ORIGINAL RESEARCH

Predicting survival in cancer patients with and without 30-day readmission of an unplanned hospitalization using a deficit accumulation approach

Timothy N. Hembree1 | Sarah Thirlwell2 | Richard R. Reich3 | Smitha Pabbathi1 | Martine Extermann4 | Asha Ramsakal1

1Department of Internal and Hospital Medicine, H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida
2Department of Supportive Care Medicine, H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida
3Biostatistics Core, H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida
4Senior Adult Oncology Program, H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida

Correspondence
Timothy N. Hembree, Department of Internal and Hospital Medicine, H. Lee Moffitt Cancer Center and Research Institute, 12902 Magnolia Drive, MCC-IHM, Tampa, Florida. Email: timothy.hembree@moffitt.org

Funding information
National Cancer Institute, Grant/Award Number: P30-CA076292

Abstract

Background: For cancer patients with an unplanned hospitalization, estimating survival has been limited. We examined factors predicting survival and investigated the concept of using a deficit-accumulation survival index (DASI) in this population.

Methods: Data were abstracted from medical records of 145 patients who had an unplanned 30-day readmission between 01/01/16 and 09/30/16. Comparison data were obtained for patients who were admitted as close in time to the date of index admission of a study patient, but who did not experience a readmission within 30 days of their discharge date. Our survival analysis compared those readmitted within 30 days versus those who were not. Scores from 23 medical record elements used in our DASI system categorized patients into low-, moderate-, and high-score groups.

Results: Thirty-day readmission was strongly associated with the survival (adjusted hazard ratio [HR] 2.39; 95% confidence interval [CI], 1.46-3.92). Patients readmitted within 30 days of discharge from index admission had a median survival of 147 days (95% CI, 85-207) versus patients not readmitted who had not reached median survival by the end of the study (P < .0001). DASI was useful in predicting the survival; median survival time was 78 days (95% CI, 61-131) for the high score, 318 days (95% CI, 207-426) for the moderate score, and not reached as of 426 days (95% CI, 251 to undetermined) for the low-score DASI group (P < .0001).

Conclusions: Patients readmitted within 30 days of an unplanned hospitalization are at higher risk of mortality than those not readmitted. A novel DASI developed from clinical documentation may help to predict survival in this population.

KEYWORDS
cancer, clinical documentation, deficit-accumulation index, late-stage cancer, survival
Several factors have been shown to influence survival in newly diagnosed cancer patients, including variables related to the tumor (size, grade, and biological characteristics, including molecular alterations), tumor stage, and those related to the nature and quality of treatment. Although these factors are useful in estimating survival and for treatment planning in the initial phase after diagnosis, these tend to be less helpful when it comes to predicting short-term outcomes in advanced states of disease. Advanced cancer is defined as cancer that is unlikely to be cured or controlled with treatment (NCI dictionary) and treatment is primarily palliative to control symptoms. Common symptoms of advanced cancer include pain, nausea, and loss of appetite, tiredness, and breathlessness.

This study is designed to help identify objective measures/factors that discriminate for more advanced disease presentations and can help to define the terminal phase of cancer. If we can define the terminal phase more objectively, we can communicate the prognosis more clearly and plan our treatment approach in accordance with the patient’s wishes.

In regards to survival, individual cancer patients exhibit a remarkable amount of variation in outcomes. To understand this variation, researchers have attempted to identify clinical factors that can be used to predict the prognosis of individual cancer patients. The magnitude of this work is staggering with one literature review identifying 887 publications documenting 169 clinical, laboratory, and molecular prognostic factors in NSCLC patients. Despite the abundance of studies, results conflict on the importance of certain markers in estimating deficits as predictors of survival in cancer patients.

We evaluated 30-day hospital readmission and accumulated deficits as predictors of survival in cancer patients with unanticipated hospital admissions. The DASI components, as listed in Table 1, were chosen based on literature review of known prognostic indicators and used together in rate as death approaches. Other more recent studies show that aggressiveness in end-of-life care for cancer patients is on the rise, which translates to more frequent and repeated hospital admissions, emergency department visits, and intensive care unit admissions. Another study reported that hospitalization may be underestimated in patients with advanced cancers. In patients with advanced cancer at the time of diagnosis (defined as stage IV for all cancers, stage IIIB for non-small-cell lung cancer, and stage III for pancreatic cancer), 71% were hospitalized at least once during the first year after diagnosis and 16% were hospitalized three times or more.

We believe that the first unplanned hospitalization event may be a harbinger that signals the transition to the terminal phase and a 30-day readmission event signifies an even stronger decline in overall ability to respond to stress and necessitates a re-evaluation of survival at the time of hospitalization. Most studies in cancer patients have attempted to model a limited number of factors to predict survival, and the prognostic models have been developed using poor methods which compromises the reliability and clinical relevance of the models, prognostic indices, and risk groups derived from them.

This study will examine survival as a function of accumulated deficits—the index created will be used as a proxy measure of vulnerability to poor outcomes/mortality. As patients experience cancer-related morbidity or treatment-related complications requiring hospitalization, we believe that their survival is a function of accumulated deficits. The Rockwood method is a model based on the accumulation of deficits that proposes that as health deficits increase so do the risk of adverse outcomes. The concept that risk is related to deficit accumulation extends to a range of illnesses, including dementia, osteoporosis, and coronary heart disease.

In these studies, deficit accumulation indicates increased disease expression and mortality risk. Deficits can be those outside of known risk factors for the disease and can include general health deficits and deficits related to special clinical populations and specific procedures. Laboratory tests and biomarkers have also been used as deficit indicators associated with risk of specific events. An advantage to the deficit accumulation approach is that it allows multiple small effects, including ones that individually are not significantly associated with the outcome of interest, to add up. A deficit-accumulation index to assess frailty in older patients undergoing chemotherapy was shown to be useful in predicting likelihood of experiencing chemother-apy-related toxicities.

We evaluated 30-day hospital readmission and accumulated deficits as predictors of survival in cancer patients with unanticipated hospital admissions. The DASI components, as listed in Table 1, were chosen based on literature review of known prognostic indicators and used together in...
The factors chosen for the deficit-accumulation survival index (DASI) included known prognostic indicators of cancer survival in the terminal cancer patient: markers of malnutrition (prognostic nutrition index [PNI], weight, and albumin level\(^{20}\)); inflammatory indices (neutrophil-to-lymphocyte ratio [NLR], platelet-to-lymphocyte ratio [PLR], and systemic immune-inflammation index [SII] \(^{27}\)); and biological factors (leukocytosis, hypercalcemia, lymphopenia, renal insufficiency, and hyponatremia \(^{33}\)). Other factors of interest included type of cancer, health care utilization in the 6 months before the index admission, 30-day readmission, length of index admission, presence of polypharmacy, marital status as proxy for social support, fall risk, reason for index admission, reason for 30-day readmission, Eastern Cooperative Oncology Group (ECOG) performance status (PS), and metastatic status.

| TABLE 1 | Twenty-three factors and cutoff levels utilized for the deficit-accumulation |
| --- | --- |
| **Factor/cutoff level** | **Deficit** |
| Readmission |  |
| Yes | 1 |
| No | 0 |
| Marital status/support |  |
| Single/divorced/widowed | 1 |
| Married | 0 |
| Language |  |
| Not english | 1 |
| English | 0 |
| Fall risk |  |
| High | 1 |
| Moderate/low | 0 |
| Health care utilization during prior 6 months (count visits) |  |
| >2 | 1 |
| <2 | 0 |
| BMI (kg/m\(^2\)) |  |
| <19 | 1 |
| >19 | 0 |
| Calcium corrected (mg/dL) |  |
| ≥11 | 1 |
| <11 | 0 |
| Creatinine (mg/dL) |  |
| >1.3 | 1 |
| <1.3 | 0 |
| ECOG performance status |  |
| 2, 3, 4 | 1 |
| 0, 1 | 0 |
| NLR (index) |  |
| >5 | 1 |
| <5 | 0 |
| Neutrophils (k/µL) |  |
| <1.8 | 1 |
| >1.8 | 0 |
| PLR (index) |  |
| >250 | 1 |
| <250 | 0 |
| Platelet count (k/µL) |  |
| >450 or <150 | 1 |
| 150-450 | 0 |
| Hemoglobin (g/dL) |  |
| <12 | 1 |
| ≥12 | 0 |
| Length of index admission (days) | (Continues) |

