Original Article

Chronic disease management practices and factors associated with health-related quality-of-life for persons with chronic myeloid leukemia receiving tyrosine kinase inhibitor therapy

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Background: The main objective of this study was to explore health-related quality of life (HRQoL) profiles, chronic disease management practices and key factors associated with HRQoL in 540 patients with chronic myeloid leukemia in chronic phase (CML-CP) administered tyrosine kinase inhibitors (TKIs).

Methods: Adult CML-CP patients treated with TKIs in Henan Cancer Hospital from March 2015 to October 2019 were assessed via questionnaires, including demographic characteristics, TKI medications, participation in CML disease management, and HRQoL, in a cross-sectional investigation. Respondents were anonymous. Functional Assessment of Cancer Therapy-Leukemia (FACT-Leu) was used to measure HRQoL. A multivariate linear regression model with stepwise entry was used to investigate variables independently associated with HRQoL domain and total scores.

Results: Totally, 540 respondents were included; 302 (55.93%) were male. Mean participant age was 42.90±13.00 years; 169 (31.3%), 178 (32.9%) and 193 (35.7%) individuals had a low, moderate or high disease management level, respectively. Except for insignificant event-free survival information, participants with higher disease management levels also had significantly higher rates of completing re-examination, drug withdrawal, cytogenetic response (CcyR) and/or major molecular response (MMR) (all P<0.01). Moreover, higher disease management level was accompanied by eight significantly higher HRQoL domains (all P<0.01). In multivariate linear regression analysis, variables significantly associated with a higher HRQoL included: (I) high disease management level (B=3.68, P=0.046); (II) transportation convenience (B=6.67, P<0.001); (III) family annual income >10,000 CNY (B=5.97, P<0.001); (IV) completed re-examination (B=4.58, P=0.036); (V) MMR (B=3.75, P=0.021) and CcyR (B=5.15, P=0.035). Female sex (B=-3.53, P=0.010), single status or divorce (B=–1.89 and –2.94, P=0.005 and 0.011), and low education level (B=–1.44, P=0.019) were significantly associated with lower HRQoL.

Conclusions: Higher disease management level was significantly associated with higher elevated treatment efficacy and HRQoL in Chinese individuals with CML-CP administered TKIs. These data indicate the importance of chronic disease management on people's HRQoL and clinical outcome.

Keywords: Chronic myeloid leukemia (CML); disease management; health-related quality of life (HRQoL); treatment effect

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Introduction

Chronic myeloid leukemia (CML) is a clonal cancer of bone marrow hematopoietic stem cells, with an annual incidence rate of (1.6–2)/10,0000 globally (1), and 0.36/10,0000 in China (2). With extensive use of first- and second-generation tyrosine kinase inhibitors (TKIs), CML patients are currently mainly treated with oral drugs and outpatient follow-up treatment, and survival is being continuously prolonged, with patients obtaining a life span similar to that of the general population (3-5). Achieving complete cytogenetic response (CcyR) and major molecular response (MMR) are the short-term goals of CML treatment, while improving the health-related quality of life (HRQoL) and functional healing are long-term goals (6,7).

Published studies provide detailed descriptions of the HRQoL of patients with CML. The quality of life may vary according sociodemographics and clinical variables, out-of-pocket expense, the type of TKI, treatment lines, medication adherence (8-11), etc. However, there is no relevant research on CML patient participation in disease management, and association between disease management and TKI treatment effectiveness and HRQoL remain unknown. In recent years, the significance of disease management based on humanistic care in patients with chronic cancer has been generally recognized. Disease management based on professional medical interventions can help patients with chronic diseases establish self-management behavior, improve compliance, strengthen doctor–patient communication, and promote benign mental stimulation, in order to improve the QOL, ameliorate prognosis and even affect the treatment outcome (12-14).

To this end, we conducted this cross-sectional study to explore HRQoL profiles, extent of involvement in chronic disease management and sociodemographic and clinical characteristics in relation to HRQoL in CML-CP patients administered TKIs. We present the following article in accordance with the SURGE reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-22-158/rc).

Methods

CML patients administered TKIs with follow-up in the outpatient department of Henan Cancer Hospital from March 2015 to October 2019 were assessed by electronic questionnaire through the Internet, patient education activities, and a hardcopy questionnaire in the hematology clinic of the hospital. Inclusion criteria were: (I) meeting the clinical diagnostic criteria of CML; (II) chronic CML; (III) exclusive treatment with TKIs; (IV) age ≥18 years; (V) clear consciousness and normal communication ability; and (VI) signed informed consent. Exclusion criteria were: (I) questionnaire not fully answered due to any reason; and (II) inability to respond to the questionnaire. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the Henan Cancer Hospital (No. 2014ys32) and informed consent was taken from all the patients.

CML disease management model

The CML disease management model used in the hospital is described.

"Henan CML corps" management mode: all CML patients (and their partners and relatives) in Henan Cancer hospital were given different forms of education, and recruited to join the "Henan CML corps". Specifically, the Hematology Department of Henan Cancer hospital was the general headquarters, with 18 regional regiments of prefectures and cities to manage CML patients and organize various activities held by the headquarters.

Regularly holding online and offline CML science education lectures, as well as various forms of popular science education activities; teaching CML patients about adverse drug reaction monitoring and treatment, medication management, diet management, exercise management, risk management, recurrence prevention, and mental health management, and issuing written health education materials.

