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ORIGINAL ARTICLE

The impact of comorbidity on health-related quality of life in elderly patients with chronic myeloid leukemia

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Abstract The primary objective of this study was to investigate whether the presence of comorbidities was associated with a lower health-related quality of life (HRQOL) in elderly patients with chronic myeloid leukemia (CML). A sample of 174 CML patients aged 60 years or above was analyzed. HRQOL was assessed with the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36). A number of pre-selected sociodemographic and disease-related factors were considered as potential confounding factors for the association between comorbidity and HRQOL. Mean age of the 174 patients analyzed was 70 years (range 60–87 years) and 55 % were male. Overall, 111 patients (64 %) reported at least one comorbidity. Analysis stratified by age group category showed a greater proportion of patients with comorbidities in the older subgroup population (≥70 years) compared to younger patients (60 to 69 years). Differences in HRQOL outcomes between patients with no comorbidity at all and those with two or more comorbid conditions were at least twice the magnitude of a clinically meaningful difference in all the physical and mental health scales of the SF-36. In multivariate analysis, after adjusting for key confounding factors, the following scales were significantly lower in those with comorbidity: general health ($p<0.001$), bodily pain ($p<0.001$), physical functioning ($p=0.002$), and vitality ($p=0.002$). Assessing comorbidity in elderly patients with CML is important to facilitate identification of those most in need of HRQOL improvements.

Introduction

The introduction of tyrosine kinase inhibitors (TKIs) in the treatment for chronic myeloid leukemia (CML) has greatly changed the prognosis of patients. With the advent of first

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TKI, namely imatinib, also elderly patients, usually candidate to palliative approach, have been treated and cured [1]. A 5-year relative survival of elderly CML patients (≥65 years) was shown to be comparable to that of younger patients [2]. As recent data from large population-based registries report a median age at diagnosis of 56 years [3], it is reasonable to consider that many of the CML patients currently under treatment have even a greater median age. Nonetheless, elderly patients and those with comorbidity have not been adequately represented in several of the pivotal clinical efficacy trials conducted so far [4–6].

While in general, elderly people are more likely to report comorbid medical conditions, recent data also shows that patients with a cancer diagnosis report significantly more comorbid conditions than do their peers without a cancer diagnosis [7]. According to Feinstein's definition [8], comorbidity is any distinct additional clinical entity pre-existent or occurring during the course of a primary disease.

The possibility to prescribe other two TKIs (i.e., nilotinib and dasatinib) as first-line treatment, in addition to imatinib, makes the selection of the most appropriate treatment for individual patients a challenge. Therefore, considering individual characteristics, including comorbidity, is critical [6, 9].

In the coming decades, the prevalence of elderly patients living with CML will substantially increase given the dramatic improvements in treatment outcomes for this disease [10, 11]. Understanding the relationships between comorbidity, treatment outcomes, and patient's health-related quality of life (HRQOL) is thus essential to robustly inform clinical decision-making.

There is convincing evidence showing that elderly patients treated with imatinib are able to achieve similar rates of cytogenetic and molecular responses compared to younger patients, although with increased incidence of temporary discontinuation or dose reduction due to toxicity [12, 13]. While some data exists on the relationships between comorbidity and clinical outcomes in CML, to our knowledge, the impact of comorbidity on patient-reported HRQOL in elderly CML patients has not been investigated. Considering the lifelong nature of current TKI therapies, even low-grade side effects can significantly impair patients' daily functioning and well-being [14]. Therefore, improving HRQOL has become an important goal of modern CML therapies [15]. We have previously shown that CML patients aged 60 years or older, who respond to imatinib therapy (i.e., at least in complete cytogenetic response), can expect to have a HRQOL profile similar to that of their peers in the general population [16].

The primary objective of this analysis was to investigate whether the presence and number of comorbidities is associated with lower physical and mental HRQOL aspects in this elderly (i.e., aged 60 or older) CML population. Secondary objectives were to assess prevalence of comorbidities and to evaluate whether these were associated with greater symptom severity.