(Continued)
Table 2: Descriptive analysis

| Variable                        | Level          | N = 266 | %   |
|---------------------------------|----------------|---------|-----|
| Readmission (Y/N)               | N              | 132     | 49.6|
|                                | Y              | 134     | 50.4|
| Sex                             | Female         | 125     | 47.0|
|                                | Male           | 141     | 53.0|
| Marital status                  | Divorced       | 27      | 10.3|
|                                | Married        | 180     | 69.0|
|                                | Single         | 33      | 12.6|
|                                | Widow          | 21      | 8.0 |
|                                | Missing        | 5       | —    |
| Language                        | English        | 255     | 95.9|
|                                | Not English    | 11      | 4.1 |
| Race                            | Not White      | 39      | 14.7|
|                                | White          | 227     | 85.3|
| Categorized Morse fall risk     | High           | 103     | 39.3|
|                                | Low            | 2       | 0.8 |
|                                | Moderate       | 148     | 56.5|
|                                | Universal      | 9       | 3.4 |
|                                | Missing        | 4       | —    |
| ECOG                            | 0              | 26      | 15.4|
|                                | 1              | 105     | 62.1|
|                                | 2              | 25      | 14.8|
|                                | 3              | 13      | 7.7 |
|                                | Missing        | 97      | —    |
| General readmission reason category | Cancer related | 64 | 24.1|
|                                | General medical | 95 | 35.7|
|                                | Treatment related | 32 | 12.0|
|                                | Uncontrolled Sx | 75 | 28.2|
| Histology category              | Carcinoma      | 195     | 73.6|
|                                | Melanoma       | 20      | 7.5 |
|                                | Other          | 30      | 11.3|
|                                | Sarcoma        | 20      | 7.5 |
|                                | Missing        | 1       | —    |
| Vital status                    | Alive          | 157     | 59.0|
|                                | Dead           | 109     | 41.0|
| Metastasis                      | 0              | 99      | 38.4|
|                                | 1              | 159     | 61.6|
|                                | Missing        | 8       | —    |
| Reason for admission            | Abnormal EKG/Lab/Image | 26 | 9.8 |
|                                | Chemotherapy side effect | 31 | 11.7|
|                                | Dehydration    | 11      | 4.1 |
|                                | Dyspnea        | 40      | 15.0|
|                                | Fever          | 26      | 9.8 |

(Continues)
| Variable                           | Level            | N = 266 | % |
|-----------------------------------|------------------|---------|---|
| Corrected calcium                 | Mean             | 9.57    | — |
|                                  | Median           | 9.50    | — |
|                                  | Minimum          | 7.50    | — |
|                                  | Maximum          | 16      | — |
|                                  | SD               | 0.91    | — |
|                                  | Missing          | 28      | — |
| Creatinine                        | Mean             | 1.02    | — |
|                                  | Median           | 0.80    | — |
|                                  | Minimum          | 0.20    | — |
|                                  | Maximum          | 7       | — |
|                                  | SD               | 0.77    | — |
|                                  | Missing          | 16      | — |
| Days between current admission and index admission | Mean | 11.06 | — |
|                                  | Median           | 10      | — |
|                                  | Minimum          | 1       | — |
|                                  | Maximum          | 27      | — |
|                                  | SD               | 7.54    | — |
|                                  | Missing          | —       | — |
| Karnofsky                         | Mean             | 77.39   | — |
|                                  | Median           | 80      | — |
|                                  | Minimum          | 40      | — |
|                                  | Maximum          | 100     | — |
|                                  | SD               | 12.53   | — |
|                                  | Missing          | 124     | — |
| Karnofsky score converted to ECOG | Mean             | 0.87    | — |
|                                  | Median           | 1       | — |
|                                  | Minimum          | 0       | — |
|                                  | Maximum          | 3       | — |
|                                  | SD               | 0.64    | — |
|                                  | Missing          | 124     | — |
| Difference between ECOG score and Karnofsky conversion | Mean | 0.29 | — |
|                                  | Median           | 0       | — |
|                                  | Minimum          | −2      | — |
|                                  | Maximum          | 3       | — |
|                                  | SD               | 0.82    | — |
|                                  | Missing          | 188     | — |
| Height(cm)                        | Mean             | 169     | — |
|                                  | Median           | 169     | — |
|                                  | Minimum          | 145     | — |
|                                  | Maximum          | 198     | — |
|                                  | SD               | 9.87    | — |
|                                  | Missing          | 34      | — |

| Variable                        | Level            | N = 266 | % |
|---------------------------------|------------------|---------|---|
| Hemoglobin                      | Mean             | 10.68   | — |
|                                  | Median           | 10.70   | — |
|                                  | Minimum          | 2       | — |
|                                  | Maximum          | 18.70   | — |
|                                  | SD               | 2.33    | — |
|                                  | Missing          | 5       | — |
| Length of index admission (days) | Mean             | 4.88    | — |
|                                  | Median           | 3       | — |
|                                  | Minimum          | 0       | — |
|                                  | Maximum          | 63      | — |
|                                  | SD               | 5.89    | — |
|                                  | Missing          | 0       | — |
| Lymphocytes                     | Mean             | 1.59    | — |
|                                  | Median           | 0.87    | — |
|                                  | Minimum          | 0.080   | — |
|                                  | Maximum          | 104     | — |
|                                  | SD               | 7.16    | — |
|                                  | Missing          | 18      | — |
| Morse fall risk                 | Mean             | 47.47   | — |
|                                  | Median           | 45      | — |
|                                  | Minimum          | 0       | — |
|                                  | Maximum          | 100     | — |
|                                  | SD               | 18.11   | — |
|                                  | Missing          | 3       | — |
| NLR                             | Mean             | 10.36   | — |
|                                  | Median           | 7.16    | — |
|                                  | Minimum          | 0.010   | — |
|                                  | Maximum          | 137     | — |
|                                  | SD               | 13.56   | — |
|                                  | Missing          | 46      | — |
| Neutrophil                      | Mean             | 7.07    | — |
|                                  | Median           | 5.73    | — |
|                                  | Minimum          | 0.010   | — |
|                                  | Maximum          | 33.24   | — |
|                                  | SD               | 4.77    | — |
|                                  | Missing          | 44      | — |
| PLR                             | Mean             | 359     | — |
|                                  | Median           | 253     | — |
|                                  | Minimum          | 1.54    | — |
|                                  | Maximum          | 3089    | — |
|                                  | SD               | 370     | — |
|                                  | Missing          | 20      | — |
In this retrospective cohort study design, we identified patients who were admitted to the Internal Hospital Medicine (IHM) service at Moffitt Cancer Center between 01/01/16 and 09/30/16 with unplanned readmissions within 30 days of discharge from an index admission. To identify a control group, we ascertained the admission date of each study patient's index admission, which ranged from 12/26/15 to 09/14/16. A specific control patient who did not experience a readmission within 30 days of discharge was chosen as a match based on the proximity of his/her first day of admission to the date and time of a study patient’s first day of admission. We identified 148 pairs of patients. On review, a few were not evaluable, resulting in 132 unplanned hospitalized patients (controls) and 139 patients with a readmission within 30-day discharge. The last date of follow-up/survival information was 4/13/2017.