Establishing a WeChat service platform to provide the latest treatment information and professional guidance for patients, and to alleviate any concerns.

Mutual management: establishing a WeChat group (Henan CML Corps 1, 2, 3) to provide a platform for communication among patients. Many patients with ideal treatment effects and good disease control played the role of

peer educators, supporting and encouraging others, sharing experience, and improving confidence in treatment.

Many forms of patient education activities (CML knowledge Grand Prix, CML knowledge game, tourism, mini marathon, CML fellowship, etc.) held every year to strengthen the relationship between doctors and patients and among patients, enrich the life experience of CML patients, and highlight their mental health.

Survey

The survey was conducted from January 2019 to January 2020. The questionnaire consisted of three parts. (I) General information of the interviewee, including age, sex, marital status, education level, transportation, insurance, family income [reported in CNY(RMB)], TKI type, drug discontinuation status, re-examination completion status, treatment response [if yes, CcyR and/or MMR], and event and occurrence time recording status. (II) Patients' participation in disease management, including the number of times the interviewee participated in online and offline education lectures, the number of interactive WeChat groups, and the number of offline patient education activities (e.g., tourism and CML knowledge). After preliminary correlation analysis, these indicators showed certain correlations. Finally, taking concept similarity as the consideration, the number of representative CML education lectures online and offline was selected as a single indicator of participation of patients in disease management. (III) Leukemia treatment function assessment using the 44-item Functional Assessment of Cancer Therapy-Leukemia (FACT-Leu) (15).

Assessment of HRQoL

HRQoL was measured using (FACT-Leu), which is a modular approach to assessing the patient's HRQoL and leukemia-specific symptoms using a 'core' set of questions (Functional Assessment of Cancer Therapy-General; FACT-G), as well as a cancer site-specific leukemia subscale. FACT-G is a 27-item compilation of general questions scored on a 5-point scale ranging from 0 = "not at all" to 4 = "very much". The items are divided into four primary HRQoL domains: Physical Well-being (PWB: 7 items, score range of 0–28); Social/Family Well-being (SWB: 7 items, score range of 0–28); Emotional Well-being (EWB: 6 items, score range of 0–24); Functional Well-being (FWB: 7 items, score range of 0–28). The leukemia-specific subscale consists of 17 items (score range of 0–68) that assess patient concerns related to leukemia. Three summary scales were used: (I) the FACT-Trial Outcome Index (TOI; score range of 0–124), a summary scale composed of PWB, FWB, and leukemia-specific subscales; (II) FACT-G (score range of 0–108); and (III) the FACT-Leukemia Total (FACT-Leu; score range of 0–176). Higher scores are reflective of higher HRQoL.

Statistical analysis

Continuous variables are reported as mean ± standard deviation (SD). Categorical variables are presented as number or percentage, and compared by the Chi-square test or Fisher's exact text (if the expected value was ≤5). One-way ANOVA or the Kruskal-Wallis test was used to compare multiple groups depending on data normality. A multivariate linear regression model with stepwise entry was used to investigate variables independently associated with HRQoL domain and total scores. A correlation matrix of all independent variables was used to investigate possible multicollinearity. If an absolute correlation coefficient of >0.7 was observed, only one variable of the related variables would be selected to enter the multivariate model. Spearman's rho and point-biserial correlation coefficient were respectively used in this analysis refer to the date property of paired variables. All analyses were performed with IBM SPSS Version 25 (SPSS Statistics V25, IBM Corporation, NY, USA). Two-tailed $P<0.05$ was considered statistically significant.

Results

As of January 2020, a total of 586 questionnaires were distributed, including 252 online (43%) and 334 paper (57%) questionnaires in patient education activities and hematology clinic of Henan Cancer hospital. Excluding 46 unqualified questionnaires, 540 valid questionnaires were included in this report, indicating an effective recovery rate of 93.17%.

Patient characteristics

Table 1 summarizes the characteristics of patients and the three disease management groups. The disease management levels were categorized by number of times of participation in education activity as low [0–1], moderate [2–3], and high [≥4]. A total of 540 patients were assessed, including 169 (31.3%) low, 178 (32.9%) moderate, and 193 (35.7%)

Table 1 Baseline patient characteristics and disease management group (n=540)

Parameter	Mean ± SD or N (%)
Disease management level	
Low	169 (31.30)
Medium	178 (32.96)
High	193 (35.74)
Age, years	42.90±13.00
Age, n (%)	
≤29 years	68 (12.93)
30–39 years	154 (29.28)
40–49 years	139 (26.43)
50–59 years	118 (22.43)
≥60 years	47 (8.94)
Sex, n (%)	
Male	302 (55.93)
Female	238 (44.07)
Marital status, n (%)	
Married	428 (79.26)
Single	83 (15.37)
Divorce	25 (4.63)
Widowed	4 (0.74)
Education level, n (%)	
College and above	177 (32.78)
Secondary and below	363 (67.22)
City or rural residence, n (%)	
City	181 (33.52)
Rural	359 (66.48)
Transport convenience, n (%)	
No	104 (19.26)
Yes	436 (80.74)
Insurance, n (%)	
Medical insurance	516 (95.56)
Own expense	24 (4.44)
Family annual income, n (%)	
<4,000 CNY	138 (25.56)
4,000–10,000 CNY	210 (38.89)
>10,000 CNY	192 (35.56)
Medicine, n (%)	
Withdrawal	25 (4.63)
Nilotinib	214 (39.63)
Imatinib	204 (37.78)
Dasatinib	97 (17.96)
Completed re-examination, n (%)	
No	62 (11.48)
Yes	478 (88.52)
Withdrawal, n (%)	
No	497 (92.04)
Yes	43 (7.96)
MMR, n (%)	
No	212 (39.26)
Yes	328 (60.74)
CcyR, n (%)	
No	55 (10.19)
Yes	485 (89.81)
EFS-related information, n (%)	
EFS, events	47 (8.70)
EFS, months	37.74±16.68
Follow-up, months	39.82±16.58
Physical well-being	20.47±5.03
Social/family well-being	19.88±5.79
Emotional well-being	18.83±4.17
Functional well-being	18.40±6.51
FACT-G	77.58±16.70
Leu subscale	50.27±9.20
FACT-Leu scale	127.85±23.43
TOI	89.14±16.84

