Background: The overall landscape of health-related quality of life (HRQoL) has not been thoroughly investigated in adolescents and young adults (AYAs) with cancer. Data are also lacking on how well HRQoL at the time of cancer diagnosis can prognosticate long-term survival in AYA survivors. Patients and Methods: We included 3,497 survivors of AYA cancer (age 15–39 years at diagnosis) who completed the Short-Form 12 Health Survey (SF-12) HRQoL questionnaire at diagnosis. Physical component summary (PCS) and mental component summary (MCS) scores were generated, with scores < 50 representing poor HRQoL. Differences in HRQoL by patient characteristics and tumor type were investigated using violin plots and t-tests/analysis of variance. The effect of HRQoL on overall survival was assessed using Kaplan-Meier plots and Cox proportional hazards models. Results: Overall mean PCS and MCS scores in this racially/ethnically diverse cohort (64% White, 19% Hispanic, 10% Black, and 7% other race/ethnicity) were 43.6 and 46.7, respectively. Women with breast cancer reported the most favorable PCS (50.8), and those with cervical cancer reported the lowest MCS (42.8). Age at diagnosis was associated positively with PCS (P < .001) and inversely with MCS (P < .001). Females had higher PCS yet lower MCS than males (both P < .001). Marginalized racial and ethnic populations reported lower PCS than White patients (P < .001). Physical and mental HRQoL were prognostic and associated with increased risk of poor survival (hazard ratio, 1.95; 95% CI, 1.72–2.21 for physical HRQoL, and 1.26; 95% CI, 1.13–1.40 for mental HRQoL). Conclusions: Physical and mental HRQoL at diagnosis vary across patient characteristics in AYA cancer survivors. Poor HRQoL at diagnosis may be a prognosticator of diminished overall survival among AYA cancer survivors.

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status–specific, consisting of 12 items derived from the longer SF-36 questionnaire.20,21 The SF-12 has been used in multiple studies in patients with cancer,22 and measures 8 domains of general HRQoL.

Patients and Methods

AYA Cancer Survivor Population

The AYA cancer survivor population was generated from a retrospective search of the MD Anderson Cancer Center’s Tumor Registry for those who were evaluated at the institution between 2000 and 2016 and diagnosed with a primary cancer during the AYA age range (15–39 years). As part of routine hospital registration practice for all patients evaluated at MD Anderson Cancer Center between 1999 and 2017, these AYAs completed a patient health intake questionnaire that included assessment of HRQoL using the validated Short-Form 12 Health Survey, Version 1 (SF-12v1) questionnaire.20 The population was restricted to those who completed the full questionnaire to enable calculation of the SF-12v1 summary scores within 6 months of cancer diagnosis. A total of 7,030 AYA patients with cancer were identified. Patients who did not complete the full questionnaire were grouped as those who completed the questionnaire >6 months after cancer diagnosis (n = 1,435) and those completing the questionnaire ≥6 months after cancer diagnosis (n = 1,435) were removed from the analysis, generating the final population of 3,497 AYA patients. The median time from diagnosis to questionnaire completion was 1.1 months (IQR, 1.0 month). Nearly 80% of the population completed the questionnaire within 2 months of diagnosis (n = 2,771). Data abstracted from the Tumor Registry included cancer diagnosis, date of diagnosis, date of birth, race/ethnicity, gender, vital status, and date of last follow-up. Patients with Asian, Native Hawaiian/Pacific Islander, American Indian/Alaska Native, or unknown race/ethnicity classification were grouped as “other.” Written informed consent was provided by all participants and the study was approved by MD Anderson’s Institutional Review Board.

SF-12 HRQoL Questionnaire and Scoring

The SF-12v1 questionnaire consists of 12 items that generate 2 composite summary scores: the physical component summary (PCS) and mental component summary (MCS).22 Scoring for the pain interference question of the SF-12 was slightly modified in the questionnaire, with responses on a scale of 0 to 10 instead of the SF-12 reported on a scale of 0 to 5. Therefore, the scores were adjusted to match the SF-12 scoring range. A norm-based scoring system was used in which the MCS and PCS scores were normalized to a mean (SD) score of 50 [10] based on SF-12 data obtained from the US general population. Higher PCS and MCS scores represent better HRQoL. Additionally, a high MCS or PCS (≥50) is indicative of a better HRQoL compared with the general population, whereas a low MCS or PCS (<50) is indicative of a poor HRQoL compared with the general population. The recall period was 4 weeks.

