Performance status of real-world oncology patients before and after first course of chemotherapy

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Background Eastern Cooperative Oncology Group Performance Status (ECOG-PS) scores are used to quantify overall disease status and are widely used to stratify participants at clinical trial entry. Longitudinal ECOG-PS measurement between 2 tumor types may provide important data for patient management in community settings.
Objective To describe oncology patients' performance status before and after their first course of chemotherapy.
Methods ECOG-PS scores from electronic medical records (EMRs) of 47 oncology clinics across the United States were retrieved. The included patients had breast, lymphoma, prostate, colorectal, or lung cancers and ECOG-PS scores within ± 14 days of initiation and completion of the first chemotherapy course. Descriptive statistics of ECOG-PS were analyzed and compared within tumor types (via the Wilcoxon signed-rank test) and between tumor types (via the Kruskal-Wallis test).
Results In all, 7,912 cancer patients were identified as having breast cancer, lymphoma, prostate cancer, colorectal cancer, or lung cancer. At baseline, patients' mean (SD) ECOG-PS scores were breast cancer, 0.51 (0.01); lymphoma, 0.82 (0.02); prostate cancer, 1.04 (0.05); colorectal cancer, 0.72 (0.02); and lung cancer, 0.97 (0.02). The percentages of patients with ECOG-PS < 2 at chemotherapy start were 94%, 86%, 78%, 89%, and 81% for each tumor, respectively; percentages at the end of the first course were 88%, 80%, 68%, 84%, and 66%, respectively. All pre- and postchemotherapy comparisons of scores between tumor types were statistically significantly different ($P < .001$), with the exceptions of lung and prostate cancer before chemotherapy, and lung, prostate, lymphoma, and colorectal cancers after chemotherapy. Changes of ECOG-PS scores from baseline to postchemotherapy assessments were statistically significant in all tumor types ($P < .01$).
Limitations The lack of a standardized method for collecting ECOG-PS scores in routine oncology practice led to the unavailability of scores for many patients.
Conclusions This study describes a national sample of community oncology patients' performance status. Even though there was a significant drop in ECOG-PS scores from pre- to postchemotherapy, good ECOG-PS scores were maintained in a majority of patients. These findings demonstrate that ECOG-PS scores can be routinely assessed and can aid in decisions throughout chemotherapy and in the planning for future treatments.
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The repeated measurement of performance status (PS) in patients with cancer has a number of applications to both routine community practice and formal clinical trials. The Eastern Cooperative Oncology Group (ECOG) has developed standard criteria for measuring a range of outcomes, including toxicity and response to treatment, to facilitate standardization among clinical trials and for comparisons between different treatment regimens. Such detailed measurements include both quantitative and qualitative but evaluable criteria of a patient's total response to treatment. One such measurement is the ECOG- Performance Status (ECOG-PS) score, which was developed as an overall assessment of patient performance status and can be applied across multiple tumor types.[1]

The use of the ECOG-PS instrument in many trials has led to a body of literature that documents the validity, reproducibility, and reliability of the measure[2-5] and its ability to stratify patients for trials, monitor progress for treatment efficacy, and assess patients' quality of survival after treatment.[6-12] Performance status has been found to be an important prognostic factor in oncology

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clinical trials and routine clinical practice.[13-16]

The ECOG-PS instrument is well suited for routine clinical practice because its scale is easily understood and the assessment can be done in very little time during a patient's examination. Detailed descriptions of performance status across tumor types in routine practice could potentially provide insights into how resources and staff training could be optimized within general oncology clinics. The utility of PS measures in routine oncology care could be helpful; however, formal research on the versatility and usefulness of available tools is required to support widespread adoption. This analysis used the largest database of routinely collected ECOG-PS measurements across tumor types. The primary objective was to describe the performance status of oncology patients with the 5 most common tumor types (breast cancer, colorectal cancer, lung cancer, prostate cancer, and lymphoma) over their first course of chemotherapy.

Methods

This was a retrospective cohort study that used data from de-identified patient electronic medical records (EMRs), which are housed in a database called OSCER (Oncology Services Comprehensive Electronic Records).

