TITLE: Comprehensive Assessment of Senior Adult Cancer Survivors

ABSTRACT
Over the past twenty-five years, the number of cancer survivors in the United States has continued to increase. As at 2007, there were over 11 million cancer survivors in the United States and this number is projected to reach 15 million by the end of 2010. An estimated 65% of all cancers occur in individuals 65 years of age and older so that the older adult population makes up a large percentage of cancer survivors in the United States. With the aging population of cancer survivors, strategies for maintaining the independence of senior adult cancer survivors, for improving the quality of day-to-day living, and for reducing further health and functional declines that can lead to institutionalization have become essential.

Cancer survivorship research focuses on the health and quality of life of a person with a history of cancer beyond the acute diagnosis and treatment phase. Survivorship research encompasses the physical, psychosocial, and economic sequelae of cancer and its treatment. It also seeks to prevent and control treatment-related outcomes such as cognitive dysfunction or 'chemo-brain', other late effects of treatment, second cancers, and poor quality of life in order to optimize survivors' health after cancer treatment. For example, some researchers have identified gross changes in health status and development of impairments (including cognitive changes ranging from subtle decrements in information processing to severe acute delirium) among cancer survivors through self-reports and interviews.[1-3] The literature, however, is sparse with regards to the availability of well-designed, formal studies that assess the health status of senior adult cancer survivors and this is a significant shortcoming in light of the increasing aging population in the United States.

Many age-related physiological changes, comorbidities, cognitive deficits and functional impairments may also exist at the time of cancer diagnosis in senior adult cancer patients. This heterogeneity in the health status of senior adult cancer patients tends to compound the clinical picture, especially with regards to treatment decision-making and treatment outcomes. Studies that will therefore take these factors into account through the assessment of senior adult cancer patients' health status and their application to predicting patients at risk for declines have become essential.

The **Long-Term Goal** of this research is to improve the care of senior adult cancer patients so that they may remain independent and active in their communities. The **Specific Aims** of this research were to:

1. Administer a comprehensive assessment to describe the prevalence and severity of health status impairments and comorbidities present at the time of diagnoses in senior adult oncology patients and compare these findings with age-matched controls from an existing database.

2. Administer a comprehensive assessment after completion of treatment to identify health status and changes from baseline that may be a result of treatment.

3. Assess the ability of baseline health status measures to predict decline in health status and performance of daily living after treatment.

LAY SUMMARY

Currently, senior adults aged 65 and older make up 60% of the population with cancer. Seniors also make up the fastest growing segment of the population in the United States and are expected to represent 20% of the overall population by 2030. As a result of the dramatic aging of our society and the increasing number of cancer survivors, studies that will seek to assess and improve quality of life for our senior adults have become necessary.

The presence of age-related bodily changes, other medical conditions, and changes in mental or functional abilities can make it difficult for older patients to tolerate cancer treatments and remain independent. After treatment is completed, senior adult cancer patients may take longer to recover from treatment-related side effects or suffer late-effects. These complications and side-effects reduce quality of life and may negatively impact senior adult patients' ability to remain independent in their community, speeding up the need for assistance or placement in nursing homes.

This study aims to describe the presence and severity of physical, functional, emotional, and mental impairments and the degree to which they influence the cancer experience of senior adults. It is the goal of this study to be able to use results obtained for improving the care of our senior adult cancer survivors so that they can live independent and functional lives.

INTRODUCTION

Cancer is the second leading cause of death in the United States today, accounting for nearly a quarter of total deaths.[4] An estimated 65% of all cancers occur in individuals 65 years of age and older.[5] In spite of cancer being the second-leading cause of death, there has been an overall decrease in mortality attributable to cancer since the early 1990s.[6] As at 2007, there were over 11 million cancer survivors in the United States and this number is projected to reach 15 million by the end of 2010.[7] Investigations into the quality of life experienced by these survivors after cancer treatment have therefore become necessary if these survivors are to be effectively managed through their course of cancer.

