Quality of Life and Its Contributors Among Adults With Late-onset Pompe Disease in China

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Research

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**Abstract**

**Background:** Pompe disease (PD), also known as glycogen storage disease type II, is an inherited disorder caused by the deficiency of acid-β-glucosidase (GAA) [1]. PD is generally classified into two forms: (1) infantile-onset PD (IOPD) when the disease is characterized by cardiomyopathy, respiratory insufficiency, and severe muscle hypotonia, and presents during the first year of life, and (2) late-onset PD (LOPD), which encompasses the remaining patients with PD who can present at less than 12 months without cardiomyopathy or present after 12 months [2]. In patients with PD, the accumulation of glycogen in the skeletal muscles, heart, liver, and nervous system causes a decline in their quality of life (QOL) and finally leads to disabilities or even death [3, 4].

The prevalence of PD is related to ethnicity or the geographic area studied [5]. According to a recent study in Taiwan, the birth prevalence of IOPD in Taiwan is 1 in 52,000, and of LOPD is about 1 in 25,000 [6]. Since mainland China does not have its own official estimates, using the Taiwanese birth prevalence as a proxy, and the number of new births in China in 2018 (15,230,000), the number of individuals born with IOPD in China in 2018 can be estimated to be at 293 (52,000/15,230,000), and individuals with LOPD at 609 (25,000/15,230,000). Although having a relatively small population size, PD is one of the 5% of all rare diseases that have certain treatments, most of which are labeled orphan drugs that often imply a small consumer market, a high price, and a heavy financial burden for their patients. As a result, the quality of life in patients with PD and those associated with them is of great concern.

International studies found that LOPD negatively influences QOL in physical health domains, while inconsistent evidence was found for QOL in mental health and functional-emotional domains [7–9]. Despite the negative consequences of PD on physical health, ongoing and chronic illness stressors may induce emotional and cognitive adjustments to the disease. Some patients may handle the psychological burden of PD relatively well, while others may not [10]. Variations in the QOL of patients with LOPD were observed across countries and ethnicities. For instance, the International Pompe Survey found that among 210 patients with LOPD in five countries, patients in the United Kingdom had significantly lower scores in vitality but much higher scores in perceived general health than American, Australian, German, and Dutch patients [8]; and in other dimensions, i.e., social and emotional functioning, Australians performed the worst among the five focal countries. Despite the emphasis on international and inter-racial variations, previous studies were mainly conducted in Europe and North America, while the situation in China has never been comprehensively reported.

Among the very few studies on the determinants of QOL in patients with PD, those in Western societies have emphasized enzyme replacement therapy (ERT) as a significant promoter of QOL, especially at the early stages of treatment. However, adverse infusion reactions have also been reported [11]. In China, it is estimated that the average annual cost of ERT for an adult PD patient is around RMB 3,000,000 (1 USD ~ 7 RMB), which is over four times the average annual household income for a Chinese family. Considering the low coverage rate of social and commercial insurance for ERT, Chinese patients with PD are fully exposed to the potentially catastrophic consequences of the disease. By the end of 2017, among the 61 patients with PD (including both IOPD and LOPD) who were registered to a national PD patient organization, only 12 had ever used the only available ERT in China, alglucosidase alfa. Among these 12, only four patients had used the medicine continuously, and none had used it up to the dosage approved by the National Medical Products Administration (i.e., 20 mg/kg every other week [12]. From 2014 to 2018, 14 child patients with PD passed away, and 11 of them had never used the drug due to unaffordability [12]. Considering the high cost and low coverage of ERT, the levels and determinants of QOL are of great concern in Chinese adult patients with LOPD. Therefore, the main objective of this study was two-fold: (1) to assess the QOL of adult patients with LOPD in China, and (2) to explore the social and economic factors that may contribute to it.

**Background:**

Pompe disease (PD) is a rare inherited disorder caused by the deficiency of acid-β-glucosidase, which leads to the impairment of organ and tissue functions and causes disabilities. As the first national survey on patients with late-onset PD (LOPD) in China, this study investigated the quality of life (QOL) of adult patients with LOPD in China and explored its contributors.