Patients and methods

Study population

Patients were previously enrolled in a large multicentre CML survivorship (n=422) study investigating long-term effects of first-line imatinib therapy. Patients' HRQOL results, inclusion criteria, and study logistic have been previously reported [16]. Briefly, patients had to be on treatment for at least 3 years and at least in complete cytogenetic response (CCyR) at the time of study entry. Patients could be enrolled regardless of number and type of comorbidity. Patients with a secondary malignancy and having psychiatric conditions or major cognitive dysfunctions hampering a self-reported evaluation, at study entry, were excluded. The current analysis is based on patients aged 60 or older (n=174) enrolled in this study [16].

Ethic committees of participating centers approved the study and all patients provided written informed consent.

Health-related quality of life and symptom severity

The Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) was used to assess HRQOL. It consists of 36 items yielding eight scales: physical functioning, role limitations due to physical problems, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems and mental health. Each scale provides a score ranging between 0 and 100 with higher scores indicating better outcomes [17].

Patient-reported symptoms were evaluated with a previously developed checklist for assessing the severity a core set of symptoms for CML patients [18]. The following symptoms were evaluated: abdominal discomfort, diarrhea, edema, fatigue, headache, muscular cramps, musculoskeletal pain, nausea, and skin problems. Each symptom was scored as: *not at all*, *a little*, *quite a bit*, *and very much*. To ease outcome interpretation in this report, and similarly to other symptom ratings included in well-validated questionnaires [19], raw scores were linearly transformed into a standardized scale ranging from 0 to 100 with higher scores indicating greater symptom severity.

Assessment of comorbidity

Patients themselves reported comorbidity at the time of HRQOL assessment by completing an adapted version of the Charlson Comorbidity Index [20]. The questionnaire addressed the following comorbidities: osteoarthritis/rheumatism, vascular pathology, diabetes, pulmonary problems, obesity, liver problems, renal pathology, myocardial infarction, ulcer, and other conditions. Also, a free text field was added to allow patients entering any other comorbidity.

Disease and sociodemographic variables analyzed

Key variables potentially contributing to explaining patient's HRQOL were considered and these were selected based on clinical relevance for the purpose of this analysis. These were grouped into (1) disease-related and (2) sociodemographic factors. Disease-related factors included time since diagnosis, Sokal risk at diagnosis, and achievement of a complete molecular response. Sociodemographic factors included age, sex, education, and social support. This latter was included being a potential determinant of HRQOL in cancer survivors and being associated with survival in elderly cancer patients [21, 22]. This was assessed with the well-validated multidimensional scale of perceived social support (MSPSS) [23] that consists of 12 items that evaluate perceptions of social support from three main sources: friends, family members, and significant others. It also yields a total score (i.e., global social support) that was used for the purpose of this analysis.

Statistical analysis

Analyses were performed on 174 CML patients aged at least 60 years. As there is paucity of research regarding HRQOL and comorbidity in elderly CML patients, all SF-36 scales were investigated in this study as primary scales. Patients were classified in three groups by number of comorbidities and categorized as *no comorbidity at all*, *one comorbidity*, and *two comorbidities or more*. Differences were investigated among such groups in self-reported symptoms and SF-36 scales by Kruskal-Wallis test ($\alpha = 0.05$). Also, multivariate analysis of covariance (ANCOVA) was used to assess differences in SF-36 scales by number of comorbidities, adjusting for other key variables selected on clinical grounds. Based on multivariate ANCOVA, the proportion of variance of SF-36 scales explained by presence of comorbidities was investigated using the total eta-square index. This index provides the specific contribution of each variable included in the model in explaining the outcome variance. For descriptive purposes, proportions of explained variance of variables other than presence of comorbidities were grouped into "disease-related" and "sociodemographic" variables. Clinical significance of differences in HRQOL outcomes was also evaluated in this study, defined as at least eight points on each SF-36 scale [24]. Statistical significance for SF-36 scales was Bonferroni corrected to account for multiple testing. All analyses were performed with SAS v.4 (SAS Institute, Inc., Cary, NC, USA) and SPSS v. 20.

Results

Mean age of the 174 patients analyzed was 70 years (range 60–87 years) and 55 % were male. Mean time between date of diagnosis and study participation was 5.5 years (SD 1.9). Seventy percent of patients were receiving a standard dose of imatinib of 400 mg/day at the time of survey. Sokal risk classification at diagnosis was low in 37 % of the patients, intermediate in 51 %, and high in 12 %. Overall, 111 patients (64 %) reported at least one comorbidity. Of the 202 comorbidities reported by these patients, these were classified as follows: osteoarthritis/rheumatism (30 % patients), vascular pathology (17 %), diabetes (10 %) and pulmonary problems (9 %), obesity (6 %), liver problems (6 %), renal pathology (5 %), myocardial infarction (4 %), ulcer (3 %), and other comorbid conditions (24 %). Sixty-three patients (36 %) did not report any comorbidity, 55 (32 %) reported only one comorbidity, and 56 (32 %) reported two or more comorbidities.