The change in cognitive status after chemotherapy ('chemo-brain') is an area of increasing interest in cancer research, especially as relates to quality of life. Several studies[1, 8] have linked cognitive changes to various cancer treatments. Cognitive changes identified have ranged from subtle decrements in information processing to severe acute delirium. In various studies[2, 3] of younger populations of cancer patients, participants linked changes in cognitive function (affecting memory, language, planning, and processing) to reductions in productivity as information processing was slowed and planning and organizing tasks had become difficult. Some participants reported avoiding socializing and those activities where cognitive difficulties might be apparent to others, thereby affecting their quality of life.[1] Based on estimates in the overall US population, 10% of persons 70 years of age and older have some degree of cognitive impairment. The presence of cognitive impairment at diagnosis and the development of new deficits after treatment can influence a senior patient's ability to comprehend and adhere to treatment requirements, thereby affecting treatment outcome and survival.

This study is unique in its goal of attempting to describe changes in the health status (including cognitive status) of senior adult cancer survivors. It is a multi-disciplinary collaborative pilot project among healthcare professionals of different specialties that involves a battery of assessments to capture overall health status. These assessments include novel and innovative performance-based tests that have not previously been routinely used in senior adult oncology patients, specifically the Executive Function Performance Test and the Activity Card Sort. The

Executive Function Performance Test and the Activity Card Sort were especially designed to better simulate everyday experiences and include a more exhaustive list of daily activities for assessing the patients' level of independence and engagement in the community. It is the hope of the investigators that information obtained from the health status assessments can be applied to identifying those senior adult patients, at the time of cancer diagnosis, at risk for negative changes in health status and cognitive decline that could affect longevity after treatment. Such insights will be valuable for the development of new strategies that can target such risk factors at an early stage to ensure optimal quality of life and decrease the requirement for institutionalization.

METHODS

Design: This was an observational longitudinal pilot study of 27 newly diagnosed senior adult oncology patients over the age of 70 years.

Recruitment: Participants were recruited from the oncology clinical practices of Washington University physicians specializing in breast, colorectal, lung, genitourinary, and head and neck cancers. The study objective and overview of participation were described to eligible patients. This was then followed by an invitation to participate in the study. Informed consent was subsequently obtained from those patients willing to enroll in the study. IRB approval was obtained from the Human Research Protection Office at Washington University.

Description of Participation: Participants completed a comprehensive assessment battery at three time-points: (1) prior to cancer therapy (2) at three months after the baseline assessment and (3) at six months after the baseline assessment. The comprehensive assessment battery was developed especially for this project through the collaboration of experts in geriatrics, oncology, nursing, and occupational therapy. The comprehensive assessment battery was designed to capture physical, functional, and cognitive status; presence and overall severity of key comorbid ailments; geriatric syndromes; nutritional status; polypharmacy; and socioeconomic resources of participants. Together, the assessments encompass all domains (function, comorbidity, socioeconomic issues, geriatric syndromes, polypharmacy, and nutrition) suggested by the Comprehensive Geriatric Assessment in the Senior Adult Oncology Practice Guidelines put forth by the National Comprehensive Cancer Network.[9] Components of the assessment battery are listed below.

a. Self-report assessments for participants to complete on their own at a study visit or at home, which included **(1)** *Demographic* forms **(2)** *Medications* form **(3)** *Center for Epidemiologic Studies Depression (CES-D) Scale*[10] *short form* **(4)** *University of Alabama Life Space Assessment (LSA)* Aids[11] form and **(5)** the *Dysexecutive questionnaire (DEX).*[12]
b. Health Status assessments completed with the research assistant which included **(1)** *Symptom Assessment* form **(2)** *Katz Index Activities of Daily Living (ADLs)*[13] **(3)** *Lawton Index of Instrumental Activities of Daily Living (IADLs)*[14] **(4)** *University of Alabama Life Space Assessment part 2 (LSA)*[11] **(5)** *Short Blessed Test (SBT)*[15] **(6)** *Mini Nutritional Assessment short form (MNA)*[16] and **(7)** *Short Physical Performance Battery (SPPB).*[17]
c. Life Participation assessments which involved a series of activities designed to assess cognition and functioning under direct observation. These included **(1)** *Delis Kaplan Executive Function Scale (DKEFS)*[18] **(2)** Activity Card Sort (ACS) **(3)** *Executive Function Performance Test (EFPT)*[19] *and* **(4)** Reintegration into Normal Living Index (RNL).[20]

Participants' medical records were also reviewed to identify and grade severity of existing comorbidities using the *ACE-27* comorbidity assessment form.[21]

RESULTS

Twenty-seven patients were successfully enrolled into the study. Of the twenty-seven, 20 participants were able to complete the Comprehensive Geriatric Assessment at the three time-points required for the study. Out of these twenty participants, only 7 participants completed the Life Participation Assessment portion of the Comprehensive Geriatric Assessment.