**Methods:** Data were derived from a nation-based, cross-sectional, self-response survey on rare diseases in early 2018. Answers from 68 adult Chinese patients with LOPD were used for data analysis. QOL was measured using the World Health Organization Quality of Life: Brief Version (WHOQOL-BREF). Covariates included age, gender, education, employment, reliance on assistive devices, medication history, social support, and disease economic burden. Data were analyzed using linear regression in R.

**Results:** For adult patients with LOPD, the average scores and standard deviations (SD) of the four dimensions of QOL were physical health=33.77 (SD=18.28), psychological health=43.81 (SD=21.70), environmental health=39.43 (SD=16.93), and social relationship=46.20 (SD=19.76); the scoring for each dimension was evaluated on a scale of 0 to 100. At the significance level of p<0.05, with increasing age, the patients experienced a significant decrease in physical health QOL (β = 0.75) and environmental health QOL (β = 0.79). Those who relied heavily on assistive devices had lower perceived physical health (β=17.8), psychological health (β=22.76), environmental health (β=17.8), and social relationships (β=22.12) than those who did not. A one-unit increase in the amount of social support, as a form of social interaction, led to a significant increase in physical health (β=0.28), psychological health (β=0.71), environmental health (β=0.72), and social relationships (β=0.70).

**Conclusion:** Adult Chinese patients with LOPD had a lower physical health and QOL compared to their counterparts with other rare diseases. Being employed was found to affect the QOL of adult Chinese patients with LOPD in almost all dimensions. Encouraging adult Chinese patients with LOPD to be socially active and help them become more involved in social life might improve their QOL.
**Methods**

**Sampling methods**

The data used for this research were derived from a large, nation-based, cross-sectional survey among people affected by rare diseases in China in 2018 [13–15]. Since no complete sample frame of rare disease patients exists due to the fact that the epidemiological information of these people is largely unknown in China, a non-probability convenience sampling method was used to recruit participants in collaboration with a variety of national rare disease patient organizations, namely the Illness Challenge Foundation and its "29 + Alliance" for rare disease patient organizations, including the China Pompe Care Center (CPCC), the only national Pompe patient organization in China. The survey details were distributed via online and offline social networks. Individual patients also shared recruitment information.

**Procedure**

The survey was conducted primarily online (www.wenjuan.com) to maximize accessibility to the dispersed population. It was approved by the Committee on the Use of Human and Animal Subjects in the Teaching and Research of Hong Kong Baptist University (No: FRG2/15–16/052).

Although the survey was self-administered, previous studies have shown that this type of survey could yield a higher response rate than the physical mail survey and more accurate results than the telephone survey [16, 17]. Participants followed a link to the survey website. Informed consent was obtained from the participants before they were presented the questionnaire. At the beginning of the questionnaire, a series of questions were used to identify the target respondents of the survey (i.e., people affected by rare diseases in China). Patients under 18 were asked to end the survey and refer the survey link to their legal guardians. Main caregivers and patients were identified and assigned to one of the two versions of the questionnaire. The two versions covered the same measures, but the questions were formed differently to retrieve more accurate answers. The survey was conducted from January 1 to February 15, 2018.

**Pompe patients in this study**

In total, 2,007 valid responses, including responses from 92 Pompe patients, were collected in the 2018 survey, which covered 94 distinct types of rare diseases. Although small in number, the 14 patients with IOPD and 78 patients with LOPD were all Pompe patients with a definitive clinical diagnosis and had registered with the CPCC by the time of the survey. In other words, these 92 patients comprised the entire population of Pompe patients that could be reached in China by February 15, 2018. In comparison, a newly published article on the Pompe registry in China mentioned that it has only 78 registered patients [18]. Thus, our sample was, in fact, a complete set of all possible observations on Chinese Pompe patients at the time of the survey.

Among the 78 surveyed patients with LOPD, 62 were adults and 16 were children. Since the scales we used to examine QOL and social support were personal measures, only adult rare disease patients could answer these questions by themselves. Hence, to maximize the reliability and accuracy of the answers, this study only included 68 adult patients.