Conformity defined by number of times patient participated in educational activity: low [0–1], medium [2–3], and high [≥4]. MMR, major molecular response; CcyR, cytogenetic response; EFS, event-free survival; FACT-G, Functional Assessment of Cancer Therapy-General; FACT-Leu, Functional Assessment of Cancer Therapy-Leukemia; TOI, FACT-Trial Outcome Index.

high disease management levels. The averaging age was 42.90±13.00 years, majorly distributed from 30 to 59 years. The gender ratio was 1.27:1 (male/female =302/238). Almost 4 out of 5 patients (79.26%) were married. Detailed characteristics were listed in *Table 1*.

Adherence

As indicated in *Table 2*, except for event-free survival (EFS)-related information (all three P>0.05), the remaining outcomes were significantly different among the three

Table 2 All characteristics *vs.* disease management levels

Parameters	Low (n=169)	Medium (n=178)	High (n=193)	All (n=540)	P
Age, year (mean ± SD)	42.43±14.04	42.58±13.84	43.62±11.10	42.90±13.00	0.642
Age, n (%)					0.068
≤29 years	26 (15.48)	25 (14.37)	17 (9.24)	68 (12.93)	
30–39 years	51 (30.36)	53 (30.46)	50 (27.17)	154 (29.28)	
40–49 years	39 (23.21)	36 (20.69)	64 (34.78)	139 (26.43)	
50–59 years	34 (20.24)	42 (24.14)	42 (22.83)	118 (22.43)	
≥60 years	18 (10.71)	18 (10.34)	11 (5.98)	47 (8.94)	
Sex, n (%)					0.948
Male	96 (56.80)	98 (55.06)	108 (55.96)	302 (55.93)	
Female	73 (43.20)	80 (44.94)	85 (44.04)	238 (44.07)	
Marriage status, n (%)					0.822
Married	129 (76.33)	140 (78.65)	159 (82.38)	428 (79.26)	
Single	30 (17.75)	29 (16.29)	24 (12.44)	83 (15.37)	
Divorce	8 (4.73)	8 (4.49)	9 (4.66)	25 (4.63)	
Widowed	2 (1.18)	1 (0.56)	1 (0.52)	4 (0.74)	
Education level, n (%)					0.131
College and above	54 (31.95)	50 (28.09)	73 (37.82)	177 (32.78)	
Secondary and below	115 (68.05)	128 (71.91)	120 (62.18)	363 (67.22)	
City or rural, n (%)					<0.001
City	35 (20.71)	64 (35.96)	82 (42.49)	181 (33.52)	
Rural	134 (79.29)	114 (64.04)	111 (57.51)	359 (66.48)	
Traffic convenience, n (%)					0.011
No	45 (26.63)	31 (17.42)	28 (14.51)	104 (19.26)	
Yes	124 (73.37)	147 (82.58)	165 (85.49)	436 (80.74)	
Insurance, n (%)					0.275
Medical insurance	159 (94.08)	169 (94.94)	188 (97.41)	516 (95.56)	
Own expense	10 (5.92)	9 (5.06)	5 (2.59)	24 (4.44)	
Family annual income, n (%)					0.487
<4,000 CNY	47 (27.81)	45 (25.28)	46 (23.83)	138 (25.56)	
4,000–10,000 CNY	71 (42.01)	64 (35.96)	75 (38.86)	210 (38.89)	
>10,000 CNY	51 (30.18)	69 (38.76)	72 (37.31)	192 (35.56)	

Table 2 (*continued*)

Table 2 (*continued*)