Analysis stratified by age group category showed a greater proportion of patients with comorbidities in the older subgroup population (≥70 years) compared to younger patients (60 to 69 years). For example, within the group of patients with no comorbidity at all, 62 % were aged between 60 to 69 years while only 38 % were aged 70 years or more. Characteristics of patients stratified by number of comorbidities are reported in Table 1.

Univariate analysis of comorbidity and health-related quality of life and symptom burden

Patients with no comorbidity (Com0) had overall statistically significant better outcomes (i.e., higher scores) across all the physical and mental health scales of the SF-36 compared to those with either one comorbidity (Com1) or two or more comorbid conditions (Com≥2) (Fig. 1).

Differences between groups Com0 and Com≥2 were at least twice the magnitude of a clinically meaningful difference for all the eight scales (physical and mental health) of the SF-36 questionnaire. The differences in bodily pain ($\Delta = 25.3$ points) and role physical ($\Delta = 24.1$ points) were at least three times the magnitude of a clinically meaningful difference. For physical functioning ($\Delta = 23$), general health ($\Delta = 22.6$), and role-emotional ($\Delta = 22.4$), the differences between Com0 and Com≥2 were just below three times the magnitude of a clinically meaningful difference.

Exploratory analysis comparing HRQOL profile of our elderly population stratified by number of comorbidities with that of the general population (adjusted by age and gender) revealed that CML patients with no comorbidity had broadly even better outcomes than their peers in some domains (data not shown).

Symptom severity by number of comorbidities is depicted in Fig. 2. Statistically significant differences were found in symptom mean scores by comorbidity for muscular cramps ($p = 0.045$), musculoskeletal pain ($p = 0.003$), edema ($p = 0.008$), and fatigue ($p < 0.001$).

Table 1 Sociodemographic and clinical characteristics of elderly CML patients by number of comorbidities

Variable	No comorbidity (n=63)	One comorbidity (n=55)	Two or more comorbidities (n=56)	Total (n=174)
Age, years				
Mean (SD)	68.89 (7.00)	71.57 (6.58)	70.70 (5.67)	70.32 (6.52)
Median	67.08	71	69.83	69.38
Range	60.08–86.83	60.67–84.25	60.58–84.50	60.08–86.83
60–69	39 (61.90)	23 (41.82)	29 (51.79)	91 (52.30)
≥70	24 (38.10)	32 (58.18)	27 (48.21)	83 (47.70)
Sex, n (%)				
Male	38 (60.32)	34 (61.82)	24 (42.86)	96 (55.17)
Female	25 (39.68)	21 (38.18)	32 (57.14)	78 (44.83)
Education, n (%)				
Primary school	39 (62.91)	38 (70.38)	40 (71.43)	117 (68.02)
High school	11 (17.74)	10 (18.51)	13 (23.21)	34 (19.78)
Master's degree and further	12 (19.35)	6 (11.11)	3 (5.36)	21 (12.20)
Missing	1	1	0	2
Living arrangements, n (%)				
Living with someone	48 (76.19)	40 (72.73)	38 (67.86)	126 (72.41)
Living alone	15 (23.81)	15 (27.27)	18 (32.14)	48 (27.59)
Global social support (MSPSS)				
Mean (SD)	5.87 (1.32)	5.73 (1.34)	5.27 (1.49)	5.63 (1.40)
Median	6.25	6.17	5.50	6
Range	1.17–7.00	1.08–7.00	1.00–7.00	1.00–7.00
ECOG performance status, n (%)				
0	35 (55.55)	36 (65.45)	33 (60.00)	104 (60.11)
1	24 (38.10)	18 (32.73)	21 (38.18)	63 (36.42)
2	4 (6.35)	1 (1.82)	1 (1.82)	6 (3.47)
3	0	0	1	1
Previous history of cancer, n (%)				
No	55 (87.3)	49 (90.74)	44 (78.57)	148 (85.55)
Yes	8 (12.7)	5 (9.26)	12 (21.43)	25 (14.45)
Missing	0	1	0	1
Sokal risk at diagnosis, n (%)				
Low (<0.8)	22 (35.48)	21 (40.38)	19 (35.18)	62 (36.90)
Intermediate (0.8–1.2)	33 (53.23)	24 (46.15)	28 (51.85)	85 (50.60)
High (>1.2)	7 (11.29)	7 (13.46)	7 (12.96)	21 (12.50)
Missing	1	3	2	6
Time since diagnosis, years				
Mean (SD)	5.58 (1.79)	5.39 (2.12)	5.40 (1.83)	5.46 (1.90)
Median	5.33	4.83	5.08	5.08
Range	3.00–12.17	3.00–11.50	3.00–10.75	3.00–12.17
Current prescribed dose of imatinib (mg/day)				
300 mg/day	12 (19.05)	12 (21.82)	5 (8.93)	29 (16.67)
400 mg/day	44 (69.84)	39 (70.91)	39 (69.64)	122 (70.11)
600 mg/day	2 (3.17)	3 (5.45)	2 (3.57)	7 (4.02)
Other	5 (7.94)	1 (1.82)	10 (17.86)	16 (9.2)
Complete molecular response, n (%)				
No	24 (38.10)	27 (49.09)	19 (33.93)	70 (40.23)
Yes	39 (61.90)	28 (50.91)	37 (66.07)	104 (59.77)

