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Living With Late-Onset Pompe Disease: The Patient and Physician Point of View

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BACKGROUND

- 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 and the current approaches to diagnosis and treatment of this disease

METHODS

- Adult patients with LOPD (aged ≥18 years) were recruited for the Pompe Patient Survey through patient associations
- Patients interested in participating who met the eligibility criteria were scheduled for a 1-hour telephone interview based on the 304-question patient survey 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

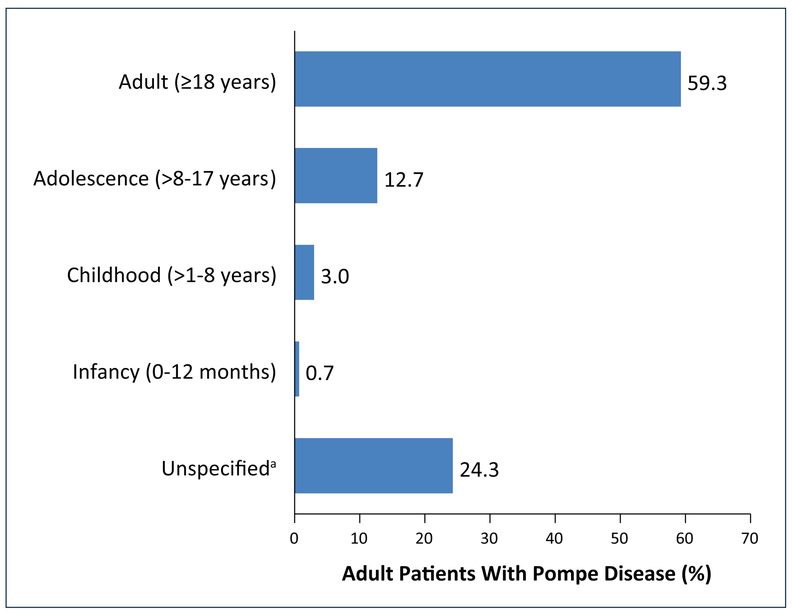
- Patients: There were 102 patient respondents; 59% were female
  - Mean (standard deviation [SD]) age at diagnosis was 38.3 (14.1) years (**Table 1**)
  - Fifty-eight (56.9%) patients were diagnosed by a neurologist
- Physicians: 15 physician respondents (13 physicians, 1 Pompe treatment center coordinator, and 1 metabolic disease unit coordinator) reported on the patients and Pompe disease management of 21 physicians
  - Physician respondents were from 9 countries: the United States (n=5), Germany (n=2), Italy (n=2), and Australia, Brazil, Canada, Spain, Taiwan, and the United Kingdom (n=1 each)
  - The most common specialties of the treating physician were neurology (n=5) and pediatrics (n=4)
- Nearly 60% of physicians stated that their patients with LOPD were diagnosed during adulthood (age ≥18 years) (**Figure 1**)

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	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]

SD=standard deviation.

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 (n=12 physician respondents), muscular dystrophy (n=7), polymyositis (n=6), and fibromyalgia (n=6)
- For the diagnosis of LOPD, genotyping (DNA test) was the most commonly employed test (85.7% of patients tested), resulting in a diagnosis in 83.3% of respondents' patients (**Table 2**)
  - Eighty-five percent of patients were cross-reactive immunologic material (CRIM)–positive; 2.2% were CRIM-negative
  - On the other hand, only 16 (16%) patients in the survey stated that they knew their Pompe mutations

Table 2. Physician Survey: Tests Used for Pompe Diagnosis and Percentage of Patients Diagnosed From Test

Test Used for Pompe Diagnosis[a]	Respondents Using Test (N=15), n	Patients Who Underwent Test (N=406), n (%)
Genotyping-DNA test	13	348 (85.7)
Dried blood spot	13	165 (40.6)
Muscle biopsy	13	100 (24.6)
Enzyme assay-serum	9	148 (36.5)
Skin biopsy	8	34 (8.4)
Other (unspecified)	1	5 (1.2)

[a]For those who said yes for a specific test, the number of patients not accounted for was 54 for the genotyping-DNA test, 54 for the dried blood spot test, 44 for the muscle biopsy, 38 for the enzyme assay-serum, and 32 for the skin biopsy.

