

Original article

Effect on postoperative survival of the status of distal ureteral margin: The necessity to achieve negative margins at the time of radical cystectomy

Marco Moschini, M.D.^{a,b,*}, Andrea Gallina, M.D.^a, Massimo Freschi, M.D.^c,
Stefano Luzzago, M.D.^a, Nicola Fossati, M.D.^a, Giorgio Gandaglia, M.D.^a,
Paolo Dell'oglio, M.D.^a, Rocco Damiano, M.D.^b, Vincenzo Serretta, M.D.^d,
Andrea Salonia, M.D.^a, Francesco Montorsi, M.D.^a, Alberto Briganti, M.D.^a,
Renzo Colombo, M.D.^a

^a Department of Urology, Urological Research Institute, Vita-Salute, University, San Raffaele Scientific Institute, Milano, Italy

^b Doctorate Research Program, Magna Graecia University of Catanzaro, Catanzaro, Italy

^c Department of Pathology, IRCCS Ospedale San Raffaele, Milan, Italy

^d Dipartimento di Discipline Chirurgiche ed Oncologiche, Università degli Studi di Palermo, Palermo, Italy

Received 24 June 2015; received in revised form 21 August 2015; accepted 1 September 2015

Abstract

Background: Despite several studies, the adequate management of positive distal ureter margins at the time of radical cystectomy (RC) remains controversial. Particularly, it is not clear whether the achievement of negative distal ureter margins at the intraoperative frozen sections (IFS) affects postoperative cancer-specific mortality (CSM).

Methods: In all, 1,447 consecutive patients treated with RC at a single center between January 1987 and August 2014 were considered. Multivariable (MVA) logistic regression analyses were used to determine predictors of positive IFS. MVA Cox regression analyses were used to test the effect on CSM of intraoperative conversion to negative margins.

Results: At IFS, 368 patients (25%) experienced at least 1 positive margin. Of these, a negative conversion of the margin at IFS occurred in 178 (48%) whereas 190 (52%) had a positive final ureteral margin. The mean follow-up was 95 months (median = 102). At MVA, history of carcinoma in situ (odds ratio = 6.40, $P < 0.001$) was predictors of positive margin at IFS. At MVA, ureteral margins that were not converted to negative (hazard ratio = 1.92, $P = 0.01$) were associated with CSM but only in patients with negative soft tissue margin and without node metastases.

Conclusions: Achieving negative IFS margins may be associated with survival benefit in patients without residual bladder cancer after RC. Patients who recorded a history of carcinoma in situ before RC are at higher risk to incur positive ureteral margin at IFS and should be investigated during RC. © 2016 Elsevier Inc. All rights reserved.

Keywords: Bladder cancer; Frozen section; Ureteral margin; Radical cystectomy; Margin

1. Introduction

Bladder cancer (BCa) represents the fifth most common malignancy in the western world with an incidence of 74,690 in 2014 and a mortality rate of 15,580 per year in the United States alone [1]. In the context of nonmetastatic BCa the current European Association of Urology guidelines recommend radical cystectomy (RC) with pelvic lymph node dissection [2].

However, the life expectancy rate even after RC is only 58% at 5 years [3]. Specifically, patients with BCa are at risk of developing concomitant upper tract disease [4] or experiencing upper urinary tract recurrences (UTR) [5–7] during the follow-up period. Both of these conditions severely affect survival expectancy [5,6,8], and have limited therapeutic options [9]. Considering that, although patients with a positive ureteral intraoperative frozen section (IFS) have been found to be at increased risk of developing UTR during follow-up [9–13], the optimal intraoperative management of patients with intraoperative positive ureteral margins is still under debate.

* Corresponding author. Tel./fax: +39-022-643-5664.

E-mail address: marco.moschini87@gmail.com (M.-A. Moschini).

Indeed, although several authors have proposed IFS and subsequent resection to obtain uninvolved ureteral margins [10–12,15,16], only 1 was able to demonstrate an improvement of UTR-free rates [14] and none were able to determine differences in terms of cancer-specific mortality (CSM) or overall mortality (OM). Moreover, several reports focused on the poor accuracy of this procedure [15,16], the difficulty in obtaining a final negative margin in patients who were found with positive margins [11,15], and the high related cost [15]. In this perspective, studies looking to determine the best candidate for this procedure have reported that patients with carcinoma in situ (CIS) [15,16], during RC, are at major risk of experiencing positive ureteral margins at IFS. In this light, using a single-institution tertiary referral cohort, we determined incidence of positive IFS at the time of RC, as well as factors associated with positive ureteral margin and prognostic effect of the achievement of negative ureteral margin.

