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ORIGINAL RESEARCH

Heterogeneity in Health-Related Quality of Life of Patients with Aplastic Anemia: A Latent Profile Analysis

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Purpose: Concerns over health-related quality of life (HRQOL) in patients with aplastic anemia (AA) have been increasing worldwide. However, most researches on HRQOL in AA patients have ignored individual-level variability. Thus, our study was designed to explore practical classification of HRQOL and related variables among AA patients.

Methods: A cross-sectional study was conducted from May 2022 to March 2023, utilizing convenience sampling to enroll AA patients. Data of HRQOL, sociodemographic characteristics, and clinical variables were collected. Latent profile analysis (LPA) was used to analyze the latent categories of HRQOL in AA patients, utilizing scores from eight subscales of the Medical Outcomes Study 36-Item Short Form Health Survey version 2.0.

Results: A total of 229 patients completed the survey and were included in the analysis. The LPA results showed significantly individual differences and identified three subgroups of HRQOL: Group 1, poor HRQOL with role emotional limitation (n=54, 23.58%); Group 2, moderate HRQOL with role physical limitation (n=56, 24.45%), and Group 3, good HRQOL (n=119, 51.97%), respectively among AA patients. Childless, no comorbidities, transfusion independence, no AA-related symptoms, and higher annual household income were associated with Group 3, whereas higher Eastern Cooperative Oncology Group performance status (ECOG-PS) scores were associated with Group 1.

Conclusion: The findings of our study revealed significant heterogeneity in HRQOL among AA patients, providing valuable information for tailoring interventions to meet individual needs, especially for those in the poor HRQOL with role emotional limitation group. To improve their quality of life, healthcare professionals should fully take into account how the HRQOL subgroups are affected by AA-related symptoms, household annual income, ECOG-PS score, children, comorbidities, and transfusion-dependence.

Keywords: aplastic anemia, health-related quality of life, latent profile analysis, influencing factors

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Introduction

Aplastic anemia (AA) is a bone marrow failure disorder characterized by peripheral pancytopenia and hypocellular bone marrow caused by many different etiologies.[1] In North America and Europe, the yearly prevalence of AA is estimated to be approximately 2.0 per million people,[2,3] while in China, the prevalence of AA is 7.4 per million people.[4] AA may occur in individuals of all age groups, with a notable prevalence among people ages 15 to 25 and 65 to 69, and there is no substantial disparity in the prevalence of AA between males and females.[5,6] AA is characterized by a complex pathophysiology, a challenging therapy process, and a substantial disease burden, particularly for severe AA (SAA) and very severe AA (VSAA), which are characterized by acute onset, rapid progression, and high mortality,[7,8] posing a critical threat to patients' lives and health. Researches on AA patients have shown significant improvements in survival rates since the introduction of hematopoietic stem cell transplantation (HSCT) and immunosuppressive therapy (IST) with anti-thymocyte globulin in the 1980s and 1990s.[9–11] Studies have shown that SAA patients treated with IST have a 4-year survival rate exceeding 80%,[12] while those who receive haploidentical HSCT have a 9-year failure-free survival and overall survival rates of 85.4% and 84.0%, respectively.[13,14]

Nevertheless, the diagnosis of AA can be a traumatic experience for both patients and their families. Patients with AA may endure not only the undesired consequences of the disease itself but also the adverse effects resulting from associated treatments. These effects frequently emerge as pathological problems, including infections, bleeding, anemia, and malnutrition.[15,16] Additionally, patients may face significant psychological pressure due to the financial strain associated with prolonged treatment and the unpredictability of disease prognosis.[17] By extension, the disease hinders their ability to resume normal family and social roles, potentially leading to psychological distress, including anxiety, depression, and even suicidal.[18] As a result, HRQOL for patients is profoundly diminished. Hence, the complete evaluation and enhancement of HRQOL for AA patients has emerged as an important concern.