Parameters	Low (n=169)	Medium (n=178)	High (n=193)	All (n=540)	P
Medicine, n (%)					0.243
Withdrawal	4 (2.37)	8 (4.49)	13 (6.74)	25 (4.63)	
Nilotinib	73 (43.20)	71 (39.89)	70 (36.27)	214 (39.63)	
Imatinib	60 (35.50)	63 (35.39)	81 (41.97)	204 (37.78)	
Dasatinib	32 (18.93)	36 (20.22)	29 (15.03)	97 (17.96)	
Finished reexamination, n (%)					<0.001
No	35 (20.71)	21 (11.80)	6 (3.11)	62 (11.48)	
Yes	134 (79.29)	157 (88.20)	187 (96.89)	478 (88.52)	
Withdrawal, n (%)					0.001
No	164 (97.04)	166 (93.26)	167 (86.53)	497 (92.04)	
Yes	5 (2.96)	12 (6.74)	26 (13.47)	43 (7.96)	
MMR, n (%)					<0.001
No	111 (65.68)	73 (41.01)	28 (14.51)	212 (39.26)	
Yes	58 (34.32)	105 (58.99)	165 (85.49)	328 (60.74)	
CcyR1, n (%)					<0.001
No	34 (20.12)	19 (10.67)	2 (1.04)	55 (10.19)	
Yes	135 (79.88)	159 (89.33)	191 (98.96)	485 (89.81)	
EFS related information					
EFS, event, n (%)	13 (7.69)	17 (9.55)	17 (8.81)	47 (8.70)	0.827
EFS, months	37.80±16.41	35.74±16.45	39.55±17.00	37.74±16.68	0.089
Follow up, months	39.47±16.59	38.20±16.53	41.62±16.52	39.82±16.58	0.132
Physical Well-being	19.18±5.94	20.05±4.47	21.99±4.21	20.47±5.03	<0.001
Social/family well-being	19.05±5.78	19.38±5.70	21.05±5.73	19.88±5.79	0.002
Emotional well-being	17.79±4.23	18.72±4.29	19.85±3.75	18.83±4.17	<0.001
Functional well-being	17.22±6.29	17.76±6.22	20.03±6.67	18.40±6.51	<0.001
FACT-G	73.24±16.66	75.92±15.95	82.93±16.05	77.58±16.70	<0.001
Leu subscale	49.41±9.35	48.85±8.96	52.33±8.95	50.27±9.20	<0.001
FACT-Leu scale	122.64±23.66	124.76±22.65	135.26±22.15	127.85±23.43	<0.001
TOI	85.80±17.32	86.66±16.08	94.35±15.90	89.14±16.84	<0.001

MMR, major molecular response; CcyR, cytogenetic response; EFS, event-free survival; FACT-G Functional Assessment of Cancer Therapy-General; FACT-Leu, Functional Assessment of Cancer Therapy-Leukemia; TOI, FACT-Trial Outcome Index.

disease management groups (all P<0.01). Patients with higher disease management also had significantly higher rates of re-examination completion, with 79.29%, 88.20% and 96.89% in the low, moderate and high groups, respectively (P<0.001, *Figure 1*).

Treatment responses and outcomes

At the end of the follow-up period, the numbers of patients with low disease management (169 cases) obtaining cumulative CcyR and MMR were 135 and 28,

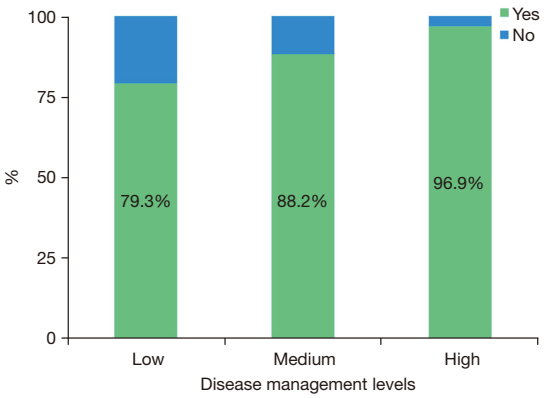

Figure 1 The rate of finish re-examination among disease management groups.

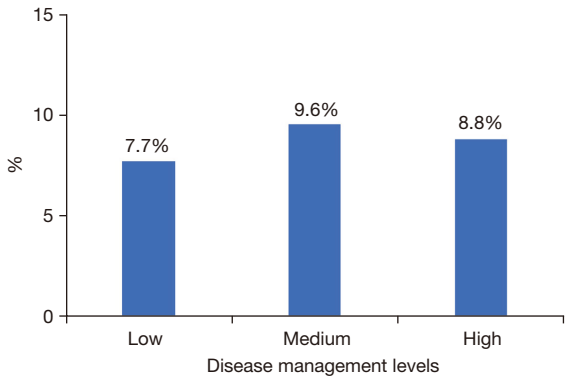

Figure 3 The EFS rates among disease management groups. EFS, event-free survival.

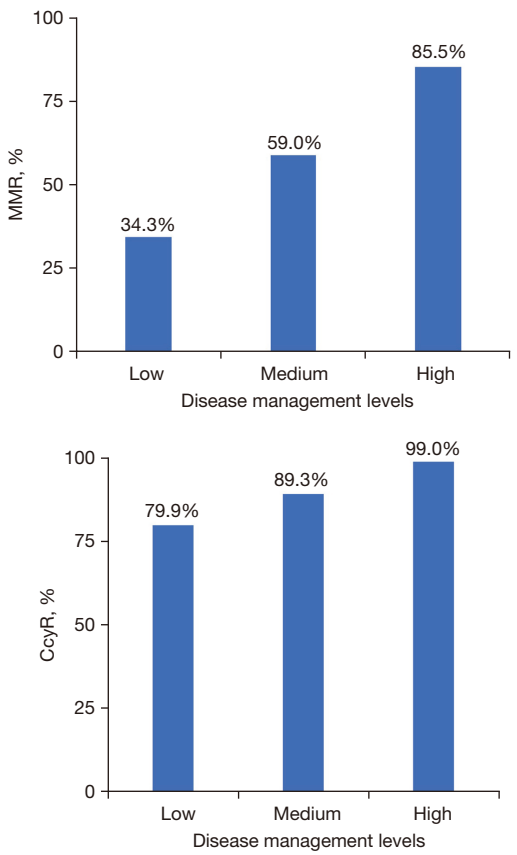

Figure 2 The rate of MMR and CcyR among disease management groups. MMR, major molecular response; CcyR, cytogenetic response.

