Usefulness of Frailty Markers in the Assessment of the Health and Functional Status of Older Cancer Patients Referred for Chemotherapy: A Pilot Study

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Background. Older cancer patients seen in an oncology clinic seem to be healthier and less disabled than traditional geriatric patients. Choosing the most sensitive tools to assess their health status is a major issue. This cross-sectional study explores the usefulness of frailty markers in detecting vulnerability in older cancer patients.

Methods. The study included cancer patients ≥70 years old referred to an oncology clinic for chemotherapy. Information on comorbidities, disability in instrumental activities of daily living (IADL) and activities of daily living (ADL), and seven frailty markers (nutrition, mobility, strength, energy, physical activity, mood, and cognition) was collected. Patients were classified into four hierarchical groups: 1- No frailty markers, IADL, or ADL disability; 2- Presence of frailty markers without IADL or ADL disability; 3- IADL disability without ADL disability; 4- ADL disability.

Results. Among the 50 patients assessed, 6 (12.0%) were classified into Group 1, 21 (42.0%) into Group 2, 15 (30.0%) into Group 3, and 8 (16.0%) into Group 4. In Group 2, 7 patients (33.3 %) had one frailty marker, and 14 (66.7%) had two or more. The most prevalent of the frailty markers were nutrition, mobility, and physical activity.

Conclusion. The assessment of seven frailty markers allowed the detection of potential vulnerability among 42% of older cancer patients that would not have been detected through an assessment of IADL and ADL disability alone. A longitudinal study is needed to determine whether the use of frailty markers can better characterize the older cancer population and predict adverse outcomes due to cancer treatment.

Key Words: Cancer—Frailty markers—Elderly—Geriatric assessment—Functional status—Disability.

Both the incidence and mortality of cancer increase with age (1,2). This increasingly older cancer population is heterogeneous. Therefore, it is crucial for clinicians to have the most accurate evaluation of the health and functional status to tailor treatment, as well as anticipate and possibly prevent complications. Geriatric assessment has been recommended for older cancer patients to identify those who may benefit from treatment and who are at higher risk of toxicity and complications (3–7).

Previous studies on older cancer patients seen in oncology have suggested that they are, for the most part, functionally independent (8–10). The usual geriatric assessment based on basic and instrumental activities of daily living (ADL and IADL, respectively) may therefore have a ceiling effect in detecting vulnerability in this population (11). Consequently, there is a need for more sensitive tools that will identify vulnerable patients who appear healthy but are susceptible to complications in response to aggressive treatments (4,6,11–13).

Frailty is a syndrome resulting from cumulative declines across multiple physiologic systems and represents a state of reduced homeostasis and resistance to stress leading to increased vulnerability and risk of adverse outcomes such as falls, disability, hospitalization, and death (14–16). Fried and colleagues (14) identified five frailty characteristics: nutrition, mobility, strength, energy, and physical activity. Several authors have recently suggested that mood and cognition should also be included as characteristics of frailty (17–20). Regardless of the number of frailty markers, the presence of at least one of these markers confers an increased risk of adverse outcomes (14,21,22).

Therefore, in the assessment of the health and functional status of older cancer patients, the concept of frailty may be a useful approach to detect vulnerability. The primary objective of this study was to assess the prevalence of seven frailty markers in older cancer patients referred to oncology for chemotherapy. The secondary objective was to classify patients into hierarchical groups based on frailty markers as well as ADL and IADL disability.

METHODS

Study Setting, Sample, and Design

This descriptive cross-sectional study was completed over a period of 4 months (from February to June 2006) at the
Segal Cancer Centre of the Jewish General Hospital, Montreal, Canada. Inclusion criteria were: outpatients, 70 years old or older, diagnosed with a solid tumor or hematological malignancy, and referred to the oncology clinic for potential chemotherapy. Exclusion criteria were: patients with a life expectancy estimated to be <3 months, patients who did not speak English or French, patients unable to give informed consent, and patients previously treated with chemotherapy.

The geriatric–oncologist (FR) regularly consulted the oncology database to identify all new patients, 70 years old or older, referred to the oncology clinic. Their charts were reviewed to identify eligible patients. The geriatric–oncologist or a geriatric nurse clinician contacted the patient at the first oncologist’s appointment to explain the study. After providing written informed consent, the patient was assessed either before or after the oncologist’s visit, or at a later date, depending on the patient’s wishes, but before the initiation of treatment. The protocol was approved by the Research Ethics Committee of the Jewish General Hospital.

Data Collection

The measurement tools were selected by a multidisciplinary team composed of geriatricians, oncologists, epidemiologists, and statisticians, based on a review of both the geriatric and oncology literature. The assessment was completed either by the geriatrician–oncologist or the geriatric nurse clinician using both self-report and performance-based measures, in addition to a medical chart review.

Age, sex, and oncology data, including type and stage of cancer, were collected from the patient’s medical chart. Other demographic data, such as level of education, social support, and living arrangement were obtained using a self-report questionnaire. The total number of comorbidities was calculated for each patient using the classification in the Cumulative Illness Rating Scale for Geriatrics (CIRS-G) (23). Performance status was assessed using the Eastern Cooperative Oncology Group Scale of Performance Status (ECOG-PS) (24).

