The Patient and Clinician Point of View: Living With Late-onset Pompe Disease

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INTRODUCTION

- Pompe disease is a rare autosomal recessive inherited glycogen storage disorder caused by deficiency of the lysosomal enzyme acid α-glucosidase (GAA), causing accumulation of lysosomal glycogen in predominantly cardiac, skeletal, and smooth muscle tissues[1]
- Glycogen accumulation within tissues leads to a broad spectrum of clinical manifestations, involving progressive debilitation, organ failure, and/or death[1]
- Late-onset Pompe disease (LOPD), with disease onset occurring after age 1 year, is characterized by progressive muscle weakness and respiratory insufficiency[1,2]
- Enzyme replacement therapy (ERT) with recombinant human GAA is approved as definitive therapy for LOPD; other management strategies include musculoskeletal rehabilitation, cardiopulmonary and gastrointestinal support, and dietary management[2,3]
- We conducted surveys to better understand the burden of LOPD from the perspectives of patients and physicians

OBJECTIVE

- To improve understanding of the impact of LOPD on patients' lives

METHODS

- Adult patients with LOPD (aged ≥18 years) were recruited to take the Pompe Patient Survey through patient associations
- Patients interested in participating who met the eligibility criteria were scheduled for a 1-hour telephone interview using a 304-question patient survey, which was administered by a trained professional
- Physicians treating adults with LOPD completed an online survey
- Both surveys collected information on demographics, disease, treatment, and effect on daily living and employment

RESULTS

Demographics

- Patients: There were 102 patient respondents from the United States; 59% were female; mean age at diagnosis was 38.3 years (standard deviation [SD], 14.1) (**Table 1**)
  - Fifty-eight (57%; N=102) patients were diagnosed by a neurologist
- Physicians: 15 physician respondents (13 physicians, 1 Pompe treatment center coordinator, and 1 metabolic disease unit coordinator) reported on the Pompe disease management of 21 physicians and their patients (n=406) (**Table 1**)
  - Physician respondents were from 9 countries: United States (n=5), Germany (n=2), Italy (n=2), Australia, Brazil, Canada, Spain, Taiwan, and United Kingdom (n=1 each)
  - The most common specialties of the treating physician were neurology (n=5) and pediatrics (n=4)

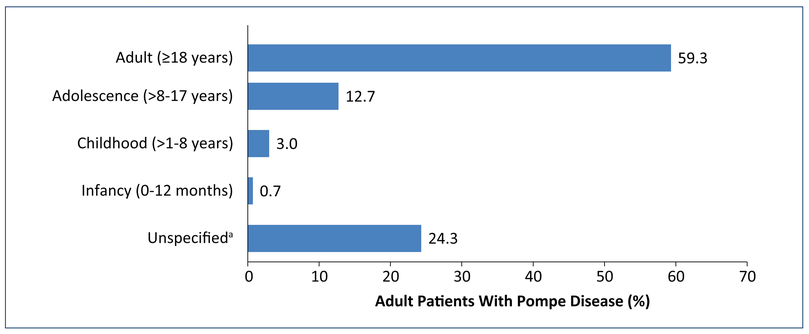
Table 1. Demographics of Survey Respondents

Patient Survey (N=102)	
Sex, n (%)	
Female	60 (58.8)
Male	42 (41.2)
Age, years, mean (SD)	
Current age	47.5 (13.2)
Age at diagnosis	38.3 (14.1)
Years since diagnosis, mean (SD)	9.2 (7.6)
Physician Survey (N=15)	
Years in practice (n=21), mean (SD) [range]	20.6 (8.4) [1-37]
Years treating patients with Pompe (n=21), mean (SD) [range]	11.2 (6.0) [1-20]
Percent of the practice devoted to the care of patients with Pompe disease, mean (SD) [range]	12.2 (10.4) [1-30]
Number of patients with LOPD routinely managed by their practice, mean (SD) [range]	27.1 (29.4) [4-100]

LOPD=Late-onset Pompe disease; SD=standard deviation

- Physicians stated that nearly 60% (159/268) of their patients with LOPD were diagnosed during adulthood (age ≥18 years) (**Figure 1**)

Figure 1. Physician Survey: Age at Diagnosis for Adult Patients With Pompe Disease (n=268 patients)



[a]Three physicians (accounting for 65 adult patients) did not answer this question.

