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Associations between age and patient-reported outcomes, emergency department visits, and hospitalizations among lung cancer patients receiving immune checkpoint inhibitors

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Abstract

Objective: Immune checkpoint inhibitors (ICIs) for lung cancer (LC) treatment have a more favorable safety profile and improved patient reported outcomes (PROs) compared to chemotherapy, suggesting that ICIs are advantageous for older populations. The impact of ICIs on PROs, clinical outcomes, and age in LC patients remains to be established. We examined associations between age and PROs, emergency department (ED) visits, and hospitalizations in LC patients receiving ICIs.

Methods: We performed retrospective analyses via *My Wellness Check* (*MWC*), an assessment and triage electronic medical record (EMR) integrated platform in LC patients receiving ICIs. Demographics, clinical characteristics, ED visits, and hospitalizations were extracted via EMR. Patient reported outcomes (PROMIS® anxiety, depression, fatigue, pain, physical function), and health-related quality of life (HRQOL; FACT-G7), were collected via *MWC*. We classified age into three categories (<65, 65–74, ≥75). Multiple regressions examined associations between PROs and age. Cox proportional hazards regressions assessed cumulative ED visits and hospitalizations.

Results: Among LC patients (N = 190) receiving ICIs, patients ≥75 had lower depression ($\beta = -5.80$, $p = 0.01$) and higher HRQOL ($\beta = 2.47$, $p = 0.05$) compared with patients <65. Relative to patients <65, patients 65–74 had lower anxiety ($\beta = -3.31$, $p = 0.05$) and pain ($\beta = -4.18$, $p = 0.03$). Patients 65–74 and ≥ 75 had lower risk of an ED visit (adjusted hazards ratio [aHR] = 0.45, $p = 0.05$ and aHR = 0.21, $p = 0.05$, respectively) and patients 65–74 had lower risk of hospitalization (aHR = 0.36, $p = 0.02$) relative to patients <65.

Conclusions: Older LC patients (65–74; ≥75) have more favorable PROs and lower risk for negative clinical outcomes than younger (<65) patients.

KEYWORDS
anxiety, cancer, depression, fatigue, hospitalization, immune checkpoint inhibitors, lung cancer, oncology, patient reported outcome measures, quality of life

1 | INTRODUCTION

Over the past decade, immune checkpoint inhibitors (ICIs) such as nivolumab, atezolizumab, and pembrolizumab have revolutionized lung cancer (LC) treatment. Numerous trials point to a superior efficacy of ICIs alone and in combination with chemotherapy in overall survival relative to chemotherapy alone.[1–4] The phase III KEYNOTE-024 and OAK trials demonstrated significant overall and progression-free survival in advanced non-small-cell LC (NSCLC) patients treated with ICIs (i.e., pembrolizumab and atezolizumab, respectively) compared with chemotherapy.[1,2] Similarly, pooled data from several clinical trials found that NSCLC patients treated with pembrolizumab plus chemotherapy demonstrated survival improvements compared to those treated with chemotherapy alone.[3] Further, results from these trials also suggest that patients receiving ICIs exhibit less adverse events (e.g., diarrhea, vomiting)[5] and improved patient-reported outcomes (PROs; e.g., health-related quality of life [HRQOL], anxiety, pain interference)[6] compared to patients receiving chemotherapy or in combination with ICIs. As such, it has been suggested that treatment with ICIs may be more tolerable for older patients.[7] However, older individuals and those with multiple comorbidities and declining overall health are underrepresented in clinical trials[8]; thus, research is needed to characterize the impact of ICIs on clinical outcomes in these populations and examine whether specific age groups may face a greater risk of poor clinical outcomes.