Several studies have been conducted to investigate the HRQOL of AA patients, with a predominant focus on specific facets of HRQOL (such as fatigue[15]) or the independent analysis of subdomains with HRQOL instruments through means-comparing tests or regression analysis.[12,14] However, the utilization of these methodologies may ignore a crucial aspect of HRQOL among AA patients: the vast heterogeneity of HRQOL among AA patients.[19] This heterogeneity can be attributed to individual differences in self-management and treatment adherence. For example, some AA patients might retain optimal physical performance following effective therapy but may suffer from social dysfunction, whereas others might experience poor sleep quality or hypertrichosis. The heterogeneity among AA patients is not captured by the overall score and cannot be accurately modeled when subscales are analyzed independently, as information regarding the relationship between these subscales would be lost.[20] Therefore, it is crucial to assess the heterogeneity of HRQOL in AA patients. Recently, many studies have used latent profile analysis (LPA) to analyze the heterogeneity of HRQOL in the field of oncology.[21,22] LPA is a statistical methodology that employs subject values on many variables to discover homogenous subgroups or classes of individuals within a heterogeneous population.[23] Unfortunately, the degree to which heterogeneity impacts our understanding of HRQOL among AA patients is still unknown. Therefore, the important aim of this study was to utilize LPA to explore potential classifications of HRQOL among AA patients. Then, we analyzed the sociodemographic and disease-related variables linked to different subgroups.

Methods

Study Design and Participants

This cross-sectional study enrolled AA patients from the Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College from May 2022 to March 2023 through convenience sampling. Participants were eligible if they were aged over 18 years old with a diagnosis of AA according to the "Guidelines for the Diagnosis and Management of Aplastic Anemia in China (2022)".[6] Individuals with profound consciousness impairments or psychiatric conditions were excluded.

When conducting multivariate logistic regression analysis, it was recommended that the sample size should be at least 5–10 times greater than the number of independent variables.[24] In this study, 21 independent variables were included. To ensure the accuracy and efficacy of the model, as well as to account for a 10% loss-to-follow-up rate, a total of 258 patients were recruited.

All patients provided written informed consent, and the study was approved by the Ethics Committee of the Institute of Hematology, Chinese Academy of Medical Sciences and Peking Union Medical College by the guidelines of the Declaration of Helsinki (No. QTJC2022035-EC-1).

Data Collection

To maintain the quality of the questionnaire results, the data collectors received training (the training was a one-time session) provided by the researchers to ensure a comprehensive understanding of the questionnaire content and scoring method. Data collectors were instructed to adhere to the established inclusion and exclusion criteria when recruiting participants. The purpose and methods of the survey were explained to patients before the survey, and only those who agreed to participate were enrolled. Any questions from the participants were addressed immediately to ensure accurate and reliable data collected. All participants completed the questionnaires independently.

Measures

HRQOL

HRQOL was measured using the Medical Outcomes Study 36-Item Short Form Health Survey version 2.0 (SF-36 v2), originally developed by the Boston Health Research Institute in 1988,[25] and subsequently revised in 1996 to improve response accuracy.[26] The SF-36 v2, a 36-item questionnaire that individuals complete to assess their HRQOL, is a globally acknowledged instrument for evaluating QOL. The instrument consists of 8 subscales that assess several aspects of HRQOL, including physical functioning (PF), mental health (MH), role emotional (RE), role physical (RP), general health (GH), social functioning (SF), vitality (VT), and bodily pain (BP). Conversion computations are required to derive the subscale scores. The subscales conversion score can be calculated using the following formula: (raw score - lowest possible score) / (highest possible score - lowest possible score) × 100. The raw score is obtained by summing the scores of the subscale items.[27] Researchers from China (Li et al) have successfully translated the SF-36 v2 into the Chinese language and culturally adapted it, ensuring its accuracy and appropriateness.[28] They have also validated its reliability and validity, making it extensive utilization of the Chinese version of the SF-36 v2 in various domains.[28] The Chinese version of SF-36 v2 was used in this study, and Cronbach's α coefficients ranged from 0.736 to 0.790. The reason why we selected the Chinese version of the SF-36 v2 is as follows. First, the choice of this scale allowed for a comparison of our results with those from other studies. Second, it covers eight dimensions of the HRQOL and is suitable for us to analyse our data with the LPA.

Sociodemographic Information

The sociodemographic information included gender (male, female), age, marital status (married, single/divorced/widowed), education level (senior or lower, college or higher), annual household income (the total income earned by all family members over a year), having children or not, healthcare payment status (insured, uninsured), employment status (employed, unemployed), smoking history (yes or no), and drinking history (yes or no).