respectively. As shown in the in *Table 2*, in the moderate disease management group (178 cases), the numbers of patients with cumulative CcyR and MMR were 159 and 73, respectively. In the high disease management group (193 cases), 191 and 111 individuals had cumulative CcyR and MMR, respectively. Cumulative CcyR rates were therefore 79.88%, 89.33% and 98.96% in the low, moderate and high groups, respectively (P<0.01), and cumulative MMR rates were 14.51%, 41.01% and 65.68%, respectively (P<0.01). The higher the degree of disease management, the higher the proportions of patients with CcyR and MMR (P<0.01) (*Figure 2*). The withdrawal rates were 2.96%, 6.74% and 13.47% in the low, moderate and high groups, respectively (P<0.01). However, no significant differences were found in EFS rate (7.69%, 9.55% and 8.81% in the low, moderate and high groups, respectively) among groups (*Figure 3*) (P>0.05).

HRQoL profiles

Means and 95% confidence intervals (CIs) of HRQoL scores by disease management level are presented in *Table 2* and *Figure 4*. The group with high disease management had the highest scores. There were significant differences in most subscales among the three cohorts (P<0.01), including PWB, SWB, EWB, FWB, FACT-G, Leu subscale, FACT-Leu scale, and TOI scores.

Independent factors associated with HRQoL results

Tables 3,*4* summarize the independent factors associated with HRQoL, including domains and total scores. In the multivariate linear regression analysis, high disease management was associated with elevated SWB component summary, FWB, FACT-G, TOI (from 1.72 to 4.74, P=0.004–0.046) and mental component summary (MCS;

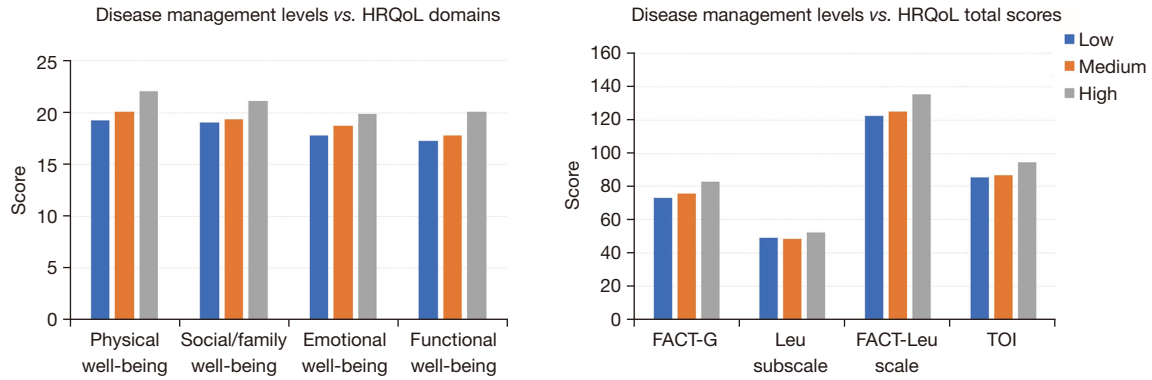

Figure 4 The results of domains among disease management groups. HRQoL, health-related quality of life; FACT-G, Functional Assessment of Cancer Therapy-General; FACT-Leu, Functional Assessment of Cancer Therapy-Leukemia; TOI, FACT-Trial Outcome Index.

–2.1 to –4.3; P=0.0394 and P=0.0080). Female participants had significantly lower total scores than male counterparts in EWB FACT-G, Leu subscale, FACT-Leu scale, and TOI (–2.64 to –5.14, P values from <0.001 to 0.046). Marital status may influence SWB; specifically, single status (–1.89, P=0.005) and divorce (–2.94, P=0.011) resulted in significantly lower SWB compared with marriage. Education level was associated with FWB domains (–1.44, P=0.019). Participants with transportation convenience had significantly higher HRQoL scores in PWB, EWB, FACT-G, Leu subscale, FACT-Leu scale and TOI (from 1.75 to 9.41, all P<0.001). Family annual income >10,000 CNY resulted in significantly higher scores in PWB, SWB, FWB, FACT-G, FACT-Leu scale, and TOI (from 1.42 to 8.90, P values from <0.001 to 0.019) (*Figure 5*). Re-examination completion may influence FWB, FACT-Leu scale, and TOI (from 1.63 to 6.38, P values from 0.010 to 0.036). Participants with MMR had higher HRQoL scores in PWB, FWB, EWB, FACT-G, FACT-Leu scale, and TOI (from 1.04 to 7.35, P values from <0.001 to 0.031); achieving CcyR was associated with PWB, EWB, Leu scale and TOI (from 1.41 to 5.15, P values from <0.001 to 0.035).

Observing common factors in the eight domain and total scores, it was found that: (I) a high disease management level usually brought elevated HRQoL scores; (II) females had significantly lower HRQoL scores in EWB, Leu subscale, and FACT-Leu total scores; (III) transportation convenience usually brought higher HRQoL scores; (IV) higher family income was also accompanied by elevated HRQoL scores; and (V) re-examination completion, MMR, and CcyR1 were associated with better HRQoL.