Our center is a free-standing comprehensive cancer center focused solely on the care of patients with a cancer diagnosis and their treatment. The Internal Hospital Medicine service admits patients for active cancer treatment, complications of cancer treatment, and morbidity associated with cancer. Patients with malignant hematologic diseases that have medical issues are rarely admitted to our service. For the purpose of this study, those with planned admissions were excluded from the 30-day readmission cohort.

We collected the following clinical data from patient electronic medical records: length of stay of index admission, occurrence of a 30-day readmission, days between readmission and discharge from index admission, age, marital status, language, reason for index admission, diagnosis(es) related to index admission, number of medications (scheduled and as needed) at discharge from index admission, number of admissions to our center in the 6 months before index admission, number of admissions to our center's intensive care unit in the 6 months before index admission, number of urgent care visits to our center's direct referral center in the 6 months before index admission, Morse fall risk level at time of index admission, weight, height, primary tumor site, number, and location of metastatic sites, ECOG PS, white blood cell count, hemoglobin level, platelet count, neutrophil count, lymphocyte count, serum sodium level, serum corrected calcium level, and serum albumin level.

We calculated NLR by dividing the number of neutrophils by the number of lymphocytes, the PLR by dividing the number of platelets by the number of lymphocytes, the SII by multiplying the PLR by the number of neutrophils, and the PNI by multiplying the albumin level by number of lymphocytes.

### Table 2 (Continued)

| Variable                  | Level | N = 266 | %  |
|---------------------------|-------|---------|----|
| Platelet Count            | Mean  | 239     | —  |
|                           | Median| 214     | —  |
|                           | Minimum| 1       | —  |
|                           | Maximum| 941     | —  |
|                           | SD    | 147     | —  |
|                           | Missing| 5       | —  |
| SII                       | Mean  | 2546    | —  |
|                           | Median| 1618    | —  |
|                           | Minimum| 0.038   | —  |
|                           | Maximum| 19293   | —  |
|                           | SD    | 2938    | —  |
|                           | Missing| 46      | —  |
| Albumin                   | Mean  | 3.42    | —  |
|                           | Median| 3.40    | —  |
|                           | Minimum| 0.30    | —  |
|                           | Maximum| 7.40    | —  |
|                           | SD    | 0.71    | —  |
|                           | Missing| 24      | —  |
| Sodium                    | Mean  | 136     | —  |
|                           | Median| 136     | —  |
|                           | Minimum| 116     | —  |
|                           | Maximum| 157     | —  |
|                           | SD    | 4.98    | —  |
|                           | Missing| 17      | —  |
| WBC                       | Mean  | 9.95    | —  |
|                           | Median| 7.92    | —  |
|                           | Minimum| 0.10    | —  |
|                           | Maximum| 138     | —  |
|                           | SD    | 11.62   | —  |
|                           | Missing| 5       | —  |
| Number of Medications on Admission | Mean | 11.36 | — |
|                           | Median| 11      | —  |
|                           | Minimum| 0       | —  |
|                           | Maximum| 31      | —  |
|                           | SD    | 4.83    | —  |
|                           | Missing| 4       | —  |
| PNI                       | Mean  | 42.53   | —  |
|                           | Median| 39.05   | —  |
|                           | Minimum| 6.85    | —  |
|                           | Maximum| 549     | —  |
|                           | SD    | 38.05   | —  |
|                           | Missing| 38      | —  |

Abbreviations: BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; NLR, neutrophil-to-lymphocyte ratio; PNI, prognostic nutrition index; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index; WBC, white blood cell count.
| Covariate                      | Statistics | Level       | Controls No N = 132 | Cases Yes N = 134 | Parametric P-value* |
|-------------------------------|------------|-------------|---------------------|-------------------|---------------------|
|                              |            |             |                     |                   |                     |
| Sex                           | N (Col %)  | Female      | 64 (48.48)          | 61 (45.52)        | .628                |
|                              | N (Col %)  | Male        | 68 (51.52)          | 73 (54.48)        |                     |
| Marital status                | N (Col %)  | Divorced    | 16 (12.21)          | 11 (8.46)         | .122                |
|                              | N (Col %)  | Married     | 91 (69.47)          | 89 (68.46)        |                     |
|                              | N (Col %)  | Single      | 11 (8.4)            | 22 (16.92)        |                     |
|                              | N (Col %)  | Widow       | 13 (9.92)           | 8 (6.15)          |                     |
| Language                      | N (Col %)  | English     | 128 (96.97)         | 127 (94.78)       | .369                |
|                              | N (Col %)  | Not English | 4 (3.03)            | 7 (5.22)          |                     |
| Race                          | N (Col %)  | Not White   | 18 (13.64)          | 21 (15.67)        | .639                |
|                              | N (Col %)  | White       | 114 (86.36)         | 113 (84.33)       |                     |
| Categorized morse fall risk  | N (Col %)  | High        | 54 (40.91)          | 49 (37.69)        | .154                |
|                              | N (Col %)  | Low         | 0 (0)               | 2 (1.54)          |                     |
|                              | N (Col %)  | Moderate    | 71 (53.79)          | 77 (59.23)        |                     |
|                              | N (Col %)  | Universal   | 7 (5.3)             | 2 (1.54)          |                     |
| ECOG                          | N (Col %)  | 0           | 14 (17.72)          | 12 (13.33)        | .156                |
|                              | N (Col %)  | 1           | 50 (63.29)          | 55 (61.11)        |                     |
|                              | N (Col %)  | 2           | 7 (8.86)            | 18 (20)           |                     |
|                              | N (Col %)  | 3           | 8 (10.13)           | 5 (5.56)          |                     |
| Admission reason             | N (Col %)  | Abnormal EKG/Lab/Image | 9 (6.82) | 17 (12.69) | .199                |
|                              | N (Col %)  | Chemotherapy side effect | 14 (10.61) | 17 (12.69) |                     |
|                              | N (Col %)  | Dehydration | 6 (4.55)            | 5 (3.73)          |                     |
|                              | N (Col %)  | Dyspnea     | 26 (19.7)           | 14 (10.45)        |                     |
|                              | N (Col %)  | Fever       | 10 (7.58)           | 16 (11.94)        |                     |
|                              | N (Col %)  | Neurological complaint | 6 (4.55) | 4 (2.99)   |                     |
|                              | N (Col %)  | Other       | 28 (21.21)          | 35 (26.12)        |                     |
|                              | N (Col %)  | Pain        | 33 (25)             | 26 (19.4)         |                     |
| Cancer type                  | N (Col %)  | Bladder     | 4 (3.03)            | 6 (4.48)          | .532                |
|                              | N (Col %)  | Breast      | 10 (7.58)           | 9 (6.72)          |                     |
|                              | N (Col %)  | GI          | 38 (28.79)          | 23 (17.16)        |                     |
|                              | N (Col %)  | Head and Neck | 5 (3.79)           | 8 (5.97)          |                     |
|                              | N (Col %)  | Hepatocellular | 2 (1.52)           | 5 (3.73)          |                     |
|                              | N (Col %)  | Lung        | 22 (16.67)          | 26 (19.4)         |                     |
|                              | N (Col %)  | Melanoma    | 11 (8.33)           | 10 (7.46)         |                     |
|                              | N (Col %)  | Neuroendocrine | 4 (3.03)          | 4 (2.99)          |                     |
|                              | N (Col %)  | Other       | 28 (21.21)          | 37 (27.61)        |                     |
|                              | N (Col %)  | Sarcoma     | 8 (6.06)            | 6 (4.48)          |                     |
| Histology category           | N (Col %)  | Carcinoma   | 101 (77.1)          | 94 (70.15)        | .583                |
|                              | N (Col %)  | Melanoma    | 8 (6.11)            | 12 (8.96)         |                     |
|                              | N (Col %)  | Other       | 14 (10.69)          | 16 (11.94)        |                     |
|                              | N (Col %)  | Sarcoma     | 8 (6.11)            | 12 (8.96)         |                     |