Data source

OSCER is a proprietary database of EMRs derived from 47 general oncology and hematology clinics located across the United States and maintained by IMS Health. These practices range in size from 10 to 1,000 hematology/oncology patients, and represent multiple locations of care. The OSCER dataset reflects true physician practice in that the EMR records provide actual practice data, rather than data from clinical trial sites or patient and physician surveys. Medical services that are delivered at other practice sites may be included, but no standard of practice has been set forth to include data from other sites in one clinic's EMR. Medical services, as well as lab tests and measurements, were prescribed at the discretion of individual physicians at each site rather than through the direction of a specific study protocol.

Patient sample

Patients in the OSCER database were analyzed over a 3-year time horizon (from January 1, 2008, through December 31, 2010). Patients had to be newly diagnosed with cancer and had to have 1 of the 5 most common tumor types: breast (ICD-9 code 174.xx), lung (ICD-9 code 162.xx), colorectal (ICD-9 code 153.xx or 154.xx), prostate (ICD-9 code 185.xx) or lymphoma (ICD-9 code 200.xx – 202.xx). Patients who had ever been on a clinical trial drug were excluded. They had to be receiving their first course of chemotherapy (defined as the start date of the patients' first regimen of chemotherapy treatment during the study period, with a 6-month clean period prior to their start date, and ended when a > 60-day gap in chemotherapy occurred or when a new chemotherapy drug was introduced).

Patients also had to have a baseline ECOG-PS score that was recorded within 14 days before or after their chemotherapy start date. Patients who had Karnofsky performance status scores available, but no ECOG-PS score, had their Karnofsky scores mapped to the appropriate ECOG score by a validated method;[4,17] these were retained for analysis (converted-score group accounted for 18% of the final sample). To be eligible for the study, patients must have had at least 2 ECOG-PS scores – the baseline ECOG score and at least one other ECOG score in the follow-up period – recorded during their course of chemotherapy. These inclusion criteria identified 7,912 patients from the OSCER database (Table 1).

Outcome measures

The main outcome measure was performance status at chemotherapy start and over the first course of chemotherapy treatment. Performance status was measured using the ECOG-PS, an ordinal scale with scores from 0-5 with associated descriptors for performance.[1] A patient with an ECOG-PS score of 0 is defined as fully active and able to carry on all predisease performance without restriction. An ECOG-PS score of 1 indicates that the patient is restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature (such as light housework or office work). A patient with an ECOG-PS score of 2 is ambulatory and capable of all self-care, but unable to carry out any work activities; this patient would be up and about more than 50% of waking hours. An ECOG-PS score of 3 refers to a patient who is capable of only limited self-care and is confined to a bed or chair more than 50% of waking hours. A patient with an ECOG-PS score of 4 is completely disabled, unable to carry on any self-care, and totally confined to a bed or chair. An ECOG-PS score of 5 indicates that the patient is deceased. (The OSCER database does not capture ECOG-PS scores of 5.).

The baseline ECOG-PS score was defined as the score that was recorded within 14 days before or after the patients' chemotherapy start date. If many ECOG-PS scores were recorded at that time, the ECOG-PS on the chemotherapy start date was used; otherwise, the score closest to the date of diagnosis was used. The ECOG score at the end of the first course of chemotherapy was defined as the score from the last date that was recorded for the patient's course, or up to 14 days after the end of the chemotherapy course. Other outcome measures included the tumor type (as recorded in the OSCER database) as well as other clinical and demographic information recorded in the EMR (Table 2).

TABLE 1 Attrition table

Metric	No. of patients	% of prior step	% of Step 1
Patients ≥ 18 years old with a cancer diagnosis (Jan 1, 2008-Dec 31, 2010)	398,261	–	100.00
Patients never on a clinical trial drug treatment	395,688	99.35	99.35
Patients with a single primary cancer diagnosis	364,006	91.99	91.40
Patients with a diagnosis of only the 5 tumor types of interest	244,005	67.03	61.27
Patients receiving first-line chemo and no chemo 6 months prior	37,937	15.55	9.53
Patients who came from a stable client ('practice') site	32,463	85.57	8.15
Patients on chemotherapy with at least 1 recorded ECOG-PS score	13,535	41.69	3.40
Patients with a recorded ECOG-PS ± 14 days of chemotherapy start	9,110	67.31	2.29
Patients with at least 2 ECOG-PS scores recorded	7,912	86.85	1.99