Patient reported outcomes (PROs) are assessments of a patient's health status provided directly by the patient that are utilized to identify often overlooked problems within a routine clinical assessment. Emerging evidence indicates that PROs are predictive factors for overall and progression-free survival. For example, pooled data from several single-arm atezolizumab trials found that patient-reported physical function, fatigue, and global health were predictive of overall survival in patients with advanced NSCLC treated with ICIs.[9] However, clinical trials are often limited to samples that may not represent patients in the real-world clinical environment (i.e., older adults) and allow for comparisons across various age groups. In a large population-based study of older adults (≥65 years old) with LC, Pinheiro et al.[10] examined the prognostic value of PROs predicting overall survival. Findings indicated that HRQOL and activities of daily living (ADL; e.g., eating, dressing, walking, and using the toilet) were significant predictors of overall survival such that lower HRQOL and the inability to preform ADL were associated with greater risk of death. However, few studies have investigated age-related differences in PROs, particularly among LC patients receiving ICIs. Several studies have found no age-related differences in HRQOL or function decline over time in LC patients receiving traditional anti-cancer treatments (e.g., chemotherapy, radiation).[11,12] Yet, emerging research indicates that younger LC patients receiving ICIs report poorer social and emotional functioning and symptom burden compared with their older counterparts.[13] Given the growing evidence that there are potential age-related differences among PROs, it is important to examine PROs not only across age groups but also in "real-world" ambulatory oncology settings.

Thus, the current retrospective cohort study examined the associations between age categories (i.e., <65, 65–74, and ≥75 years old) and PROs (i.e., anxiety, depression, fatigue, pain interference, physical function, quality of life) in a diverse ambulatory LC population receiving ICIs. We also assessed whether age categories and sociodemographic and clinical characteristics were associated with emergency department (ED) visits and hospitalization.

2 | METHOD

2.1 | Program description

A routine electronic health record (EHR)-integrated PRO screening system (*My Wellness Check [MWC]*) was implemented across ambulatory oncology clinics of Sylvester Comprehensive Cancer Center (SCCC) at University of Miami (UM), FL.[14] The *MWC* assessment platform is designed to assess emotional and physical symptoms, as well as supportive care needs and triage patients attending ambulatory oncology clinics at SCCC. Patients scheduled for an oncology visit receive the *MWC* assessment via the patient portal. The questionnaire is scored and populated in real-time, with best practice alerts (BPAs) generated based on clinical cutoffs or reported supportive care needs. Patients can answer the *MWC* questionnaire through the patient portal up to 72 h before their appointment. The *MWC* questionnaire is available in English and Spanish based on the patients' preferred language.

2.2 | Symptom assessment

The *MWC* assessment consists of five PROMIS® computerized adaptive tests (anxiety, depression, pain interference, fatigue, and physical function) to assess emotional and physical symptoms commonly experienced by cancer patients. PROMIS® measures use a T-score metric where 50 is the mean of a relevant reference population and 10 is the standard deviation. Higher scores indicate an increase in the construct being measured (e.g., higher anxiety, higher depression).[15–18] PROMIS® pain interference (T-score ≥70), fatigue (T-score ≥70), physical function (T-score ≤30), depression (T-score ≥60), and anxiety (T-score ≥65) were considered moderate or severe elevations and triggered a BPA, triaging the information to the clinical team. The *MWC* assessment also evaluates supportive care needs (e.g., transportation, childcare) and HRQOL with the Functional Assessment of Cancer Therapy-General (7-item version; FACT-G7).[19] Low HRQOL was defined as a FACT-G7 score of ≤13. The *MWC* questionnaire takes approximately 8–12 min to complete depending on patients' symptom severity. *My Wellness Check* questionnaires are voluntary, and patients can skip any question.

2.3 | Patient population

Patients with LC who completed the *MWC* questionnaire within 90 days from receiving ICIs between October 2019–March 2023 were included in this study. The ICI treatment was defined as receipt of any of following drugs: Pembrolizumab, Nivolumab, Duralumab, Cemiplimab, Atezolizumab, Ipilimumab, Avelumab, and Dostarlimab. The study protocol was approved by the institutional review board at UM (ePROST#20230178). Informed consent was waived.

2.4 | Data collection

2.4.1 | Outcome measures

The primary outcomes were the T-scores of five PROMIS®-CATs and FACT-G7 score in the first *MWC* questionnaires that eligible patients completed during ICI treatment. Scores were treated as continuous variables. Exploratory outcomes were time to an ED visit and hospitalization, which were calculated in days from the first *MWC* questionnaire and the first event, respectively. All ED visits and hospitalizations in the UM Health System were captured from the electronic data warehouse (EDW) which houses EHR data. No outside-of-network events were captured.

