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Chemotherapy in the oldest old: The feasibility of delivering cytotoxic therapy to patients 80 years old and older

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ABSTRACT

Objectives: Cancer is predominantly a disease of the elderly. While "older" patients are frequently considered for chemotherapy, little data exist in the population 80 years and older (80+). We investigated outcomes of patients 80+ who received chemotherapy at our institution.
Materials and Methods: A retrospective chart review of patients 80+ initiating chemotherapy for malignant solid tumors from 2005 to 2010 was performed. Baseline demographics, cancer type and chemotherapy data were collected. Primary outcome was the rate of discontinuation due to toxicity. Secondary outcomes included the rate of dose reduction/omission/delay (ROD), hospitalization and blood transfusion.
Results: Chemotherapy was initiated in 318 patients. Baseline demographics included the following: median age 82 years (80–92 years), 56% male, 55% ECOG PS 0-1, 43% Charlson index score of 0–1; 38% were taking ≥6 prescription medications. Common malignancies were colorectal (32%), lung (20%), and breast (12%). Most patients (68%) had metastatic disease or received palliative intent therapy (71%). Treatment was first line in 89% of patients, and an upfront dose reduction was ordered in 41%. Toxicity caused therapy discontinuation in 32% of cases, while 52% experienced dose ROD. Hospitalization occurred in 32%; 18% required blood transfusions. Baseline polypharmacy was associated with increased hospitalization risk (OR 2.28, 95% CI 1.34–3.88, $p = 0.002$), but dose adjustments were not correlated with any outcome.
Conclusion: In this study, we observed a high risk of hospitalization or treatment discontinuation due to toxicity, despite frequent dose modifications. As the cancer population ages, validated tools are needed to better select patients for therapy.

1. Introduction

As the risk of developing and dying of cancer increases steadily with age, cancer can be thought of as primarily a disease of the elderly.[1,2] It is well recognized that men and women over the age of 80 years (80+) constitute one of the fastest growing segments of the North American population.[3,4] Thus, increasing numbers of elderly patients will be candidates for cancer therapy. With respect to the use of systemic cytotoxic chemotherapy, relatively little is known about the outcomes of patients 80+ either enrolled in clinical trials[5–7] or treated in the non-trial setting.[8,9] In fact, most studies evaluating cancer treatment in the elderly focus on patients aged 65–79 years.

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Given the paucity of descriptive research and therapeutic trial evidence to guide management of cancer in those over 80, we designed this exploratory analysis to investigate the feasibility and tolerability of chemotherapy in a cohort of patients 80+. Further goals are to identify which of the very elderly may be the best candidates for systemic treatment, and to create predictive tools to help guide clinicians when faced with such treatment decisions.

2. Materials and Methods

2.1. Patients

With approval from our institutional review board, we undertook a retrospective chart review of all patients aged 80 years and above initiating a course of chemotherapy for a solid tumor at The Ottawa Hospital between June 2005 and January 2010. These dates were chosen to capture a large number of patients and to reflect a diversity of therapy regimens. Our cancer center is the sole provider of medical oncology and radiation oncology services to a mixed urban and rural population of approximately 1.5 million.

Data were extracted by two of the authors from paper charts, electronic medical records and electronic chemotherapy ordering systems. We collected baseline data on each patient, including both standard and population-specific demographics—age, gender, ECOG performance status (PS), smoking history, baseline number of prescription medications and living situation prior to initiation of chemotherapy. Patient co-morbidities, excluding primary cancer diagnosis, were identified to calculate individual Charlson co-morbidity index (CCI) scores.[10] Cancer type and stage, the chemotherapy planned (regimen, intent and line of therapy, setting of initial regimen delivery, dose adjustment prior to the first cycle) and baseline blood parameters were recorded.

Eligible patients were those aged 80+ years at the start of a course of chemotherapy, including clinical trial patients. We excluded patients who started chemotherapy before the age of 80 years but continued on the same regimen after turning 80 years old. In patients who initiated multiple lines of chemotherapy after the age of 80 years, only data from the first initiation of chemotherapy were recorded. Patients receiving only biological or hormonal therapy were excluded. The line of therapy took into account all previous lines of systemic treatment irrespective of differing intent. If a therapy was interrupted for more than 4 months, resumption of the same drug constituted a new line. Dose adjustments made prior to the start of the first cycle and any subsequent cycle dose reductions, omissions and delays of greater than one week were also noted.

2.2. Outcomes

The primary end point was the rate of therapy discontinuations attributable to toxicity. Secondary end points included the rates of dose reductions, delays and omissions (ROD), rates of hospitalization and frequency of blood transfusions. Only hospital stays of more than 24 h were recorded as hospitalizations. Both hospitalizations and blood transfusions were included only if they occurred while the patient was actively receiving chemotherapy or within 30 days thereafter.

2.3. Statistical Analysis

We summarized patients' baseline characteristics and outcomes. Age was reported as median with range. Other categorical demographics, cancer characteristics and chemotherapy characteristics as well as the rates of primary outcome and secondary outcomes were reported as percentages. Each patient starting chemotherapy for the first time since reaching the age of 80 years represented the basic unit of analysis.

In order to investigate the association between baseline factors and the risk of hospitalization or discontinuation due to toxicity, a logistic regression model was applied for multivariable analysis. Both unadjusted and adjusted odds ratios with their 95% confidence limits were calculated.

All statistical analyses were performed using the SAS, version 9.3 (SAS institute, North Carolina).

3. Results

3.1. Demographics

Between June 2005 and January 2010, chemotherapy was initiated in 318 patients aged 80+ years. Baseline demographics are shown in Table 1. The patients ranged from 80 to 92 years old, with a median age of 82 years. The majority of patients were male (56%), ex-smokers (52%) and lived with their family (66%). ECOG PS was available in 79% of patients, and among them the majority (55%) were of PS 0-1. Regarding co-morbidity, 43% of patients had a CCI score of 0-1 (excluding the cancer diagnosis). Just over a third

Table 1 – Baseline patient demographics, tumor types and stage distribution (n = 318).

Age median (range)	82	80–92
Gender	Male	56%
	Female	44%
ECOG	0–1	55%
	2	14%
	3–4	9%
	Unknown	22%
Medications	<6	59%
	≥6	38%
	Unknown	3%
Smoking history	Never	30%
	Ex-smoker	52%
	Current smoker	6%
	Unknown	12%
Charlson	0–1	43%
	≥2	56%
	Unknown	1%
Living situation	Alone	23%
	With family	66%
	Retirement home or nursing home	5%
	Unknown	6%
Tumor type	Colorectal	32%
	Lung	20%
	Breast	12%
	Prostate	10%
	Other	26%
Tumor stage	Stages 1–3	32%
	Stage 4	68%