Clinical Information

The clinical information included Eastern Cooperative Oncology Group performance status (ECOG-PS), comorbidity (heart failure, diabetes, hypertension, etc.), transfusion-dependence (transfusion-dependence was defined as at least one transfusion of platelets or red blood cells every 8 weeks, on average, for a duration of 4 months[6]), AA-related symptoms (fever, bleeding, fatigue, etc.), medication adherence status (we asked, "How often have you taken the prescription given by your doctor in the past three months?" The potential responses were nearly all of the time (>90%, classified as "excellent"), most of the time (75%, classified as "good"), approximately half the time (50%, classified as "fair"), or less than half the time (<50%, classified as "poor"),[29] hemoglobin (HGB), neutrophil (N), platelet (PLT), disease severity (non-severe AA (NSAA), SAA, VSAA), time since diagnosis (years), and regular follow-up status (yes or no).

Statistical Analyses

Statistics were analyzed using SPSS 26.0 and Mplus 7.0. Continuous variables that followed a normal distribution were presented as the mean with standard deviations and were compared using one-way ANOVA. Conversely, non-normally distributed variables were compared using the Kruskal–Wallis *H*-test and were reported as medians with interquartile range (IQR). The Spearman correlation test was used to analyze the correlation. Categorical variables were depicted as frequency counts and percentages, with Chi-square tests or Fisher tests employed for group comparisons.

LPA was used to analyze the latent categories of HRQOL levels among AA patients based on the eight subscales scores of the SF-36 v2. The iterative procedure began with a one-class model and progressively expanded the number of categories until optimal fit indices were achieved.

The indicators for model fitting included the following: (1) the model fit improved as the akaike information criterion (AIC), bayesian information criterion (BIC), and sample size-adjusted BIC (aBIC) decreased; (2) The $p< 0.05$ for the lo-Mendell-Rubin likelihood ratio test (LMR) and bootstrapped likelihood ratio test (BLRT) indicated that the current model fit (N = k) was better than that of the former model (N = k-1); and (3) entropy (which ranges between 0 and 1) was greater than 0.8, indicating a good model fit.[30] The final classification of the model was determined based on model fit metrics and clinical significance.[31] Afterwards, we used multivariable logistic regression analysis to examine how sociodemographic and clinical variables influenced various categories of HRQOL.

Results

Sociodemographic and Clinical Characteristics of the Participants

Among 258 eligible participants, 29 individuals were excluded due to incomplete responses, resulting in a final 229 (88.76%) individuals who completed the survey. The median age of the participants was 30 (IQR 22.00–40.50) years, with over half being male (55.45%), married (54.15%), childless (55.46%), unemployed (54.59%), had no history of smoking (51.97%), free of comorbidities (52.40%), and without AA-related symptoms (52.84%). The majority of participants were diagnosed with NSAA (79.91%), reported a history of drinking alcohol (69.87%), good/excellent compliance with medication (78.17%), and regular follow-up (75.11%). More than one-third of participants (41.05%) possessed a college education or higher, and a smaller percentage (18.34%) were uninsured. The median time since diagnosis was 6.00 (IQR 4.00–10.80) years, and the household annual income of the patients was 71.21 (IQR 50.00–71.21) thousand Chinese yuan.

The PF domain exhibited the highest median score (85.00, IQR 70.00, 95.00), while the GH domain displayed the lowest median score (60.00, IQR 45.00, 77.00), and slight variation in the median scores among the eight dimensions. According to the correlation analysis, there were strong, positive correlations between PF and RP ($r = 0.545$, $p \leq 0.001$), RE and RP ($r = 0.612$, $p \leq 0.001$), GH and VT ($r = 0.505$, $p \leq 0.001$), and MH and VT ($r = 0.623$, $p \leq 0.001$).

