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Original article

Variations in pelvic lymph node dissection in invasive bladder cancer: A Dutch nationwide population-based study during centralization of care

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Abstract

Objectives: To assess temporal trends in radical cystectomy (RC) and pelvic lymph node dissection (PLND) and the effect of centralization of care in the Netherlands between 2006 and 2012.

Patients and methods: This nationwide population-based study included 3524 patients from the Netherlands Cancer Registry who underwent RC as the primary treatment for cT1–4a, N0 or Nx, M0 urothelial carcinoma. Annual application rates of PLND, median LNC, and rates of node-positive disease (pN+) were compared by linear-by-linear association. Multivariable logistic regression was performed to identify patients' and hospital characteristics associated with PLND and LNC $\geq$10, and to study associations between LNC and pN+ disease.

Results: In total, 3,191 (91%) patients had PLND during RC and the use increased from 84% in 2006 to 96% in 2012 ($P < 0.001$). Owing to centralization of care in 2010 (at least 10 RCs/y/hospital), significantly more patients were treated in high-volume hospitals ($\geq$20 RC per year) in 2011 and 2012. PLND use was highest in males, younger patients and in academic, teaching, and high-volume hospitals ($\geq$20 RC per year). In 2012, PLND application rates were comparable for academic, teaching, and nonteaching hospitals ($P = 0.344$). Median LNC increased from 7 in 2006 to 13 in 2012 ($P < 0.001$), 55% had an LNC $\geq$10 (63% in 2012). Furthermore, lymph node count (LNC) $\geq$10 was associated with cT3–4a and, pN+ disease, R0 and treatment in academic, teaching, or high-volume hospitals ($\geq$20 RC per year). Rate of pN+ disease increased from 18% to 24% between 2006 and 2012 ($P = 0.014$). This trend was significantly associated with increased LNC on a continuous scale (odds ratio = 1.03).

Conclusions: After centralization of care, PLND during RC for cT1–4a, N0 or Nx, M0 urothelial carcinoma has become standard in all types of Dutch hospitals. The increase in LNC between 2006 and 2012 was associated with a higher incidence of pN+ disease and suggests more adequate template extension and adherence to contemporary guidelines in recent years.

Keywords: Bladder cancer; Centralization; Lymph node count; Lymph node dissection; Population-based; Staging

1. Introduction

Pelvic lymph node dissection (PLND) during radical cystectomy (RC) for bladder cancer (BC) is described as early as 1962 [1]. At present, it is considered essential for staging and prognostic purposes and to direct adjuvant therapy [2,3]. Another reason to perform PLND during RC is a potential higher survival rate in both node-negative and

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node-positive disease [4–6]. Lymph node metastases are present in 26% of PLND specimens of patients who undergo RC for BC [2]. Furthermore, in epidemiological studies, omission of PLND during RC is associated with inferior long-term overall survival (OS) and cancer-specific survival (CSS) [7,8]. Nevertheless, population-based studies from the United States and Canada have reported rates of PLND omission up to 18% [7,9]. We assessed PLND rates and associated quality-of-care parameters in 3,524 patients who underwent RC for cT1–4a, N0 or Nx, M0 UC in the Netherlands between 2006 and 2012. Of note, in 2010, the Dutch Urological Association started to centralize muscle-invasive BC care. To meet quality criteria, hospitals had to perform at least 10 RCs per year. In 2015, this number increased to 20. Additionally, we analyzed whether lymph node count (LNC) was associated with the incidence of pathological node-positive disease (pN+).

2. Patients and methods

2.1. Patients

We included all patients from the Netherlands Cancer Registry (NCR) who underwent RC as primary treatment for cT1–4a, N0 or Nx, M0 urothelial carcinoma (UC) between 2006 and 2012. Patients who underwent salvage procedures or partial cystectomy were excluded. Patients who underwent RC for progression of non–muscle-invasive UC (pT1) were not accounted for because the National Register of Citizens registers only primary treatment.

2.2. Netherlands Cancer Registry

The nationwide population-based NCR includes all newly diagnosed malignancies. Notification is obtained from the national network and registry of histopathology and cytopathology in the Netherlands (PALGA) and the National Registry of Hospital Discharge Diagnosis [10]. Independent and trained registration assistants from the NCR collect data on patient, tumor, and treatment characteristics from patient files. Topography and morphology are coded according to the International Classification of Diseases for Oncology [11], and tumor stage is coded according to the tumor, node, and metastasis (TNM) classification system [12]. Vital status of all patients is retrieved by linkage to the nationwide municipal population register. Hospitals were categorized into nonteaching, teaching, and academic. In the Netherlands, academic hospitals are government funded and linked to a university that supports in scientific research. Teaching and non-teaching hospitals are not government funded and not part of a university. Residents are trained in both academic and teaching hospitals. Hospital volume was categorized as low, intermediate, or high if <10, 10–19, or ≥ 20 cystectomies were performed annually.

2.3. Statistical analyses

Patient, hospital, and tumor characteristics were compared by chi-square tests if variables were categorical and by Kruskal-Wallis tests if variables were continuous. Linear-by-linear association compared temporal trends in the use of PLND during RC, median LNC, and pN+ disease. Factors associated with having PLND during RC were determined by multivariable logistic regression. The following variables were included: age, sex, clinical stage of disease, year of cystectomy, neoadjuvant chemotherapy, type of hospital, and hospital volume. Furthermore, for patients who did undergo PLND during RC, multivariable logistic regression analysis was performed to identify patients' and hospital factors associated with an LNC of <10 vs. ≥ 10. In multiple reports, an LNC ≥ 10 was associated with superior survival rates and used as a quality-of-care parameter [4–9]. Additionally, a multivariable logistic regression analysis was performed to determine the association between pN+ and LNC adjusted for year of cystectomy, sex, age, neoadjuvant chemotherapy administration, pT-stage, hospital type, and hospital volume. A 5-year OS rate was compared for academic, teaching, and nonteaching hospitals in a univariable and multivariable fashion. The Kaplan-Meier method was used to generate OS rates, and equality of distributions were compared by Log-rank tests. A multivariable Cox regression model was performed to assess the prognostic value of PLND and type of hospital on OS. Statistical analyses were performed with SPSS statistical software (version 19.0; SPSS Inc., Chicago, III). P values were considered statistically significant at <0.05.

3. Results

In total, 3,524 patients who underwent RC as primary treatment for cT1–4a, N0 or Nx, M0 UC between 2006 and 2012 were included (cNx, $N = 503$, 14%). Patient characteristics per type of hospital are displayed in Table 1. Clinical stages of disease were evenly distributed over the study period. In total, 3,191 (91%) patients underwent RC plus PLND. During the study period, the PLND application rate increased from 84% in 2006 to 96% in 2012 ($P < 0.001$) (Table 2). Table 2 also shows the number of patients treated in high-volume hospitals during the study period. After centralization in 2010, this number significantly increased in 2011 and 2012. PLND was omitted in 5% of patients in academic hospitals vs. 8% in teaching hospitals and 12% in nonteaching hospitals ($P < 0.001$). In 2012, these rates were 5% vs. 3% and 5%, respectively ($P = 0.304$). Multivariable logistic regression analysis identified that the chance of having PLND during RC was highest in males and younger patients, patients operated on in recent years, and those operated on in academic and teaching hospitals. In