2.4.2 | Covariates

Self-reported demographics (e.g., race, ethnicity, marital status) and clinical characteristics (e.g., cancer stage, Charlson Comorbidity Index [CCI][20]), were collected from the EDW. Age was categorized as <65, 65–74, or ≥75 years based on categories utilized in previous LC clinical trials (e.g., Impower130,[21] Checkmate017[22] Checkmate227[23]) to facilitate meaningful comparisons across studies. Other demographics (ethnicity, marital status, health insurance) were categorized into two groups: Hispanic versus non-Hispanic, having a partner versus no partner, and insured (managed care, Medicare, Medicaid) versus uninsured (self-pay). Time since cancer diagnosis was calculated in years from cancer diagnosis to the *MWC* assessment date and was log transformed to reduce skewness.

2.5 | Statistical analysis

Descriptive statistics were calculated for demographics, clinical characteristics, and responses to the *MWC* questionnaire. Multiple linear regression models examined demographics and clinical characteristics that were associated with PRO scores (i.e., anxiety, depression, fatigue, pain interference, physical function, quality of life). Adjusted coefficients (β) and 95% confidence intervals (CIs) were obtained. The cumulative incidence function of ED visits and hospitalizations were estimated by the Kaplan-Meier method, which estimates the probability of an event (e.g., ED visit, hospitalization) occurring at a specific time point among those who have not yet experienced that event. Patients who were lost to follow-up or died were censored. The log-rank test was used to compare the outcomes among three age groups. The log-rank test is a nonparametric hypothesis test to compare the observed number of events (e.g., ED visit, hospitalization) in each age group to what would be expected if the null hypothesis were true (i.e., if the Kaplan-Meier curves are identical). Further analyses were performed using Cox proportional hazards regression models to compare the cumulative incidence of ED visits and hospitalizations between age groups adjusting for patient demographics and clinical characteristics. Cox proportional hazards regression models were utilized as they investigate the association between the time to an event and multiple predictor variables. The Cox proportional hazards model assumptions were examined and were both met. All p values were two-sided, with <0.05 considered statistically significant. Analyses were performed with SAS v9.4 and RStudio version 4.2.3 using the following packages: lavaan, survival, survminer, and ggsurvfit.

3 | RESULTS

3.1 | Patient demographics

Between October 2019–March 2023, 190 LC patients completed the *MWC* questionnaire while receiving ICIs (monotherapy or in combination with another ICI). The mean age was 66.8 (SD = 9.8) years old, and the sample was categorized into three groups: patients <65 years old (n = 87; 45.8%), 65–74 (n = 63; 33.2%), and ≥75 years (n = 40; 21.1%). Patients were White (n = 177; 93.2%) and distributed equally among ethnicity groups (n = 96; 50.5% Hispanic vs. n = 88; 46.3% non-Hispanic). Table 1 presents demographics and clinical characteristics.

3.2 | Factors associated with PROs

3.2.1 | Depression

Moderate to severe depression was reported by 15.3% of patients (n = 29; M = 48.8, SD = 10.7). Results from the multiple linear regression model showed that patients aged ≥75 had significantly lower depression scores (β = −5.80; 95% CI, −9.92–1.51; p = 0.01) compared with patients <65 years old. Having a partner (β = −3.39; 95% CI, −6.90–0.19; p = 0.04) and CCI (β = 0.80; 95% CI, 0.20–1.43; p = 0.01) was also significantly associated with depression scores. Patients who reported having a partner had lower depression scores than those who did not have a partner. Further, those with higher CCI scores reported higher depression scores.

TABLE 1 Sample demographics & clinical characteristics.

Demographics & clinical characteristics (*N* = 190)	Mean (*SD*)
Age	66.8 (9.8)
Charlson comorbidity index	9.5 (2.6)
Years since diagnosis	1.72 (2.1)
	N (%)
Sex	
Male	98 (51.6)
Female	92 (48.4)
Race	
White	177 (93.2)
African American	11 (5.8)
Refused/Not reported	2 (1.0)
Ethnicity	
Hispanic/Latino	96 (50.5)
Non-Hispanic/Latino	88 (46.3)
Refused/Not reported	6 (3.2)
Relationship status	
Married/Partner	111 (58.4)
Divorced	25 (13.2)
Single	33 (17.4)
Widowed	18 (9.5)
Unknown	3 (1.6)
Insurance	
Commercial	89 (46.8)
Medicare/Medicaid	68 (35.8)
Self-pay	11 (5.8)
Other	22 (11.6)
Preferred language	
English	109 (57.4)
Spanish	76 (40.0)
Other	5 (2.6)
Cancer stage	
Stage I	4 (2.1)
Stage II	4 (2.1)
Stage III	20 (10.5)
Stage IV	31 (16.3)
Unknown	131 (68.9)
Age categories	
Aged <65	87 (45.8)
Aged 65–74	63 (33.2)
Aged ≥75	40 (21.1)