Table 1 (continued)

Variable	No comorbidity ($n=63$)	One comorbidity ($n=55$)	Two or more comorbidities ($n=56$)	Total ($n=174$)
Adverse events (any grade), n (%)				
Yes	22 (34.92)	19 (34.55)	27 (48.21)	68 (39.08)
No	41 (65.08)	36 (65.45)	29 (51.79)	106 (60.92)

SD standard deviation, *ECOG* Eastern Cooperative Oncology Group, *MSPSS* multidimensional scale of perceived social support

Multivariate analysis of the association of comorbidity and health-related quality of life

In a multivariate ANCOVA, we adjusted the comparison of the three comorbidity groups with regard to the SF-36 domains for important sociodemographic and disease-related patient characteristics. In this analysis, four out of eight SF-36 scales (physical functioning, bodily pain, general health, and vitality) remained significantly different among comorbidity groups even after Bonferroni correction for multiple testing. Details for this analysis are given in Tables 2 and 3.

To investigate the relative importance of comorbidity in comparison with disease-related and sociodemographic factors, we calculated proportions of explained variance in terms of total eta-square index (Fig. 3). For each scale, we report proportions of variance which are uniquely explained by either presence of
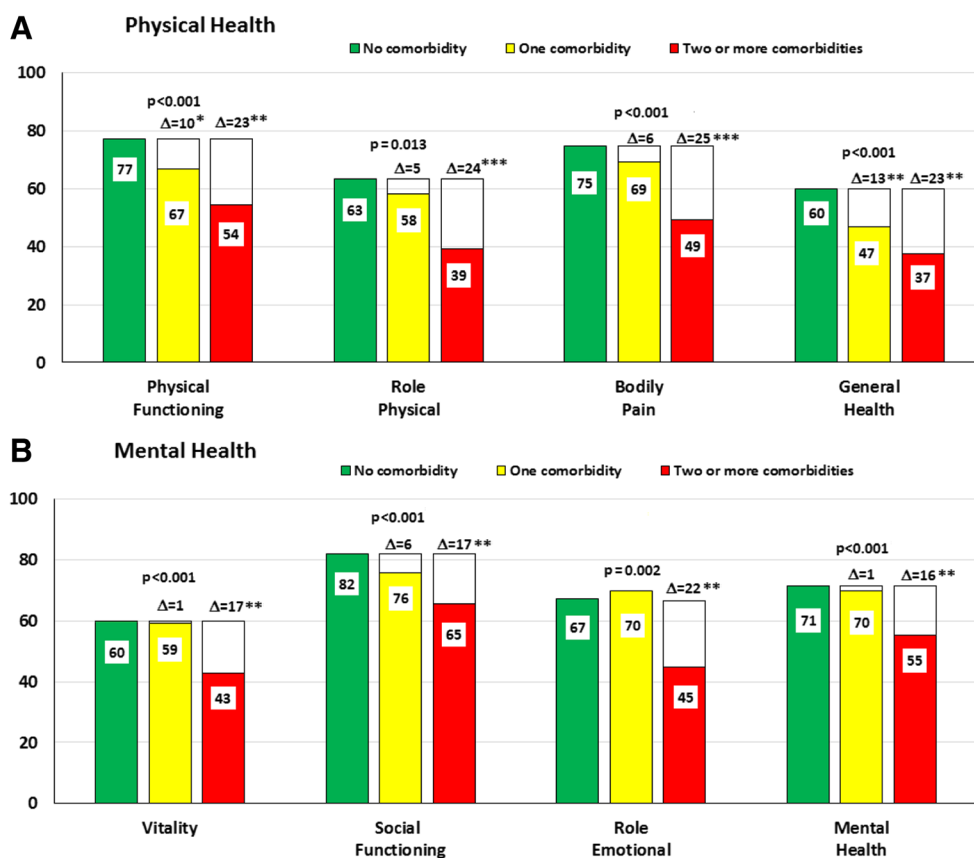