(Continues)
| Covariate                  | Statistics | Level      | Controls No N = 132 | Cases Yes N = 134 | Parametric P-value* |
|---------------------------|------------|------------|---------------------|-------------------|---------------------|
| Clinic                    | N (Col %)  | Breast     | 10 (7.58)           | 9 (6.72)          | .920                |
|                           | N (Col %)  | Cutaneous  | 13 (9.85)           | 12 (8.96)         |                     |
|                           | N (Col %)  | Endocrine  | 1 (0.76)            | 2 (1.49)          |                     |
|                           | N (Col %)  | GI         | 46 (34.85)          | 40 (29.85)        |                     |
|                           | N (Col %)  | GU         | 12 (9.09)           | 17 (12.69)        |                     |
|                           | N (Col %)  | Gyn        | 0 (0)               | 2 (1.49)          |                     |
|                           | N (Col %)  | Head and Neck | 9 (6.82)          | 9 (6.72)          |                     |
|                           | N (Col %)  | Malignant heme | 8 (6.06)           | 6 (4.48)          |                     |
|                           | N (Col %)  | Neuro-onc  | 1 (0.76)            | 1 (0.75)          |                     |
|                           | N (Col %)  | Sarcoma    | 10 (7.58)           | 9 (6.72)          |                     |
|                           | N (Col %)  | Thoracic   | 22 (16.67)          | 27 (20.15)        |                     |
| DASI                      | N (Col %)  | HIG        | 25 (18.94)          | 54 (40.3)         | <.001               |
|                           | N (Col %)  | MOD        | 69 (52.27)          | 64 (47.76)        |                     |
|                           | N (Col %)  | LOW        | 38 (28.79)          | 16 (11.94)        |                     |
| Metastasis                | N (Col %)  | 0          | 49 (37.98)          | 50 (38.76)        | .898                |
|                           | N (Col %)  | 1          | 80 (62.02)          | 79 (61.24)        |                     |
| Age                       | N          |            | 132                 | 134               | .048                |
|                           | Mean       |            | 63.22               | 60.06             |                     |
|                           | Median     |            | 65                  | 63                |                     |
| Health care visits previous 6 months | N | 132             | 134               | .045               |
|                           | Mean       |            | 0.53                | 0.77              |                     |
|                           | Median     |            | 0                   | 0                 |                     |
| SCMC visits previous 6 months | N | 132             | 134               | .232               |
|                           | Mean       |            | 0.25                | 0.42              |                     |
|                           | Median     |            | 0                   | 0                 |                     |
| Weight                    | N          |            | 124                 | 133               | .630                |
|                           | Mean       |            | 77.47               | 76.24             |                     |
|                           | Median     |            | 72.85               | 74.7              |                     |
| Corrected Calcium         | N          |            | 119                 | 119               | .258                |
|                           | Mean       |            | 9.51                | 9.64              |                     |
|                           | Median     |            | 9.5                 | 9.5               |                     |
| Creatinine                | N          |            | 124                 | 126               | .959                |
|                           | Mean       |            | 1.02                | 1.02              |                     |
|                           | Median     |            | 0.8                 | 0.8               |                     |
| ECOG                      | N          |            | 79                  | 90                | .592                |
|                           | Mean       |            | 1.11                | 1.18              |                     |
|                           | Median     |            | 1                   | 1                 |                     |
| Karnofsky                 | N          |            | 68                  | 74                | .568                |
|                           | Mean       |            | 76.76               | 77.97             |                     |
|                           | Median     |            | 80                  | 80                |                     |
| Hemoglobin                | N          |            | 129                 | 132               | .868                |
|                           | Mean       |            | 10.66               | 10.7              |                     |
|                           | Median     |            | 10.8                | 10.65             |                     |

(Continues)
### TABLE 3 (Continued)

| Covariate                        | Statistics | Level | Controls | Cases | Parametric P-value* |
|----------------------------------|------------|-------|----------|-------|---------------------|
|                                  |            |       | No N = 132 | Yes N = 134 |                      |
| Length of index admission (days) | N          |       | 132      | 134   | <.001               |
|                                  | Mean       |       | 3.61     | 6.12  |                     |
|                                  | Median     |       | 3        | 4     |                     |
| Lymphocytes                      | N          |       | 119      | 129   | .773                |
|                                  | Mean       |       | 1.45     | 1.71  |                     |
|                                  | Median     |       | 0.96     | 0.77  |                     |
| NLR                              | N          |       | 112      | 108   | .018                |
|                                  | Mean       |       | 8.23     | 12.56 |                     |
|                                  | Median     |       | 6.22     | 7.73  |                     |
| Neutrophil                       | N          |       | 113      | 109   | .132                |
|                                  | Mean       |       | 6.59     | 7.56  |                     |
|                                  | Median     |       | 5.5      | 6.35  |                     |
| PLR                              | N          |       | 119      | 127   | .858                |
|                                  | Mean       |       | 363.37   | 354.89|                     |
|                                  | Median     |       | 250      | 268.24|                     |
| Platelet count                   | N          |       | 129      | 132   | .598                |
|                                  | Mean       |       | 243.63   | 234.02|                     |
|                                  | Median     |       | 208      | 218.5 |                     |
| SII                              | N          |       | 112      | 108   | .282                |
|                                  | Mean       |       | 2336.75  | 2763.63|                     |
|                                  | Median     |       | 1400.96  | 2056.93|                     |
| Albumin                          | N          |       | 121      | 121   | .119                |
|                                  | Mean       |       | 3.49     | 3.35  |                     |
|                                  | Median     |       | 3.5      | 3.4   |                     |
| Sodium                           | N          |       | 124      | 125   | .951                |
|                                  | Mean       |       | 135.86   | 135.82|                     |
|                                  | Median     |       | 136      | 136   |                     |
| WBC                              | N          |       | 129      | 132   | .952                |
|                                  | Mean       |       | 9.99     | 9.9   |                     |
|                                  | Median     |       | 7.99     | 7.74  |                     |
| Weight                           | N          |       | 124      | 133   | .630                |
|                                  | Mean       |       | 77.47    | 76.24 |                     |
|                                  | Median     |       | 72.85    | 74.7  |                     |
| Number of medications on admission | N        |       | 131      | 131   | .019                |
|                                  | Mean       |       | 10.66    | 12.06 |                     |
|                                  | Median     |       | 10       | 12    |                     |
| PNI                              | N          |       | 112      | 116   | .987                |
|                                  | Mean       |       | 42.57    | 42.49 |                     |
|                                  | Median     |       | 39.28    | 38.63 |                     |

Abbreviations: BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; NLR, neutrophil-to-lymphocyte ratio; PNI, prognostic nutrition index; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index; WBC, white cell blood count.

Bold values significance p values <0.05.

*The parametric P-value is calculated by ANOVA for numerical covariates and chi-square test for categorical covariates.
The reason for admission variable (chief complaint) was determined by review of patient history and physical assessment at time of admission. If there were multiple similar reasons for admission (chief complaints), these were then grouped for statistical analysis. The groupings are as follows: (a) pain (back pain, neoplasm-related pain, abdominal pain); (b) neurologic complaints (syncope, dizziness, headache, diplopia, ataxia); (c) dyspnea (shortness of breath, hypoxia); (d) adverse effects of chemotherapy (nausea, vomiting, diarrhea within 1 week of chemotherapy); (e) abnormal findings on electrocardiogram, laboratory values, or radiographic imaging (combined group); and (f) other (any “reason” with count <10). Regarding the variable of “cancer type,” for any type with a count of <10, it was grouped into the category of “other.”