3.2.2 | Anxiety

Moderate to severe anxiety was reported by 12.1% of patients ($n = 23$; $M = 52.4$, $SD = 10.6$). Patients aged between 65 and 74 had significantly lower anxiety scores ($\beta = -3.31$; 95% CI, −6.70–0.04; $p = 0.05$) compared with patients <65. Hispanic ethnicity ($\beta = 5.26$; 95% CI, 0.63–9.90; $p = 0.03$) and higher CCI ($\beta = 0.69$; 95% CI, 0.11–1.27; $p = 0.02$) had significant positive associations with anxiety scores.

3.2.3 | HRQOL

There were 41 patients (21.6%) with low HRQOL scores. The mean score was 17.4 (SD = 6.2). Patients aged ≥75 had higher HRQOL scores ($\beta = 2.47$; 95% CI, −0.27–4.74; $p = 0.05$) than patients aged <65. Patients living with a partner also had higher HRQOL scores than patients without a partner ($\beta = 1.04$; 95% CI, 0.26–4.36; $p = 0.03$).

3.2.4 | Fatigue

Moderate to severe fatigue was reported by 13 patients (6.8%) and the mean score was 45.6 ($SD = 11.5$). A multiple linear regression did not show any associations between fatigue and demographics.

3.2.5 | Pain

Moderate to severe pain was reported by 16 patients (8.4%) and the mean score was 53.6 ($SD = 11.8$). Patients aged 65–74 had significantly lower pain scores ($\beta = -4.18$; 95% CI, −7.08–0.73; $p = 0.03$) than patients <65. Also, higher CCI was positively associated with pain scores ($\beta = 0.96$; 95% CI, 0.36–1.66; $p < 0.0001$).

3.2.6 | Physical function

Moderate to severe declined physical function was reported by 29 patients (15.3%) and the mean score was 40.3 ($SD = 10.7$). Age was not associated with physical functioning scores. Years since cancer diagnosis was positively associated with physical functioning scores ($\beta = 1.74$; 95% CI, 0.28–3.20; $p = 0.02$).

Table 2 presents multiple regression results for depression, anxiety, HRQOL, fatigue, pain, and physical function.

3.3 | Clinical outcomes by age groups

The Kaplan-Meier estimates of cumulative incidence of ED visits significantly differed among age groups (39.6% vs. 28.0% vs. 24.1% at

TABLE 2 Factors associated with depression, anxiety, HRQOL, fatigue, pain, & physical functioning.