In the correlation coefficient analysis, almost all absolute values of coefficients were <0.5. Only a large correlation coefficient r=0.85 (P<0.001) was found between EFS time (months) and follow-up time (months). However, both variables were not included in multivariate models.

Other results

We next tested for an interaction effect on HRQoL between disease management and family annual income. *Figure 5* displays means and 95%CIs of HRQoL scores in various subscales. In the stratified analyses of family annual income and disease management versus HRQoL scores, patients with a high disease management level had higher average HRQoL scores compared with the medium and low groups in almost all domains and total scores. Further, 80% of the subgroups based on disease management level had significant differences and trends in HRQoL scores (all P<0.05).

Discussion

This is the first study to explore the status of disease management for Chinese CML patients. The results showed that among 540 cases, 68.7% (371 cases) were moderately or highly involved in their disease management, and the overall level of participation was moderate to high. In addition, univariate analysis of the demographic characteristics showed that the degree of patient participation in disease management was affected by residence and transportation convenience. Patients living in cities with convenient transportation had an elevated participation rate in disease management, which may be related to the city's cultural

Table 3 The independent factors associated to each HRQoL domains

Parameter	Physical well-being		Social/family well-being		Emotional well-being		Functional well-being	
	Estimate (SE)	P	Estimate (SE)	P	Estimate (SE)	P	Estimate (SE)	P
Disease management level								
Low	Ref.	–	Ref.	–			Ref.	–
Medium	–0.26 (0.50)	0.605	0.09 (0.60)	0.879			0.24 (0.69)	0.728
High	1.04 (0.55)	0.059	1.72 (0.59)	0.004			1.82 (0.73)	0.013
Age group								
≤29 years	Ref.	–			Ref.	–	Ref.	–
30–39 years	–0.11 (0.66)	0.870			0.02 (0.56)	0.971	–0.29 (0.90)	0.749
40–49 years	–0.45 (0.68)	0.502			0.01 (0.57)	0.992	–1.62 (0.93)	0.081
50–59 years	–0.24 (0.69)	0.727			0.85 (0.59)	0.151	–0.17 (0.95)	0.860
≥60 years	–1.98 (0.87)	0.023			–0.32 (0.74)	0.667	–1.39 (1.19)	0.243
Sex								
Male					Ref.	–		
Female					–1.07 (0.34)	0.002		
Marital status								
Married			Ref.	–				
Single			–1.89 (0.67)	0.005				
Divorce			–2.94 (1.15)	0.011				
Widowed			–4.33 (2.83)	0.126				
Education level								
College and above							Ref.	–
Secondary and below							–1.44 (0.61)	0.019
Transportation convenience								
No	Ref.	–			Ref.	–	Ref.	–
Yes	2.31 (0.52)	<0.001			1.75 (0.44)	<0.001	1.35 (0.71)	0.056
Insurance								
Medical insurance	Ref.	–						
Own expense	2.22 (0.97)	0.023						
Family annual income, CNY								
<4,000	Ref.	–	Ref.	–	Ref.	–	Ref.	–
4,000–10,000	–0.20 (0.51)	0.697	0.21 (0.62)	0.733	-0.02 (0.44)	0.960	0.54 (0.69)	0.431
>10,000	1.42 (0.53)	0.008	2.19 (0.63)	<0.001	0.72 (0.45)	0.112	1.74 (0.74)	0.019
Medicine								
Withdrawal							Ref.	–
Nilotinib							2.74 (1.34)	0.040
Imatinib							3.87 (1.32)	0.004
Dasatinib							2.64 (1.43)	0.065

Table 3 (*continued*)

Table 3 (*continued*)

Parameter	Physical well-being		Social/family well-being		Emotional well-being		Functional well-being	
	Estimate (SE)	P	Estimate (SE)	P	Estimate (SE)	P	Estimate (SE)	P
Completed re-examination								
No	Ref.	–			Ref.	–		
Yes	1.63 (0.63)	0.010			1.05 (0.54)	0.052		
Withdrawal								
No	Ref.	–			Ref.	–		
Yes	1.69 (0.74)	0.023			1.83 (0.63)	0.004		
MMR								
No	Ref.	–			Ref.	–	Ref.	–
Yes	1.04 (0.48)	0.031			1.28 (0.39)	0.001	1.41 (0.62)	0.025
CcyR								
No	Ref.	–			Ref.	–		
Yes	2.62 (0.72)	<0.001			1.41 (0.61)	0.021		

HRQoL, health-related quality of life; MMR, major molecular response; CcyR, cytogenetic response.

atmosphere, economic conditions, and more accessibility to disease-related knowledge; conversely, the inconvenience for patients with poor transportation could explain their low participation in offline patient education activities. Henan Province is a large agricultural province; about 66.48% of CML patients come from rural areas, and have a low education level. From this point of view, health professionals should consider developing remote network platforms for disease management and providing simple CML knowledge lectures and website application guidance before each patient receives the network platform service. This would ensure that patients can correctly use the network platform, which could provide prevention, diagnosis and follow-up services to help rural patients improve their self-management ability and QOL.