Participants included 9 males (33.3%) and 18 females (66.7%). Fourteen participants (53.8%) had completed their education up to the high school level, 9 (34.6%) up to college level, and 3 (11.5%) up to the graduate/professional level. Seven of the participants lived alone (25.9%) while others lived with either their spouses or other relatives. Twenty-three (88.5%) participants reported not having had any fall in the preceding year while 3 (11.5%) reported an occurrence of at least one fall in the preceding year.

Preliminary analysis of baseline, three-month and six-month data indicated that the Self-Report and Health Status assessments did not capture changes that community-dwelling senior adults undergo while receiving cancer therapy (see Table 1 below). No significant differences were found between scores on these assessments at the three time-points

Table 1: Comparisons between baseline, three-month and six-month Self-Report and Health Status assessment scores.

Self- reported assessments	**Baseline**	**3 month**	**6 month**	**p-value**
Dex score, mean (SD)	11.8 (10.3)	11.4 (9.8)	11.6 (9.2)	0.94**
median (min-max)	10.5 (1-46)	8 (0-29)	9.5 (0-29.0)	
CESD score, mean (SD)	1.5 (1.5)	1.6 (1.4)	1.9 (1.9)	0.81**
median (min-max)	1 (0-6)	1 (0-5)	1 (0-5)	
Health Status assessments	**Baseline**	**3 month**	**6 month**	**p-value**
Total ADL score by participant, mean (SD)	17.6 (0.6)	16.7 (3.7)	17.6 (0.8)	0.31*
median (min-max)	18 (16-18)	17 (0-19)	18.0 (15-18)	
Total IADL score by participant, mean (SD)	24.3 (1.5)	12.4 (1.9)	23.5 (3.2)	0.20*
median (min-max)	25.0 (18-25)	25 (16-25)	25 (15-25)	
Mini nutritional score, mean (SD)	11.3 (2.9)	12.4 (1.9)	11.5 (3.4)	0.32*
median (min-max)	12 (3-14)	13 (8-14)	12 (0-14)	
Physical performance score, mean (SD)	8.9 (3)	10.2 (1.0)	9.4 (2.3)	0.33*
median (min-max)	10 (2-12)	10 (9-12)	10 (3-12)	