Statistical Methods

Violin plots were used to visualize the distribution and probability density of PCS and MCS scores by tumor type, age at diagnosis, gender, and race/ethnicity. Differences in mean MCS and PCS scores by these characteristics were assessed using independent samples t tests or analysis of variance (ANOVA) for binomial or multinomial independent variables, respectively. Survival was defined as date of diagnosis to date of death or last follow-up, with ascertainment of follow-up through 2022. Survival estimates were calculated by Kaplan-Meier method with corresponding log-rank P values. An overall multivariable Cox proportional hazards model was created to identify independent risk factors associated with OS, and included PCS, MCS, gender, race/ethnicity, age at diagnosis, tumor type, and year of diagnosis.

Results

Study Population

A total of 3,497 AYA patients with cancer were included in the analysis (Table 1). The distribution of patient variables for those included in the analysis compared with those excluded (n = 3,533) were comparable, with only slight increases in White patients and those with more favorable diagnoses (eg, breast cancer and HL) in the final patient population compared with those who were removed during the selection process. The median age at diagnosis across the AYA age range was 32 years (IQR, 10 years). Breast cancer was the most frequent diagnosis (20.4%), followed by sarcoma (12.8%) and leukemia (10.5%). Our patient population was diverse, including 35.7% of participants who self-identified as Black, Hispanic, or other. The median follow-up time was 9.2 years (IQR, 11.7 years), with 1,402 deaths recorded during this period.

PCS and MCS Score Distribution and OS

The distributions of PCS and MCS scores and impact on OS are shown in Figure 1. PCS scores in the overall cohort ranged from 11.3 to 70 with a mean (SD) of 43.6 [11.9] (Figure 1A). The mean (SD) MCS score was slightly higher at 46.7 [10.7] (range, 10–69; Figure 1C). AYA cancer survivors with poor PCS (<50) at time of cancer diagnosis had lower OS durations than their counterparts with PCS ≥50 (log-rank P < .001), resulting in a >20% reduction in the 5-year survival rate from 78.9% to 56.0% (Figure 1B). Poor PCS was associated with increased risk of death (hazard ratio [HR], 1.95; 95% CI, 1.72–2.21; P < .001). Poor MCS (<50) at diagnosis compared with MCS ≥50 was associated with decreased survival (log-rank P < .001) (Figure 1D) and increased risk of death (HR, 1.26; 95% CI, 1.13–1.40; P < .001).

PCS and MCS by Tumor Type

Mean PCS (P < .001) and MCS (P < .001) scores varied by tumor type (Table 1). Patients with breast cancer reported the most favorable PCS (50.8) at diagnosis, yet among the lowest MCS (46.3). The distributions of PCS and MCS scores were unique for each tumor type (Figure S1A in the supplementary material, available online with this article). Apart from breast cancer, all tumor types had median PCS scores <50, and the proportions of PCS scores <40 were pronounced for cervical cancer, colorectal cancer, leukemia, and sarcoma. Combined, patients with solid tumors had more favorable PCS compared with those diagnosed with hematological malignancies (P < .001). There was less variation in MCS by tumor type compared with PCS scores. The distributions of MCS scores tended to be more unimodal across all 10 tumor types analyzed, with only patients with cervical cancer reporting a mean MCS score of <45 (Table 1).

OS by tumor type is shown in Figure 2A. Patients diagnosed with central nervous system (CNS) tumors, colorectal cancer,
leukemia, sarcoma, and the other tumors group had 5-year survival rates <60%. When stratified by tumor type, poor PCS at diagnosis was associated with inferior survival for patients with breast cancer, CNS tumors, colorectal cancer, HL, leukemia, sarcoma, and other tumors (Figure 2B). Poor MCS was associated with lower survival in patients with HL (log-rank P = .0093), germ cell tumors (log-rank P = .038), and other tumor types (log-rank P = .002; Figure 2C).

