Format: Abstract

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Ulceration in bladder cancer associates with extravesical disease, independent of cell cycle, or hypoxia pathways status: Integrating gross morphology and expression profiles in cystectomies.

Schultz L[1], Spagnul SJT[1], Damm GR[1], da Cunha IW[2], Bezerra SM[3], da Costa WH[4], Guimaraes GC[5], Zequi SD[5], Soares FA[2].

Author information

Abstract

OBJECTIVE: Ulceration is common in bladder tumors, but its prognostic role, although intuitive, is not established. We aim to explore the presence of gross ulceration and its relationship with other morphological and biological features classically associated with extravesical disease, in patients submitted to radical cystectomy.

METHODS: Tumor size and morphology were noted on 101 cystectomy patients (2000-2010). Papillary, exophytic, and vegetant tumors were grouped as "papillary" and solid/nodular, ulcerated and infiltrative as "nonpapillary." Ulceration was noted grossly in every case as a binary parameter, regardless of morphology. Immunohistochemistry was performed for hypoxia (hypoxia-inducible factor-1α and vascular endothelial growth factor), and cell cycle proteins (pRb, p53, and cyclin D1).

RESULTS: Mean age was 66.7 year, male:female ratio was 2:1, 20 patients received bacillus Calmette-Guerin and 10 neoadjuvant chemotherapy. Upstaging rate was 56.4%. Ulcerated lesions presented mostly as nonpapillary and nonorgan confined (nOC), whereas nonulcerated tumors were often papillary and organ confined (OC). Tumor size was smaller in nonpapillary tumors (P = 0.002), but did not associate with altered hypoxia or cell cycle expressions. pRb and cyclin D1 loss and p53 overexpression were more frequent in ulcerated and non-OC tumors as did the phenotype vascular endothelial growth factor-negative/hypoxia-inducible factor-1α-low (P<0.001). On a multivariate model, ulceration was an independent predictor of non-OC and extravesical disease.

CONCLUSION: Patients with ulcerated tumors were often staged with extravesical disease, independent of other morphologic and biological features known to affect prognosis. Prospective studies are needed to confirm the predictive value of tumor ulceration at cystoscopy, which could

improve patient stratification for neoadjuvant chemotherapy.

KEYWORDS: Bladder cancer; Cell cycle; Hypoxia; Morphology; Ulceration; pappilary

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