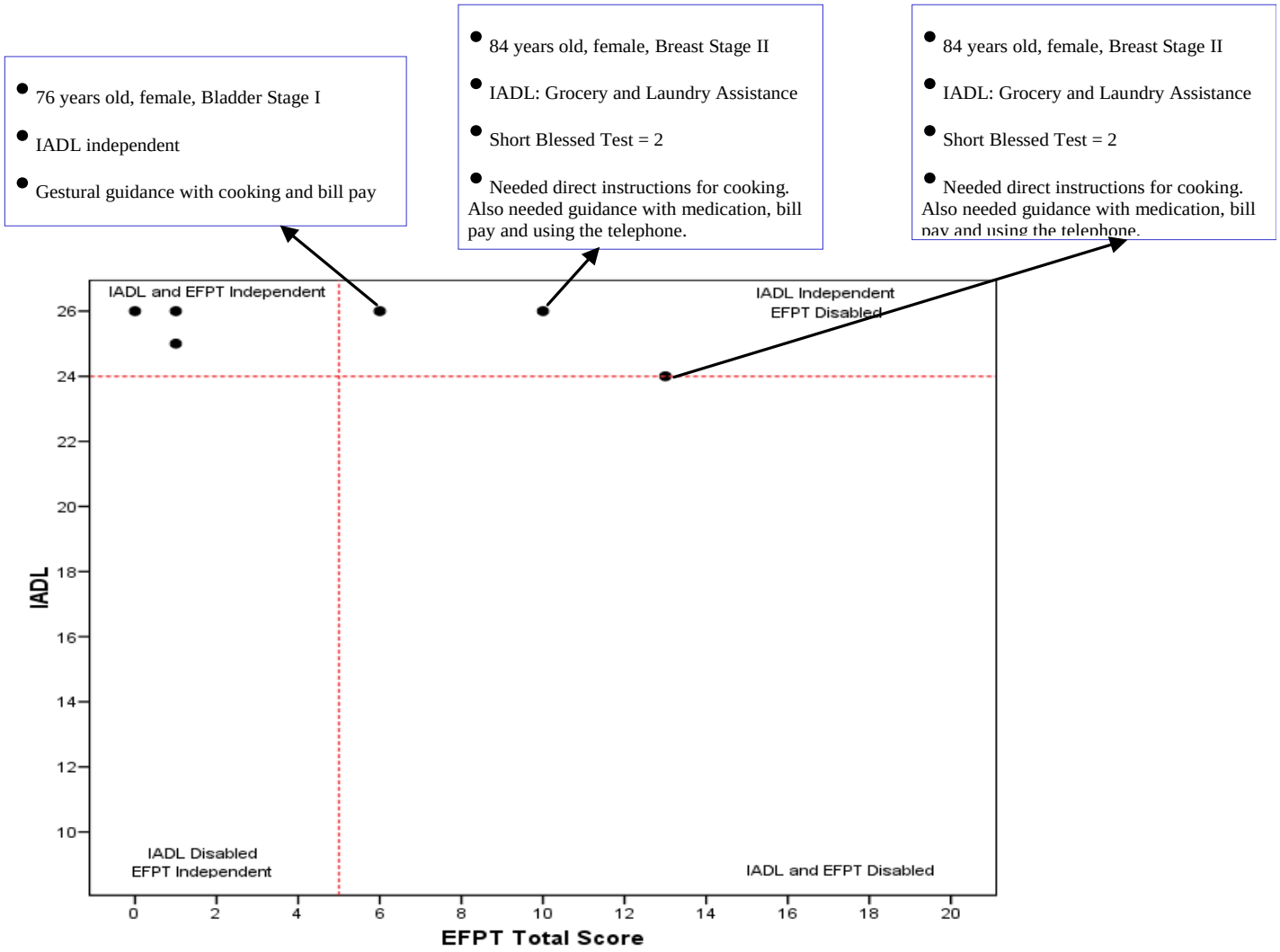
Short blessed score, mean (SD)	2.9 (3.8)	3.1 (5.0)	1.5 (1.9)	0.46**
median (min-max)	2 (0-16)	2 (0-22)	1 (0-6)	
Total symptoms, mean (SD)	4.4 (3.6)	4.4 (3.1)	3.8 (3.7)	0.52**
median (min-max)	4 (0-18)	4 (0-11)	3 (0-15)	
Reintegration of normal living, mean (SD)	47.6 (5.7)	49.5 (7.0)	47.7 (8.3)	0.14*
median (min-max)	48.0 (38-55)	53 (30-55)	50.5 (30-55)	
UAB life-space assessment				
Global UAB score, mean (SD)	72.3 (22.6)	73.8 (21.1)	68.9 (28.6)	0.34*
median (min-max)	80 (25-104)	75 (32-102)	74 (19-114)	
Adult comorbidity score, n (%)				
None	1 (3.7)	1 (4.5)	1 (4.5)	
Mild	7 (25.9)	6 (27.3)	7 (31.8)	
Moderate	10 (37.0)	8 (36.4)	9 (40.9)	
Severe	9 (33.3)	7 (31.8)	5 (22.7)	
Total	27	22	22	

* One-way ANOVA ** Wilcoxon-Mann-Whitney test

However, among the 7 participants who completed the Life Participation Assessment portion of the battery, specifically the EFPT, discrepancies in the ability to safely perform activities of daily living were identified between the results of the EFPT and the though the Health Status assessments (see Figure 1).

Figure 1 below shows 4 categories that participants may fall into based on their scores after completing their patient-based (Lawton's Index in this case, with normal ranging from 24-26) and performance-based testing (EFPT in this case, with normal <5). The optimal situation is the left-upper quadrant where participants are deemed truly functional based on agreement between scores obtained on the IADL and EFPT. The worst situation is the right-lower quadrant where the participant is truly not able to function independently due to abnormal scores on both tests. The right-upper and left-lower quadrants represent areas where discrepancies exist between the scores of the IADL and EFPT. The figure shows that 3 of the 7 participants (in the left upper quadrant) were actually able to perform under direct observation (EFPT) those daily tasks they had alluded to being able to independently perform on their Lawton's IADL. However, **3 of the 7 participants (right upper quadrant) were found to not be as functional** as they had initially indicated on their IADL after EFPT was performed. 1 of the 7 participants is not displayed in the figure due to failure to complete a part of the EFPT.