**PCS and MCS by Race/Ethnicity**

Marginalized racial and ethnic AYA patients with cancer had significantly worse PCS than White AYA patients with cancer (P = .0023). Black AYA patients with cancer reported the lowest PCS at diagnosis, with 67.8% reporting PCS <50 compared with 60.9% of Hispanic and 58.0% of White patients. No significant differences were observed for MCS by race/ethnicity (Table 1) and the distributions were similar across groups (Supplementary Figure S1B).

Black patients had a 5-year survival rate of 53.2% that was nearly 10% lower than White and Hispanic patients (64% for each; Figure 3A). Survival differed by race/ethnicity (log-rank P <.001). When stratified by race/ethnicity, a significant reduction in survival by poor PCS was observed for Black (log-rank P = .0026), Hispanic (log-rank P <.001), White (log-rank P <.001), and other race/ethnicity (log-rank P = .0021) (Figure 3B). MCS did not differ by race/ethnicity (P = .26; Table 1), yet the effect of poor MCS on shorter survival was observed in the Hispanic (log-rank P = .024) and White (log-rank P = .0019) AYA cancer patient populations (Figure 3C).

**PCS and MCS by Age at Diagnosis**

Older age at diagnosis was associated with a higher mean PCS; however, a lower mean MCS (P < .001 for each; Table 1). The distribution of PCS and MCS scores stratified by diagnosis age categories show similar features (Supplementary Figure S1C)—a greater proportion of poor PCS scores was observed for adolescent patients (age 15–18 years) and lower MCS scores for young adult patients (age 26–39 years). Survival also differed by age category, with adolescents having a higher 5-year survival rate compared with both emerging adults (age 19–25 years) and young adults (Supplementary Figure S2A). When stratified by age categories, PCS was a significant prognostic feature for all 3 age categories (Supplementary Figure S2B), yet MCS was prognostic for only emerging and young adults (Supplementary Figure S2C).

**PCS and MCS by Gender**

Female AYA survivors had significantly higher PCS, yet lower MCS compared with male AYA patients (both P < .001; Table 1, Supplementary Figure S1D). Males had an increased risk of death compared with females (log-rank P = .0031; Supplementary Figure S3A). The negative effect of poor PCS on survival was evident in both male and female AYA survivors (both log-rank P < .0001; Supplementary Figure S3B). MCS was also associated with survival in males (log-rank P < .0006) and females (log-rank P = .0051; Supplementary Figure S3C).

**HRQoL as a Predictor of OS**

Low PCS (HR, 1.91; 95% CI, 1.69–2.17; P < .001) and low MCS (HR, 1.18; 95% CI, 1.06–1.32; P < .001) at diagnosis were independent