	β	SE β	95% CIs (LL, UL)	p	β	SE β	95% CIs (LL, UL)	p	β	SE β	95% CIs (LL, UL)	p
Demographics	**Depression**				**Anxiety**				**HRQOL**			
Aged <65 (ref)												
Aged 65–74	−3.06	1.77	(−5.90, −1.29)	0.08	**−3.31**	**1.72**	**(−6.70, 0.04)**	**0.05**	0.77	1.12	(−2.00, 2.47)	0.49
Aged ≥75	**−5.80**	**2.09**	**(−9.92, −1.51)**	**0.01**	−3.17	2.00	(−7.07, 0.73)	0.11	**2.47**	**1.27**	**(−0.27, 4.74)**	**0.05**
Male (ref: female)	−2.77	1.60	(−5.63, 0.89)	0.09	−2.99	1.56	(−6.03, 0.06)	0.06	−0.55	1.00	(−2.79, 1.22)	0.59
White race (ref: Black)	2.37	3.25	(−4.28, 8.61)	0.47	4.01	3.21	(−2.28, 10.30)	0.21	−1.51	2.04	(−5.26, 2.60)	0.46
Hispanic (ref: non-Hispanic)	1.59	2.40	(−3.34, 6.24)	0.51	**5.26**	**2.36**	**(0.63, 9.90)**	**0.03**	−1.43	1.48	(−4.11, 1.61)	0.33
Spanish Speaker (ref. English)	−2.07	2.39	(−6.96, 2.58)	0.39	−3.63	2.35	(−8.23, 1.00)	0.12	1.90	1.48	(−1.24, 4.51)	0.20
Uninsured (ref: insured)	−0.72	3.35	(−7.10, 6.18)	0.83	−1.11	3.18	(−7.33, 5.14)	0.73	−0.54	2.09	(−4.72, 3.41)	0.80
Has a partner (ref: no partner)	**−3.39**	**1.67**	**(−6.90, −0.19)**	**0.04**	−1.69	1.60	(−4.82, 1.43)	0.30	**2.30**	**1.04**	**(0.26, 4.36)**	**0.03**
CCI	**0.80**	**0.31**	**(0.20, 1.43)**	**0.01**	**0.69**	**0.30**	**(0.11, 1.27)**	**0.02**	−0.27	0.20	(−0.71, 0.07)	0.18
Years since diagnosis	−1.08	0.71	(−2.41, 0.48)	0.13	−0.90	0.70	(−2.25, 0.44)	0.19	0.73	0.45	(−0.28, 1.50)	0.10
	β	SE β	95% CIs (LL, UL)	p	β	SE β	95% CIs (LL, UL)	p	β	SE β	95% CIs (LL, UL)	p
Demographics	**Fatigue**				**Pain**				**Physical functioning**			
Aged <65 (ref)												
Aged 65–74	3.07	1.87	(−0.59, 6.73)	0.10	**−4.18**	**1.96**	**(−7.08, 0.73)**	**0.03**	2.56	1.85	(−1.07, 6.19)	0.17
Aged ≥75	−1.58	2.17	(−5.83, 2.66)	0.47	−2.50	2.29	(−6.67, 2.34)	0.28	−1.62	2.12	(−5.77, 2.53)	0.44
Male (ref: female)	1.77	1.65	(−1.47, 5.00)	0.29	−0.49	1.78	(−3.39, 3.67)	0.78	1.96	1.66	(−1.29, 5.22)	0.24
White race (ref: Black)	−1.58	3.33	(−8.11, 4.96)	0.64	−1.68	3.74	(−9.18, 5.25)	0.65	−3.13	3.30	(−5.95, 3.34)	0.34
Hispanic (ref: non-Hispanic)	−0.42	1.69	(−3.73, 2.89)	0.80	2.05	2.71	(−3.39, 6.97)	0.45	2.05	2.47	(−2.78, 6.88)	0.41
Spanish Speaker (ref: English)	−1.73	1.72	(−5.09, 1.64)	0.31	−0.19	2.68	(−4.82, 5.53)	0.94	−2.66	2.48	(−7.52, 2.21)	0.28
Uninsured (ref: insured)	**−7.08**	**3.30**	**(−13.54, −0.62)**	**0.03**	6.54	3.55	(−0.15, 13.63)	0.07	−5.00	3.27	(−11.30, 1.51)	0.13
Has a partner (ref: no partner)	2.61	1.68	(−0.68, 5.89)	0.12	−0.76	1.83	(−4.52, 2.67)	0.68	1.87	1.72	(−1.49, 5.23)	0.28
CCI	−0.15	0.32	(−0.77, 0.47)	0.63	**0.96**	**0.33**	**(0.36, 1.66)**	**0.00**	−0.38	0.31	(−1.00, 0.24)	0.23
Years since diagnosis	**1.72**	**0.73**	**(0.28, 3.15)**	**0.02**	−1.08	0.79	(−2.44, 0.68)	0.17	**1.74**	**0.75**	**(0.28, 3.20)**	**0.02**

Note: Bold text indicates *p*-values < 0.05.

Abbreviations: β, regression coefficient; CCI, Charlson Comorbidity Index; CI, confidence interval; LL, lower limit; ref, reference; SE β, standard error of regression coefficient; UL, upper limit.

