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# How I treat bladder cancer in elderly patients



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ABSTRACT

Bladder cancer is a disease of the elderly. There is a disconnect between the efficacy of treatments for patients with advanced disease, and their effectiveness, at least in part related to the advanced age at diagnosis. Standard treatments for patients with locally advanced or metastatic bladder cancer include radical cystectomy and/or cisplatin-based combination chemotherapy. However, there is significant potential for morbidity, and even mortality, with these treatments necessitating tools to risk stratify elderly patients to optimize the safety and benefit of treatments and alternative strategies in situations where the potential risks are likely to outweigh the potential benefits. This review considers the current standard treatments for advanced bladder cancer, approaches to risk stratify elderly patients, and highlights our relatively poor knowledge base regarding the optimal care of elderly patients with this disease.

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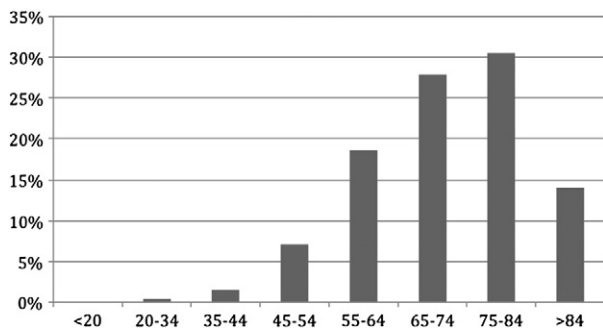
## 1. Introduction

Bladder cancer is a disease of the elderly (Fig. 1). The median age of diagnosis of bladder cancer in the United States is 73 years old and the median age of death is 79 years old. Due to the advanced age at the time of diagnosis, at least in part,

there is a major disconnect between the efficacy of treatment of patients with advanced bladder cancer, as established through clinical trials, and the effectiveness of such treatment when applied to the general population of patients with the disease. The “gold standard” treatments for advanced bladder cancer are associated with significant potential for morbidity

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**Fig. 1 – Age distribution of new bladder cancer diagnoses in the United States (data derived from the Surveillance, Epidemiology, and End Results Program\*).**

\*<http://seer.cancer.gov/statfacts/html/urinb.html>.

and even mortality. A radical cystectomy with pelvic lymph node dissection, with diversion or reconstruction of the urinary tract, involves major abdominal surgery and typically a prolonged recovery period. When systemic chemotherapy is utilized, cisplatin-based combination chemotherapy is supported by Level I evidence. Unfortunately, the bulk of evidence establishing these treatments as “gold standards” has been generated in younger patients. For example, Hutchins and colleagues reported that at a time when >75% of patients with bladder cancer in the United States were  $\geq 65$  years old, only 55% of patients with bladder cancer participating in Southwest Oncology Group (SWOG) trials were  $\geq 65$  years old [1]. Further complicating an evidenced-based approach to the management of elderly patients with bladder cancer is a lack of uniform reporting guidelines regarding the age of participants in clinical trial publications. While some trials report the percentage of enrolled patients above a certain age (e.g., percent  $\geq 65$  years old), most trials only report median age, and range, preventing a full appreciation for the number of elderly patients included.

Of course, care decisions in patients with bladder cancer, and other malignancies, are not optimally based on chronological age but rather functional age. Measures of functional status or frailty are generally much more important determinants of treatment tolerability, and benefit, than age alone. Nonetheless, there is physiologic decline in virtually every organ system associated with aging, functional reserve may differ in younger and older patients with the same baseline functional status, and chronological age still contributes to medical decision-making. The chronological age that defines “elderly” is arbitrary and most analyses have used a cut-off of  $\geq 65$  or  $\geq 70$  to define an elderly population.

With this background, the care of the elderly patient with advanced bladder cancer is probably best discussed within the context of a case. An 80 year-old woman undergoes a cystoscopy and transurethral resection of bladder tumor, after presenting with gross hematuria, and is diagnosed with muscle-invasive urothelial cancer. She undergoes a computed tomography scan of the chest, abdomen, and pelvis that reveals no radiographic evidence of metastatic disease. She has hypertension and type II diabetes mellitus and a creatinine of 1.5. Her Eastern Cooperative Oncology Group (ECOG) performance status is 2.

What else do we need to know about this patient to guide management? There are several other aspects to her history and physical that may be important to clinical decision making, most of which are important to elicit in the work-up of any patient, but some that may be particularly germane to the elderly patient. Has cognition been adequately assessed? What is the patient’s level of mobility, living situation, and social support system? How is her nutritional status? Does she prepare her own meals? How many other medications is she taking and who administers these medications? Has organ function been adequately assessed? When feasible, these domains are likely best assessed in the setting of a Comprehensive Geriatric Assessment (CGA) [2] or a formal geriatrics consultation, though key information can often be ascertained through a more detailed history.

*As we dig a bit deeper, we learn that our patient suffers from mild dementia. She lives in an assisted living facility. She has a very supportive family that accompanies her to appointments and assists with transportation. She needs assistance with her instrumental activities of daily living.*

## 2. Treatment of Muscle-Invasive Bladder Cancer in the Elderly

Treatment options for clinically localized muscle-invasive bladder cancer (i.e., cT2-4a) include radical cystectomy with or without perioperative chemotherapy, radiation therapy with or without concomitant chemotherapy, or transurethral resection of bladder tumor/supportive care alone. In the United States, radical cystectomy is the preferred treatment for patients with muscle-invasive bladder cancer and is potentially curative. Long-term outcomes are correlated highly with pathologic stage of disease with approximately 80%, 70%, and 30%, of patients remaining disease-free with organ-confined disease, extravesical disease, and lymph node-positive disease, respectively [3]. Unfortunately, clinical staging in bladder cancer poorly predicts pathologic stage such that such refined risk stratification information is not available prior to surgery, when treatment decisions need to be made [4]. Not surprisingly, as radical cystectomy is a major surgical procedure, population-based data suggest that this operation is performed much less commonly in elderly patients. In an analysis of the National Cancer Database (NCDB), Fedeli et al. demonstrated that approximately 40–50% and 13–30% of septuagenarians and octogenarians with muscle-invasive bladder cancer, respectively, underwent radical cystectomy [5]. Gore et al. examined a cohort of 3262 Medicare beneficiaries aged 66 or older with muscle-invasive bladder cancer using Surveillance, Epidemiology, and End Results-Medicare data. These investigators determined that only 21% of patients underwent cystectomy; notably, overall survival was better for patients that underwent cystectomy [6]. Similar findings have been confirmed in a more contemporary analysis of NCDB data also highlighting that similar survival outcomes were achieved with either cystectomy or concurrent chemoradiation, both of which were better than other therapies or no treatment [7].

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