FIGURE1: Discrepancies between Patient-Based and Performance-based assessments



*Patient number 7 did not complete Medication task due to inability to swallow.
IADL score = 26; EFPT Total Score for 3 tasks = 7 (above threshold).

DISCUSSION

Cognitive and functional deficits appear to be present in senior adult cancer survivors. Sometimes, these deficits may be so subtle that they are not captured by routine subjective measures of health status assessments. This was illustrated well in our study where no statistically significant differences were found in the scores obtained at the three different time-points (all p-values > 0.05). When viewed apart from the results of the Life Participation assessment, the results from these assessments indicated that participants were functionally and mentally competent enough to perform necessary tasks for living.

However, discrepancies were found to be present on cognitive and functional ability when the results of the EFPT, one of the Life Participation assessments, were assessed. As previously mentioned, only 3 of the 7 participants (in the left upper quadrant) were actually able to perform under direct observation (EFPT) those daily tasks they had alluded to being able to independently perform on their Lawton's IADL. Another **3 of the 7 participants (right upper**

quadrant) were found to not be as functional as they had initially indicated on their IADL after EFPT was performed. They had passed their IADL but were actually not able to perform under direct observation those daily tasks they had alluded to being able to perform independently.

These results attest to the unique ability of the EFPT to capture functional deficits that may have otherwise gone unnoticed. This is especially important for senior adult cancer patients who are already at risk for less independence due to their advanced age, comorbidities and existing impairments at time of cancer diagnosis. Unnoticed impairments may therefore be significant in hastening the requirement for institutionalization in this important population since majority of those affected will not be on the radar for the close monitoring of such deficits.

Importantly, the presence of comorbidities in senior adults at the time of cancer diagnosis was well exemplified by this study. At baseline testing, 70.3% of the participants already had "moderate" or "severe" grades of comorbidities and this continued to be echoed at the subsequent time-points. With a high burden of moderate or severe comorbidities, the impact of these comorbidities on cancer treatment can no longer be ignored- they are bound to affect treatment decisions, treatment compliance and survival. It is important for the management team to be abreast of senior adult patients' comorbidities as they will impact the treatment landscape.

Several limitations were encountered in this study. First of all, the study had a small sample size. While statistical analysis was still feasible with 20 patients, we believe that expanding the cancer sites to increase the recruitment pool and sample size will generate better power to detect differences in the variables studied. Secondly, only 7 participants were able to perform the Life Participation assessments. This was much less than desirable. One reason for the low participation rate may have been the fact that this part of the testing was done at a distance (4444 Forest Park Avenue) from the recruitment clinics (Siteman Cancer Center), which may have been an extra inconvenience to participants. Plans to secure an area within the Siteman cancer center building in which assessments can be done, limiting the need to travel an extra distance for this section of the testing, will help to decrease the likelihood of this occurring in the future. Thirdly, not all assessments as outlined in the *methods* section were completed by all participants. We believe that better standardization of the testing protocols will facilitate completion of the assessment battery.

FUTURE PLANS

The data gained from this pilot project has only begun to enhance our understanding of the health limitations, especially functional and cognitive issues that may impair daily function and self-care throughout cancer treatment and survival. Larger studies to better investigate these deficits are therefore required. The investigators plan to use the experience and data gained from this pilot study to apply for extramural R21 and R01 funding from the National Cancer Institute and the National Institute for Aging. In the future, we would like to conduct longitudinal studies to investigate the types of deficits present at the start of treatment that persist after cancer treatment; the types of functional and cognitive deficits (i.e., 'chemo-brain') that develop as a consequence of treatment; and the ability of performance-based tests to identify newly diagnosed cancer patients at risk for functional declines during and after completion of cancer therapy. We believe that the results of such studies will help to pave the way for the development of interventions and strategies to ameliorate difficulties with independence and quality of life that may be encountered as a result of cancer treatment in our senior adult cancer survivor population.

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