The outcome of interest was survival. The 23 factors used for DASI calculation and cutoff levels are shown in Table 1. This study was approved by the Chesapeake Institutional Review Board, which met the criteria for waiver of consent and of Health Insurance Portability and Accountability Act authorization.

2.1 | Statistical analyses

One goal of this analysis was to examine the relation between hospital readmission in cancer patients and overall survival. A Cox proportional hazards model tested time from initial hospital admission until death, with censoring at last follow-up for living patients. A hazard ratio (HR) with a 95% confidence interval (CI) described the relation between hospital readmission and survival, with Kaplan-Meier curves used to depict this relation. Also of interest was whether this relation remained statistically significant while accounting for other demographic (e.g. sex) and clinical (e.g. type of cancer) variables.

Univariate models were tested to determine which variables should be included in a single multivariable Cox model (P < .05). NLR, neutrophil, PLR, platelet, and SII were all highly correlated; hence, only NLR was carried into multivariable analysis. Our multivariable model required the inclusion of cancer type, regardless of its statistical significance, to demonstrate that, in the terminal stage, the type of cancer does not play a prominent role in time to death. We also planned to include recent health care utilization regardless in the multivariable model. The outcome of interest in the multivariable model was the relation between hospital readmission and survival. With 271 patients, we were able to include as many as 13 covariates with minimal concern for model overfitting. We ended up including nine variables in the model.

Another goal of this study was to use an accumulation of deficits approach to predict survival. Deficits were summed across 23 factors and divided by the number of factors to create the DASI. DASI scores were then used to categorize patients into 3 groups: low (cutoff value of <0.30), moderate (cutoff value of 0.31-0.48), and high (cutoff value of >0.48).

We used the Cox proportional hazards model and HR and 95% CI to describe the relation between deficit score and survival. A Kaplan-Meier curve depicted this relation for the low, medium, and high deficit score groups. Data were analyzed using SAS 9.4 (SAS Institute Inc, Cary, NC).

With 271 patients, we had 80% statistical power to detect a hazard ratio of 1.54 or greater for the readmission outcome, and 1.69 or greater for the DASI outcome (assuming a 2-sided test with a nominal alpha of 0.05).

3 | RESULTS

Table 2 shows characteristics of the 271 patients. The median age of patients was 63 years (range, 19-92 years). Most patients were white (86%), English speaking (96%), and married (68%), with 51% male and 49% female.

Patients with gastrointestinal cancers (23%) and lung cancers (16%) were most commonly represented among those who had an unplanned admission to our hospital (Table 2). Greater than 61% had documented metastatic disease; most patients were admitted with a chief complaint associated with common symptoms of advanced cancer (pain (21%), chemotherapy side effect (11%), dyspnea (15%), or fever (8%). However, reason for index admission was not a statistically significant predictor of survival in multivariable analysis (see Table 5).
| Covariate                      | Level          | N     | Hazard Ratio (95% CI) | HR P-value |
|-------------------------------|----------------|-------|-----------------------|------------|
| Sex                           | Female         | 132   | 0.99 (0.69-1.43)      | .971       |
|                               | Male           | 139   | —                     | —          |
| Marital status                | Divorced       | 28    | 0.87 (0.47-1.60)      | .644       |
|                               | Single         | 35    | 0.71 (0.39-1.31)      | .272       |
|                               | Widow          | 22    | 1.33 (0.72-2.45)      | .361       |
|                               | Married        | 180   | —                     | —          |
| Language                      | Not English    | 11    | 1.12 (0.41-3.03)      | .830       |
|                               | English        | 260   | —                     | —          |
| Race                          | Not White      | 38    | 1.05 (0.61-1.82)      | .850       |
|                               | White          | 233   | —                     | —          |
| Categorized morse fall risk   | Low            | 2     | 0.00 (0.00-)          | .983       |
|                               | Moderate       | 150   | 0.71 (0.49-1.03)      | .074       |
|                               | Universal      | 10    | 0.14 (0.02-1.04)      | .055       |
|                               | High           | 105   | —                     | —          |
| ECOG                          | 1              | 109   | 1.37 (0.64-2.94)      | .413       |
|                               | 2              | 28    | 2.15 (0.89-5.19)      | .088       |
|                               | 3              | 15    | 2.54 (0.99-6.49)      | .052       |
|                               | 0              | 23    | —                     | —          |
| Reason for admission          | Abnormal EKG/Lab/Image | 26 | 0.64 (0.32-1.27) | .201 |
|                               | Chemotherapy Side Effect | 30 | 0.48 (0.23-0.98) | **.045** |
|                               | Dehydration    | 11    | 0.21 (0.05-0.89)      | **.035**   |
|                               | Dyspnea        | 41    | 0.98 (0.57-1.69)      | .937       |
|                               | Fever          | 21    | 0.54 (0.25-1.18)      | .123       |
|                               | Neurological Complaint | 8 | 0.13 (0.02-0.93) | **.042** |
|                               | Other          | 78    | 0.59 (0.35-0.99)      | **.044**   |
|                               | Pain           | 56    | —                     | —          |
| Cancer type                   | Bladder        | 9     | 3.96 (1.46-10.74)     | **.007**   |
|                               | Breast         | 16    | 0.84 (0.33-2.09)      | .702       |
|                               | GI             | 62    | 1.17 (0.66-2.09)      | .584       |
|                               | Head and neck  | 13    | 1.42 (0.56-3.55)      | .459       |
|                               | Hepatocellular | 7     | 2.86 (1.14-7.21)      | **.025**   |
|                               | Melanoma       | 22    | 0.80 (0.35-1.83)      | .590       |
|                               | Neuroendocrine | 8     | 0.26 (0.03-1.93)      | .187       |
|                               | Other          | 76    | 0.89 (0.50-1.59)      | .697       |
|                               | Sarcoma        | 14    | 0.75 (0.26-2.22)      | .608       |
|                               | Lung           | 44    | —                     | —          |
| Histology category            | Melanoma       | 22    | 0.80 (0.39-1.65)      | .548       |
|                               | Other          | 29    | 1.02 (0.57-1.83)      | .943       |
|                               | Sarcoma        | 22    | 0.71 (0.33-1.54)      | .385       |
|                               | Carcinoma      | 197   | —                     | —          |
| Dasi                          | Moderate       | 139   | 1.88 (1.00-3.52)      | **.049**   |
|                               | High           | 84    | 4.71 (2.48-8.95)      | **<.001**  |
|                               | Low            | 48    | —                     | —          |

(Continues)
Few differences reached statistical significance ($P < .05$). The few differences included age, with readmitted patients being slightly younger. The readmitted patients also had higher health care visits, length of index admission, medications, and NLR. Not surprisingly, the DASI was higher in readmitted patients.

A 30-day readmission event was strongly associated with survival, with an adjusted hazard ratio (HR) of 2.39\% and a 95\% confidence interval (CI) of 1.46-3.92. Patients who were readmitted within 30 days of discharge from their index admission had a median survival of 147 days compared with patients not readmitted who had not reached median survival by the end of the study ($P < .0001$) (Figure 1). In addition to 30-day readmission, other significant predictors of survival identified in univariate Cox regression analyses included ECOG PS, metastasis, corrected calcium, length of index admission, inflammation indices (NLR, PLR, and SII), PNI, and leukocytosis (WBCs) (Table 4). Also notable, certain reasons for index admission (chemotherapy side effect, dehydration, neurological complaints, and “other” conditions); and two types of cancer (bladder and hepatocellular) were statistically significant predictors of survival. In the final multivariable Cox model, factors remaining statistically significant were 30-day readmission event (HR = 2.44; 95\% CI = 1.44-4.12), corrected calcium, PNI, and leukocytosis (WBCs) (Table 5).

Table 3 compares each variable by 30-day readmission.