Compliance of CML patients with medications and regular follow-up play a key role in the degree of treatment response at the molecular level (16). Patients with poor compliance tend to have poor treatment effects and high medical costs (17,18). However, due to the complexity of compliance evaluation, there is no gold standard for measuring treatment compliance in IM (19,20). We attempted to analyze the compliance of CML patients by assessing whether they were monitored regularly during TKI treatment. The present survey showed that compliance rates in the three groups with different levels of disease management were 79.29%, 88.20% and 96.89% for the low, moderate and high groups, respectively, indicating a statistically significant difference (P<0.001). These results suggested that disease management can significantly improve patient compliance. The higher the degree of disease management, the higher the proportions of cumulative MMR and CcyR, and the higher the proportion of patients with drug withdrawal. These findings indicate that disease management significantly improves the treatment response of patients, possibly because disease management improves the treatment enthusiasm of patients, which improves drug and follow-up compliance. The EFS rates of the three groups were not statistically significant. Although disease management had a positive effect on patients, recurrence, progression and drug resistance are more often related to poor patient prognosis.

HRQoL is a subjective feeling of one's own QOL against the background of a given cultural and value system. It is influenced by the individual's goals, expectations and concerns (21). Considering the need for life-long treatment by CML patients, HRQoL has become an important index for evaluating the prognosis of CML-CP patients (22).

In this study, multiple linear regression analysis of HRQoL-related independent factors was performed in CML patients, with the following results. (I) Cumulative differences in the FACT-Leu questionnaire scores of the three disease management groups were statistically significant (P<0.001), suggesting that CML patients

Table 4 Independent factors associated with Leu subscale and total scores

Parameter	FACT-G		Leu subscale		FACT-Leu scale		TOI	
	Estimate (SE)	P	Estimate (SE)	P	Estimate (SE)	P	Estimate (SE)	P
Disease management level								
Low	Ref.	–	Ref.	–	Ref.	–	Ref.	–
Medium	–0.21 (1.69)	0.900	–1.15 (0.95)	0.226	–1.69 (2.38)	0.477	–1.94 (1.72)	0.260
High	4.74 (1.80)	0.009	1.72 (0.97)	0.077	6.05 (2.54)	0.018	3.68 (1.84)	0.046
Sex								
Male	Ref.	–	Ref.	–	Ref.	–	Ref.	–
Female	–2.67 (1.33)	0.046	–2.64 (0.76)	<0.001	–5.14 (1.88)	0.007	–3.53 (1.36)	0.010
Transportation convenience								
No	Ref.	–	Ref.	–	Ref.	–	Ref.	–
Yes	6.67 (1.72)	<0.001	3.12 (0.97)	0.001	9.41 (2.43)	<0.001	6.67 (1.75)	<0.001
Insurance								
Medical insurance			Ref.	–				
Own expense			4.02 (1.84)	0.030				
Family annual income, CNY								
<4,000	Ref.	–			Ref.	–	Ref.	–
4,000–10,000	1.26 (1.69)	0.456			1.81 (2.38)	0.447	1.45 (1.72)	0.398
>10,000	6.94 (1.75)	<0.001			8.90 (2.48)	<0.001	5.97 (1.79)	<0.001
Completed re-examination								
No	Ref.	–			Ref.	–	Ref.	–
Yes	4.05 (2.14)	0.058			6.38 (3.01)	0.035	4.58 (2.18)	0.036
Withdrawal								
No			Ref.	–				
Yes			3.98 (1.41)	0.005				
MMR								
No	Ref.	–			Ref.	–	Ref.	–
Yes	5.85 (1.51)	<0.001			7.35 (2.13)	<0.001	3.75 (1.63)	0.021
CcyR								
No			Ref.	–			Ref.	–
Yes			3.14 (1.29)	0.015			5.15 (2.43)	0.035
EFS-related information								
EFS, events			–3.25 (1.34)	0.016				

FACT-G, Functional Assessment of Cancer Therapy-General; FACT-Leu, Functional Assessment of Cancer Therapy-Leukemia; TOI, FACT-Trial Outcome Index; MMR, major molecular response; CcyR, cytogenetic response; EFS, event-free survival.