Selection and Naming of the Models

We examined potential profile models ranging from 1 to 6, as presented in Table 1. The AIC, BIC, and aBIC showed a decrease as the number of class profiles increased. The entropy values for model 1 to model 6 all exceeded 0.8. However, the LMR of Model 2 and Model 6 did not significantly differ. Model 3 and Model 5, which had entropy values closest to 1, exhibited statistically significant results for both LMR (Model 3: $p= 0.005$; Model 5: $p= 0.023$) and BLRT (Model 3: $p< 0.001$; Model 5: $p< 0.001$). Additionally, they met the requirement of having at least 3% of cases in each potential category.[20] However, for Model 5, the minimum number of samples was 14, which may considerably restrict its representativeness. After comparing the model fit indices of each model, Model 3 was selected as the best-fitting model. The probabilities of correct attribution for a patient with AA to each category were 0.972, 0.956, and 0.996, respectively (Table 2). These results indicated that the optimal model derived from the potential profile analysis in this study exhibited reliability and a robust capacity for differentiation across categories.

Statistically significant differences were observed in the PF, RP, BP, GH, VT, SF, RE, and MH scores for Model 3. The study analyzed the characteristics of three potential groups of HRQOL in AA patients by plotting line graphs of the eight subscale scores of the SF-36 v2 (Figure 1). These groups were named based on the fluctuations in the mean values

Table 1 Comparison of Model Fit Evaluation Results for the Different Groups

	AIC	BIC	aBIC	Entropy	*p*		Class Probability
					LMR	BLRT	
1	16,380.721	16,435.661	16,384.951				
2	15,922.350	16,008.193	15,928.959	0.918	0.397	<0.001	0.314/0.686
3	15,769.473	15,886.220	15,778.461	0.952	0.005	<0.001	0.236/0.245/0.520
4	15,706.068	15,853.718	15,717.436	0.883	0.004	<0.001	0.245/0.188/0.236/0.332
5	15,641.403	15,819.957	15,655.150	0.952	0.023	<0.001	0.114/0.197/0.170/0.061/0.459
6	15,593.959	15,803.416	15,610.086	0.907	0.055	<0.001	0.114/0.061/0.197/0.170/0.135/0.323

Abbreviations: AIC, the Akaike Information Criterion; BIC, Bayesian Information Criterion; aBIC, sample size-adjusted BIC; LMR, Lo-Mendell-Rubin likelihood ratio test; BLRT, Bootstrapped likelihood ratio test.

Table 2 Classification Probabilities for the Most Likely Latent Group Membership(Column) by Latent Group(Row)

	Group 1	Group 2	Group 3
Group 1	0.972	0.028	0.000
Group 2	0.042	0.956	0.001
Group 3	0.000	0.004	0.996

of the subscale items. 54 (23.58%) patients were in Group 1, exhibiting lower HRQOL scores compared to the other two groups. Additionally, this group was classified as the "poor HRQOL with RE limitations" group showed a bipartition trend in the RE subscale compared to the other two groups. There were 56 patients (24.45%) in Group 2 whose HRQOL scores fell between Group 1 and Group 3, and significantly lower scores on RP. As a result, these participants were classified into the "moderate HRQOL with RP limitation" group. Group 3, consisting of 119 patients (51.97%), exhibited higher HRQOL scores compared to the other two groups. Therefore, this group was named the "good HRQOL" group. Figure 2 shows the trends of HRQOL curves for all three groups.

Predictors of HRQOL Groups

The findings of the intergroup comparison analysis demonstrated statistically disparities ($p < 0.05$) in the three groups of HRQOL among AA patients in terms of household annual income, having children or not, ECOG-PS score, comorbidity, transfusion-dependence, AA-related symptoms, and time since diagnosis (Table 3).

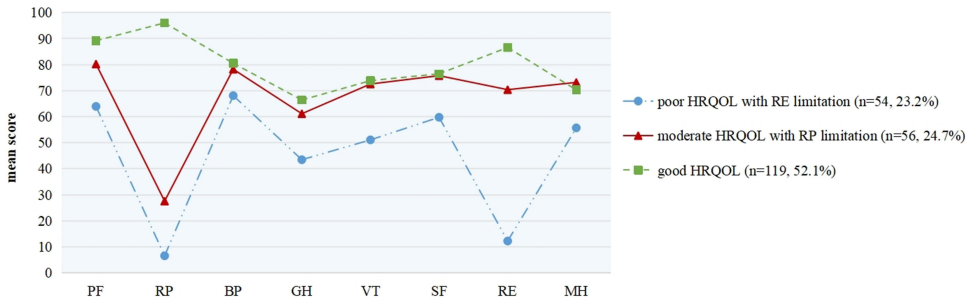

Figure 1 The predicted mean HRQOL for each trajectory group.
Abbreviations: PF, physical functioning; MH, mental health; RE, role emotional; RP, role physical; GH, general health; SF, social functioning; VT, vitality; BP, bodily pain.

