjects with AS
- Patients with Alport syndrome were followed up to 24 months with serial collection of kidney function, proteinuria, renal biomarker data
- SF-36 questionnaire completed at baseline and weeks 24, 48, 72, 96 and 120
- Mixed-Effect Model Repeated Measure (MMRM) used to determine impact of variables on SF-36 components
- GFR slope (cc/min/1.73m^2/year) derived using linear regression at subject level based on change from baseline

Methods

- Controlled for
  - Time
  - Baseline SF-36 component score
  - CKD subgroup (Stage 1,2 vs. 3,4)
  - Gender
  - Genetics (autosomal vs X-linked)
  - GFR
  - GFR slope

Table 1
Baseline Characteristics

N	165
Age (range)	44.8 (15-80)
Male (%)	56 (33.9)
Ethnicity (%)	
White	137 (83)
Asian	7 (4.2)
Hispanic	2 (1.2)
African American	1 (0.6)
Other	20 (12.1)
GFR cc/min/1.73m^2 (range)	56.3 (30.8-95.6)
GFR slope/year (SD)	-1.03 (12.42)
Genotype	
COL4A3	44 (26.7)
COL4A4	47 (28.5)
Col4A5	112 (67.9)
Unknown	13 (7.9)
Mutation type	
Missense/splice site	118 (71.5)
Deletion/truncating	26 (15.7)
SF 36 Results (SD)	
Physical Component	52.5 (6.7)
Mental Component	49.7 (10.1)
Physical Functioning	53.5 (5.4)
Role-physical	52.6 (6.9)
Bodily Pain	52.5 (8.7)
General Health	48.1 (9.8)
Vitality	50.8 (9.0)
Social Functioning	50.9 (8.9)
Role-emotional	51.1 (8.3)
Mental Health	50.4 (9.6)

Table 2
Changes in SF-36 Scoring from Baseline

SF-36 Component	Coefficient Estimate (p-value) Time (weeks)	Baseline Score
Bodily Pain	-.02 (.04)	-.5 (<.0001)
General Health	-.017 (.033)	-.24(<.0001)
Mental Comp	-.022 (.019)	-.4 (<.0001)
Mental Health	-.02 (.028)	-.4 (<.0001)
Physical Comp	-.013 (.06)	-.37(<.0001)
Physical Function	-.005 (0.44)	-.36(<.0001)
Role-Emotional	-.027 (.007)	-.48(<.0001)
Role-Physical	-.029 (.001)	-.59(<.0001)
Social Function	-.020 (.037)	-.51(<.0001)
Vitality	-.006 (.483)	-.30(<.0001)

Results

Baseline results (Table 1)

- 165 patients enrolled
- Mean age 44.8 years, 66.1% female
- 67.9% with X-linked mutations
- mGFR 56.3 cc/min/1.73m^2
- SF-36 scores low

Table 2:

- All SF-36 component scores decreased with time except Physical Component, Physical Functionality and Vitality
- Higher baseline SF-36 component scores associated with larger drops with time
- GFR>60cc/min/1.73m2 was associated with higher component scores for General Health and Role-Emotional (not shown)
- Gender and mode of inheritance not associated with changes in SF-36 scores (not shown)
- Physical Functionality and Vitality not associated with changes in SF-36 results in any model

Discussion

- Patient-centered outcomes increasingly important when designing clinical trials
- QOL scores decrease with GFR in CKD
- Patients with AS have additional factors that impact QOL: Hearing and vision involvement, having rare progressive inherited disease without proven therapy
- The ATHENA trial was first prospective cohort trial to characterize QOL changes over time in patients with AS
- QOL, as measured by SF-36, was low for the study cohort regardless of GFR, comparable to advanced CKD population
- All SF-36 components significantly decreased with time, regardless of baseline GFR or slope of GFR decline
- Higher SF-36 component scores at baseline were associated with larger decreases in scores over time
- Baseline CKD stage, gender and mode of inheritance did not significantly impact QOL scores

Conclusions

- Patients with Alport syndrome have low QOL as measured by SF-36
- QOL scores similar to CKD 3b, 4
- Higher baseline QOL associated with larger decreases over time
- Female gender and mode of inheritance did not impact QOL scores
- Understanding QOL in Alport syndrome is important when planning trials to assess impact of therapy on QOL

References

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