Disease Diagnosis

Physician Survey

- The most common misdiagnoses were limb girdle dystrophy (LGMD; physician respondents, n=12), muscular dystrophy (n=7), polymyositis (n=6), and fibromyalgia (n=6)
- LOPD was commonly diagnosed using genotyping (DNA test), which was used in 86% of patients tested, and resulted in a diagnosis in 83% of respondents' patients
  - Eighty-five percent (345/406) of patients were cross-reactive immunologic material (CRIM)–positive; 2% (9/406) were CRIM-negative
  - Conversely, only 16% (16/102) of patients in the patient survey stated that they knew their Pompe mutations

Treatment

Physician Survey

- Most patients visited their physician every 6 months (57%) or annually (35%)
- Mean duration of first ERT infusion was 4.3 hours (SD, 1.1)
- Satisfaction with efficacy and tolerability of ERT were rated as 4.7/10 and 7/10, respectively, based on a 10-point scale (0=not at all; 10=extremely)
- Thirty-three percent (5/15) of physicians reported infusion-associated fatigue in their patients

Patient Survey

- Approximately half of patients (49%; 50/102) reported being cared for by a cardiologist: 28% (29/102) had received a cardiac magnetic resonance imaging test, 89% (91/102) had received an echocardiogram, and 88% (90/102) had received an electrocardiogram
- Almost all (97%; 99/102) patients with LOPD reported ever receiving ERT, with 95 patients currently receiving ERT
  - Ninety-six percent (91/95) receive ERT every 2 weeks; 4% (4/95) receive ERT weekly
- Mean delay between diagnosis and starting ERT was 4.0 years (SD, 5.8) and mean age at ERT initiation was 42.2 years (SD, 13.8)
- Sixty-seven percent (64/95) of patients reported a mean infusion duration between 4-5.9 hours; 17% (16/95) reported a duration of 6-7.9 hours and 4% (4/95) a duration of 8-9.9 hours
- Satisfaction with efficacy of ERT was rated as 7.2/10 and tolerability as 8.7/10
- Infusion-associated fatigue was reported by 36% (34/95) of patients

Effect on Daily Living and Employment

- Physicians reported that 115/268 (43%) and 41/268 (15%) patients had moderate and severe limitations in walking/moving around, respectively
- Seventy percent (68/97) of patients reported difficulty getting up from a lying or sitting position all of the time (**Table 2**)

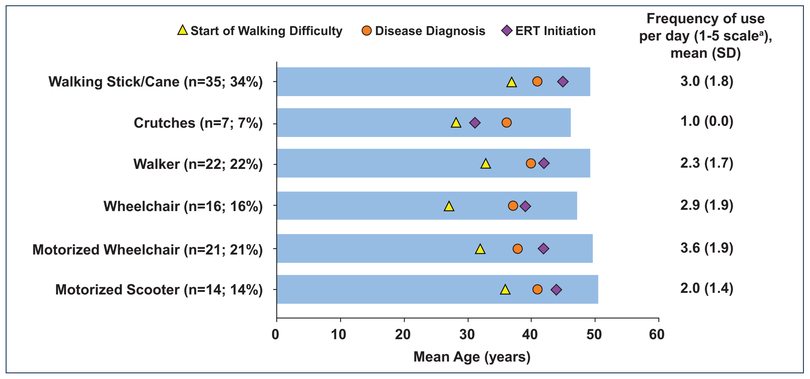
Table 2. Summary of Daily Living and Employment Difficulties