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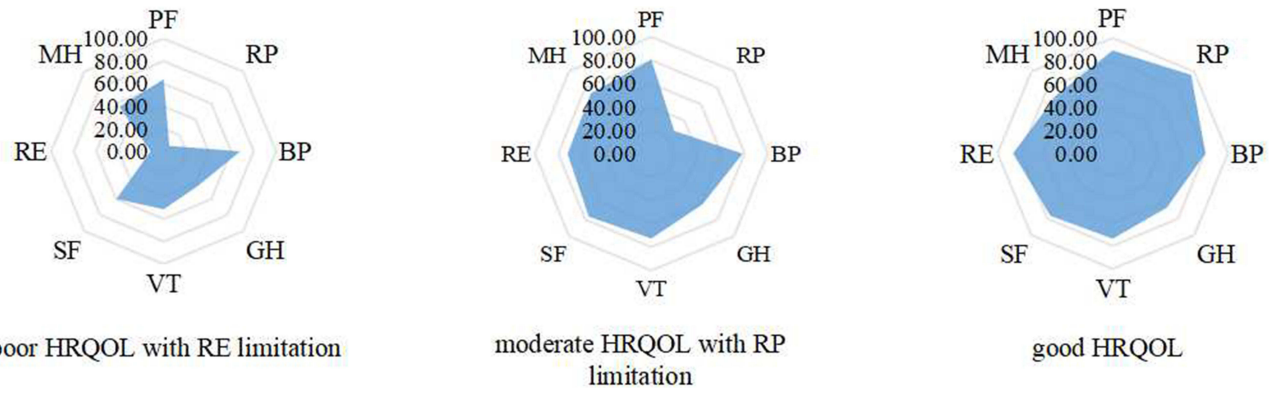

Figure 2 Tendencies of the three distinctive HRQOL groups.
Abbreviations: PF, physical functioning; MH, mental health; RE, role emotional; RP, role physical; GH, general health; SF, social functioning; VT, vitality; BP, bodily pain.

In this study, we utilized these statistically significant variables as independent variables and potential profile categories of HRQOL as dependent variables in an unordered multicategorical logistic regression analysis, with the "poor HRQOL with RE limitation" group served as the reference group.

The results presented in Table 4, indicated that patients without AA-related symptoms or with a higher annual household income were more likely to be classified in the "moderate HRQOL with RP limitation" group. Conversely,

Table 3 Comparison of Sociodemographic Characteristics Among the Different HRQOL Groups

Variables	Poor HRQOL with RE Limitation (n=54)	Moderate HRQOL with RP Limitation (n=56)	Good HRQOL (n=119)	*Fisher/* χ^2*/H*	*p*
Gender					
Male	30	34	63	0.932	0.628
Female	24	22	56		
Age (IQR)	32.00 (23.75, 40.00)	30.50 (23.25, 39.75)	29.00 (20.00, 39.00)	2.268	0.322
Marital status					
Single/Divorced/Widowed	20	24	61	3.294	0.193
Married	34	32	58		
Education					
Senior or lower	33	35	67	0.741	0.691
College or higher	21	21	52		
Annual household income *(thousand Chinese Yuan*, IQR)	60.00 (30.00, 71.21)	71.21 (52.50, 71.21)	71.21 (50.00, 100.00)	10.604	0.005
Children					
With	32	26	44	7.574	0.023
Without	22	30	75		
Healthcare payment					
Insured	43	47	97	0.343	0.842
Uninsured	11	9	22		
Employment					
Employed	26	24	54	0.311	0.856
Unemployed	28	32	65		
Smoking history					
Yes	31	23	56	3.034	0.219
No	23	33	63		

(*Continued*)

Table 3 (Continued).