TABLE 4 (Continued)

| Covariate                              | Level  | N   | Hazard Ratio (95\% CI) | HR P-value |
|----------------------------------------|--------|-----|------------------------|------------|
| Metastasis                             | Yes    | 159 | 1.79 (1.19-2.70)       | .005       |
|                                        | No     | 103 | —                      | —          |
| Readmission (Y/N)                      | Yes    | 139 | 2.08 (1.42-3.05)       | <.001      |
|                                        | No     | 132 | —                      | —          |
| Age                                    |        |    | 1.01 (0.99-1.02)       | .286       |
| Health care visits previous 6 months   |        |    | 1.06 (0.89-1.25)       | .532       |
| SCMC visits previous 6 months          |        |    | 0.94 (0.78-1.13)       | .514       |
| Weight                                 |        |    | 0.99 (0.98-1.00)       | .154       |
| Corrected calcium (Log transformed)    |        |    | 145.28 (23.09-914.27)   | <.001      |
| Creatinine (Log Transformed)           |        |    | 0.74 (0.31-1.75)       | .487       |
| Days between current admission and index admission |        |    | 1.00 (0.97-1.03)       | .829       |
| ECOG                                   |        | 175 | 1.39 (1.07-1.82)       | .015       |
| Karnofsky                              |        | 151 | 0.99 (0.97-1.01)       | .507       |
| Height(cm)                             |        | 240 | 1.00 (0.98-1.02)       | .679       |
| Hemoglobin                             |        | 267 | 1.02 (0.94-1.11)       | .628       |
| Length of index admission(days)(Log Transformed) |        |    | 1.33 (1.02-1.73)       | .034       |
| Lymphocytes                            |        | 254 | 0.86 (0.63-1.19)       | .359       |
| NLR (Log transformed)                  |        | 226 | 1.71 (1.36-2.16)       | <.001      |
| Neutrophil (Log transformed)           |        | 227 | 2.41 (1.66-3.50)       | <.001      |
| PLR (Log transformed)                  |        | 252 | 1.34 (1.08-1.67)       | .008       |
| Platelet count (Log transformed)       |        | 267 | 1.58 (1.15-2.15)       | .004       |
| SII (Log transformed)                  |        | 225 | 1.65 (1.36-2.00)       | <.001      |
| Albumin                                |        | 248 | 0.53 (0.40-0.72)       | <.001      |
| PNI                                    |        | 234 | 0.95 (0.93-0.98)       | <.001      |
| Sodium                                 |        | 254 | 0.99 (0.95-1.03)       | .503       |
| WBC (Log transformed)                  |        | 267 | 1.45 (1.13-1.85)       | .004       |
| Weight                                 |        | 265 | 0.99 (0.98-1.00)       | .154       |
| Number of diagnoses (Log transformed)  |        | 265 | 0.99 (0.98-1.00)       | .154       |
| Number of medications on admission     |        | 267 | 1.01 (0.97-1.05)       | .807       |

Abbreviations: BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; NLR, neutrophil-to-lymphocyte ratio; PNI, prognostic nutrition index; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index; WBC, white cell blood count.

Bold values significance $p$ values <.05.
To test whether missing data biased our results, we created 20 datasets with complete data using multiple imputations to estimate missing values. We tested these 20 datasets on the final multivariate Cox regression model. The range of the hazard ratios for readmission using these 20 tests was: 1.8-2.0. All were statistically significant at the \( P \leq .01 \) level.

The DASI was a prominent predictor of survival. Relative to results in the low-score group, hazard ratios in the moderate- and high-score groups were 1.88 (95% CI, 1.00-3.53; \( P = .049 \)) and 4.71 (95% CI, 2.48-8.95; \( P = .0001 \)). The median survival time was 78 days (95% CI, 61-131 days) for the high-score group (cutoff value > 0.48), 318 days (95% CI, 207-426 days) for the moderate-score group (cutoff value, 0.31-0.48), and not reached as of 426 days (\( P < .001 \)) for the low-score group (cutoff value < 0.31) (Figure 2).

### TABLE 5  Multivariable survival analysis

| Covariate                                      | Level       | Hazard ratio | HR \( P \)-value |
|------------------------------------------------|-------------|--------------|-----------------|
| Readmission (Y/N)                              | Yes         | 2.44 (1.44-4.12) | <.001           |
|                                                 | No          | —            | —               |
| Health care visits previous 6 months           |             | 0.95 (0.75-1.20) | .672            |
| Cancer type                                    | Bladder     | 2.79 (0.69-11.30) | .150            |
|                                                 | Breast      | 1.03 (0.34-3.07) | .961            |
|                                                 | GI          | 1.27 (0.58-2.80) | .553            |
|                                                 | Head and Neck | 2.22 (0.64-7.66) | .207            |
|                                                 | Hepatocellular | 4.74 (0.42-53.14) | .207            |
|                                                 | Melanoma    | 0.65 (0.26-1.65) | .366            |
|                                                 | Neuroendocrine | 0.47 (0.06-3.96) | .486            |
|                                                 | Other       | 1.46 (0.66-3.24) | .351            |
|                                                 | Sarcoma     | 0.93 (0.26-3.29) | .914            |
|                                                 | Lung        | —            | —               |
| Metastasis                                     | Yes         | 1.35 (0.79-2.30) | .266            |
|                                                 | No          | —            | —               |
| Reason for admission                           | Abnormal EKG/Lab/Image | 0.75 (0.27-2.09) | .580            |
|                                                 | Chemotherapy side effect | 1.08 (0.46-2.53) | .859            |
|                                                 | Dehydration | 0.32 (0.07-1.56) | .160            |
|                                                 | Dyspnea     | 0.94 (0.42-2.12) | .887            |
|                                                 | Fever       | 0.47 (0.16-1.41) | .179            |
|                                                 | Neurological complaint | 0.61 (0.08-4.93) | .647            |
|                                                 | Other       | 0.80 (0.41-1.55) | .508            |
|                                                 | Pain        | —            | —               |
| Corrected calcium                              |             | 1.55 (1.16-2.06) | .003            |
| Length of index admission (days) (Log transformed) |     | 0.87 (0.60-1.26) | .464            |
| NLR (Log transformed)                          |             | 0.83 (0.54-1.30) | .423            |
| PNI                                            |             | 0.94 (0.90-0.99) | .013            |
| WBC (Log transformed)                          |             | 2.21 (1.18-4.12) | .013            |

To test whether missing data biased our results, we created 20 datasets with complete data using multiple imputations to estimate missing values. We tested these 20 datasets on the final multivariate Cox regression model. The range of the hazard ratios for readmission using these 20 tests was: 1.8-2.0. All were statistically significant at the \( P \leq .01 \) level.

The DASI was a prominent predictor of survival. Relative to results in the low-score group, hazard ratios in the moderate- and high-score groups were 1.88 (95% CI, 1.00-3.53; \( P = .049 \)) and 4.71 (95% CI, 2.48-8.95; \( P = .0001 \)). The median survival time was 78 days (95% CI, 61-131 days) for the high-score group (cutoff value > 0.48), 318 days (95% CI, 207-426 days) for the moderate-score group (cutoff value, 0.31-0.48), and not reached as of 426 days (\( P < .001 \)) for the low-score group (cutoff value < 0.31) (Figure 2).

4  | DISCUSSION

Providing survival estimates is important for decision making in oncology care. Our anecdotal experience tells us that an unplanned acute hospitalization can signify a deterioration of performance status, often indicating a
serious worsening of prognosis. However, being able to quantify this change in prognosis objectively has remained elusive. Our methodologic approach to estimate survival at the time of unplanned hospitalization and 30‐day readmission supports our experience. For patients with unplanned hospitalization followed by readmission within 30 days, median survival was 147 days. This worsening of survival in readmitted patients supports the use of readmission as a signal of the transition from the progressive to the terminal cancer phase.

