ELSEVIER

Urologic Oncology: Seminars and Original Investigations 32 (2014) 391–395

UROLOGIC ONCOLOGY

Review article

Why is perioperative chemotherapy for bladder cancer underutilized?

Francis M. Patafio, M.D., William J. Mackillop, M.B.Ch.B., Deb Feldman-Stewart, Ph.D., David Robert Siemens, M.D., Christopher M. Booth, M.D.*,[1]

Division of Cancer Care and Epidemiology, Queen's University Cancer Research Institute, Kingston, Canada

Received 1 October 2013; received in revised form 29 October 2013; accepted 7 November 2013

Abstract

Despite clinical evidence and recommendations from international treatment guidelines, the use of perioperative chemotherapy for muscle-invasive bladder cancer in routine practice remains low. Although multiple studies have described underutilization, there is an urgent need to better understand the elements contributing to the observed gaps in care. In this commentary, we explore what is known about the factors contributing to underutilization of perioperative chemotherapy for muscle-invasive bladder cancer. We also propose a framework to guide future knowledge translation activities in an effort to improve the care and outcomes of patients with this disease.

Keywords: bladder cancer; chemotherapy; quality of care; health policy; knowledge translation; practice patterns; medical decision making

1. Introduction

A substantial proportion of patients who undergo cystectomy for muscle-invasive bladder cancer (MIBC) ultimately have recurrence and die from their disease [1]. Beginning in the late 1990s, a series of randomized controlled trials and 2 meta-analyses have reported that long-term survival is improved by approximately 5% with a course of neoadjuvant chemotherapy (NACT) [2–5]. Based on these data, international guidelines recommend the use of NACT for patients with T2-T4 bladder cancer [6–8]. The evidence in support of adjuvant chemotherapy (ACT) also suggests that it improves patient outcomes [9,10]. However, the quality of the data is more limited, and therefore ACT is not as strongly endorsed by practice guidelines [7,11].

Despite level I evidence and practice guideline recommendations, numerous studies have reported low rates of perioperative chemotherapy in routine care. Porter et al. used Surveillance, Epidemiology and End Results Program-Medicare data to describe the use of NACT among 40,660 patients with MIBC in the United States from 1992 to 2003. They found that NACT was delivered to 1%, 7%, and 11% of patients with stages 2, 3, and 4 disease, respectively [12]. David et al. [13] used records from the National Cancer Data Base in the United States to describe treatment of 7,161 patients with stage III bladder cancer diagnosed between 1998 and 2003. They found that 10% of patients received ACT, whereas only 1% received NACT. In our own population-based study of practice patterns in Ontario, NACT was used in only 4% of the 2,738 patients with MIBC diagnosed between 1994 and 2008 [14]. Moreover, treatment rates did not substantially increase over time: 5% from 1994 to 1998, 3% from 1999 to 2003, and 6% from 2004 to 2008. Contrary to the existing Ontario practice guidelines, the use of ACT was more common than NACT and increased over time: 16% from 1994 to 1998, 19% from 1999 to 2003, and 23% from 2004 to 2008.

In general, patients with MIBC are eligible for perioperative chemotherapy if they have T2-T4 disease, no clinical evidence of metastatic disease, an Eastern Cooperative Oncology Group performance status 0 to 1, and adequate renal function. Raj et al. reviewed the use of NACT at a single tertiary referral center during 2003 to 2008 and found that NACT was given to only 32 of 145 (22%) patients [11]. Among these 145 patients, 70% were eligible based on calculated renal function. Among the 113 patients not treated with NACT, a satisfactory reason for not using NACT was not identified in 66 cases (58%). In the remaining patients, contributing reasons included concerns

* Corresponding author. Tel.: +1-613-533-6895; fax: +1-613-533-6794.
E-mail address: boothc@kgh.kari.net (C.M. Booth).

[1]This work was funded through salary support provided to Dr Booth as a Cancer Care Ontario Chair in Health Services Research.

1078-1439/$ – see front matter
http://dx.doi.org/10.1016/j.urolonc.2013.11.003

over age/comorbidity (26%), patient preference (8%), concerns of NACT toxicity (8%), symptoms or active bleeding (5%), and clinically localized disease (17%).

2. What factors might be driving physician and patient decision making?

In Fig., we depict the care pathway for patients with MIBC and potential provider- and patient-level barriers to the use of NACT/ACT. An important and common up-front barrier is the fact that 30% to 50% of patients are not eligible for treatment on the basis of impaired renal function [15,16]. In the subsequent sections, we summarize what is known from the published literature about provider- and patient-level barriers to NACT/ACT.