2. Materials and methods

Data from 1,447 patients with BCa treated with RC for nonmetastatic BCa between 1987 and 2014 at a tertiary referral center were included in the study. Patients were staged preoperatively with pelvic/abdominal computerized tomography, bone scan, and chest x-ray tests. In all, 7 surgeons performed RC using a standardized technique with ureteral resection approximately 1 cm proximal to the ureterovesical junction. Distal ureteral segments were analyzed with IFS and additional ureteral tissue was resected as needed until IFS revealed no further tumor or the surgeon deemed that inadequate length remained for additional resection. The ureteral margin was evaluated with IFS by a specialized uropathologist and was classified as positive or negative. Margins with high-grade atypia were classified as positive. Postoperatively, ureter margins were analyzed with permanent hematoxylin and eosin section. Negative margin status was achieved when both ureteral margins were negative at the final ureteral section at IFS. Postoperative follow-up was not standardized owing to the retrospective nature of the study. However, patients were generally evaluated postoperatively every 3 to 4 months for the first year, semiannually for the second year, and annually thereafter. Examinations included radiological imaging with computerized tomographic scan or magnetic resonance imaging in all patients. In addition to a physical examination with laboratory testing, intravenous pyelography, cystoscopy, urine cytology, urethral washings, and bone scans were carried out if indicated. UTR was defined as any documented radiographic, endoscopic, or pathologically demonstrated recurrence in the kidneys or ureters. The institutional review board approved the study (IRB: Vescica/2012).

3. Variable definition

All patients included in this study had complete clinical and pathology data that consisted of information regarding age at

surgery, gender (male vs. female), body mass index, preoperative hemoglobin levels, history of CIS before RC, clinical T stage (cT1–T2 vs. cT3 vs. cT4), clinical N stage (cN0 vs. cN+), number of nodes removed, number of positive nodes, blood loss during surgery, lymph vascular invasion, soft tissue surgical margin (STSM), pathological stage (pT0–T2 vs. pT3 vs. pT4), lymph node invasion (LNI), neoadjuvant chemotherapy administration, and adjuvant chemotherapy administration. IFS variables included the evaluation of the first section (positive vs. negative), number of sections analyzed, and the evaluation of the last section (positive vs. negative). These parameters were available for both left and right ureters.

4. Statistical analyses

Descriptive statistics of categorical variables focused on frequencies and proportions. Means, medians, and interquartile ranges were reported for continuously coded variables. Chi-square and Mann-Whitney tests were used to compare the statistical significance of differences in proportions and medians, respectively. Our statistical analyses consisted of 4 steps. First, multivariate logistic regression was performed to assess the relationship between all potential confounders and the possibility of achieving a positive ureteral margin at IFS and at permanent section analyses (PSA). Second, using multivariate Cox regression analyses predicting CSM we assessed the value of the conversion to a negative final ureteral margin at IFS in overall population and subsequently in considering only patients with negative STSM and absence of any nodal metastases. Third, we used Kaplan-Meier curves to estimate CSM-free, OM-free, and UTR-free rates after stratifying patients according to the status of the final ureteral margin at IFS (primary positive and negative status achieved vs. primary negative vs. primary positive and negative status not achieved). Finally, sensitivity and specificity of the first ureteral IFS margin were analyzed considering final pathological evaluation as a reference. Sensitivity was defined as the number of true-positive IFS results divided by the overall number of positive ureter margins at final pathology evaluation. Specificity was defined as the number of true-negative IFS results divided by the overall number of true-negative ureter margins at the final pathology evaluation. The area under the curve (AUC) of the receiver operating characteristics curve quantified the discriminative ability of ureteral frozen section in the prediction of positive ureteral margins. Statistical analyses were performed using the R statistical package (R Foundation for Statistical Computing, Vienna, Austria) and SPSS v. 20.0 (IBM Corp., Armonk, NY), considering a statistical significance at $P < 0.05$.

5. Results

5.1. Baseline patient characteristics

Clinical and pathological demographics of the cohort, stratified by ureteral margin status, are reported in [Table 1](#).

Download English Version:

<https://daneshyari.com/en/article/3999360>

Download Persian Version:

<https://daneshyari.com/article/3999360>

[Daneshyari.com](https://daneshyari.com)