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**Table 1. Baseline Characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (%)</th>
<th>PCS Mean [SD]</th>
<th>P Value*</th>
<th>MCS Mean [SD]</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total, N</td>
<td>3,497</td>
<td>43.6 [11.9]</td>
<td>&lt;.001</td>
<td>46.7 [10.7]</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Tumor type</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>712 (20)</td>
<td>50.8 [9.3]</td>
<td>46.3 [10.4]</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Sarcoma</td>
<td>448 (13)</td>
<td>39.7 [12.1]</td>
<td>48.3 [10.8]</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Leukemia</td>
<td>366 (11)</td>
<td>41.7 [10.7]</td>
<td>47.4 [10.2]</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>HL</td>
<td>287 (8.2)</td>
<td>45.1 [11.1]</td>
<td>48.0 [10.3]</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>NHL</td>
<td>284 (8.1)</td>
<td>42.3 [12.2]</td>
<td>46.4 [10.7]</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>GCT</td>
<td>226 (6.5)</td>
<td>44.0 [10.9]</td>
<td>47.7 [10.1]</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>CRC</td>
<td>215 (6.5)</td>
<td>41.0 [12.1]</td>
<td>46.0 [11.2]</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>CNS</td>
<td>128 (3.7)</td>
<td>43.8 [10.2]</td>
<td>46.9 [10.6]</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Cervical</td>
<td>120 (3.4)</td>
<td>42.3 [13.2]</td>
<td>42.8 [11.6]</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>711 (20)</td>
<td>40.7 [11.9]</td>
<td>45.9 [11.2]</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Age at diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adolescent (15–18 y)</td>
<td>205 (5.9)</td>
<td>42.0 [11.4]</td>
<td>49.4 [11.1]</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Emerging adult (19–25 y)</td>
<td>629 (18)</td>
<td>42.1 [12.1]</td>
<td>48.1 [10.6]</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Young adult (26–39 y)</td>
<td>2,463 (76)</td>
<td>44.1 [11.8]</td>
<td>46.2 [10.7]</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>2,006 (57)</td>
<td>44.5 [11.9]</td>
<td>45.6 [10.7]</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1,491 (43)</td>
<td>42.5 [11.7]</td>
<td>48.2 [10.6]</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>2,248 (64)</td>
<td>44.1 [11.9]</td>
<td>46.7 [10.7]</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>657 (19)</td>
<td>43.2 [11.8]</td>
<td>46.1 [11.0]</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>345 (9.9)</td>
<td>41.2 [11.9]</td>
<td>47.4 [11.0]</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>OtherB</td>
<td>247 (7.1)</td>
<td>43.9 [11.4]</td>
<td>47.0 [10.2]</td>
<td>&lt;.001</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CNS, central nervous system; CRC, colorectal cancer; GCT, germ cell tumor; HL, Hodgkin lymphoma; MCS, mental component summary; NHL, non-Hodgkin lymphoma; PCS, physical component summary.

*Bold indicates statistically significant P value.

BAsian, Native Hawaiian/Pacific Islander, American Indian/Alaska Native, or unknown.
predictors of diminished OS in multivariable Cox proportional hazards regression model that included gender, diagnosis age, race/ethnicity, tumor type, and year of diagnosis (Table 2).

**Discussion**

In this large, diverse cohort of AYA patients with cancer, HRQoL at diagnosis was impacted by tumor type, age at diagnosis, race/ethnicity, and gender. Low physical (PCS) and mental (MCS) HRQoL at diagnosis were independent predictors of diminished survival among AYAs with cancer. To the best of our knowledge, this study is the first to show that patient-reported HRQoL at diagnosis is predictive of lower OS in AYAs with cancer.

The present study identified distinctive distributions of PCS and MCS scores at diagnosis across the most common tumor types diagnosed in the AYA population, such as CNS tumors, HL, non-Hodgkin lymphoma, leukemia, breast cancer, and cervical cancers, for which data on PCS and MCS in AYAs are often lacking. Our physical HRQoL results across individual tumor types extends findings by Smith et al, which found poorer PCS in AYA patients with sarcoma compared with germ cell tumors. However, our finding of differences in physical HRQoL by tumor type contrasts with results from Siembida et al, which showed that physical HRQoL did not differ by whether patients had hematologic or solid tumors in their sample of 572 AYAs. The finding of an association between poor PCS at diagnosis and reduced OS in AYAs patients, particularly those with sarcoma, colorectal cancer, CNS tumors, breast cancer, HL, and leukemia, could potentially guide the identification of those in greatest need of supportive interventions to improve overall health and well-being long-term.

Age at diagnosis was an important factor modulating the variation observed in PCS and MCS. The finding that younger AYAs (adolescents and emerging adults) with cancer had worse PCS than older AYAs (young adults) may be due to younger AYAs having more aggressive tumors than older AYAs. For example, in a study of breast cancer, Murphy et al found that AYAs aged 15 to 29 years were more likely to have more advanced stages of disease and HER2-positive or triple-negative breast cancer than AYAs aged 30 to 39 years. However, in the analysis by Siembida et al, older, off-treatment AYA patients had a higher burden of poor HRQoL than patients aged 15 to 17 years. The superior MCS scores in younger AYAs compared with older AYAs in the present study may be explained, in part, by younger AYAs having less financial toxicity than older AYAs, or perhaps by younger AYAs still enjoying greater active parental support and still living with their parents, whereas older AYAs may also experience greater psychosocial pressures from less tangible family support and having to live independently, possibly starting a career, and perhaps bearing greater worry/responsibility.