ECOG-PS, Eastern Cooperative Oncology Group Performance Status

Statistical analysis

Descriptive statistics were analyzed as means with standard deviations. The ECOG-PS scores at the start of chemotherapy (baseline) and after the first chemotherapy course (as measured in days from the chemotherapy start) were analyzed and compared within tumor types via the Wilcoxon signed-rank test and between tumor types using Kruskal-Wallis tests. Chi-square tests were performed to analyze the differences between ECOG-PS scores over time for each tumor type. Analysis was conducted with SAS Base 9.2 (SAS Institute Inc, Cary, North Carolina).

Results

In all, 7,912 cancer patients were identified from the EMRs, of whom 3,147 (39.8%) had breast cancer, 1,044 (13.2%) had lymphoma, 251 (3.2%) had prostate cancer, 1,477 (18.7%) had colorectal cancer, and 1,993 (25.2%) had lung cancer (Table 2, p. 166). The mean age for the total sample was 60.6 years (median, 61 years), with mean ages for breast cancer at 55.6 years (median, 56), for lymphoma at 64.1 years (median, 66), for prostate cancer at 70.7 years (median, 71), for colorectal cancer at 60.4 years (median, 61), and for lung cancer at 65.8 years (median, 66). Because of the large number of breast cancer patients, women accounted for 65.8% of patients in the total sample

At baseline, the mean (SD) ECOG-PS scores were 0.52 (0.01) for breast cancer, 0.82 (0.02) for lymphoma, 1.04 (0.0) for prostate cancer, 0.72 (0.02) for colorectal cancer, and 0.97 (0.02) for lung cancer. The baseline comparison of ECOG-PS scores between tumor types was statistically significantly different ($P < .001$), except for the comparison of lung and prostate cancers, which was not statistically significant ($P > .05$). The distributions of ECOG-PS scores at baseline and after the first course of chemotherapy are displayed in Figure 1 and Table 3. Postchemotherapy comparisons of ECOG-PS scores between tumor types were statistically significantly different ($P < .001$), except for the comparison of lung and prostate cancers and of lymphoma and colorectal cancers, which were not statistically significant ($P > .05$). Within tumor type, the comparisons from pre- to postchemotherapy showed that all decreases in ECOG-PS scores were statistically significant from baseline ($P < .01$; Table 3, p. 167).

The proportions of patients with baseline ECOG-PS < 2, representing patients who were starting chemotherapy with relatively high function, were 94% for breast cancer, 86% for lymphoma, 78% for prostate cancer, 89% for colorectal cancer, and 81% for lung cancer. At the end of the first course of chemotherapy, ECOG-PS < 2 were 88%, 80%, 68%, 84%, and 66%, respectively. Figure 1 and Table 3 display the shift in ECOG scores over the first course of chemotherapy.

Shifts in the distribution of scores over time were analyzed by tumor type. For breast cancer, baseline ECOG-PS scores 0, 1, 2, and 3 had statistically significant drops from pre- to postchemotherapy ($P < .001$); except for ECOG-PS score 4. Lung cancer was similar with ECOG-PS scores 0, 1, 2, and 3 having statistically significant drops ($P < .05$); except for ECOG-PS score 4. Colorectal cancer had ECOG-PS scores 0, 1, and 2 as statistically significant ($P < .01$); except for ECOG-PS 3 and 4. Lymphoma and prostate cancer were the same with statistically significant decreases in ECOG-PS scores 0 and 2 ($P < .01$), but not 1, 3, and 4.

Figure 2 (p. 168) displays the distribution of ECOG scores over the first cycle of chemotherapy. Only days 0, 7, 14, and 21 are shown because the other days contained minimal data; however, visits on these days reflect normal care of oncology

TABLE 2 Patient demographics and clinical characteristics by tumor type (N = 7,912)