Fig. 1 **a**, **b** Health-related quality of life profile of elderly CML patients by number of comorbidities. Mean outcomes for the eight scales of the SF-36 questionnaire by number of patients' self-reported current comorbidities are shown. For each scale, higher scores denote better outcomes and lower scores worse outcomes. *p* value refers to the overall comparison of mean scores among patients with no, one, or at least two comorbidities, under the null hypothesis of no difference. Δ represents the positive score difference between patients with no comorbidities at all and those with either one or at least two comorbidities. Values reported in the figure were rounded. A *single asterisk* denotes that the score difference exceeds the minimally important difference (i.e., 8 points). *Double asterisks* indicate that the score difference equals to or exceeds twice the minimally important difference. *Triple asterisks* entail that the score difference equals to or exceeds three times the minimally important difference
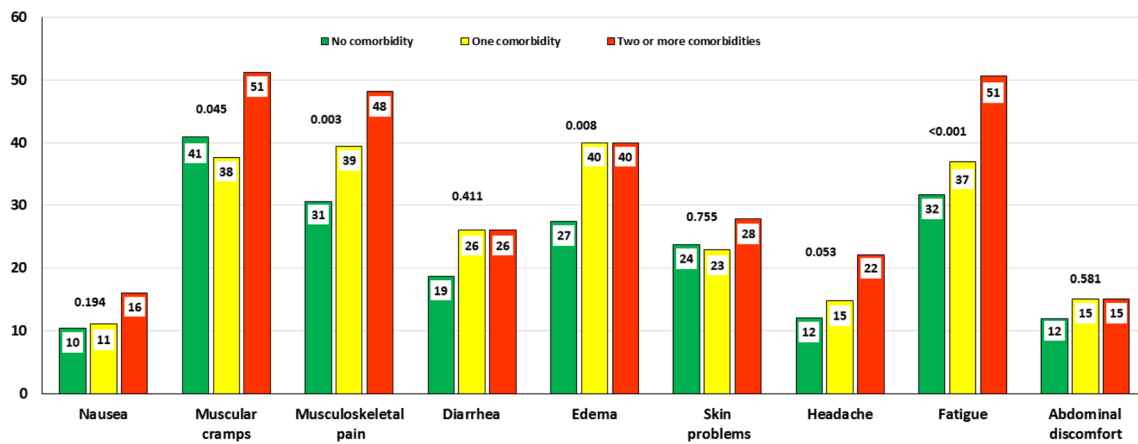
Fig. 2 Self-reported symptom severity of elderly CML patients by number of comorbidities. For each symptom, higher scores denote higher symptom severity while lower scores indicate lower symptom severity. Values reported in the figure were rounded. *p* value refers to the overall comparison of mean scores among patients with no, one, or at least two comorbidities, under the null hypothesis of no difference

comorbidities, disease-related, or sociodemographic variables. We found that for general health (15 % explained variance) and bodily pain (12 % explained variance), the presence of co-morbidities explained substantially more variance than disease-related or sociodemographic variables.