Variables	Poor HRQOL with RE Limitation (n=54)	Moderate HRQOL with RP Limitation (n=56)	Good HRQOL (n=119)	*Fisher/* χ^2*/H*	*p*
Drinking history					
Yes	41	38	81	1.232	0.540
No	13	18	38		
ECOG-PS					
<2	34	50	102	15.766	< 0.001
≥2	20	6	17		
Comorbidity					
With	34	31	44	11.847	0.003
Without	20	25	75		
Transfusion-dependence					
Yes	38	31	50	12.305	0.002
No	16	25	69		
AA-related symptoms					
With	39	25	44	18.707	< 0.001
Without	15	31	75		
Medication adherence					
Excellence	29	35	67	8.176	0.225
Good	16	10	22		
Fair	6	9	28		
Poor	3	2	2		
HGB (g/L, IQR)	100.00 (60.00, 132.25)	81.50 (64.55, 122.50)	92.00 (64.00, 126.00)	0.529	0.767
N ($\times 10^9$/L, IQR)	54.00 (25.50, 108.00)	66.00 (26.00, 186.00)	72.00 (28.00, 166.00)	1.422	0.491
PLT ($\times 10^9$/L, IQR)	1.88 (0.99, 5.38)	2.02 (1.26, 6.17)	1.86 (1.08, 4.92)	1.593	0.451
Disease severity					
NSAA	40	43	90	2.743	0.605
SAA	11	12	20		
VSAA	3	1	9		
Time since diagnosis *(years*, IQR)	6.00 (3.00, 10.08)	5.00 (4.00, 7.30)	6.90 (4.10, 11.00)	9.393	0.009
Regular follow-up					
Yes	37	42	93	1.844	0.398
No	17	14	26		

patients with higher ECOG-PS scores were more likely to be categorized in the "poor HRQOL with RE limitation" group, and these findings were observed when comparing the "poor HRQOL with RE limitation" with the "moderate HRQOL with RP limitation" subgroups. Patients in the "good HRQOL" group, compared to those in the "poor HRQOL with RE limitation" group, were more likely to be childless, transfusion-independent, and had no comorbidities, AA-related symptoms, and a higher annual household income.

Discussion

In this study, we explored the HRQOL of patients with AA by utilizing LPA to investigate the heterogeneity of their HRQOL and identify the factors contributing to the various latent groups. To our knowledge, this is the first study to use LPA to explore the heterogeneity of HRQOL among AA patients. Our study revealed significant individual differences of HRQOL among AA patients, who were classified into three groups: the poor HRQOL with RE limitation, the moderate HRQOL with RP limitation, and the good HRQOL subgroups, respectively. These characteristics used to define these

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Table 4 Logistic Regression Analysis of Categories of HRQOL Trajectories in AA Patients

Variables	Group 2 (n=56)		Group 3 (n=119)	
	OR (95% CI)	*p*	*OR (95% CI)*	*p*
Children [Without]	1.94(0.84, 4.49)	0.121	2.90(1.31, 6.39)	0.008
Comorbidity [Without]	2.19(0.91, 5.29)	0.082	5.11(2.21, 11.81)	<0.001
Transfusion-dependent [No]	1.82(0.78, 4.30)	0.169	3.17(1.42, 7.07)	0.005
AA-related symptoms [Without]	3.50(1.47, 8.33)	0.005	4.92(2.17, 11.16)	<0.001
Annual household income (*thousand Chinese yuan*)	1.18(1.04, 1.33)	0.008	1.21(1.08, 1.37)	0.001
Time since diagnosis (years)	0.96(0.88, 1.06)	0.417	1.06(0.99, 1.14)	0.097
ECOG-PS [<2]	5.75(1.92, 8.33)	0.002	5.32(2.04, 13.91)	0.001

Notes: The reference group = Group 1: poor HRQOL with RE limitation (n=54).
Abbreviations: *OR*, odds ratio; *CI*, confidence interval.

groups were similar to those utilized by Băjenaru et al to define the potential categories for exploring HRQOL among older age groups through LPA.[32] The HRQOL for the three groups, as determined by LPA, showed statistically significant, which indicated that the categorization results were reasonable to some extent. Our findings confirmed that household annual income, having children or not, comorbidities, transfusion-dependence, and AA-related symptoms were all significant factors associated with the identified HRQOL groups.