IADL disability was assessed using the seven Older American Resources and Services (OARS) items (25): use of the phone, transportation, shopping, meal preparation, housework, medication, and finances. The denominator was adjusted to take into account patients who did not normally perform an activity such as cooking or laundry. ADL disability was assessed using six tasks of the Katz index (26): bathing, dressing, toileting, transferring, continence, and feeding. Disability in IADL or ADL was defined as the need for assistance to complete at least one IADL or ADL, respectively.

Nutritional status was assessed by body mass index (BMI) and two self-report questions: “In the last year, have you lost more than 10 pounds unintentionally?” (14) and “During the last 3 months, was food intake decreased for whatever cause?” (27). A BMI ≤ 18.5 was considered underweight and indicated undernutrition (28). An affirmative answer to one of the two questions or a low BMI indicated a positive marker of frailty for nutrition.

Mobility was assessed by the number of falls reported by the patient in the last 6 months and by the Timed Up and Go test (TUG) (29). Presence of one or more falls or a TUG time >10 seconds (29) was considered a positive marker of frailty for mobility.

Strength was assessed by three measurements of grip strength (in kilograms) in the dominant hand using a Jamar handheld dynamometer. The maximal grip strength was selected for the analysis. The lowest quintile by sex and BMI was considered a positive marker of frailty for strength (14).

Energy was assessed using a visual scale ranging from 0 (no energy) to 10 (full of energy). A score ≤ 3 indicated a positive marker of frailty for energy (16).

Physical activity was assessed by a validated self-report question from the Canadian Study of Health and Aging Risk Factor Questionnaire (RFQ) (30). No exercise or a low level of exercise was considered a positive marker of frailty for physical activity.

Mood was assessed by the Hospital Anxiety and Depression scale (HADS) (31). A total score ≥15 in the total scales was considered a positive marker of frailty for mood (32).

Cognition was assessed by the Mini-Mental State Examination (MMSE) (33) and the Montreal Cognitive Assessment (MoCA) (34). The MoCA is a test developed to identify patients who perform well on the MMSE but who present mild cognitive impairment (MCI). A score <26 on one or both measurement tools was considered a positive marker of frailty for cognition.

Data Analysis

Summary statistics of the demographics, tumor type and stage, health and functional status, and frailty markers were obtained. Patients were classified into four hierarchical groups based on the results of their assessment: 1- No frailty markers, IADL or ADL disability; 2- Presence of frailty markers without IADL or ADL disability; 3- IADL disability without ADL disability; 4- ADL disability.

Results

Eighty-two patients were screened during the study period. Based on the exclusion criteria (Figure 1), 29 were not eligible. Of the 53 eligible patients, 3 refused to participate. Overall, 50 patients were evaluated for a response rate of 94%.

Table 1 presents the demographics, oncology, and health and functional status data of the study group. The mean age of the patients was 76.8 years (standard deviation 5.2); 56.0% were women. For solid tumors, breast cancer was the most common diagnosis, followed by lung cancer and colorectal cancer; almost half had metastases. For hematological malignancies, leukemia was the most common diagnosis. Among the 50 patients, 13 (26.0%) had >3 comorbidities, 21 (42.0%) had IADL disability, and 8 (16.0%) had ADL disability. The most prevalent IADL and ADL disabilities were shopping (30.0%) and incontinence (12.0%) respectively.

Among the 50 patients, 88% had at least one frailty marker; 52% had three or more (Table 2). The most prevalent of the seven frailty markers were nutrition (62.0%), mobility (58.0%), physical activity (42.0%), and cognition
(42.0%). More specifically, among the 38 patients with an MMSE score of ≥26, 12 (31.6%) had a MoCA score <26, suggesting MCI.

Figure 2 illustrates the distribution of the 50 patients among the four previously defined groups: Group 1: 6 (12.0%) patients with no frailty marker, IADL or ADL disability; Group 2: 21 (42.0%) patients with presence of frailty markers without IADL or ADL disability; Group 3: 15 (30.0%) patients with IADL disability but without ADL disability; and Group 4: 8 (16.0%) patients with ADL disability. All patients with ADL or IADL disability had at least one frailty marker.

Among the 21 patients (42.0%) in Group 2, 7 (33.3%) had one frailty marker; 6 (28.6%) had two; and 8 (38.1%) had three or more. The most prevalent frailty markers in this group were the same as in the whole study sample, with nutrition and mobility being the most common.

**DISCUSSION**

To our knowledge, this is the first study to assess simultaneously seven frailty markers, IADL, ADL, and comorbidities in older cancer patients. Although more than half the patients in our study sample had no IADL or ADL disability, a large proportion had frailty markers, and only six (12.0%) had none. Moreover, 42.0% of patients presented at least one frailty marker without any IADL or ADL disability. Previous studies on health and functional status of older cancer patients (8–11), reporting primarily on IADL and ADL assessment but inconsistently on markers such as BMI, cognition, and mood, might not have identified a large proportion of those potentially vulnerable to the adverse outcomes of cancer treatment.