2.1. The urologist

The urologist is the gatekeeper to NACT/ACT as they determine whether or not a patient is referred to a medical oncologist. Outside of academic medical centers, urologists may have more limited access to medical oncologists. Assuming there is access to medical oncology consultation, there are 2 general reasons why a urologist may not refer to medical oncology. First, some urologists may not be aware of the evidence and guidelines in support of NACT. A study reported in 1988 surveyed 153 urologists and oncologists asking them what treatment they would choose if they were diagnosed with MIBC. They found that 56% of North American urologists would undergo cystectomy alone, whereas only 11% would add chemotherapy to their surgical management. In comparison, 29% of medical oncologists would undergo cystectomy alone and 25% of them would include chemotherapy in their treatment [17]. A follow-up survey of the same urologists/oncologists 2 years later provided a summary of the initial results and asked whether knowing about their colleagues choices would change their management decision [18]. The researchers found that knowing colleagues' opinions did influence respondents' subsequent stated management preferences. Compared with the initial survey, a considerably greater proportion of Canadian urologists (14% vs. 5% previously), US urologists (36% vs. 20% previously), and medical oncologists (61% vs. 25% previously) stated they would incorporate chemotherapy with surgical management. It is worth noting that these studies were conducted before publication of the pivotal randomized controlled trials of NACT. Bower et al. [19] surveyed 273 UK urologists and surgeons in 1996 regarding their management of patients with bladder cancer and found that only 2% of respondents would refer a patient with MIBC to an oncologist. Publication and dissemination of clinical practice guidelines (CPGs) may mitigate this potential barrier. Miles et al. evaluated rates of referral to medical oncology and the use of NACT before and after publication of a 2005 CPG in Alberta, Canada. Among 236 patients with T2-T4 MIBC, medical oncology referral rates increased from 2%

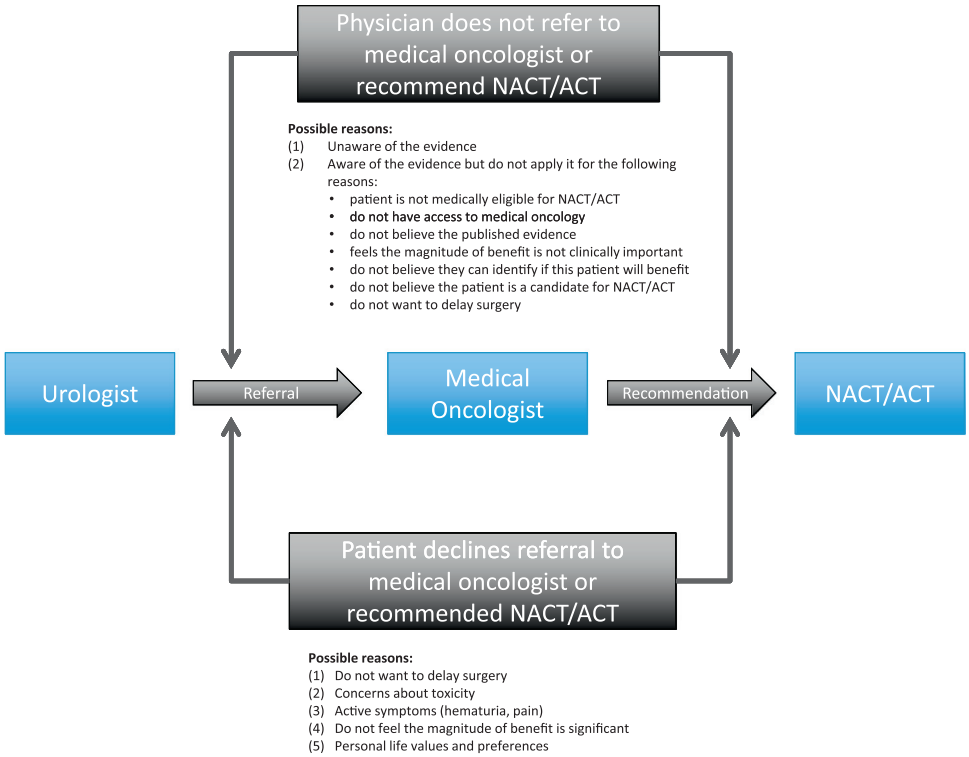

Fig. Potential barriers to the use of perioperative chemotherapy along the care pathway for patients with muscle-invasive bladder cancer. (Color version of figure is available online.)