Discussion

We have found that some two thirds of CML patients aged 60 years or above reported at least one comorbidity and that the presence of this was associated with important impairments in both physical and mental health domains. This negative association with HRQOL outcomes was particularly remarkable in patients who reported two or more comorbid conditions.

In a recent large population-based registry study, it was found that 55 % of the 2904 CML patients analyzed had at least one comorbidity. Although this percentage is slightly lower than that found in our study (i.e., 64 %), it should be noted that in this registry, also patients younger than 60 years were represented.

Saussele and colleagues [25] recently showed that comorbidity at diagnosis was an independent prognostic factor for shorter survival in imatinib-treated CML patients regardless of age. They concluded that the presence of comorbidity is more important than the disease itself in determining the survival of patients. Our findings complement this remarkable data [25] by showing that comorbidity also heavily influence HRQOL of elderly patients. Notably, in our analysis of variance, the presence of co-morbidities was by far the most important contributor in determining the subjective general health status scale of the SF-36.

Considering the paucity of research on this topic, it is difficult to compare our findings with other similar CML studies. However, our results are broadly consistent with the few studies conducted in patients with other hematologic malignancies

(mainly Hodgkin's and non-Hodgkin's lymphoma patients) indicating the negative impact of comorbidities on patients' HRQOL [26–28].

In our previous study [29] analyzing the whole sample, we found that fatigue was independently associated with all HRQOL physical and mental health domains of the SF-36. In this analysis, specifically investigating the role of comorbidity on HRQOL in the elderly sub-population (i.e., with a substantial higher number of comorbid conditions), we found that comorbidity was associated with both HRQOL and fatigue. Taken together, both findings might suggest that, in elderly patients, comorbidity could possibly impair HRQOL by raising patients' fatigue levels. Whether the presence of comorbidities can determine an increased symptom severity, which can in turn negatively affect more general aspects of HRQOL, should be investigated in future prospective studies. The identification of a causal model on the pathways of how comorbidity could influence the various aspects of HRQOL, would be important to inform the development of future intervention studies in elderly patients.

Our findings have two important implications. From a clinical practice perspective, our results suggest that elderly patients with comorbidities should be more closely monitored due to their poorer HRQOL outcomes. They might represent a specific population who can benefit the most from supportive care programs. Another implication is for better designing and interpreting future HRQOL research studies of elderly CML patients. Our results indicate that comorbidity should be considered as a key variable to adjust for, in order to increase robustness of study results and outcome interpretation. Therefore, routinely collecting and quantifying comorbid conditions possibly using well-validated indices in clinical practice and research is strongly recommended.

Our study has limitations. First, given the cross-sectional design, we cannot draw conclusions on causal relationships

Table 2 Multivariate ANCOVA on physical health-related aspects of elderly CML patients

Variable	Physical functioning		Role physical		Bodily pain		General health	
	β (95 % CI)	p	β (95 % CI)	p	β (95 % CI)	p	β (95 % CI)	p
Comorbidity		0.002*		<0.001*		0.042		<0.001*
One vs not at all	−4.331 (−13.317; 4.655)		−7.439 (−23.924; 9.046)		−3.846 (−13.699; 6.008)		−13.032 (−21.325; −4.738)	
Two or more vs not at all	−15.863 (−24.700; −7.026)		−20.755 (−36.967; −4.542)		−22.000 (−31.691; −12.309)		−20.950 (−29.106; −12.794)	
Sokal risk (ref. high)	0.876 (−7.029;8.871)	0.827	2.376 (−12.126; 16.879)	0.746	−0.305 (−8.974; 8.364)	0.945	−0.200 (−7.496; 7.096)	0.957
Complete molecular response (ref. yes)	4.660 (−2.844; 12.165)	0.222	1.328 (−12.439; 15.095)	0.849	−3.537 (−11.766; 4.692)	0.397	3.018 (−3.908; 9.944)	0.390
Sex (ref. female)	15.562 (7.960; 23.165)	<0.001*	24.371 (10.423; 38.319)	0.001*	12.168 (3.831; 20.505)	0.005*	9.016 (1.999; 16.032)	0.012
Education (ref. high)	−7.820 (−15.759; 0.118)	0.053	−10.583 (−25.147; 3.980)	0.153	−6.577 (−15.282; 2.128)	0.137	−3.132 (−10.459; 4.194)	0.399
Age (years)	−0.988 (−1.585; −0.390)	0.001*	−0.596 (−1.692; 0.501)	0.285	−0.214 (−0.870; 0.441)	0.519	0.051 (−0.501; 0.602)	0.856
Social support[a]	0.916 (−1.861; 3.693)	0.515	−0.584 (−5.679; 4.511)	0.821	0.816 (−2.229; 3.862)	0.597	0.521 (−2.042; 3.084)	0.688
Time since diagnosis (years)	0.624 (−1.407; 2.655)	0.544	0.723 (−3.004; 4.450)	0.702	0.855 (−1.372; 3.083)	0.449	0.027 (−1.848; 1.902)	0.977