Group 1, which had members of all the diagnostic groupings, was the smallest group (23.58%). Focusing on each subscale of the SF-36 v2, Group 1 had the lowest RP and RE scores. Moreover, the RE subscale scores exhibited the greatest discrepancy with those of Group 2 and Group 3, indicating a polarized state. This implies that compared to PF, MH might be the primary factor influencing the lowest level of HRQOL for individuals with AA. AA patients experience psychological symptoms that impede their ability to engage in work and daily activities, potentially leading to reduced treatment adherence, poorer prognosis, and lower HRQOL. Prince et al emphasized the unique impacts of both physical and mental illnesses on mortality and disability, and argued that the lack of MH is equivalent to the absence of PF.[33] Thus, it is imperative for medical staff in clinical practice to focus not only on physical symptoms of AA patients but also their psychological problems, and to provide tailored interventions to patients in need of help.

The composition of Group 2 was very interesting. Despite displaying a positive psychological state, these patients still encountered notable limitation in RP, such as limited mobility and decreased independence, due to physical health issues. Compared with those in the other two groups, more than 50% of the patients in Group 2 exhibited a higher prevalence of comorbidities, transfusion-dependence, and had the shortest time since diagnosis. Notably, RP was strongly correlated with RE in AA patients in this study. Thus, it may be necessary for health professionals to tailor individualized interventions for patients in this group in order to decrease the probability of progression to Group 1. Ohmberger et al stated that PF can influence MH through lifestyle choices and social capital.[34] In clinical practice, healthcare professionals can enhance patients' health through health investments (such as health education) and social interactions (such as patients' families participate in decision-making). Furthermore, the composition of Group 2 highlighted the advantages of using LPA to analyze HRQOL, and identifying AA patients with this specific level of HRQOL solely based on the characteristics of the SF-36 v2 can pose a significant challenge.

Group 3 was characterized by high levels of HRQOL, even exceeding the average HRQOL level of the general population (matched for age and sex[28]). Patients within this group demonstrated the highest scores across all subscales of the SF-36 v2 scale (Figure 2). Moreover, Group 3 also has the most members of patients (51.97%), encompassing individuals from various diagnostic groups, underscoring the prognostic significance of HRQOL for a substantial portion of AA patients. Response shift has been extensively documented in HRQOL researches,[35,36] indicating that the experience of a condition such as cancer can alter survivors' perceptions of their HRQOL.[20] AA patients who possess a redefined perception of HRQOL and adjusted expectations during the period from diagnosis to treatment may

demonstrated unexpectedly elevated levels of HRQOL in this study. Furthermore, these patients exhibited favorable prognosis following prompt initiation of treatment, which may also explain the high proportion of patients in this group.

Previous studies have validated the clinical significance of the ECOG-PS score, indicating an association between a worse prognosis and higher scores, which was consistent with the findings of this study.[37,38] Patients with higher ECOG-PS scores were more likely to be classified into the "poor HRQOL with RE limitation" group. This relationship can be attributed to the decline in physical condition, activity endurance, and overall PF associated as the ECOG-PS scores increased, which heightens the likelihood of experiencing severe somatic symptoms. On the other hand, the ECOG-PS can also indirectly impact the HRQOL of patients by affecting negative emotions.[39] The deterioration in physical health may lead to changes in patients' original life status and negative emotions due to unfulfilled social roles, ultimately leading to a diminished HRQOL.[34] Due to its 5-level scale, the ECOG-PS score is simple and allows medical staff to evaluate a patient's physical status quickly.[40] It could be an effective tool for assessing and examining a patient's HRQOL in clinical practice.

Consistent with previous studies, AA patients with higher annual household incomes tend to report higher levels of HRQOL.[41–43] However, our study diverges from prior studies by demonstrating that AA patients without children exhibited a higher HRQOL.[44,45] This discrepancy may be attributed to the reduced financial burden diminished family management-related issues and the absence of worry about the fate of children. Nevertheless, a study by Hurmuz et al indicated that intimate interpersonal relationships can provide emotional support, maintain and enhance patients' physiological functioning, and increase motivation for recovery.[44] Thus, medical staff should prioritize the evaluation of AA patients' financial capacity, promptly identify patients facing financial difficulties, and increase the reasonable utilization of healthcare. Moreover, medical staff should encourage patients' families to participate in patient care as much as possible to ensure that patients receive more positive social support.[46]