**Measurements**

**Dependent variable: Quality of life**

Quality of life was measured by the World Health Organization Quality of Life: Brief Version (WHOQOL-BREF), which was developed collaboratively by experts around the world and has been widely field-tested [19]. In an international survey of 11,830 adults from 23 countries, the WHOQOL group reported that WHOQOL-BREF was a reliable and cross-culturally valid assessment of QOL across all four domains [20]. According to the same research, the Cronbach's alpha for the four domains in a Chinese sample was acceptable for the physical domain (0.82), the psychological domain (0.89), the social domain (0.76), and the environment domain (0.70). In addition, WHOQOL-BREF was extensively used in China to measure the QOL of older adults [21], patients with specific diseases [22–25], and patients with rare diseases [26]. The WHOQOL-BREF assesses individuals' perceptions in the context of their culture and value systems and their personal goals, standards, and concerns. The instrument comprises 26 items that measure the following broad domains: physical, psychological, social relationships, and environment. The physical domain refers to the pain, energy, sleep, mobility, activities, medication, and work of a patient. The psychological domain emphasizes patients' positive/negative feelings, cognitions, self-esteem, body image, and spirituality. The social domain evaluates personal relationships, and social and sex activities. The environmental domain focuses on patients' subjective perceptions of safety, home environment, leisure, transportation, and health/social facilities [19, 20]. A guideline published by the WHO illustrated in detail the scores calculated for each domain [19]. The calculated maximum score is 100 in all domains, and scores are scaled in a positive direction (i.e., higher scores denote higher levels of quality of life). It has been noted that the cut-off for the WHOQOL-BREF varies among different groups of people. Elderly studies found a critical value of 60 as the best cut-off point [27]. Yet another study on urban residents in China revealed that the two cut-off standards for low QOL, "70% of the maximum score" and "1 SD below the mean", produced very different results for the probable prevalence of low QOL in the population under investigation [28].

**Independent variables**

The independent variables in this study included sociodemographic variables (age, gender, education, employment status, and residence), medication history, disease economic burden, reliance on assistive devices, and social support.
Medication history was assessed by asking the respondents whether they received ERT with recombinant human GAA (rhGAA, Myozyme) during the past 12 months. Economic burden was measured in terms of catastrophic health expenditure (CHE). When the cost of treatment for a disease exceeds a certain percentage of income, the disease is considered to cause CHE for the patient. There is no commonly accepted criterion for defining CHE [29], and it varies from 10% of income [30, 31], or 10% of household consumption [32] to 40% of disposable income [33, 34]. In this study, we regarded out-of-pocket health expenditures in excess of 10% of annual family income as an indicator of CHE. Reliance on assistive devices is an important indicator of disability status, and was measured with patients’ self-reports on the degree to which they needed to rely on assistive devices in their daily lives. Social support was measured with the Chinese Mandarin version of the Medical Outcomes Study Social Support Survey (MOS-SSS-CM), which is a brief, multidimensional, self-administered instrument developed for patients with chronic conditions and has been validated previously among patients in mainland China [35]. The MOS-SSS-CM consists of 20 questions. One single item measured the structural support by asking “How many close friends and relatives (refers to people who you can get along with and talk about your concerns) do you have?”. The other 19 items measured functional support from four subscales (emotional/informational support, tangible support, affectionate support, and positive social interaction) [36].

Data analysis

In this study, the QOL was analyzed as sub-dimensional scores rather than a total score in order to reveal more specific information. Descriptive analyses included means and standard deviations of the continuous variables and percentages of categorical data. Univariate analysis of QOL included a t-test for binary variables, ANOVA test for categorical variables with more than two categories, and the Pearson correlation test for continuous variables.

To help understand that a certain contributing factor in excess could reduce the QOL and vice versa, we conducted a multivariable linear regression. Variables with $p < 0.1$ in the univariate analysis were included in the linear regression for multivariable analysis. All statistical analyses were conducted using R software (version 3.5.0), including packages of dplyr (version 0.8.0.1) and stats (version 3.6.0). Statistical significance was defined as $P < 0.05$.