1 year for aged <65, 65–74, and ≥75, respectively [$p = 0.01$]; Figure 1). For hospitalization, the cumulative incidence was 40.8% versus 22.2% versus 19.5% at 1 year for aged <65, 65–74, and ≥75, respectively, and there was a significant difference [$p = 0.01$]; Figure 2). When Cox proportional hazards regression models were applied (See Supplementary Table S1), the risk of an ED visit for patients aged 65–74 and patients ≥75 years old were significantly lower than that of patients <65 (adjusted hazard ratio [aHR], 0.45 [95% CI, 0.20–0.99] for patients aged 65–74, aHR, 0.21 [95% CI, 0.04–0.99] for patients ≥75). In addition, patients who were uninsured (vs. insured) and had higher CCI had a significantly higher risk of an ED visit (aHR, 4.10 [95% CI, 1.56–10.78] and aHR, 1.29 [95% CI, 1.12–1.50], respectively). Adjusted HR of an ED visit could not be estimated for the race category because there were no events of interest among the non-White group ($n = 13$). For the risk of hospitalization, we found that patients aged 65–74 had a significantly lower risk of hospitalization than patients <65 (aHR, 0.36 [95% CI, 0.15–0.83]), but the model was not significant for patients ≥75 (aHR, 0.50 [95% CI, 0.14–1.79]). Other factors associated with increased risk of hospitalization include being uninsured (aHR, 4.81 [95% CI, 1.90–12.22]), higher CCI (aHR, 1.23 [95% CI, 1.06–1.41]), and depression scores (aHR, 1.08 [95% CI, 1.01–1.15]). Also, higher physical function scores were associated with a lower risk of hospitalization (aHR, 0.99 [95% CI, 0.84–0.99]).

4 | DISCUSSION

The current study examines the associations between age and PROs as well as whether age and sociodemographic and clinical characteristics were associated with ED visits and hospitalizations in a diverse ambulatory LC population receiving ICIs. Overall, we found

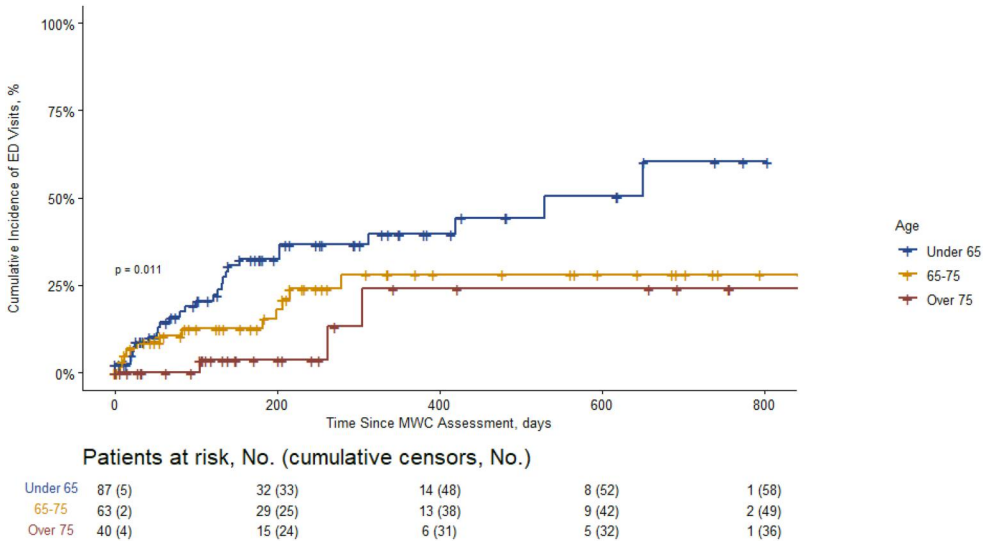

FIGURE 1 Cumulative Incidence of emergency department visits among patients by age group. *MWC* indicates *My Wellness Check*.