	Breast		Colorectal		Lung		Lymphoma		Prostate		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Total	**3,147**	**39.8**	**1,477**	**18.7**	**1,993**	**25.2**	**1,044**	**13.2**	**251**	**3.2%**	**7,912**	**100**
Age												
< 65 years	2,438	77.5	895	60.6	840	42.2	498	47.7	64	25.5	4,735	59.9
≤ 65 years	709	22.5	582	39.4	1,153	57.9	546	52.3	187	74.5	3,177	40.1
Sex												
Male	0	0	821	55.6	1,072	53.8	563	53.9	251	100	2,707	34.2
Female	3,147	100	657	44.4	921	46.2	481	46.1	0	0	5,205	65.8
Race												
Black	451	14.3	155	10.5	169	8.5	64	6.1	40	15.9	879	11.1
Asian	15	0.5	8	0.5	3	0.2	2	0.2	0	0	28	0.4
White	936	29.7	531	36.0	799	40.1	356	34.1	64	25.5	2,686	34
HIspanic	46	1.5	14	1.0	10	0.5	10	1.0	2	0.8	82	1.0
Other	23	0.7	23	1.5	13	0.7	7	0.7	2	0.8	68	0.9
Unknown	1,676	53.3	746	50.5	999	50.1	605	58	143	57	4,169	52.7
Primary insurance type												
Medicare	316	10	265	17.9	498	25.0	197	18.9	79	31.5	1,355	17.1
Medicaid	86	2.7	48	3.3	46	2.3	21	2.0	2	0.8	203	2.6
Commercial	1,563	49.7	673	45.6	908	45.6	422	40.4	98	39.0	3,664	46.3
Cash	6	0.2	3	0.2	4	0.2	3	0.3	0	0	16	0.2
Other	74	2.4	34	2.3	41	2.1	12	1.2	2	0.8	163	2.1
Unknown	1,102	35	454	30.7	496	24.9	389	37.3	70	27.9	2,511	31.7
Stage at diagnosis												
0	16	0.5	0	0	0	0	–	–	0	0	16	0.2
I	570	18.1	22	1.5	117	5.9	–	–	1	0.4	710	9
II	1,123	35.7	215	14.6	115	5.8	–	–	25	10	1,478	18.7
III	488	15.5	506	34.3	462	23.2	–	–	11	4.4	1,467	18.5
IV	222	7.1	397	26.9	626	31.4	–	–	97	38.7	1,342	17
X[a]	314	10	81	5.5	86	4.3	–	–	18	7.2	499	6.3
Missing	414	13.2	256	17.3	587	29.5	1,044	100	99	39.4	2,400	30.3
Metastatic status												
Adjuvant	2,487	79.0	920	62.3	963	48.3	–	–	47	18.7	4,417	64.3
Metastatic	660	21.0	557	37.7	1,030	51.7	–	–	204	81.3	2,451	35.7
Chemotherapy schedule												
n[b]	3,070	–	1,413	–	1,861	–	884	–	237	–	7,465	–
QW	612	19.9	346	24.5	811	43.6	36	4.1	57	24	1,862	24.9
Q2W	720	23.5	926	65.5	69	3.7	45	5.1	8	3.4	1,768	23.7
Q3W	1,676	54.6	112	7.9	781	42	642	72.6	162	68.4	3,373	45.2
Q4W	45	1.5	13	0.9	164	8.8	118	13.4	5	2.1	345	4.6
Other	17	0.6	16	1.1	36	1.9	43	4.9	5	2.1	117	1.6
Duration of first course of chemotherapy (days)												
Mean (SD)	103.1 (105.9)		110.1 (84.7)		76.6 (63.4)		84.6 (51.3)		120.3 (97.3)		95.8 (87.4)	
Median	64		99		64		91		107		66	
25th percentile	43		36		36		43		57		43	
75th percentile	106		162		106		111		160		117	

QW, weekly dosing; Q2W, every-other-week dosing; Q3W, every-third-week dosing; Q4W, every-fourth-week dosing; SD, standard deviation

[a]Stage X represents a stage that was recorded but is considered unknown. [b]In all, 859 patients were not included because they had therapy for only 1 day; therefore no schedule could be calculated.