Results

Descriptive statistics
Table 1
Basic descriptive statistics

|                                | Adult patients with LOPD | Adult patients with other rare diseases (Non-Pompe) | p-value |
|--------------------------------|--------------------------|-----------------------------------------------------|---------|
| **Age (years)**                | 30.00(7.39)              | 35.71(11.21)                                        | < 0.001 |
| Age at the onset of symptoms   | 20.68(6.71)              | 22.06(15.60)                                        | 0.148   |
| Time between the onset of symptoms and first time to seek diagnosis | 0.12(4.73)              | 2.75(6.28)                                         | < 0.001 |
| Time between the first time to seek diagnosis and being diagnosed | 4.25(5.03)              | 3.23(6.25)                                         | < 0.001 |
| **Gender (= male%)**           | 47.06(32/68)             | 46.20(493/1,067)                                    | 0.991   |
| **Education(%)**               |                          |                                                    |         |
| Primary school or lower (6 year of edu) | 7.35(5/68)              | 12.00(128/1,067)                                   | 0.505   |
| Middle school (9 year of edu)  | 22.06(15/68)             | 21.84(233/1,067)                                   |         |
| High school or above (12 year of edu) | 70.59(48/68)            | 66.17(706/1,067)                                   |         |
| **Employment (= yes%)**        | 20.59(14/68)             | 52.67(562/1,067)                                   | < 0.001 |
| **Catastrophic health expenditure (CHE) (= yes%)** | 67.21(41/61)            | 70.03(687/981)                                     | 0.748   |
| **Rural/Urban (= rural%)**     | 35.29(24/68)             | 24.55(262/1,067)                                   | 0.067   |
| **Reliance on Assistive Devices (%)** |                      |                                                    |         |
| None                           | 8.82(6/68)               | 57.73(616/1,067)                                   | < 0.001 |
| Some                           | 50.00(34/68)             | 27.09(289/1,067)                                   |         |
| A lot                          | 41.18(28/68)             | 15.18(162/1,067)                                   |         |
| **Medicated (= yes% "used ERT in the past 12 months")** | 10.29(7/68)             | -                                                   |         |
| **Social Support (out of 100 points)** |                      |                                                    |         |
| Tangible support               | 72.87(15.72)             | 64.78(20.43)                                        | < 0.001 |
| Emotional/informational support| 55.70(16.01)             | 54.86(18.21)                                        | 0.680   |
| Positive social interaction    | 52.65(15.85)             | 53.72(18.89)                                        | 0.594   |
| Affectionate support           | 55.78(17.35)             | 56.48(20.10)                                        | 0.751   |
| Structural support             | 5.63(5.83)               | 5.62(10.25)                                         | 0.990   |
| **Quality of Life (out of 100 points)** |                      |                                                    |         |
| Physical health                | 33.77(18.28)             | 48.22(20.87)                                        | < 0.001 |
| Psychological health           | 43.81(21.7)              | 43.25(20.76)                                        | 0.837   |
| Environmental health           | 39.43(16.93)             | 42.70(17.80)                                        | 0.127   |
| Social relationships           | 46.20(19.76)             | 48.56(19.54)                                        | 0.342   |

† SD refers to the standard deviation. "-" means ERT is not available or applicable to adult patients with other rare diseases under our survey.

Table 1 summarizes the main variables investigated in this study. A total of 68 adult patients with LOPD were included in the study. To better outline Pompe patients' social, medical, and economic characteristics, we compared them with those of patients with other rare diseases who participated in the same cross-sectional survey.
The average age of adult patients with LOPD was 30 years. The male-to-female ratio was around 1:1.1. About two-fifths of the participants lived in rural areas. More than 92% of them completed the nine-year mandatory education (or reached the level of middle school), while more than 70% completed 12 years of education (or reached the level of high school or above). Approximately one in five adult patients with LOPD is currently employed. Only 10% of the 68 patients used Myozyme in the past 12 months, and their average age was younger than that of non-users (27.9 years vs. 30.2 years). Nevertheless, nearly 70% of them suffered from CHE. Half of the adult patients with LOPD relied moderately on assistive devices, and around 40% relied heavily on them.

Compared with the 1,067 adult patients with rare diseases other than PD, the 68 patients with LOPD were younger (30.0 years among patients with LOPD vs. 35.7 years among patients with other rare diseases), experienced a shorter period between the onset of symptoms and first time to seek diagnosis (0.12 years vs. 2.75 years), yet a longer period between the first time to seek diagnosis and finally being diagnosed (4.25 years vs. 3.23 years). Patients with LOPD are also less likely to be employed (20.6% vs. 52.7%), more likely to come from rural areas (35.3% vs. 24.6%) and more likely to rely on assistive devices (91.18% vs. 42.27%). The other factors, including gender, education, and CHE, were similar between the two groups.