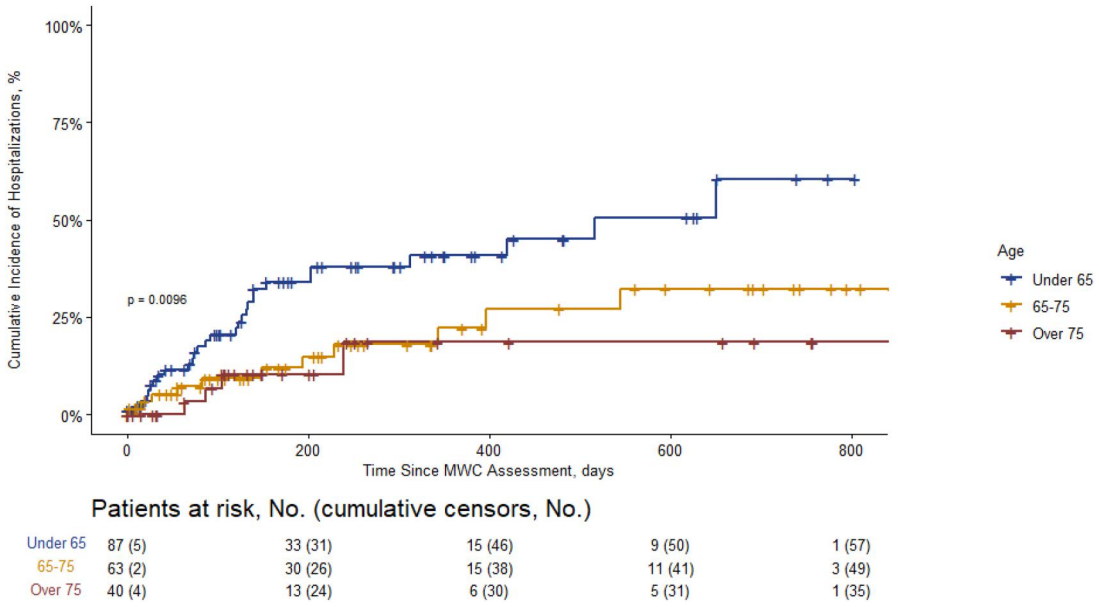

FIGURE 2 Cumulative incidence of hospitalizations among patients by age group. *MWC* indicates *My Wellness Check*.

that moderate to severe depression, anxiety, and poor physical function were experienced by 15.3%, 12.1%, and 15.3% of patients, respectively. There were 41 (21.6%) patients who reported having low HRQOL (FACT-G7 score of <13). Lower numbers of patients reported experiencing moderate to severe fatigue (6.8%) and pain (8.4%). Our data support previous findings that LC patients commonly experience moderate to severe distressing psychological (e.g., anxiety, depression) and physical symptoms (e.g., pain, declining physical function).[24] However, the degree to which LC patients experience these symptoms may differ based on factors such as cancer stage, treatment type, and age.

Overall, patients in the youngest age category (<65) had worse PROs and clinical outcomes when compared to patients in the older age categories (i.e., 65–74 and ≥ 75). Specifically, we found that patients <65 years old had significantly higher depression and lower HRQOL when compared with patients ≥75 years of age, and significantly higher anxiety and pain compared with patients aged 65–74. There were no significant differences in fatigue and physical function among age groups. Researchers have theorized that the mechanism by which ICIs work, immune system activation, may cause increased immune related adverse events (irAEs) and subsequently poorer PROs in younger adults.[25,26] However, immune activation may be muted in older adults potentially leading to less irAEs and more favorable PROs.[27] Although there is no definitive research supporting this theory, previous studies demonstrate that the human immune system begins to downregulate with age.[28] In fact, vaccine

research among older adults supports this theory as vaccine responses are impaired in older individuals.[29] We also posit that in comparison to adults >65, those aged <65 are often still employed and playing an active role in their children's lives. These additional responsibilities may result in increased stress when coping with cancer and treatment which may lead to worse PROs. Similarly, Diefenbach and colleagues[30] found that older and unemployed prostate cancer survivors, compared to younger and employed survivors had more frequent worries about cancer recurrence and higher stress associated with lower levels of QOL.

Furthermore, the worse PROs reported in participants who were <65 can potentially be explained by the age-related positivity effect.[31] This effect, which has been replicated in over 100 studies, suggests that relative to younger adults, older adults focus more on positive and less on negative emotional stimuli.[32]

Study results found that having a partner was associated with lower depression scores and higher HRQOL. This is not surprising given that this aligns with one of the most well-accepted beliefs that cancer patients with a stable partner have better clinical outcomes including longer survival.[33,34] We also found that patients having more comorbidities had higher depression, anxiety, and pain. This finding is consistent with studies examining the impact of comorbidity on cancer outcomes.[35,36] Similar to previous studies on psychosocial outcomes in Hispanic/Latino cancer patients,[37,38] we found that patients who reported being Hispanic had higher anxiety compared with their non-Hispanic counterparts.