TABLE 3 Mean ECOG-PS scores at baseline (Pre) and after first course of chemotherapy (Post)

	Pre				Post					
Cancer type	n	Mean	Median	SD	n	Mean	Median	SD	% change over time	*P* value[a]
Breast	3,147	0.5154	0.0	0.0112	2,238	0.7837	1.0	0.0149	52%	< .0001
Prostate	251	1.0398	1.0	0.0482	186	1.2312	1.0	0.0558	18%	.0058
Lymphoma	1,044	0.8209	1.0	0.0218	701	0.9900	1.0	0.0282	21%	< .0001
Colorectal	1,477	0.7204	1.0	0.0179	1,000	0.9380	1.0	0.0222	30%	< .0001
Lung	1,993	0.9749	1.0	0.0161	1,331	1.2682	1.0	0.0217	30%	< .0001

ECOG-PS, Eastern Cooperative Oncology Group Performance Status; SD, standard deviation [a]*P* values represent comparisons within tumor categories before and after chemotherapy

patients due to various chemotherapy regimens, safety monitoring, and hematologic toxicity assessment. For most tumor types, ECOG scores of 0 and 1 were recorded for about 70% of all evaluable subjects during the first cycle of chemotherapy (prostate and lung cancers being slightly lower); very good performance status was maintained during the first cycle of chemotherapy from the majority of patients in this observational cohort. Figure 2 suggests that although adverse events, missed appointments, varying treatment schedules, and physician preference not to measure subsequent ECOG-PS decrease the number of subjects available for successive determination of performance status at later time points, the overall performance of those who presented for follow-up was preserved. The many observations recorded on days 7, 14, and 21 may reflect the schedule of administration of the subcomponents of certain regimens, as well as high compliance with follow-up assessments for toxicity.

Discussion

This study provides a description of a national sampling

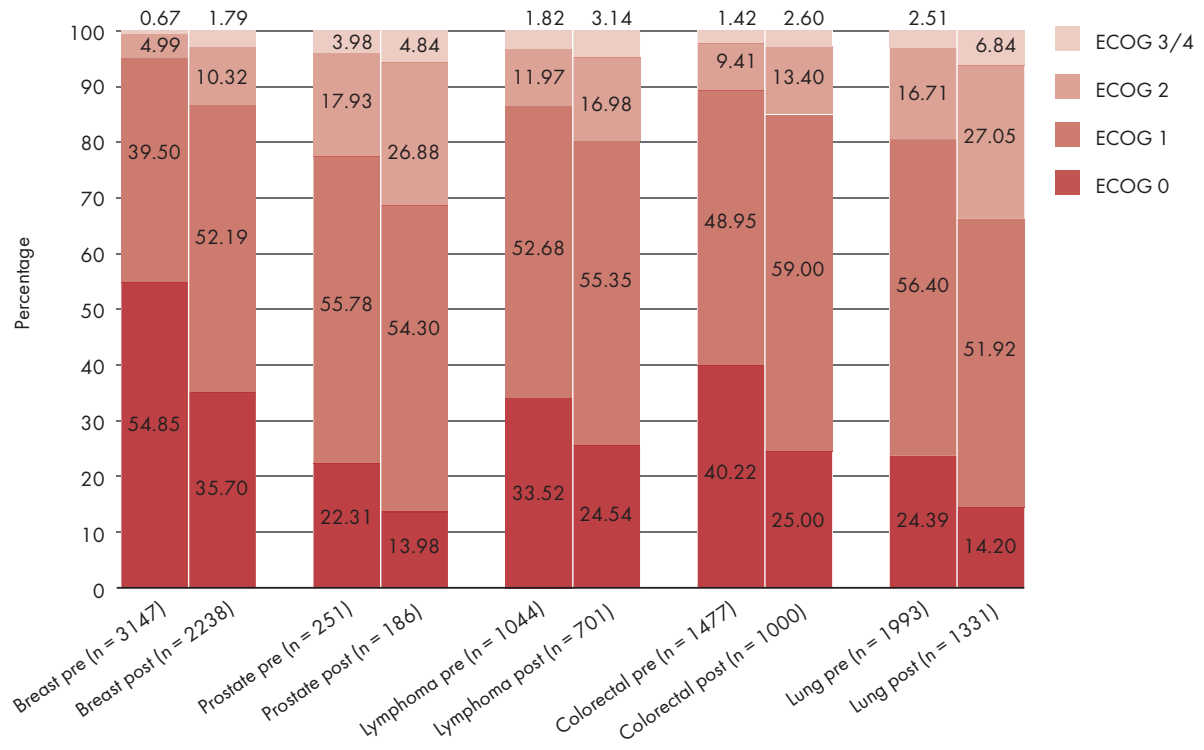

FIGURE 1 Distribution of ECOG-PS scores at baseline (Pre) and after first course of chemotherapy (Post)

ECOG-PS, Eastern Cooperative Oncology Group Performance Status

[a]Percentage does not equal 100% because of rounding. Lower sample sizes post first course of chemotherapy can be attributed to patient death, transfer out of care of the medical system using the EMR, or physician preference not to assess ECOG-PS at end of therapy.

