Clinical Oncology xxx (2016) 1–9

Contents lists available at ScienceDirect

Clinical Oncology

journal homepage: www.clinicaloncologyonline.net

Original Article

The Patterns of Practice and Outcomes of Penile Cancer in Ontario

A. Mahmud *, X. Qu *, D. Yip *, M. Leveridge †, W. Mackillop *

* Department of Oncology, Queen's University, Cancer Centre of Southeastern Ontario at Kingston General Hospital, Kingston, Ontario, Canada

† Department of Urology, Queen's University, Kingston General Hospital, Kingston, Ontario, Canada

Received 12 August 2016; received in revised form 15 November 2016; accepted 21 November 2016

Abstract

Aims: Penile cancer is a rare malignancy in Western countries. The management guidelines are mainly derived from retrospective studies as there are no randomised trials. The primary objective of this study was to assess patterns of practice and outcomes of penile squamous cell carcinoma in Ontario. Secondary objectives included examining trends in incidence, pathological characteristics and prognostic factors.

Materials and methods: All patients diagnosed with penile cancer between 2000 and 2010 were identified from the Ontario Cancer Registry and all available pathology reports related to penile cancer during this period were reviewed.

Results: Pathology reports of 419 new cases of penile squamous cell carcinoma were reviewed. There was a significant improvement in completeness of the pathology reports in recent years. The age-adjusted incidence was 0.9 per 100 000 person-years. Most patients presented with a pT1 lesion (63%). A partial penectomy (40%) was the most common surgical procedure. Over 38% of patients identified to be eligible for organ-sparing surgery had a total or partial penectomy. Only 23% of the eligible patients identified to require lymph node dissection underwent the procedure. The 5 year disease-specific survival for stage 0, I, II, III were 94%, 93%, 74% and 52%, respectively.

Conclusions: There is a significant variation in the patterns of practice in Ontario. A large proportion of patients in this cohort were probably overtreated for the primary malignancy and undertreated for the regional nodes.

Key words: Incidence; outcome; pathology; penile cancer; practice pattern

Introduction

Penile cancer is an uncommon malignancy in Europe and North America, with an incidence less than 1 per 100 000 person-years [1]. However, in parts of Africa, Asia and South America, penile cancer accounts for about 10% of all malignancies in men [2]. In Canada, penile cancer accounts for about 200 new cases and 30 related deaths per year [3]. Squamous cell carcinoma (SCC) is the most common histology and accounts for 95% all penile cancer [4].

Due to the low incidence of penile cancer in the Western hemisphere, management is often guided by small case series, single centre retrospective studies and local experience [5,6]. Current guidelines, such as European Association of Urology (EAU), National Comprehensive Cancer Network (NCCN) and Canadian Association of Genitourinary Medical Oncologists (CAGMO), are mainly derived from retrospective single centre studies, as well as registry databases from Europe and the USA [1,5,7]. There are no randomised studies available to guide penile cancer management and there was a call for a Canadian registry study from the CAGMO guideline [5].

Penile cancer requires complex management [8]. Only 4.1% of urologists in the USA carry out penile surgery and 1.5% carry out lymph node dissection (LND), whereas about 60% of cases are managed in the community [8]. Centralised management has been shown to improve outcomes on the population level, specifically in cancers with a lower incidence, such as oesophageal and pancreatic cancer [9]. A supra-regional network in Europe has resulted in an increased number of cases seen at higher-volume centres, greater utilisation of penile-sparing procedures, more

Author for correspondence: A. Mahmud, Department of Oncology at Queen's University, Cancer Centre of Southeastern Ontario, 25 King St W, Kingston, Ontario, K7L 5P9 Canada. Tel: +1-613-5442631x4506; Fax: +1-613-5481355.

E-mail address: aamer.mahmud@krcc.on.ca (A. Mahmud).

http://dx.doi.org/10.1016/j.clon.2016.12.006

Please cite this article in press as: Mahmud A, et al., The Patterns of Practice and Outcomes of Penile Cancer in Ontario, Clinical Oncology (2016), http://dx.doi.org/10.1016/j.clon.2016.12.006

appropriateness of LND and improvements in patient satisfaction [10].

Currently, management for penile cancer in Canada is not centralised. There is a lack of data on how well Canadian physicians adhere to practice guideline. The primary objective of this study was to assess patterns of practice and outcome of penile SCC in Ontario. Secondary objectives included examining the trend in incidence, pathological characteristics and prognostic factors from a large Canadian cohort.