Our results are consistent with previous studies indicating that roughly 80% of older cancer outpatients are independent in ADL (9–11); more than half are independent in IADL (9–11); two-thirds are cognitively intact (10.35) and a majority have ≤3 comorbidities (9,10). These patients are generally more independent than older persons seen in specialized geriatric programs and home care services (8,36). The approach based on geriatric assessment has proven useful for patients experiencing multiple disabilities in ADL, interacting medical and social problems, and typical geriatric syndromes (falls, incontinence, dementia) (12,37). However, there is limited evidence of the effectiveness of this approach in independent older patients who are affected by a severe medical condition such as cancer (12,37). In a recent longitudinal study on women receiving adjuvant chemotherapy for breast cancer, Hurria and colleagues (11) found a high level of toxicity to treatment despite no change in IADL and ADL. These findings suggest that an approach based primarily on the assessment of IADL and ADL might have a potential ceiling effect in detecting vulnerability in the population of older cancer patients.

Using data from the Cardiovascular Health Study, which included community-dwelling American men and women 65 years old or older, Fried and colleagues (14) reported that older persons with at least three of five frailty markers are at a significantly increased risk of suffering from adverse outcomes such as falls, worsening mobility, ADL disability, hospitalization, and death within 3 years. Moreover, each of these frailty markers represents an independent predictor of adverse outcomes. Our results suggest that using frailty

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**Table 1. Demographic, Oncology, and Health and Functional Status Data of the Study Group (N = 50)**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mean ± SD, [Min-Max]; N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>76.8 ± 5.2, [70–92]; 28 (56.0%)</td>
</tr>
<tr>
<td>Female</td>
<td>28 (56.0%)</td>
</tr>
<tr>
<td>Cancer type</td>
<td>Breast: 12 (24.0%); Lung: 10 (20.0%); Colorectal: 8 (16.0%); Leukemia: 4 (8.0%); Prostate: 4 (8.0%); Other: 12 (24.0%)</td>
</tr>
<tr>
<td>Metastatic tumor (n = 44)*</td>
<td>Present: 19 (43.2%); Absent: 20 (45.4%); Unknown: 5 (11.4%)</td>
</tr>
<tr>
<td>Level of education (≥13 y)</td>
<td>27 (54.0%); Living at home: 47 (94.0%); Presence of social support: 42 (84.0%)</td>
</tr>
<tr>
<td>Source of social support (n = 42)</td>
<td>Spouse: 20 (47.6%); Children: 15 (35.7%); Other: 7 (16.7%)</td>
</tr>
<tr>
<td>Comorbidities &gt; 3</td>
<td>13 (26.0%)</td>
</tr>
<tr>
<td>Functional status</td>
<td>ECOG-PS ≥ 2: 9 (18.0%); IADL disability: 21 (42.0%); ADL disability: 8 (16.0%)</td>
</tr>
</tbody>
</table>

**Notes:** *Patients with hematological malignancies (leukemia or lymphoma) were excluded (n = 6). SD = standard deviation; ECOG-PS = Eastern Cooperative Oncology Group Scale of Performance Status; IADL = instrumental activities of daily living; ADL = activities of daily living.
markers could help to better identify those highly functional independent older cancer patients who may be vulnerable to complications in response to aggressive treatments.

Choosing the most sensitive tools to assess health status is a major issue in geriatric oncology. For example, in the case of older cancer patients requiring chemotherapy, in particular adjuvant chemotherapy, a sensitive evaluation of the cognitive status is crucial. Patients with MCI are, in fact, at increased risk for developing delirium and eventually dementia (38,39). In our study, 12 of the 38 patients with a normal MMSE score had a MoCA suggestive of MCI. These patients would not have been identified as having a frailty marker for cognition had we relied solely on the MMSE score. This finding emphasizes the need to use more sensitive measurement tools in this population of older cancer patients.

Two important strengths of this study are the use of validated self-report and performance tests and the high mean age of our sample (77 years). This cross-sectional pilot study is the first step toward establishing an optimal approach to defining clinically relevant markers and measurement tools of health and functional status in this population.

There are limitations to this study. This is a cross-sectional study, restricted to a small number of patients from a single institution, which may not be representative of other centers. This study included only patients referred for chemotherapy who may be healthier than the general population of older cancer patients, owing to the potential referral bias. Although patients with various types of tumors and treatments were included in the sample, this design was selected to have a picture of the health and functional status of the older cancer patients referred to an oncology clinic.

**Conclusion**

Our results suggest that the usual geriatric assessment tools would have a ceiling effect and might not be intended for patients affected by only one severe medical condition such as cancer. Frailty markers may be a useful approach to detect potential vulnerability in older cancer patients. Longitudinal studies adequately powered to stratify by tumor and treatment type are needed to test the predictive validity of frailty markers in this population.

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