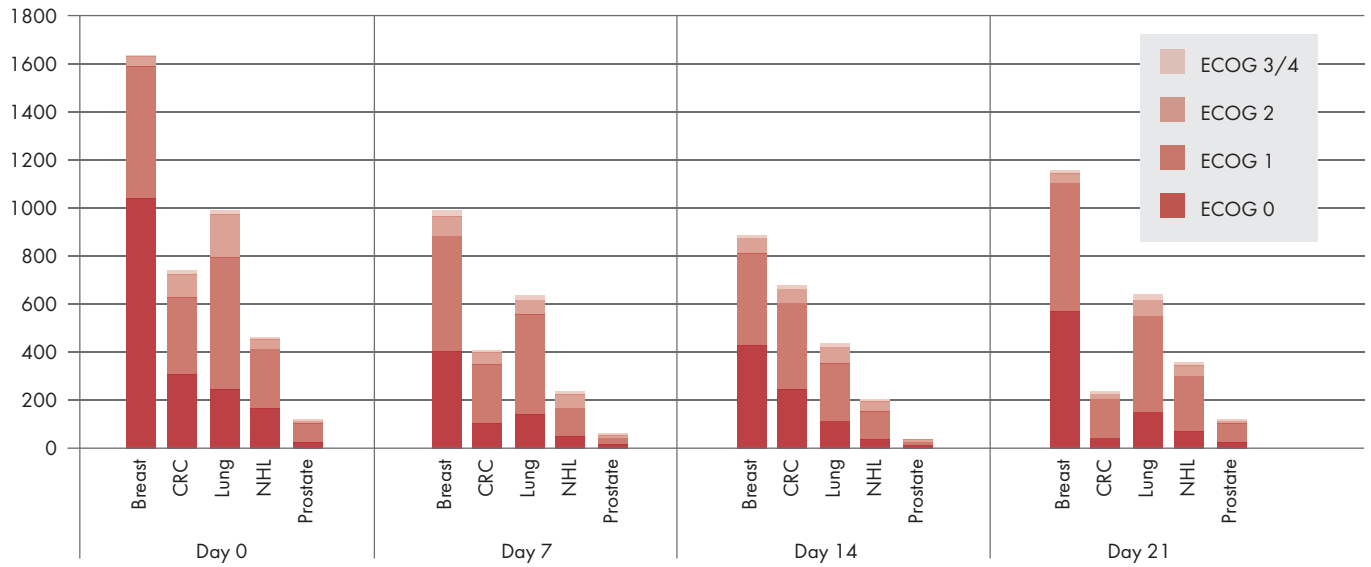

FIGURE 2 ECOG-PS distribution over the first 21 days of treatment, by tumor type

ECOG-PS, Eastern Cooperative Oncology Group Performance Status CRC, colorectal cancer; NHL, non-Hodgkin lymphoma

of community oncology patients' performance status over their first course of chemotherapy. Significant differences between tumor types were found; however, good performance status in all 5 tumor types over time contrasts with the poor status of patients in randomized clinical trials (RCTs).[18-19] Performance status is commonly used for clinician determination of suitability for subsequent chemotherapy, as well as for enrollment in RCTs.[1] In fact, the ECOG-PS is the key for entry into RCTs and for the assessment of baseline randomization efforts.[20-22] Its ubiquity is a function of its applicability to all types of cancer, as well as robust findings of association with both treatment response and mortality. In our study, we found that the performance status of community oncology patients was much better than what RCTs have reported, which could imply that community oncology patients are not as sick as the patients who enroll in RCTs. Community oncologists should be aware of this when they counsel patients regarding prognosis.