Conversely, the perceived social support of adult patients with LOPD in China appears to be similar to that of other Chinese rare disease patients. For patients with LOPD, the average scores of the four dimensions of social support were $\bar{x}=72.87$ (SD = 15.12) for tangible support, $\bar{x}=55.70$ (SD = 16.01) for emotional/informational support, $\bar{x}=52.65$ (SD = 15.85) for positive social interaction, and $\bar{x}=55.78$ (SD = 17.35) for affectionate support. In terms of structural support, i.e., the average number of close friends and relatives that adult patients with LOPD feel at ease with and can talk to was 5.63. Patients with LOPD perceived that they received more tangible social support than other adult rare disease patients ($\bar{x}=72.9$ vs. $\bar{x}=64.8$, p < 0.001). However, in the other three dimensions, the amount of perceived social support or structural support did not seem to differ significantly between the patients with LOPD and those with other rare diseases.

In terms of QOL of adult patients with LOPD, the average scores for the four dimensions were: $\bar{x}=33.77$ (SD = 18.28) for physical health, $\bar{x}=43.81$ (SD = 21.70) for psychological health, $\bar{x}=39.43$ (SD = 16.93) for environmental health, and $\bar{x}=46.20$ (SD = 19.76) for social relationships. Compared with other adult rare disease patients, the physical health QOL of people with LOPD was significantly lower ($\bar{x}=33.8$ vs. $\bar{x}=48.2$, p < 0.001), whereas their QOL in the other three dimensions did not differ significantly from those of other rare disease patients.

**Univariate analysis**
Table 2 presents the results of the univariate analysis of the four dimensions of QOL. At the level of \( p < 0.05 \), factors that significantly contributed to adult patients’ physical health QOL were age, reliance on assistive devices, and positive social interaction as an aspect of social support. As for psychological health QOL, the significant contributors were employment status, reliance on assistive devices, and positive social interaction. As for environmental health QOL, the significant contributors were age, employment status, reliance on assistive devices, and positive social interaction. As for social relationship QOL, the significant contributors were employment status, reliance on assistive devices, and positive social interaction.
Results from the multiple linear regression are presented in Table 3.

Age significantly influenced physical and environmental health QOL. With increased age, the patients experienced a significant decrease in their physical health QOL ($\beta=-0.75, p < 0.01$) and environmental health QOL ($\beta=-0.79, p < 0.01$).

Educational level and CHE did not seem to affect the QOL among adult patients with LOPD in any dimension. Being employed led to a significant increase in psychological health ($\beta=11.67, p < 0.05$), environmental health ($\beta=11.29, p < 0.05$), and social relationship QOL ($\beta=11.53, p < 0.05$). Those who relied heavily on assistive devices had lower physical health ($\beta=-17.8, p < 0.05$), lower psychological health ($\beta=-22.67, p < 0.05$), lower environmental health ($\beta=-17.8, p < 0.05$), and lower social relationship QOL ($\beta=-22.12, p < 0.01$) than those who did not. Those who relied on assistive devices to some extent also had lower psychological health ($\beta=-16.12, p < 0.01$) and lower social relationship QOL ($\beta=-15.89, p < 0.05$) than those who did not. A one-unit increase in positive social interaction as a form of social support led to a significant increase in physical health ($\beta=0.28, p < 0.05$), psychological health ($\beta=0.70, p < 0.01$), environmental health ($\beta=0.72, p < 0.01$), and social relationships ($\beta=0.70, p < 0.01$).

Discussion

To the best of our knowledge, this study is the first to comprehensively explore the levels and factors associated with QOL among patients with LOPD in China. Compared to previous research that compared Pompe patients with the healthy population, our study makes a significant contribution in that we took other rare disease patients as the comparison group. We believe that our choice of comparison group better highlights the problems faced by adult patients with LOPD, which are otherwise neglected by the existing health care and support systems in China. Another contribution of our study is that we focused on sub-dimensional scores rather than the total score of QOL, which can provide more specific suggestions for rare disease healthcare policymaking.
We found that adult patients with LOPD and non-Pompe rare disease patients in China had similar QOL in the domains of psychological and environmental health and social relationships; however, the former suffered an even lower QOL in the domain of physical health than the latter. This is, to some extent, consistent with previous findings in the literature where patients with PD were compared with the general population [8, 37, 38]. This is due to the fact that the special pathological features of PD, which cause the accumulation of glycogen in the skeletal muscles, heart, liver, and nervous system, may substantially restrain Pompe patients’ ability to move or breathe [37]. Our study notes that physical vulnerability features may influence patients with LOPD more than patients with other rare diseases. This finding calls for more efforts to promote physical-health-related QOL among people with LOPD. Since ERT has proven to be an important treatment for patients with PD, it is critical to enhance its affordability and accessibility in China. Meanwhile, as the study reveals, positive social interaction plays a very important role in increasing patients’ QOL across all domains. Hence, elevating the awareness of the public on PD, and encouraging them to get to know the patients with PD will mobilize more positive interactions between the patient community and the public. Moreover, effective community-based social support programs should also be conceived to create a more supportive social environment for patients with LOPD.