Materials and Methods

Patient Population

All patients diagnosed with penile cancer between 1 January 2000 and 31 December 2010 were identified from the Ontario Cancer Registry (OCR) based on International Classification of Diseases, 10th revision (ICD-10) code C.60-malignant neoplasm of penis. All available pathology reports related to a penile cancer diagnosis were obtained through Cancer Care Ontario. The date of diagnosis, vital status, cause of death and date of death were obtained from the OCR.

Pathology Data

All pathology reports were reviewed by two physicians and audited by a third physician. The date of diagnosis based on pathology reports was used. All surgical procedures that occurred within the 3 months of diagnosis were considered as initial management that provided pathological staging information. Pathological tumour (pT) and nodal (pN) stages were described according to the American Joint Committee on Cancer (AJCC) 7th edition. pT1 lesions were assigned to pT1a stage when neither lymphovascular invasion status or grade was known. Patients who did not undergo upfront surgical nodal staging (pNx) were considered N0 for overall staging.

We described the proportion of cases managed by organ-sparing surgery (OSS) and LND as a proxy for the appropriateness of surgical management, as previously described [8]. Patients who had pT1 tumours with a histological grade of 1 or 2, regardless of nodal status, were considered eligible for OSS as per NCCN guidelines (v 1.2016) [7]. OSS is defined as a procedure less extensive than a partial or total penectomy. Patients who had pT1b or greater, grade 3 or 4, and/or biopsy-proven regional lymph nodes were considered as candidates for LND [7].

Radiation Data

The radiotherapy data were obtained from Cancer Care Ontario. The intent of radiotherapy was determined based on timing corresponding to surgical procedures, treatment site and dose/fractionation. Radiotherapy was considered palliative when dose ≤ 30 Gy and fractionation ≤ 10. Radiotherapy was considered adjuvant when given within 6 months of a curative surgical procedure and it was considered radical when patients underwent biopsy alone.

Statistical Analysis

The age-adjusted incidence rate was calculated by direct standardisation adjusting to the age distribution of the 2006 Ontario population [11]. Age-specific incidence rates were calculated for 10 year age groups. We used Joinpoint Regression Program 4.2.0.1 (National Cancer Institute; Bethesda, Maryland, USA) to assess trends in incidence analysis. This software fits the simplest joinpoint model by starting with the minimum number of joinpoints and assessing whether more joinpoints were necessary [12]. The annual percentage change in incidence was obtained from this method.

The chi-squared test and *t*-test/Wilcoxon test were used to evaluate the difference between groups for categorical and continuous variables, respectively. Continuous variables, such as depth of invasion and tumour size, were dichotomised based on literature, whereas age was dichotomised based on statistical property for confounding adjustment. The Kaplan–Meier method was used for the analysis of survival and recurrence. Overall survival was censored on 31 December 2012, whereas disease-specific survival (DSS) was censored on 31 December 2010 because the information for cause of death was 2 years behind. Cause of death other than ICD-9 187 was censored for DSS analysis. Local and regional recurrence was censored on 31 December 2010. The time-to-event outcome was defined as the time from pathological diagnosis to the event. Outcomes between groups were compared using the Log-rank test. Cox proportional hazard regression models were used to assess prognostic factors for DSS and local recurrence, respectively. Patient's age, type of initial management, multiple pathological factors of the primary tumour, local and regional recurrence (as time-varying covariates) were all considered in multivariate analysis. Backward elimination was used with a threshold of P-value < 0.05. The hazard rate over time was graphed with Kernel estimation. Proportional hazard assumption was tested by time-varying covariate analysis. The pattern of missing data was verified and multiple imputations were carried out using patient age and available pathological features to impute missing data on pathological features by regression models. Results from multiple imputations were compared with results from the complete dataset. The complete dataset contained all patients with complete information on variables that were selected from multivariate analysis. A two-sided P-value < 0.05 was considered statistically significant. Statistical analyses were carried out using SAS 9.3 (SAS Institute, Cary, North Carolina, USA).

This study was approved by the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethic Board.

Results

Incidence

In total, 533 patients with penile cancer were identified from the OCR in 2000–2010; 795 pathology reports were

Please cite this article in press as: Mahmud A, et al., The Patterns of Practice and Outcomes of Penile Cancer in Ontario, Clinical Oncology (2016), http://dx.doi.org/10.1016/j.clon.2016.12.006