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Brief Correspondence

Outcomes for Patients with Clinical Lymphadenopathy Treated with Radical Prostatectomy

Marco Moschini [a,b], *Alberto Briganti* [b], *Christopher R. Murphy* [a], *Marco Bianchi* [b], *Giorgio Gandaglia* [b], *Francesco Montorsi* [b], *J. Fernando Quevedo* [c], *Rachel Carlson* [d], *Eugene Kwon* [a], *R. Jeffrey Karnes* [a,*]

[a] *Department of Urology, Mayo Clinic, Rochester, MN, USA;* [b] *Unit of Urology/Division of Oncology; IRCCS Ospedale San Raffaele; URI Milan, Italy;* [c] *Division of Medical Oncology, Mayo Clinic, Rochester, MN, USA;* [d] *Division of Biomedical Statistics and Informatics, Mayo Clinic, Rochester, MN, USA*

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Abstract

Clinical lymphadenopathy (cN+) from prostate cancer (PCa) identified on imaging remains a contraindication to radical prostatectomy (RP) according to guidelines. We tested the hypothesis that there would be no difference in survival between patients with and without cN+ on preoperative imaging who underwent RP and pelvic lymph node dissection with detection of pelvic lymph node metastasis (LNM). A total of 302 patients with LNM were retrospectively reviewed (1988–2003) and stratified according to cN status on the basis of preoperative imaging. Univariable and multivariable Cox regression analyses were performed to evaluate cN+ as a predictor of survival. Of the 302 patients, 50 (17%) had cN+; the 252 (83%) patients with negative preoperative imaging comprised the cN0 group. During median follow-up of 17.4 yr, 161 deaths were recorded, 70 of which were from PCa. Among the entire LNM cohort, the number of positive lymph nodes (hazard ratio [HR] 1.10; $p = 0.02$) and pathologic Gleason score 8–10 versus $\leq$6 (HR 2.37; $p = 0.04$) were significant predictors of cancer-specific mortality (CSM). cN+ was not a significant predictor of CSM ($p = 0.6$). Selected patients with cN+ have similar clinical outcomes to those with normal preoperative imaging in the setting of LNM.

Patient summary: Clinical lymph node metastases are not a factor in determining survival after radical prostatectomy and pelvic lymph node dissection in patients with prostate cancer. Thus, the presence of clinical lymph node metastases should not be considered as an absolute contraindication to treatment with curative intent.

* Corresponding author. Department of Urology, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA. Tel. +1 507 2669968; Fax: +1 507 2844951.
E-mail address: karnes.r@mayo.edu (R.J. Karnes).

Lymph node metastasis (LNM) at the time of radical prostatectomy (RP) is a known factor for poor prognosis and increases the estimated risk of cancer-specific mortality (CSM) to 23–43% [1,2]. However, growing evidence suggest acceptable long-term survival for such patients who have undergone RP with pelvic lymph node dissection (PLND) [3,4] and further therapeutic strategies are potentially helpful in this patient population [5,6]. During preoperative evaluation, routine cross-sectional imaging is suggested for staging of higher-risk prostate cancer and is known for its poor accuracy in detecting small LNM [7]. The National Comprehensive Cancer Network guidelines [8], among others, do not mention RP/PLND as an option in clinical lymphadenopathy (cN+). Against this background, we provide an analysis of the

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impact of cN+ on survival in a pN+/LNM population for the first time in the literature.

Data for 302 LNM patients treated with RP and PLND between 1988 and 2003 at two tertiary referral centers were included in the study. PLND consisted of excision of fibro-fatty tissue from the obturator, internal, and external iliac chains, although some patients could have undergone a more extended procedure including the presacral and/or common iliac chains. All of the patients had been staged preoperatively using verifiable abdominopelvic computed tomography (CT) and/or magnetic resonance imaging. Preoperative radiology reports and/or images were reviewed to determine if patients had clinically suspicious lymphadenopathy (cN+). Patients were categorized as being either cN+ or clinically node-negative (cN0) on the basis of radiographic interpretation. Typically, a node was considered to be malignant or suspicious if the short axis was >8 mm for a round node or >10 mm for an oval node. Neoadjuvant and adjuvant (<90 d after RP) treatments were recorded. Postoperatively, patients received adjuvant hormonal therapy (aHT) and/or radiotherapy (aRT) according to physician and/or patient preferences and cancer characteristics. It was intended that aHT would be lifelong; however, given the retrospective nature of the cohort, it is uncertain whether patients discontinued treatment after a period of time. Both institutional review boards approved the study. Univariable and multivariable Cox regression analyses were performed to analyze cN+ as a predictor of CSM.