For patients in our study group, factors associated with survival were not cancer specific, nor were they specific to the admitting diagnosis at the time of hospitalization, when combined with readmission in a multivariable statistical model. Rather, they represented general features common to the terminal cancer patient, such as widespread inflammation, malnutrition, biological disarrangements (such as hypercalcemia and leukocytosis). Correlations observed between NLR, PLR, and SII, but not PNI, suggested that the different inflammation indices were measuring the same thing in our study and suggested that PNI might be measuring a separate factor (malnutrition or cachexia). The identification of common features across cancer types supports the notion that the course of most cancers eventuates in a fairly universal clinical picture.

As a further refinement to our survival estimation, our formulated DASI system was found to be highly effective in predicting survival. The high‐score group had a median survival of 78 days vs >426 days in the low‐score group. Identifying patients who fall into the high‐score category will allow us to have a robust and timely discussion about end‐of‐life planning without having patients undergo unnecessary and costly medical interventions. To our knowledge, this is the first time this approach has been applied to cancer patients at the time of unplanned hospitalization. Our next step will be to prospectively validate this approach with attention to limitations related to existing clinical documentation.

Although our cohort mostly comprised patients with gastrointestinal and lung cancers and those having pain and dyspnea as their chief complaint, these factors were not statistically significant drivers of survival in our study. This is consistent with observations that quality of life indicators (including nausea and emesis, dyspnea, pain, and weakness) provide prognostic clues in patients with terminal cancer. Symptoms of dyspnea and pain may reflect progress of patients toward this terminal syndrome.41

A significant limitation is that our data were limited to those available in the electronic medical record. In certain instances, we used existing data such as nursing documentation of fall risk as a proxy for debility/robustness of the individual. We recognize that a true objective measure would be more informative, such as the validated Timed Up and Go study.42 We utilized “marital status” as a proxy for social support in lieu of the validated Social Support Questionnaire.43 We also recognize that we did not have adequate data on comorbidities and that implementation of tools such as the Charlson Comorbidity Index44 would be helpful. Hence, the fact that these variables were not significant in our analysis could be more a function of the limitations of our available data.

As a further refinement to our survival estimation, our formulated DASI system was found to be highly effective in predicting survival. The high‐score group had a median survival of 78 days vs >426 days in the low‐score group. Identifying patients who fall into the high‐score category will allow us to have a robust and timely discussion about end‐of‐life planning without having patients undergo unnecessary and costly medical interventions. To our knowledge, this is the first time this approach has been applied to cancer patients at the time of unplanned hospitalization. Our next step will be to prospectively validate this approach with attention to limitations related to existing clinical documentation.

Although our cohort mostly comprised patients with gastrointestinal and lung cancers and those having pain and dyspnea as their chief complaint, these factors were not statistically significant drivers of survival in our study. This is consistent with observations that quality of life indicators (including nausea and emesis, dyspnea, pain, and weakness) provide prognostic clues in patients with terminal cancer. Symptoms of dyspnea and pain may reflect progress of patients toward this terminal syndrome.41

A significant limitation is that our data were limited to those available in the electronic medical record. In certain instances, we used existing data such as nursing documentation of fall risk as a proxy for debility/robustness of the individual. We recognize that a true objective measure would be more informative, such as the validated Timed Up and Go study.42 We utilized “marital status” as a proxy for social support in lieu of the validated Social Support Questionnaire.43 We also recognize that we did not have adequate data on comorbidities and that implementation of tools such as the Charlson Comorbidity Index44 would be helpful. Hence, the fact that these variables were not significant in our analysis could be more a function of the limitations of our available data.

Although ECOG PS has long been accepted as a strong predictor of survival in cancer patients and was a significant predictor in our univariate analysis, our ECOG PS data may perhaps be not generalizable. The ECOG PS data were missing in 36% (186/287) of our cohort and 76% (142/186) had a documented ECOG PS of 1 or 0. The low ECOG PS may not be representative of the true clinical status of patients at the time of unplanned hospitalization. Because of lack of good quality data, we omitted ECOG PS from the multivariable analysis.

Although ECOG PS has long been accepted as a strong predictor of survival in cancer patients and was a significant predictor in our univariate analysis, our ECOG PS data may perhaps be not generalizable. The ECOG PS data were missing in 36% (186/287) of our cohort and 76% (142/186) had a documented ECOG PS of 1 or 0. The low ECOG PS may not be representative of the true clinical status of patients at the time of unplanned hospitalization. Because of lack of good quality data, we omitted ECOG PS from the multivariable analysis.

This study focused on patients receiving care at our free‐standing oncology center, resulting in limitations related to a lack of diversity among patients and lack of data for health care utilization at other sites. We recognize that further study is required to include cancer patients receiving care beyond our institution and service area.

This study represents a significant advancement in the methodology for assessment of survival at the time of unplanned hospitalization. We found that unplanned hospitalization followed by a 30‐day readmission event and our DASI system were important predictors of survival. The identified
deficits found to be significant represent features common to the terminal cancer patient, such as widespread inflammation, malnutrition, biological disarrangements, and increased healthcare utilization. Utilization of a 30-day readmission event and the DASI system could improve our current means of survival estimation in cancer patients with unplanned hospitalization. Future work will focus on prospective validation of our model with attention to overcome the limitations described above.

ACKNOWLEDGMENT

We thank Rasa Hamilton (Moffitt Cancer Center) for editorial assistance.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

RESEARCH SUPPORT

This work has been supported in part by the Shared Resources at the H. Lee Moffitt Cancer Center & Research Institute, an NCI designated Comprehensive Cancer Center (P30-CA076292).

PREVIOUS PRESENTATION

Contents of the manuscript have not been presented previously.

CONFLICTS OF INTEREST

None.