No statistical differences were observed in the domains of psychological health, environmental health, and social relationships of QOL. The impact of rare diseases on psychological, environmental, and social QOL may be more closely related to social misconceptions and even stigma of PD and RD patients than to the physiological nature of the diseases themselves [39]. Hence, regardless of the type of rare disease patients, their perceptions of psychological stress, a sense of security from the environment, and social interactions with others could be similar. Recent research has emphasized that psychological adjustments are beneficial to patients’ well-being [40]. More studies are needed to identify practical and effective ways for patients with LOPD and other rare diseases to improve their mental health.

Most patients with LOPD will not be cured in their lifetimes; hence, identifying ways to improve their QOL should be a core mission of patient-centered care. This study sought to contribute to this mission by exploring the contributors of patients’ QOL. Among all the potential contributors that we included in this study, gender did not seem to make a difference in terms of the four domains of QOL among the patients with LOPD in China. Age was negatively associated with the physical and environmental health domains of QOL, but it had no significant association with mental health or social relationships.

A systematic review among 1,214 rare disease patients in the United States noted that income level is positively associated with QOL in all domains [41]. Our study partly echoes these findings. On one hand, we found that employment is significantly correlated with patients’ psychological, environmental, and social relationship QOL. This is reasonable because employed patients tend to perform better in their social roles and have more chances to interact with other people. Meanwhile, higher levels of QOL may also allow patients to have a higher employment rate. On the other hand, the influences of employment on physical health were significant in univariate analysis but became non-significant in the multivariable model, implying a weak association between employment and patients’ physical health. Such a weak association may further suggest that physical condition may not be an obstacle for patients with LOPD to engage in work; rather, having a job may increase their subjective feelings of physical health. Therefore, policymakers and caregivers may need to think about how to create work opportunities that are suitable for these patients.

One surprising finding of our study is that there was no statistical difference between patients with LOPD and those with other rare diseases in terms of the proportion of patients suffering from CHE, even though ERT is recognized as one of the most expensive orphan drugs in the world. We think the most likely reason lies in the indicator of CHE itself. CHE is a binary indicator used for all populations and does not take into consideration disease-specific characteristics. Studies have indicated that rare diseases tend to pose a high economic burden on patients [42, 43], in other words, the existing benchmark for judging CHE may be able to distinguish between rare and common diseases, but lacks sufficient sensitivity to distinguish between PD and other rare diseases. This inadequate sensitivity may also explain why nearly 70% of rare disease patients with and without PD both suffer from CHE, which is much higher than the average proportion of CHE among the general population (12.9%) [44].

The problem faced by patients with PD i.e., high healthcare expenditures, does not exist in China alone—in Europe, the average cost of ERT for PD is approximately EUR 300,000 (approximately RMB 2,360,000) per patient per year [1]. The financial burden of patients with PD in China can be even more devastating, because almost all patients with PD must pay out-of-pocket. There is almost no insurance coverage from the government or the market to help alleviate the burden.

Another noteworthy finding of our study was that CHE had no significant influence on the QOL in patients with LOPD compared with other non-PD rare disease patients, which is inconsistent with studies conducted in the United States and Europe [45, 46]. Although patients can have adverse infusion reactions, the expensive ERT has been highlighted in Western societies as a significant promoter of QOL, especially at the early stages of treatment [47]. Given the high price of ERT and the nearly complete lack of health insurance coverage on it in China at the time of this survey, a higher CHE may indicate the utilization of ERT or other forms of treatment, which should have potentially helped, at least, increase the patients’ physical health. However, this is not what we found in our study. Although no existing literature could provide explanation to such a finding, based our knowledge on the community of patients with LOPD in China, the majority of the patients who received ERT used the medicine neither continuously nor with sufficient doses. As a result, the effectiveness of the treatment was quite limited.