The mean ECOG-PS scores at baseline, from lowest to highest, were breast, colorectal, lymphoma, lung, and prostate. Numerous factors may account for this ordering, including the current treatment regimens for specific tumors, the stage in the natural history of the tumor, and when outpatient chemotherapy was administered. Given the emphasis on screening and early detection of breast cancer patients and a well-supported rationale for early-stage, systemic chemotherapy in selected breast cancers, it is plausible to suggest that these subjects usually access an oncology provider early in their disease process, compared with prostate cancer patients, who are not candidates for chemotherapy until much later in the natural history of their disease. After the first course of chemotherapy, the order of mean ECOG-PS scores was the same, except for prostate cancer, which was a bit better than lung cancer. This could be owing to the aggressive nature of lung cancers, and/or the known hematologic toxicity associated with combination carboplatin plus taxane regimens. We also found a substantial drop in performance status after the first course of treatment in all nearly tumor types, including the doubling of the percentage of those patients with grade 3-4 status, which may be expected as a function of cumulative toxicity or tumor progression.

Many other studies have used PS measures to evaluate patients; however, most studies are confined to 1 tumor type or represent international samples, making them difficult to compare with US community oncology patients. In a recent US community oncology study,[23] 11% of patients with non–small-cell lung cancer had ECOG-PS 3-4 at baseline and received first-line chemotherapy, which was slightly higher than what we found here for lung cancer patients (2.5%); but could be attributable to our sample being a combination of small cell and non–small-cell lung cancers, thereby decreasing our proportion of lung cancer patients with low performance status. The prognostic utility of ECOG-PS in a large international study of urothelial cancer found that the 5-year recurrence-free, cancer-specific, and overall survival estimates were 10% to 15% better in the ECOG-PS 0 patients, compared with the estimates in patients who had higher ECOG scores at baseline.[24] ECOG status was found to be a prognostic factor for 90-day mortality in patients with advanced or

metastatic soft tissue sarcoma who were treated with first-line chemotherapy; patients with an ECOG-PS of 1 had a 3.83 times higher odds of early death, compared with those having an ECOG-PS of 0 (12.00 higher odds for an ECOG-PS of 2).[25] And lastly, in a recent Canadian study, community oncology patients' performance status steadily declined over their last 6 months of life.[26]

The ECOG-PS is not thought to be a very sensitive or disease-specific measure of quality of life, but it is a routinely applied, standardized measure that does provide an assessment of the patient's general well-being. Although it is not a patient-reported outcome measure and may reflect the biases and experiences of the clinicians who record it, the information is useful for many different applications, including quick and efficient monitoring of patient progress throughout treatment. With its high acceptability and ease of use, it can increase the likelihood of routine screening use in clinical practice.

The limitations of our research include the lack of true representativeness of all patients being treated in the United States, as well as our use of primarily community oncology practices, which may not be reflective of treatment in academic medical centers. Regarding prostate cancer patients, it is important to note that data collected from the EMRs of urology practices were not represented in this sample. In addition, a substantial number of patients had to be dropped from the analysis because of missing ECOG-PS scores, which may have introduced bias. Finally, database design and clinician bias can influence the perception of the utility of performance status as assessed by ECOG-PS. That is, the assessment may be performed regularly, but our data suggest that it may not have been entered into the EMR as frequently as utility may warrant. For example, a structured data field for performance status may not exist in the software, or ECOG-PS may be recorded in the clinical notes (which were not accessible for this study because of privacy protections under the Health Insurance Portability and Accountability Act).

In our review of the available literature, we found that rarely, if ever, are ECOG-PS scores compared across different cancer types or over time, as reported here. They are most commonly reported as part of the baseline health status assessment at the start of RCTs with small sample sizes, thus increasing the difficulty of interpreting the scores' representativeness, as well as the significance of observed differences in baseline or subsequent scores between groups. The data reported here may be quite useful in the evaluation of the RCT literature and in the consideration of any performance status–associated adverse events, compared with those in standard-of-care populations. The extrapolation of clinical trial results to results seen in standard-of-care settings may be facilitated by considering differences in performance status in the broader population of cancer patients who are under treatment in the real-world setting. In addition, these findings offer community oncology providers data demonstrating that performance status can be easily and routinely assessed, can aid in decisions regarding the patient's status and the tolerability of chemotherapy, and may aid in planning for future treatments.

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