The current study showed a significant difference in clinical outcomes between age groups such that younger LC patients receiving ICIs had higher risks of ED visits and hospitalizations. Specifically, when compared to patients aged 65–74 years old, patients <65 had a 2.22 higher risk of an ED visits and 2.79 higher risk of hospitalizations, even when adjusting for sociodemographic and clinical characteristics. Additionally, patients <65 years old had a 4.76 higher risk of an ED visit compared with patients >75. Results indicate that older age may potentially be a protective factor against negative clinical outcomes in LC patients receiving ICIs. As discussed previously, a heightened immune response in younger patients receiving ICIs may increase the number of irAEs contributing to ED visits and hospitalizations. Further research is needed to examine the mechanisms by which ICIs have greater adverse clinical outcomes in younger patients.

Study findings also suggest that patients who were uninsured and had more comorbidities also had higher risks for ED visits. Zhou and colleagues[39] found that among working aged adults, the uninsured use the ED more than those who are privately insured. However, in the current study, only 5.8% (n = 11) of participants were uninsured, potentially because Medicare is offered for individuals who are >65 years old. Not surprisingly, patients who were uninsured, had more comorbidities and indicated higher depression scores and lower physical function had higher risks for ED visits and hospitalizations. Patients who have LC and overall declining health may seek care at the ED and be hospitalized.

4.1 | Study limitations

While this study significantly contributed to our understanding of the associations between age and PROs and the associations between sociodemographic, clinical characteristics, and clinical outcomes in an ethnically diverse ambulatory LC population receiving ICIs, limitations should be considered. First, most patients assessed (n = 131) had missing cancer staging (i.e., Stage I-IV) and LC type (e.g., NSCLC, small cell LC) within the electronic medical record data-pull; therefore, we could not examine the impact of cancer stage on PROs and clinical outcomes. Future studies should assess LC histology (i.e., cancer stage, type) as well as the mechanism by which ICIs have greater adverse effects in younger cancer patients. Second, only patients who completed a *MWC* assessment were included in the study. Patients who completed one or more *MWC* assessments potentially were in overall better health than those who did not complete an assessment. Despite Faverio[40] finding that 75% of those who are 65 years and older are competent Internet users, older adults who have challenges associated with completing online questionnaires may have been self-excluded from the study, creating a bias toward those who are more technologically adept. Third, although we examined an ethnically diverse population (50.5% Hispanic/Latino), 93.2% of all respondents identified as White. Therefore, findings may not generalize to other populations. Fourth, few patients (n = 7) who completed a *MWC* assessment were receiving combination ICIs, so we were unable to examine if treatment with multiple ICIs impact PROs or clinical outcomes. Fourth, despite prospectively examining ED visits and hospitalizations, PROs were only assessed only at the first *MWC* completion. A longitudinal study that examines the change in PROs over time is warranted. Lastly, we were unable to determine the reason for ED visits and hospitalizations, consequently, pre-planned hospitalizations and non-oncology-related ED visits were included in our outcomes.

4.2 | Clinical implications

Younger patients (<65 years old) may have worse PROs and clinical outcomes in certain domains, such as depression, anxiety, and HRQOL. Younger patients might require additional support and resources to address these issues. Our findings suggest that age is an important factor in predicting PROs and clinical outcomes, and healthcare providers should consider age-specific interventions to address the unique needs and challenges of patients in different age groups.

5 | CONCLUSION

In this cohort study of ambulatory oncology patients, younger (<65) LC patients had higher depression, anxiety, pain and lower HRQOL scores than older patients. Younger patients also had high risks for of

ED visits and hospitalizations than older patients. These findings suggest that older LC patients have favorable PROs and a reduced risk for negative clinical outcomes than younger LC patients.

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CONFLICT OF INTEREST STATEMENT

Authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

De-identified data from this study are not available in a public archive; however, de-identified data from this study is available (as allowable according to institutional IRB standards) by emailing the corresponding author.

ETHICS STATEMENT

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

PATIENT CONSENT STATEMENT

This is a retrospective study and does not require informed consent.

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