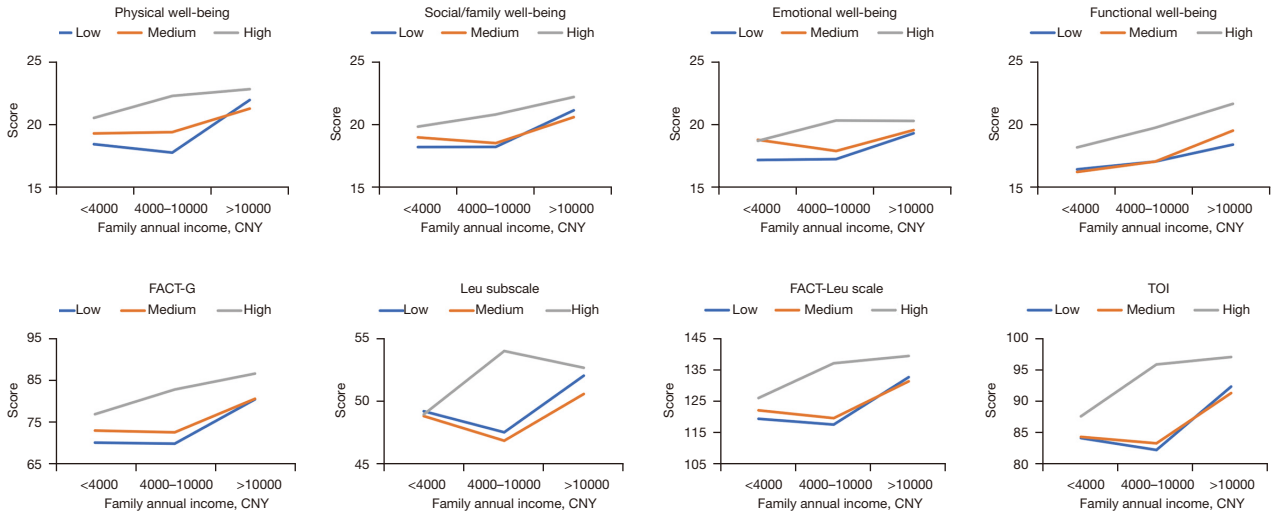

Figure 5 The interaction mean plots of family annual income cross disease management on HRQoL scores. FACT-G, functional assessment of cancer therapy-general; FACT-Leu, Functional Assessment of Cancer Therapy-Leukemia; TOI, FACT-Trial Outcome Index; HRQoL, health-related quality of life.

participating in disease management projects can have improved QOL. (II) The self-rated QOL scores of female patients were lower than those of male patients, and the domain of female self-rated QOL was mainly EWB, corroborating Breccia M's (23) study. Female patients should pay attention to their chief complaints and seek emotional and psychological supports. (III) Marital status may affect SWB; specifically, single and divorced participants had significantly lower SWB than married counterparts. Education level was associated with FWB scores in CML patients. Larfors *et al.* (24) analyzed 980 CML patients in Sweden, and showed that low income, low education level, living alone and other factors were associated with shorter survival time. (IV) The results of this study suggested that patients with convenient transportation and higher family income had higher HRQoL. Smith *et al.* (25) analyzed data from the UK blood tumor research network, and found that with free treatment, therapeutic outcomes in CML patients were similar to those reported by clinical trials, suggesting that drug cost is indeed an important factor affecting curative effects in patients. At the same time, the latter study also speculated that different socioeconomic status determines patient compliance, further leading to poor treatment results in patients from poor areas. Jiang *et al.* (8) also confirmed that patients with lower co-payment of TKI drug expenses achieved better physical and psychological outcomes. Therefore, financial difficulties can weaken the QOL of patients.

In this study, the associations of disease management with annual family income and HRQoL were examined. The results showed that annual income was an important factor influencing HRQoL in patients, because CML is a chronic disease that requires long-term treatment. The more expensive the TKI drug treatment, the more likely it is that poor patients will stop taking the medicine or not take the drug according to the physician's advice, resulting in unsatisfactory treatment effects and lower QOL. Therefore, China's medical reform should pay close attention to the medical insurance system, expanding the coverage area, increasing the proportion of insurance reimbursement, narrowing the gap between urban and rural areas, and promoting the fairness of medical insurance; meanwhile, citizens should improve their understanding of medical insurance and actively obtain appropriate insurance to reduce their economic burden in case of illness. As TKI costs are gradually included in the scope of medical insurance payment in all provinces and cities, more patients will enjoy preferential policies from medical insurance, which should improve medication compliance and the QOL in patients. (VI) The present results also suggested that re-examination completion, MMR, and CcyR were associated with higher HRQoL. In CML patients, an analysis of a phase III clinical trial of TKIs (9) showed that better response to TKI treatment was generally associated with improved HRQoL. In

patients who achieved MMR, EWB and leukemia-specific domains showed the greatest improvements (P<0.001). These results showed that acquisition of MMR had an important positive significance with empirical well-being, FACT-G, FACT-Leu scale scores. The reason may be that responders with MMR may be less worried about disease recurrence or progression to the acute phase. In the studies assessing CML patients by Unnikrishnan *et al.* (26) and Sacha *et al.* (27), lower HRQoL was associated with poor medication compliance. The main causes of low compliance were adverse drug reactions, economic pressure and forgetting to take the medicine (18,28,29). A cross-sectional study of CML patients in China found that the rate of rural household registration was low, as well as the frequency of treatment. In this case, patients often had poor treatment compliance, resulting in poor therapeutic effects and reduced QOL (30), which further suggests that attention should be paid to the education and management of rural patients with registered permanent residence, encouraging them to participate in decision-making for their own treatment and increasing their awareness of the importance of regular medication and monitoring. This would improve treatment response and ultimately increase patient survival and QOL.

This study had several limitations. First, it was a cross-sectional study involving a patient survey; all results were from patients' self-reports, and the integrity and accuracy of the reported data could not be verified. In addition, since the respondents of this survey are from the Internet, outpatient clinics of Henan Cancer Hospital and those who participate in patient education activities, some patients (the elderly or those with serious diseases, etc.) cannot participate in the survey, and the information may be omitted. Furthermore, this was a single-center study, with standardized monitoring and strict management of CML patients. Therefore, the current findings need further verification.

Nevertheless, this was the first real-world study in China evaluating disease management in patients with CML. The present results indicate that disease management significantly improves patient compliance, treatment response, and HRQoL, providing new insights into the importance of disease management in CML patients.

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Footnote

Reporting Checklist: The authors have completed the SURGE reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-22-158/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-22-158/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the Henan Cancer Hospital (No. 2014ys32) and informed consent was taken from all the patients.

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