Verifiable preoperative imaging was available for 302 patients with LNM at RP/PLND. Among these 302 patients, 50 (17%) had clinically suspicious lymph nodes on imaging, comprising the cN+ group, while 252 (83%) patients had negative imaging and comprised the cN0 group. All patients had negative bone scans. No patient had a preoperative lymph node biopsy or an abandoned RP (Table 1). The mean and median follow-up was 16.4 and 17.4 yr (interquartile range 15.6–17.2 yr). There were 161 deaths, of which 70 were attributable to prostate cancer. CSM was 26% (13/50) for the cN+ and 23% (57/252) for the cN0 group. Kaplan-Meier survival analysis revealed no difference between the groups for cancer-specific survival ($p = 0.5$; Supplementary Fig. 1A) and overall survival ($p = 0.6$; Supplementary Fig. 1B), with 5-, 10-, 15-, and 20-yr cancer-specific survival of 92%, 82%, 75%, and 70% for the cN0 group, and 91%, 82%, 69%, and 58%, respectively, for the cN+ group. Table 2 lists risk factors for CSM. Among the entire cohort, the number of positive lymph nodes (hazard ratio [HR] 1.10; $p = 0.02$) and pathologic Gleason score 8–10 versus ≤6 (HR 2.37; $p = 0.04$) were significant multivariable predictors of CSM. cN+ was not a significant predictor of CSM ($p = 0.6$).

Although some differences were observed between the groups (Table 1), cN status had no impact on survival in

Table 1 – Descriptive statistics stratified according to clinical node status for the 302 patients with lymph node metastatic prostate cancer treated with radical prostatectomy between 1988 and 2003 at two tertiary care centers

	Overall ($n = 302$, 100%)	Clinical N+ ($n = 50$, 17%)	Clinical N– ($n = 252$, 83%)	p value
Age at surgery (yr)				
Mean	63.9	62.1	64.2	0.07
Median (IQR)	64.2 (59–69)	61.5 (57–68)	65.0 (59–70)	
Preoperative PSA				
Mean	32.2	27.8	33.0	0.4
Median (IQR)	18.9 (9.5–41.3)	14.2 (4.5–40.8)	19.1 (10.1–42.2)	
NCCN risk, *n* (%)				
Missing	13 (4.3)	3 (6.0)	10 (4.0)	
Low	13 (4.3)		13 (5.2)	0.07
Intermediate	78 (25.8)	11 (22.0)	67 (26.6)	
High	198 (65.6)	36 (72.0)	162 (64.3)	
Nodes removed (*n*)				
Mean	13.2	12.6	13.4	0.5
Median (IQR)	13 (8–17)	11 (7–17)	13 (8–17)	
Positive nodes (*n*)				
Mean	2.4	3.6	2.1	<0.001
Median (IQR)	1 (1–2)	2 (1–4)	1 (1–2)	
Pathologic stage, *n* (%)				
pT2–T3a	81 (26.8)	12 (24.0)	69 (27.4)	
pT3b	200 (66.2)	32 (64.0)	168 (66.7)	0.3
pT4	21 (7.0)	6 (12.0)	15 (6.0)	
Pathologic GS, *n* (%)				
2–6	52 (17.2)	5 (10.0)	47 (18.7)	
7	143 (47.4)	16 (32.0)	127 (50.3)	0.01
8–10	107 (35.4)	29 (58.0)	78 (31.0)	
Positive surgical margin, *n* (%)	165 (55)	22 (44)	143 (57)	0.1
Neoadjuvant hormone therapy	24 (8)	14 (28)	10 (4)	<0.001
Adjuvant hormone therapy	228 (75)	35 (70)	193 (77)	0.4
Adjuvant radiotherapy	91 (30)	10 (20)	81 (32)	0.09
Cancer-specific mortality, *n* (%)	70 (23)	13 (26)	57 (23)	0.5
Overall mortality, *n* (%)	161 (53)	29 (58)	132 (52)	0.5

IQR = interquartile range; PSA = prostate-specific antigen; NCCN = National Comprehensive Cancer Network; GS = Gleason score.

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