**Figure 1.** (A) Distribution of PCS scores, (B) survival curves stratified by PCS ≥50, (C) distribution of MCS scores, and (D) survival curves stratified by MCS ≥50 in AYA patients with cancer.

Abbreviations: AYA, adolescent and young adult; MCS, mental component summary; PCS, physical component summary.
Figure 2. (A) Overall survival by tumor type, and survival curves stratified by (B) PCS ≥50 and (C) MCS ≥50 in AYA patients. Solid line: PCS/MCS ≥50; dotted line: PCS/MCS <50.

Abbreviations: AYA, adolescent and young adult; CNS, central nervous system; CRC, colorectal cancer; GCT, germ cell tumor; HL, Hodgkin lymphoma; MCS, mental component summary; NHL, non-Hodgkin lymphoma; PCS, physical component summary.
regarding their own future and the future of their possibly young families/children.

Few studies have reported on the relationship between race/ethnicity and HRQoL in the AYA cancer patient population. Keegan et al.\(^{26}\) previously reported that AYA patients from marginalized racial and ethnic groups are more likely to be diagnosed with cancer at a later stage of disease than non-Hispanic White AYAs. In an analysis of HRQoL in adult patients with colorectal cancer from MD Anderson, the relationship between poor HRQoL and survival was evident in patients with stage III and IV disease, while attenuated for those with stages I and II at diagnosis.\(^{15}\) Data on stage at diagnosis were not available.
The prognostic value of PROs is of interest because it is a cost-effective alternative when compared with laboratory-based markers of prognosis. It also facilitates access to specific potential interventions (ie, targeting physical functioning and/or mental health) that could improve the patient’s well-being and thus the possibility of altering patients’ long-term prognoses. With the increasing interest in PROs, studies focusing on potential interventions to improve outcomes are emerging. Kent et al33 used PROs related to pain and pain-related interference with daily activities to determine patient eligibility for a randomized intervention trial. Intervention included cognitive functional therapy with or without wearable-generated movement sensor biofeedback. This intervention produced significant and durable improvements in patient-reported activity limitations and pain scores among this low HRQoL population. In a phase II randomized, controlled trial, fatigue scores from a symptom assessment scale were used as an eligibility criterion to identify participants with cancer-related fatigue who were subsequently randomized to a successful multimodal intervention of physical activity and dexamethasone aimed at alleviating cancer-related fatigue.34 Several physical activity interventions utilizing varying characteristics, including individualized physical activity prescriptions, supervised structure, goal setting, and wearable devices, have been reported to improve HRQoL, anxiety, and depression among AYA cancer survivors.35

Potential limitations include that this study encompasses a single, albeit large, tertiary comprehensive cancer center, making it unclear whether these findings are generalizable to other cancer care settings, such as community practices. HRQoL was assessed within 6 months of diagnosis, with a median time to questionnaire completion of 1.1 months. This approach was taken to minimize the impact of treatment on HRQoL, but a portion of the participants may have been in active treatment at the time of assessment, potentially inflating the levels of “baseline” HRQoL. Availability of specific treatment and stage information would have been informative in our analyses of HRQoL and OS. The lack of information on how HRQoL changed longitudinally between baseline and the first 2 years of survival is a potential limitation as well, given that a study by Husson et al9 has shown that HRQoL can improve significantly in AYAs between the time of initial cancer diagnosis and 1 year postdiagnosis.

Conclusions

Our findings suggest that patient-reported HRQoL in AYAs diagnosed with cancer varies by cancer type and patient demographics, and that poor HRQoL at diagnosis can be used as a potential biomarker of poor prognosis. Furthermore, our study highlights the importance of collecting HRQoL among AYAs at diagnosis, so that they can be offered appropriate interventions to improve their HRQoL and physical and psychological functioning. Further studies are needed to identify these targeted interventions to improve outcomes for AYAs with cancer.

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References


5. US Food and Drug Administration. Core patient-reported outcomes in cancer clinical trials: guidance for industry. Accessed April 1, 2024. Available at: https://www.fda.gov/media/149994/download