Treatment

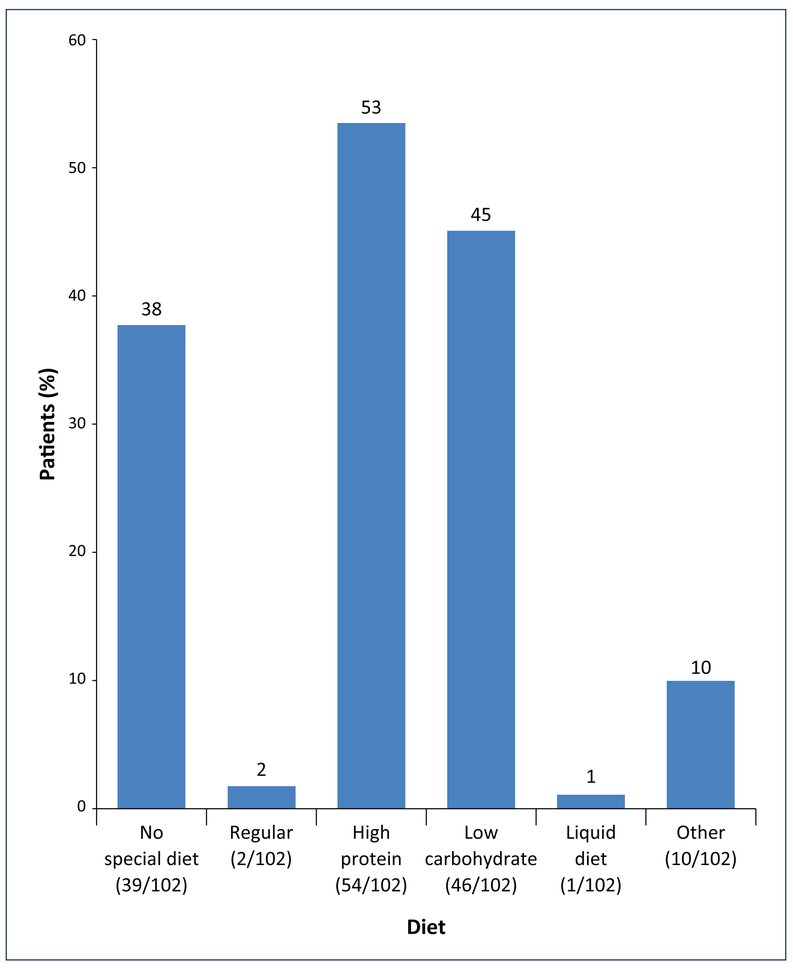
Physician Survey

- Most of the patients visited their physician every 6 months (56.7%) or annually (34.7%)
- Mean (SD) duration of first ERT infusion was 4.3 (1.1) hours
- Efficacy and tolerability of ERT were rated as 4.7/10 and 7/10, respectively
- Infusion-associated fatigue was reported in 22.8% of patients

Patient Survey

- Approximately half of patients (49%) reported being cared for by a cardiologist: 28% had received a cardiac magnetic resonance imaging test, 89% had received an echocardiogram, and 88% had received an electrocardiogram
- A range of diets were reported by patients (**Figure 2**); however, only 17% of patients were followed by a nutritionist/dietician

Figure 2. Patient Survey: Type of Diet[a]



[a]Patient responses in the "Other" Category included gluten free (n=2); gluten free due to celiac disease; avoids processed food; can't eat much due to gastrointestinal problems, get bloated and spends hours burping so she does not eat much; feeding tube at night; mechanical soft; no sweets or carbs; chooses to eat healthy on her own not based on a diet; she struggles with it.