	Physician Survey	Patient Survey
Mobility	43% and 15% of patients had moderate or severe limitations, respectively	81% and 58% had limitations or required assistance in walking and moving around, respectively
Getting up from lying position	67% of patients had significant difficulty	89% of patients reported difficulty
Swallowing or respiratory difficulty	19% of patients had difficulty swallowing	57% of patients required respiratory assistance; 1/3 reported respiratory infection within the last year
Employment/ school	56% of patients were working or in school	41% of patients were employed or in school 63% of unemployed patients reported that Pompe disease was the reason for unemployment Working patients missed an average of 2.1 work days per month due to infusions
Out-of-pocket expenses	Mean $385 (SD, $744) per infusion for US-based respondents Mean $56 (SD, $76) per infusion for non-US-based respondents	27% of patients reported out-of-pocket ERT expenses Average financial burden of infusion therapy was 2 (based on 1-4 scale)

ERT, enzyme replacement therapy.

- Limits in walking and moving around all of the time were reported by 57 (56% ; N=102) patients (**Figure 2**)
  - Patients used a mean of 2 different devices with more than 10% of patients requiring the use of 6 different devices

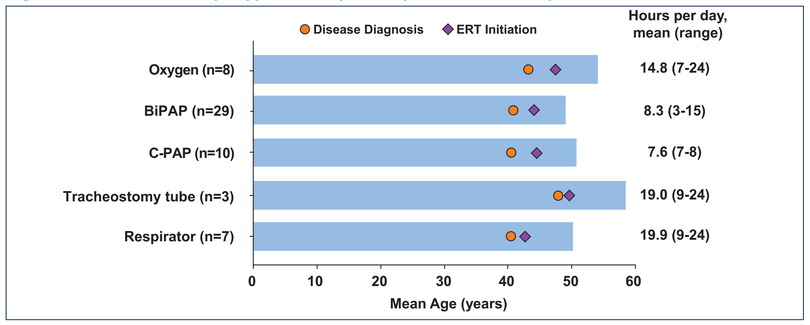
Figure 2. Patient Survey: Devices Used for Assistance With Walking and Moving Around (N=102)



Length of bar indicates current mean age of patient group.
Patients could use more than one device.
[a]1=a little of the time; 5=all of the time.

- Fifty-seven percent (58/102) of patients reported using some kind of respiratory assistance (**Figure 3**)

Figure 3. Patient Survey: Type of Respiratory Assistance Required



BiPAP=bilevel positive airway pressure; C-PAP=continuous positive airway pressure.
Length of bar indicates current mean age of patient group.
Three patients used 2 types of respiratory assistance (BiPAP and oxygen; tracheostomy and oxygen; respirator and tracheostomy); 1 patient used 3 types of respiratory assistance (respirator, tracheostomy, and diaphragmatic pacemaker). Nine patients reported using another type of respiratory assistance than shown in the figure.

- Twenty-six percent (27/102) of patients had difficulty swallowing, with a mean age of difficulty onset of 38 years (SD, 18.9)
- Six percent (5/101) of patients required a G-tube for feeding; the mean age when G-tube feeding started was 9.6 years (SD, 10.9)

CONCLUSIONS

- The survey confirms that there is considerable misdiagnosis of LOPD with other more common inherited muscle disorders, such as LGMD, because of similarities in phenotype
- There is a significant delay (approximately 4 years) between diagnosis and initiation of ERT; delay in diagnosis is also related to earlier wheelchair use
- Survey results demonstrate the significant burden of LOPD on physical, social, and financial quality of life
  - By age 46, 58% of surveyed patients required ambulatory assistance devices
  - More than 50% of patients required respiratory assistance
- Swallowing difficulty is under-recognized; our survey indicated that about one fourth of patients have dysphagia, which is higher than reported in the literature
- There is a discordance between the physicians' perception and patients' own report regarding the impact of Pompe disease on mobility and employment. Physicians tend to underestimate the burden of disease

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DISCLOSURES

Conflicts of Interest

NP, S Sathe, VJ, CV, JAB, and S Sitaraman are employees of and hold stock in Amicus Therapeutics. KP does not have anything to disclose.

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