CI confidence interval

*Statistically significant after Bonferroni correction for multiple testing (p<0.006)

[a] Higher scores indicate greater support

Table 3 Multivariate ANCOVA on mental health-related aspects of elderly CML patients

Variable	Vitality		Social functioning		Role emotional		Mental health	
	β (95 % CI)	p	β (95 % CI)	p	β (95 % CI)	p	β (95 % CI)	p
Comorbidity		0.002*		0.025		0.021		0.010
One vs not at all	0.591 (−7.424; 8.606)		−6.224 (−15.184;2.735)		−0.138 (−16.464; 16.188)		−1.978 (−9.540; 5.585)	
Two or more vs not at all	−12.802 (−20.685; −4.920)		−12.247 (−21.058; −3.435)		−20.435 (−36.491; −4.378)		−11.072 (−18.510; −3.635)	
Sokal risk (ref. high)	2.129 (−4.922; 9.180)	0.551	−2.064 (−9.947; 5.818)	0.605	4.298 (−10.065; 18.661)	0.555	1.611 (−5.043; 8.264)	0.633
Complete molecular response (ref. yes)	1.232 (−5.462; 7.925)	0.717	2.880 (−4.603; 10.363)	0.448	2.972 (−10.662; 16.607)	0.667	3.075 (−3.241; 9.391)	0.337
Sex (ref. female)	14.305 (7.524; 21.086)	<0.001*	7.883 (0.303; 15.464)	0.042	19.729 (5.915; 33.542)	0.005*	13.763 (7.365; 20.162)	<0.001*
Education (ref. high)	−0.961 (−8.042; 6.119)	0.789	0.891 (−7.024; 8.807)	0.824	−4.540 (−18.964; 9.883)	0.535	2.071 (−4.610; 8.752)	0.541
Age (years)	−0.263 (−0.796; .270)	0.331	−0.091 (−0.687; 0.0505)	0.763	−0.597 (−1.683; 0.489)	0.279	−0.289 (−0.792; 0.214)	0.258
Social support[a]	2.160 (−0.317; 4.637)	0.087	4.225 (1.456; 6.994)	0.003*	0.249 (−4.797; 5.295)	0.922	3.114 (0.776; 5.451)	0.009
Time since diagnosis (years)	1.105 (−0.707; 2.917)	0.230	1.088 (−0.937; 3.114)	0.290	−0.586 (−4.277; 3.104)	0.754	0.585 (−1.125; 2.294)	0.500

CI confidence interval

*Statistically significant after Bonferroni correction for multiple testing (p<0.006)