- Almost all (n=99; 97%) patients with LOPD reported receiving ERT; 96% receive ERT biweekly whereas 4% receive ERT weekly
- Mean (SD) age at the initiation of ERT was 42.2 (13.8) years
- Mean (SD) delay between diagnosis and starting ERT was 4.0 (5.8) years
- Sixty-seven percent of patients reported the mean duration of infusion to be 4-5.9 hours; 16.8% reported it as 6-7.9 hours and 4.2% as 8-9.9 hours
- The efficacy of ERT was rated as 7.2/10 and tolerability as 8.7/10
- Infusion-associated fatigue was reported by 35.8% of patients

Effect on Daily Living and Employment

- Physicians reported that 115 (42.9%) and 41 (15.3%) patients had moderate and severe limitations, respectively
- Sixty-eight (70.1%) patients reported difficulty with getting up from a lying or sitting position all of the time (**Table 3**)

Table 3. Summary of Daily Living and Employment Difficulties

	Physician Survey	Patient Survey
Mobility	42.9% and 15.3% of patients had moderate or severe limitation, respectively	81% and 58% had limitations or required assistance in walking and moving around, respectively
Getting up from lying position	66.8% of patients had significant difficulty	88.7% of patients reported difficulty
Difficulty in swallowing	19.4% of patients	26% of patients reported trouble swallowing; 6% required a G-tube for feeding
Respiratory assistance	--	57% of patients required respiratory assistance; 1/3 reported respiratory infection within the last year
Employment/ school	56.3% of patients were working or in school	41.2% 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 (SD)	$385 ($744) per infusion for US-based respondents $56 ($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%) patients (**Table 4**)

Table 4. Use of Devices for Assistance With Walking and Moving Around

Device	Physician Survey		Patient Survey	
	Respondents, n (N=15)	Patients Using the Device, n (%) (N=268)	Patients Using the Device, n (%)	Frequency of Use Per Day on a Scale of 1 to 5[a], Mean (SD)
Walking stick/cane	11	71 (26.5)	35 (34.3)	3.0 (1.8)
Wheelchair	9	30 (11.2)	16 (15.7)	2.9 (1.9)
Walker	8	27 (10.1)	22 (21.6)	2.3 (1.7)
Motorized scooter	7	15 (5.6)	14 (13.7)	2.0 (1.4)
Motorized wheelchair	6	16 (6.0)	21 (20.6)	3.6 (1.9)
Crutches	4	4 (1.5)	7 (6.9)	1.0 (0.0)
Other (unspecified)	1	1 (0.3)	3 (2.9)	5.0 (0.0)

[a]1=a little of the time; 5=all of the time.

- Fifty-eight patients reported using some kind of respiratory assistance (**Table 5**)
- Respiratory infections in the last year were reported by about one-third of patients

Table 5. Patient Survey: Type of Respiratory Assistance Required

Type[a]	Yes, n (%)	Hours Per Day, Mean (range)
BiPAP	29 (50)	8.3 (3–15)
C-PAP	10 (17.2)	7.6 (7–8)
Oxygen therapy	8 (13.8)	14.8 (7–24)
Respirator	7 (12.1)	19.9 (9–24)
Tracheostomy tube	3 (5.2)	19.0 (9–24)
Other[b]	9 (15.5)	-
No response	2 (3.4)	-

BiPAP=bilevel positive airway pressure; C-PAP, continuous positive airway pressure.
[a]Three patients had 2 types of respiratory assistance (BiPAP and oxygen, tracheostomy and oxygen, and respirator and tracheostomy) and 1 patient had 3 types of respiratory assistance (respirator, tracheostomy, and diaphragmatic pacemaker)
[b]Answers in the "Other" category included: diaphragmatic pace maker; nebulizer and inhaler; ventilator 24 hours; G tube overnight for nutritional assistance (8 hours); will be starting C-PAP next week, patient is unable to walk or breathe on own; patient weight 375 lbs and requires help all the time to move; if a lot of walking is required, uses a wheelchair, is looking at a lift chair, hand rails in restrooms; currently being evaluated, just recently diagnosed.

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
- High-protein/low-carbohydrate diet was followed by half the patients; the majority of the patients did not seek a nutritionist's advice on their diet
- Dysphagia is underrecognized in LOPD; about one-fourth of patients may suffer from difficulty swallowing
- Infusion-related fatigue is common in patients with LOPD
- Respiratory-tract infections are frequent, with a third of the patients reporting at least 1 within the past year

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DISCLOSURES

Conflicts of Interest

NP, S Sathe, CV, JAB, and S Sitaraman are employees of and hold stock in Amicus Therapeutics. DD serves as a consultant for Amicus Therapeutics.

For questions, please contact Sheela Sitaraman at ssitaraman@amicusrx.com.

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