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Curative Treatment for Muscle Invasive Bladder Cancer in Elderly Patients: A Systematic Review

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Abstract

Context: The incidence of muscle invasive bladder cancer (MIBC) increases with age. With increased life expectancy the number of elderly MIBC patients is expected to increase**.** Existing guidelines on management of MIBC do not preclude curative treatments for elderly patients. However, it is necessary to assess the risks and benefits of a treatment to avoid overtreatment that results in decreased health-related quality of life without prolonging survival.
Objective: To report on overall survival (OS), cancer specific survival (CSS), and morbidity after curative treatment in elderly patients, defined as age >70 yr, with nonmetastatic MIBC and to compare this with the outcome of younger MIBC patients.
Evidence acquisition: A systematic review was performed using Medline, PubMed, and Embase databases. Articles were included if they addressed one of the three research questions:

1) Does a geriatric assessment improve outcome in elderly patients with MIBC?
2) Do elderly patients have inferior survival, both CSS and OS, after curative therapy compared to younger patients with MIBC?
3) Do elderly patients have an increased complication rate, defined as perioperative mortality (POM) and both early and late complication rate, after curative therapy compared to younger patients with MIBC?

Only articles including >100 patients and with a clear age–stratification were included.
Evidence synthesis: Forty-two articles were retrieved for review. No article directly addressed the use of geriatric assessment. OS and CSS worsen significantly with age both after radical cystectomy and radiotherapy regimens. While POM significantly increases with age, morbidity seems comparable between younger and older patients.
Conclusions: Although a proportion of elderly patients with MIBC will benefit from curative treatment, we observed worse OS, CSS, and POM with age. The impact of age on

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late morbidity is less clear. Prospective studies evaluating geriatric assessments are critically needed to optimize MIBC management in the elderly.

Patient summary: We performed a systematic review to evaluate the outcome and complication rate in elderly patients with muscle invasive bladder cancer. We observed that overall survival and cancer specific survival significantly decrease and perioperative mortality significantly increases with age. The impact of age on late morbidity is less clear. There is a need for geriatric assessments to select those patients that will benefit from curative treatment.

1. Introduction

Bladder cancer is the ninth most frequently diagnosed cancer worldwide. Although the mortality rate of bladder cancer tends to decrease, bladder cancer still ranks 13th in terms of causes of death [1]. The incidence of bladder cancer increases steadily with age and due to an increase in overall life expectancy, population ages exponentially. Consequently, the number of elderly patients with bladder cancer is expected to further increase in the future.

Radical cystectomy (RC) with extended pelvic lymph node dissection is considered to be the standard of care for nonmetastatic muscle invasive bladder cancer (MIBC) [2]. External beam radiotherapy combined with concomitant chemotherapy is an alternative to RC for carefully selected patients [2].

Existing guidelines for the management of MIBC do not preclude curative treatments for elderly patients and it is suggested that the decision to treat cancer patients should not be based solely on age, though life expectancy should be considered [3]. A thorough geriatric assessment (GA) can help avoid both undertreatment and overtreatment of elderly patients, both of which could result in decreased health-related quality of life [3].

The aim of this systematic review is to report on overall survival (OS) and cancer specific survival (CSS) as well as morbidity after curative treatment in elderly patients, defined as age >70 yr, with nonmetastatic MIBC, and to compare this with the outcome observed in a younger population with MIBC.

2. Evidence acquisition

2.1. Study design

A systematic review was conducted to identify studies of relevance for the predefined research questions:

1) Does a GA improve outcome in elderly patients with MIBC?
2) Do elderly patients have inferior survival, both cancer specific survival (CSS) and overall survival (OS), after curative therapy compared with younger patients with MIBC?
3) Do elderly patients have an increased complication rate, defined as perioperative mortality (POM) and both early and late complication rate, after curative therapy compared to younger patients with MIBC?

2.2. Search strategy

Search strings were used to interrogate the following databases: Medline, PubMed, and Embase. Potential articles were identified using the National Library of Medicine's Medical Subject Headings: "(urinary bladder neoplasms[mh] OR <bladder$* adj3 (cancer$ or carcinoma$ or neoplasm$ or tumor$)[mp]>) AND (Frail Elderly[mh] OR Aged[mh] OR elder$.ti,ab OR Geriatric$.ti,ab[tw] OR older person.ti,ab[tw] OR older adult.ti,ab[tw] OR octogenerians.ti,ab. [tw]) AND (Cystectomy[mh] OR surgery[mh] OR radiotherapy[mh] OR drug therapy[mh] OR resection.ti,ab OR radiotherapy.ti,ab OR radiation. ti,ab OR chemothera$ .ti,ab OR antineoplastic$.ti,ab) AND (treatment outcome[mh] OR survival rate[mh] OR effectiveness.ti,ab OR efficacy.ti,ab OR survival benefit ti,ab). The search was finalized on December 21, 2016. Relevant articles found in the reference section of the retrieved articles were also retained for evaluation.

2.3. Eligibility criteria

Longitudinal and population-based studies as well as consecutive and nonconsecutive surgical series, reporting on CSS, OS, POM, or complication rate after radical treatment for MIBC, were included.

Articles needed to be published in English. Only full papers were included. Articles reporting on at least 100 patients were maintained. Articles could still be rejected, despite inclusion of >100 patients, if the total number of patients in the younger or elderly group separately was <50 patients. Only articles comparing outcomes between different age groups were considered for inclusion. Age stratification was thus mandatory for being eligible.

2.4. Selection of relevant articles

The selection of relevant articles was conducted in two steps. As a first step, one reviewer (V.F.) excluded clearly irrelevant studies or studies not meeting the eligibility criteria based on title and abstract. Two reviewers (V.F. and P.O.) performed the final selection based on review of the full text manuscripts.

2.5. Data extraction

Point estimates, p values, and confidence intervals for effectiveness (CSS and OS) and safety outcomes (POM and complication rate) were extracted. It was decided a priori to

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