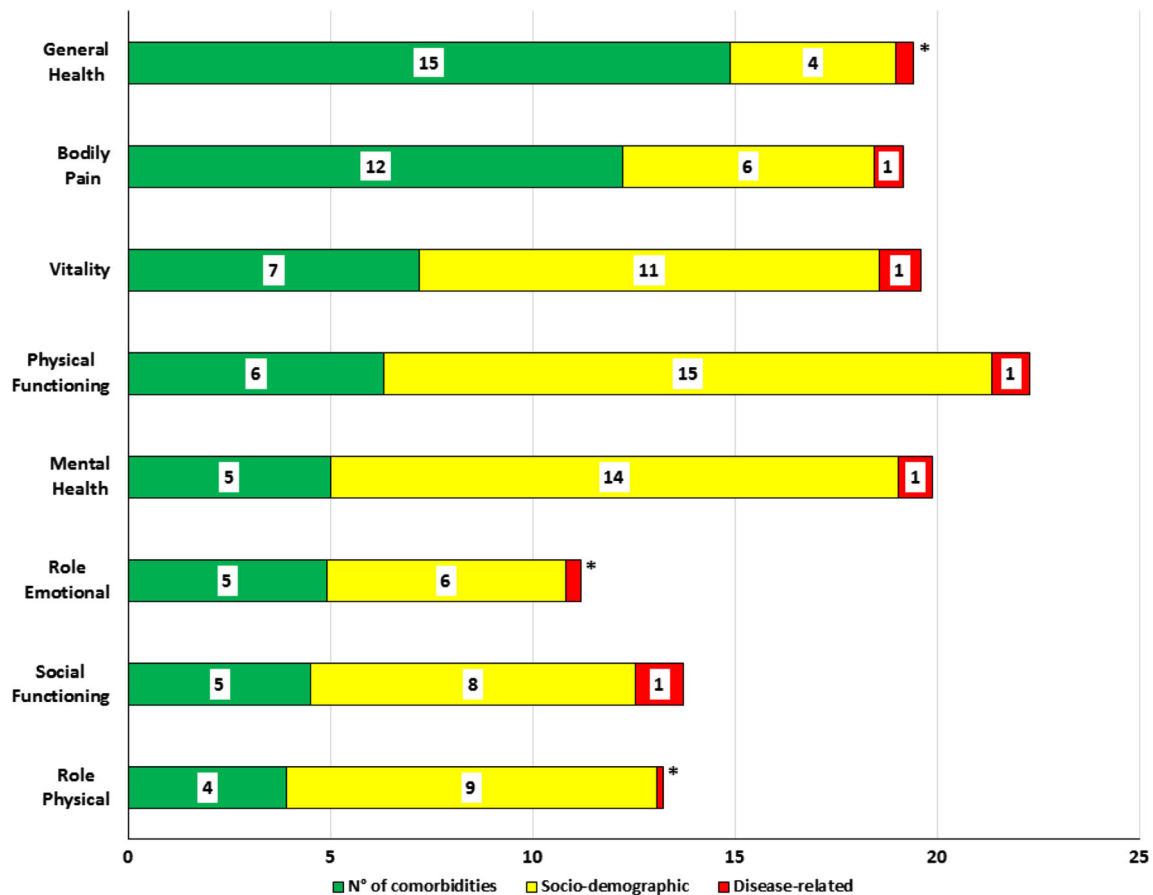[a] Higher scores indicate greater support

Fig. 3 Explained variance (%) of health-related quality of life of elderly CML patients. Mean outcomes for the eight scales of the SF-36 questionnaire are shown. For each scale, the figure shows the percentage of variance (total eta-squared) explained in the multivariate ANCOVA model (as reported in Tables 2 and 3), by presence of comorbidities, sociodemographic factors (age, sex, education, and social support), and disease-related variables (Sokal risk, complete molecular response, time since diagnosis). Values reported in the figure were rounded. A *single asterisk* signifies that the explained variance is less than 1 %

between comorbidity and HRQOL or specific symptoms. Also, given the self-reported nature of comorbidity data collection, we cannot rule out the possibility of underreporting of comorbid conditions. For example, as major cognitive dysfunction or psychiatric problems were an exclusion criterion of the original study, this might have contributed to the underreporting of psychological-related comorbidities.

These limitations notwithstanding, our study also has strengths. Our sample was homogenous with regard to therapy received, thus ruling out the potential confounding effect of type and schedule of therapy when analyzing the association between comorbidity and HRQOL. Also, we accounted for the role of social support, which might be particularly important in determining HRQOL of elderly people. Finally, our results have been generated in an observational setting thus most likely to be generalizable to CML patients seen in daily practice.

In conclusion, the presence of comorbidity in elderly CML patients is associated with diminished physical and mental health well-being. Therefore, assessing comorbidity in elderly patients is important to facilitate identification of those most in need of HRQOL improvements. It is likely that assessing comorbidities is also equally important in younger patients and this should be examined in future studies.

Authors' contributions   FE, MB, MBA, and GR did the conception and design of this study. FC and FE completed the statistical analysis. FE, FC, GR, and MB carried out manuscript writing. All authors did the collection and assembly of data and the final approval of manuscript.

Compliance with ethical standards   Ethic committees of participating centers approved the study. All patients provided written informed consent.

Conflict of interest   The authors declare that they have no conflict of interest.

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