Our study findings revealed that the likelihood of transfusion-independent patients being attributed to "good HRQOL" group was 3.174 times greater than that of patients being attributed to 'poor HRQOL with RE limitation' group. Vaht et al discovered that the lifespan of AA patients with transfusion dependence was considerably shorter than that of those without.[9] Frequent blood transfusions during treatment may result in complications such as transfusion-related infections, iron overload, and inefficient transfusions, which can significantly impact the survival and HRQOL of these patients.[47,48] Clinical staff should pay close attention to the HRQOL of AA patients who are transfusion-dependent. Furthermore, AA patients who are transfusion-dependent tend to have more severe disease and experience more clinical symptoms than those who are not.[49] The results of our study indicated that patients with AA-related symptoms were more likely to be in the "poor HRQOL with RE limitation" group. AA patients with clinical symptoms tend to be more concerned and excessively worried about any changes in their bodies,[15] potentially exacerbating disease burden, resulting in poor HRQOL. Thus, health education should be improved to enhance patients' awareness of disease understanding and provide tailored interventions for AA-related symptoms to prevent and minimize complications, alleviate disease burden, and improve patients' HRQOL.

Limitations

Our study was designed initially as cross-sectional, preventing the determination of changes in HRQOL groups for AA patients over time and whether the predictors of their group status had changed. Hence, a future study with a longitudinal design is required to track changes in HRQOL over time among different subgroups. Second, the participants in our study were all recruited from a single hospital, which may restrict the generalizability of the results. Multicenter, large-sample studies are needed to further validate the present results. What's more, using convenience sampling to recruit participants might limit how widely our findings can be applied. Nonetheless, our study provides a new direction for exploring the HRQOL of AA patients. Last but not least, in our study, we only explored the effects of sociodemographic and disease factors on different groups of HRQOL in AA patients. However, other significant factors, such as social support and psychological resilience, were not evaluated in this study and warrant further investigation.

Conclusion

This study could make a contribution to the awareness of HRQOL among AA patients. Our study revealed that LPA offers notable benefits in addressing the complexity and diversity of data related to HRQOL measures among AA patients. Utilizing this model, we successfully categorized the HRQOL of AA patients into three subgroups: Group 1, poor HRQOL with role emotional limitation; Group 2, moderate HRQOL with role physical limitation, and Group 3, good HRQOL, respectively. Factors such as AA-related symptoms, household annual income, ECOG-PS score, children, comorbidities, and transfusion-dependence were found to significantly impact the patients' HRQOL. The findings of our study also provided a better understanding of the heterogeneity in HRQOL among AA patients, it could be useful to guide clinicians to timely identify patients at heightened risk for diminished HRQOL in the context of limited healthcare resources.

Abbreviations

HRQOL, health-related quality of life; LPA, latent profile analysis; AA, aplastic anemia; NSAA, non-very severe aplastic anemia; SAA, severe aplastic anemia; VSAA, very severe aplastic anemia; HSCT, hematopoietic stem cell transplantation; IST, immunosuppressive therapy; ATG, anti-thymocyte globulin; PF, Physical functioning; MH, Mental health; RE, role emotional; RP, role physical; GH, general health; SF, social functioning; VT, vitality; BP, bodily pain; SF-36 v2, the Mos 36-Item Short Form Health Survey version 2.0; AIC, the Akaike Information Criterion; BIC, Bayesian Information Criterion; aBIC, sample size-adjusted BIC; LMR, Lo-Mendell-Rubin likelihood ratio test; BLRT, Bootstrapped likelihood ratio test; ECOG-PS, Eastern Cooperative Oncology Group performance status; IQR, inter-quartile range; CI, confidence interval; SE, Standard Error; OR, odds ratio; HGB, hemoglobin; N, neutrophil; PLT, platelet.

Data Sharing Statement

The data supporting the findings of this study can be obtained from the corresponding author, upon reasonable request.

Ethics Approval

The study was approved by the Ethics Committees of the Institute of Hematology, Chinese Academy of Medical Sciences & Peking Union Medical College according to the guidelines of the Declaration of Helsinki.

Consent to Participate

All patients provided written informed consent.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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