ORCID

Timothy N. Hembree https://orcid.org/0000-0002-7276-0952

REFERENCES

1. Woodard GA, Jones KD, Jablons DM. Lung cancer staging and prognosis. In: Reckamp KL, ed. Lung Cancer: treatment and research. Cham, Switzerland: Springer International Publishing; 2016:p. 47-75.
2. Lagman RL, Davis MP, LeGrand SB, Walsh D. Common symptoms in advanced cancer. Surg Clin North Am. 2005;85(2):237-255.
3. Brundage MD, Davies D, Mackillop WJ. Prognostic factors in non-small cell lung cancer. A decade of progress. Chest. 2002;122:1037-1057.
4. Altman DG. Studies investigating prognostic factors: conduct and evaluation. In: Gospodarowicz MK, O’Sullivan B, Sobin H, eds. Prognostic factors in Cancer, 3rd edn. Hoboken, NJ: Wiley-Liss; 2006:p. 39-54.
5. Salpeter SR, Malter DS, Luo EJ, Lin AY, Stuart B. Systematic review of cancer presentations with a median survival of six months or less. J Palliat Med. 2012;15:175-185.
6. Huang J, Boyd C, Tyldesley S, Zhang-Salomons J, Groome PA, Mackillop WJ. Time spent in hospital in the last six months of life in patients who died of cancer in Ontario. J Clin Oncol. 2002;20:1584-1592.
7. Wang S-Y, Hall J, Pollack CE, et al. Trends in end-of-life cancer care in the Medicare program. J Geriatr Oncol. 2016;7:116-125.
8. Earle CC, Landrum MB, Souza JM, Neville BA, Weeks JC, Ayanian JZ. Aggressiveness of cancer care near the end of life: is it a quality-of-care issue? J Clin Oncol. 2008;26:3860-3866.
9. Whitney RL, Bell JF, Tancredi DJ, Romano PS, Bold RJ, Joseph JG. Hospitalization rates and predictors of rehospitalization among individuals with advanced cancer in the year after diagnosis. J Clin Oncol. 2017;35(31):3610-3617.
10. Mallett S, Royston P, Waters R, Dutton S, Altman DG. Reporting performance of prognostic models in cancer: a review. BMC Med. 2010;8:21-21.
11. Rockwood K, Mitnitski A. Frailty in relation to the accumulation of deficits. J Gerontol A Biol Sci Med Sci. 2007;62:722-727.
12. Song X, Mitnitski A, Rockwood K. Age-related deficit accumulation and the risk of late-life dementia. Alzheimers Res Ther. 2014;6:54.
13. Kennedy CC, Ioannidis G, Rockwood K, et al. A frailty index predicts 10-year fracture risk in adults age 25 years and older: results from the Canadian Multicentre Osteoporosis Study (CaMos). Osteoporos Int. 2014;25:2825-2832.
14. Wallace L, Theou O, Kirkland SA, et al. Accumulation of non-traditional risk factors for coronary heart disease is associated with incident coronary heart disease hospitalization and death. PLoS ONE. 2014;9:e90475.
15. Howlett SE, Rockwood M, Mitnitski A, Rockwood K. Standard laboratory tests to identify older adults at increased risk of death. BMC Med. 2014;12:171.
16. Mitnitski A, Collerton J, Martin-Ruiz C, et al. Age-related frailty and its association with biological markers of ageing. BMC Med. 2015;13:161.
17. Cohen HJ, Smith D, Sun C-L, et al. Frailty as determined by a comprehensive geriatric assessment-derived deficit-accumulation index in older patients with cancer who receive chemotherapy. Cancer. 2016;122:3865-3872.
18. Pinato DJ, North BV, Sharma R. A novel, externally validated inflammation-based prognostic algorithm in hepatocellular carcinoma: the prognostic nutritional index (PNI). Br J Cancer. 2012;106:1439-1445.
19. Langius J, Bakker S, Rietveld D, et al. Critical weight loss is a major prognostic indicator for disease-specific survival in patients with head and neck cancer receiving radiotherapy. Br J Cancer. 2013;109:1093-1099.
20. Djaladat H, Bruins HM, Miranda G, Cai J, Skinner EC, Daneshmand S. The association of preoperative serum albumin level and American Society of Anesthesiologists (ASA) score on early complications and survival of patients undergoing radical cystectomy for urothelial bladder cancer. BJU Int. 2014;113:887-893.
21. Kang MH, Go S-I, Song H-N, et al. The prognostic impact of the neutrophil-to-lymphocyte ratio in patients with small-cell lung cancer. Br J Cancer. 2014;111:452-460.
22. Ethier J-L, Desautels DN, Templeton AJ, Oza A, Amir E, Lheureux S. Is the neutrophil-to-lymphocyte ratio prognostic of survival outcomes in gynecologic cancers? A systematic review and meta-analysis. *Gynecol Oncol*. 2017;145:584-594.

23. Zhou X-L, Li Y-Q, Zhu W-G, et al. Neutrophil-to-lymphocyte ratio as a prognostic biomarker for patients with locally advanced esophageal squamous cell carcinoma treated with definitive chemoradiotherapy. *Sci Rep*. 2017;7:42581.

24. Yodying H, Matsuda A, Miyashita M, et al. Prognostic significance of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in oncologic outcomes of esophageal cancer: a systematic review and meta-analysis. *Ann Surg Oncol*. 2016;23:646-654.

25. Lee S, Oh SY, Kim SH, et al. Prognostic significance of neutrophil lymphocyte ratio and platelet lymphocyte ratio in advanced gastric cancer patients treated with FOLFOX chemotherapy. *BMC Cancer*. 2013;13:330.

26. Guo Y-H, Sun H-F, Zhang Y-B, et al. The clinical use of the platelet/lymphocyte ratio and lymphocyte/monocyte ratio as prognostic predictors in colorectal cancer: a meta-analysis. *Oncotarget*. 2017;8:20011-20024.

27. Hong X, Cui B, Wang M, Yang Z, Wang L, Xu Q. Systemic immune-inflammation index, based on platelet counts and neutrophil-lymphocyte ratio, is useful for predicting prognosis in small cell lung cancer. *Tohoku J Exp Med*. 2015;236:297-304.

28. Kasuga I, Makino S, Kiyokawa H, Katoh H, Ebihara Y, Ohyashiki K. Tumor-related leucocytosis is linked with poor prognosis in patients with lung carcinoma. *Cancer*. 2001;92:2399-2405.

29. Hutchesson AC, Bundre NJ, Ratcliffe WA. Survival in hypercalcemic patients with cancer and co-existing primary hyperparathyroidism. *Postgrad Med J*. 1995;71:28-31.

30. De Giorgi U, Mego M, Scarpi E, et al. Relationship between lymphopenia and circulating tumor cells as prognostic factors for overall survival in metastatic breast cancer. *Clin Breast Cancer*. 2012;12:264-269.

31. Samuels J, Ng CS, Nates J, et al. Small increases in serum creatinine are associated with prolonged ICU stay and increased hospital mortality in critically ill patients with cancer. *Support Care Cancer*. 2011;19:1527-1532.

32. Soares M, Salluh J, Carvalho MS, Darmon M, Rocco JR, Spector N. Prognosis of critically ill patients with cancer and acute renal dysfunction. *J Clin Oncol*. 2006;24:4003-4010.

33. Berardi R, Caramanti M, Castagnani M, et al. Hyponatremia is a predictor of hospital length and cost of stay and outcome in cancer patients. *Support Care Cancer*. 2015;23:3095-3101.

34. Howlader N, Noone AM, Krapcho M, et al. *SEER cancer statistics review, 1975-2014*. Bethesda, MD: National Cancer Institute; 2017.

35. Gnijdic D, Hilmer SN, Blyth FM, et al. Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. *J Clin Epidemiol*. 2012;65:989-995.

36. Maggiore RJ, Gross CP, Hurria A. Polypharmacy in older adults with cancer. *Oncologist*. 2010;15:507-522.

37. Aizer AA, Chen M-H, McCarthy EP, et al. Marital status and survival in patients with cancer. *J Clin Oncol*. 2013;31:3869-3876.

38. Granda-Cameron C, Behta M, Hovinga M, Rundio AL, Mintzer D. Risk factors associated with unplanned hospital readmissions in adults with cancer. *Oncol Nurs Forum*. 2015;42:E257-268.

39. Zuber CS, Frei EI, Brandley C, et al. Appraisal of methods for the study of chemotherapy in man: comparative therapeutic trial of nitrogen mustard and triethylene thiophosphoramide. *J Chron Dis*. 1960;11:7-38.

40. Harrell FE. *Regression modeling strategies*, 2nd edn. New York, NY: Springer; 2001.

41. Viganò A, Donaldson N, Higginson IJ, Bruera E, Mahmud S, Suarez-Almazor M. Quality of life and survival prediction in terminal cancer patients: a multicenter study. *Cancer*. 2004;101:1090-1098.

42. Schoene D, Wu S-S, Mikolaizak AS, et al. Discriminative ability and predictive validity of the timed up and go test in identifying older people who fall: systematic review and meta-analysis. *J Am Geriatr Soc*. 2013;61:202-208.

43. Saracino R, Kolva E, Rosenfeld B, Breitbart W. Measuring social support in patients with advanced medical illnesses: an analysis of the Duke-UNC Functional Social Support Questionnaire. *Palliat Support Care*. 2015;13:1153-1163.

44. Suzuki H, Hanai N, Nishikawa D, et al. The Charlson comorbidity index is a prognostic factor in sinonasal tract squamous cell carcinoma. *Jpn J Clin Oncol*. 2016;46:646-651.

---

**How to cite this article:** Hembree TN, Thirlwell S, Reich RR, Pabbathi S, Extermann M, Ramsakal A. Predicting survival in cancer patients with and without 30-day readmission of an unplanned hospitalization using a deficit accumulation approach. *Cancer Med*. 2019;8:6503–6518. [https://doi.org/10.1002/cam4.2472](https://doi.org/10.1002/cam4.2472)