This study found that a higher level of reliance on assistive devices was negatively associated with all four dimensions of QOL. A large-scale study using the International Pompe Survey also revealed that wheelchair- and ventilator-dependent patients were more likely to report lower health-related QOL in terms of physical functioning, physical role functioning, and social functioning than the general population [8]. Yet in the same study, functional disability was not found to influence mental health-related QOL. However, our study found otherwise; that is, the influence of functional disability was
pervasive on QOL in patients with LOPD. This may be because patients who rely heavily on assistive devices are less likely to go outdoors and have fewer chances to interact with others. More attention should be paid to these socially isolated patients. Future research should explore the impact of an active lifestyle, especially among patients who require assistive devices. The findings should be tested to determine whether they can be generalized to the global context.

Previous studies on QOL in patients with LOPD mostly focused on the financial and physical burdens presented by the disease; however, the humanistic aspect was largely overlooked. Dekker et al. indicated that the painful processes of learning, coping, and adapting to disease-related psychology could induce a humanistic burden on the social capital and social support of the patients and their caregivers [10]. Our findings indicated that promoting positive, successful interactions should be emphasized in improving QOL in patients with LOPD beyond the conventional emphasis on medication. Patient organizations may consider providing opportunities for patients to talk with their peers and share good news with friends in their programs. This study also found that unlike social interaction, tangible emotional/informational and affectionate social support might not be associated with patients’ QOL. However, one review of the spiritual needs of chronic disease patients emphasized that the feeling of being in charge or being helpful is more effective in improving patients' psychological resilience than the feeling of being weak or being helped [48]. Therefore, when promoting social interactions, QOL promotional programs and patient organizations may try to offer more opportunities for reciprocal interactions rather than treating the patients as recipients alone.

Limitations

There are a few limitations to this study. First, this is a self-response cross-sectional survey that involves a rather small sample size. The inference made from this sample needs to be carefully examined. Second, the data were collected by an online survey. Although this approach could maximize the coverage of patients residing sporadically over a large country, whether or not the subjects would be able to understand the questions correctly or to provide authentic answers are of concern. Third, we did not include other possible factors associated with LOPD or QOL, such as comorbidities, clinical symptoms, and accessibility to medical resources. Fourth, there is neither a specific QOL scale for rare disease patients nor for patients with LOPD in particular. Therefore, we used the WHOQOL-BREF, which consists of abstract questions that are not suitable for children. Hence, non-adult patients with LOPD or IOPD were excluded from our study. Further relevant studies are warranted.

Conclusion

This study comprehensively explored the levels of and contributors to the QOL of adult patients with LOPD in China. Measured by the WHOQOL-BREF, the average physical health QOL for this group of patients was very low. However, social interactions, especially those realized via employment, were found to play an important role in QOL in patients with LOPD in almost all dimensions. Compared with offering tangible, informational, or affectionate social support, it might be more important to encourage patients with LOPD to be socially active and to help them better including in social life. Besides, most Chinese patients with LOPD cannot afford ERT due to inadequate financial support. They inevitably become disabled at an earlier age, which will, in turn, constrain their social life and decrease their QOL. Hence, how to provide adult patients with LOPD equal or even more opportunities to be socially engaged is something that healthcare providers and policymakers need to consider.

Abbreviations

CHE: Catastrophic health expenditure
ERT: Enzyme replacement therapy
IOPD: Infantile onset Pompe disease
LOPD: Late onset Pompe disease
MOS-SSS-CM: Chinese Mandarin version of the Medical Outcomes Study Social Support Survey
PD: Pompe disease
QOL: Quality of life
WHOQOL-BREF: World Health Organization Quality of Life: Brief Version

Declarations

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Availability of data and materials
Not applicable.

Authors’ contributions
DD developed the survey questionnaire, collected the data, and conducted a preliminary analysis. SC and JXW conducted the full data analysis and wrote the initial draft of the manuscript. All authors contributed to the final version of the manuscript. All authors have read and approved the final manuscript.

Ethics approval and consent to participate
The study was approved by the Committee on the Use of Human and Animal Subjects in Teaching and Research, Hong Kong Baptist University (HASC no: FRG2/15-16/052). All participants provided informed consent before the survey was conducted.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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