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Original Article

Curative Therapy for Bladder Cancer in Routine Clinical Practice: A Population-based Outcomes Study

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Abstract

Aims: Definitive therapy of bladder cancer involves cystectomy or radiotherapy; controversy exists regarding optimal management. Here we describe the management and outcomes of patients treated in routine practice.
Materials and methods: Treatment records were linked to the Ontario Cancer Registry to identify all cases of bladder cancer in Ontario treated with cystectomy or radiotherapy in 1994–2008. Practice patterns are described in three study periods: 1994–1998, 1999–2003, 2004–2008. Logistic regression, Cox model and propensity score analyses were used to evaluate factors associated with treatment choice and survival.
Results: In total, 3879 cases (74%) underwent cystectomy and 1380 (26%) were treated with primary radiotherapy. Cystectomy use increased over time (66, 75, 78%), whereas radiotherapy decreased (34, 25, 22%), $P < 0.001$. There was substantial regional variation in the proportion of cases undergoing radiotherapy (range 16–51%). Five year cancer-specific survival (CSS) and overall survival were 40 and 36% for surgical cases and 35 and 26% for radiotherapy cases ($P < 0.001$). In multivariate Cox model and propensity score analyses, there was no significant difference in CSS between surgery and radiotherapy (hazard ratio 0.99, 95% confidence interval 0.91–1.08); radiotherapy was associated with slightly inferior overall survival (hazard ratio 1.08, 95% confidence interval 1.00–1.16).
Conclusion: Utilisation of cystectomy for bladder cancer in routine practice has increased over time with no evidence of a significant difference in CSS between radiotherapy and cystectomy.

Key words: Bladder cancer; cystectomy; health services; outcomes; quality of care; radiation

Introduction

Initial local therapies for muscle-invasive bladder cancer include cystectomy or radiotherapy. Outcomes achieved with either modality are good in highly selected series from centres of excellence [1,2] and there is no strong evidence showing the superiority of one modality over the other. Accordingly, controversy exists as to what treatment is preferred and whether in fact there is an optimal treatment strategy. This controversy is evident in the discordance of international treatment guidelines, with some strongly recommending cystectomy over radiotherapy [3–5] and others concluding that both forms of treatment are acceptable [6,7]. These recommendations are not based on high-level evidence, as there are no contemporary randomised controlled trials (RCTs) that have systematically compared these two treatment modalities.

Population-based outcome studies provide insight into patterns of care and outcomes among patients treated in routine clinical practice [8]. They can minimise sources of selection and referral bias that often limit single institution-based studies. These studies may also contribute to an

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understanding about effectiveness of medical therapies when there are no randomised data to guide patient care. Only a handful of population-based studies have reported practice and outcomes of cystectomy and radiotherapy for bladder cancer and these studies primarily described patients treated in the 1980s and 1990s [9–12]. It remains unclear if clinical features of bladder cancer have changed over time and how surgical and radiotherapy treatments may have evolved. We undertook the current population-based cohort study to evaluate the use of surgery and radiotherapy for patients with bladder cancer in the contemporary era and provide insights into the outcomes achieved in routine clinical practice.

Materials and Methods

Study Design and Population

This was a population-based, retrospective cohort study to describe the management and outcome of muscle-invasive bladder cancer in the Canadian province of Ontario. Ontario has a population of about 13.5 million people and a single-payer universal health insurance programme. All incident cases of bladder cancer in Ontario with transitional cell, adenocarcinoma and squamous cell histology who underwent cystectomy or radical radiotherapy in 1994–2008 were included. The study population was classified into three temporal periods: 1994–1998, 1999–2003, 2004–2008.

Data Sources

The Ontario Cancer Registry (OCR) is a passive, population-based cancer registry that captures diagnostic and demographic information on at least 98% of all incident cases of cancer in the province of Ontario [13]. The OCR does not compile information about the extent of disease or treatment. Accordingly, we obtained surgical pathology reports for patients with cystectomy. Indicators of the socioeconomic status of the community in which patients resided at diagnosis were linked, as described previously [14].

A variety of electronic administrative health databases were linked to the OCR. Records of hospitalisation from the Canadian Institute for Health Information (CIHI) provided information about surgical interventions; these records are known to be consistent and complete [15]. The clinical databases of Ontario's comprehensive cancer centres provided records of radiotherapy and chemotherapy. These centres are the only providers of radiotherapy in the province and the electronic radiotherapy records are known to be 95% complete and 99% accurate with respect to total dose, number of fractions, date of therapy, body region irradiated and treatment intent [16]. Provincial physician billing records and treatment records from regional cancer centres were used to identify chemotherapy utilisation – these records are created in the act of prescribing treatment. Surgical pathology reports were obtained from the OCR and reviewed by a team of data abstractors.

Definitions of Comorbidity, Management and Outcomes

Comorbidity was classified using the Charlson Index modified for administrative data based on all non-cancer diagnoses recorded during any hospital admission within 5 years before surgery [17]. Cases treated with radical radiotherapy were identified from the radiotherapy treatment records of the regional cancer centres. Cases treated to the bladder or pelvis with curative intent were included, as were those with missing intent who were treated with <250 cGy/fraction. Cases treated with surgery and radiotherapy were further classified based on the sequence and timing of both modalities: surgical cases with preoperative radiotherapy (radiotherapy first with surgery <16 weeks after completing radiotherapy); radiotherapy case with salvage surgery (radiotherapy first with surgery >16 weeks from the end date of radiotherapy); surgical cases with postoperative radiotherapy (surgery first with radiotherapy starting within <16 weeks); surgical cases with salvage radiotherapy (surgery first with radiotherapy starting >16 weeks from surgery). The primary outcome end point was cancer-specific survival (CSS). To account for possible cause of death miscoding, CSS included death from any cancer. CSS was prioritised over overall survival, as it was felt to be less vulnerable to bias from unmeasured prognostic factors.

Statistical Analysis

Comparisons of proportions between study groups were made using the chi-squared test. Survival was determined from the date of surgery/radical radiotherapy using the Kaplan–Meier technique and comparisons between groups were made using the Log-rank test. Factors associated with surgery/radiotherapy were evaluated by logistic regression. Factors associated with overall survival/CSS were evaluated using the Cox proportional hazards regression model. To control observed confounding variables when exploring the association between surgery/radiotherapy and survival, we also used the propensity score technique in the Cox proportional hazards model. The propensity score is the probability that a case would have surgery and it was modelled with observed confounding variables using the logistic regression model. Propensity scores allowed us to create five propensity strata with balanced confounding variables between surgery cases and radiotherapy cases. Survival of cases treated with surgery was compared with that of those treated with radiotherapy within each stratum using a Cox proportional hazards model; a summary hazard ratio combining the results across quintiles was calculated based on the stratified Cox's PH model [18,19]. Because propensity score analyses may better control for known confounders than traditional Cox analyses, the primary analysis of CSS used the propensity score technique. Results were considered statistically significant at $P < 0.05$. All analyses were carried out using SAS version 9.1 (SAS Institute, Cary, NC, USA).