



Sentinel Node Biopsy for Anal Carcinoma

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Abstract

Background: Anal squamous cell carcinoma is a rare neoplasm. Inguinal lymph nodes metastases are an independent prognostic factor in predicting tumor recurrence and overall survival in patients affected by anal canal cancer. Nowadays there is not an adequate tool to diagnose inguinal lymph node metastases. In recent years the role of sentinel node biopsy in this topic was investigated.

Methods: A review of the Literature was performed to this purpose.

Results: All reports agree that SLNB biopsy is a feasible and effective method for defining the inguinal node status in these patients. It may help to detect occult inguinal metastatic disease, in order to select patients to submit to inguinal radiotherapy. This approach permits a selection of patients who could take advantage of inguinal sparing irradiation, thus avoiding toxic side effects, which were reported to be as high as 33%, with 15% of patients requiring major medical or surgical intervention.

Conclusions: Nowadays sentinel lymph node biopsy seems to be the best toll for staging inguinal status in patients affected by anal cancer. It permits a new individualized and tailored approach to anal cancer based on the results of these exams in order to select patients to be submitted to inguinal radiotherapy, avoiding morbidity associated to this treatment in patients negative for inguinal MTS.

Keywords: Anal cancer; Squamous cancer; Staging; PET-CT scan; Sentinel lymph node; Inguinal lymph node; FNA

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Introduction

Anal cancer remains a rare disease even if its incidence is increasing, mainly in association with Human Papilloma Viruses (HPV) infection. Dailing and Coll assessed that the incidence of anal cancer increased among both men (160%) and women (78%) from 1973 to 2000 in the USA [1]. An estimated 8200 new cases (2950 men and 5250 women) were supposed to occur in the United States in 2017, accounting for approximately 2.6% of digestive system cancers. Moreover it has been calculated that 1100 deaths due to anal cancer will occur in U.S. alone in 2017 [2].

Nowadays the overall 5-year survival rate reaches 70% in the absence of inguinal metastases [3], that are an independent prognostic factor for local failure and overall mortality according to a multivariate analysis in a phase 3 EORTC trial [4]. The average incidence rate of synchronous inguinal MTS is 13% (range 3%-23%) but if metachronous inguinal MTS are taken into account the overall rate of inguinal involvement reaches 24% (16%-36%) [3]. Inguinal involvement is usually unilateral, with <5% bilateral either synchronous or metachronous extension [3]. Gerard and Coll reported a severe prognosis for patients with clinically large inguinal lymph nodes (37% 5 year overall survival rate for patients with lymph nodes >2 cm in greatest dimension). Otherwise the presence of concomitant perirectal lymph nodes did not significantly affect the prognosis [3].

Considering these aspects inguinal lymph nodes' detection is mandatory for an adequate treatment and for patients' prognosis.

Sentinel Node Biopsy in Anal Cancer

The classical recommended clinical workup in the staging of inguinal lymph nodes includes inguinal lymph nodes' palpation, abdominal Computed Tomography (CT scan) and inguinal endosonography that could be associated with Fine Needle Aspiration (FNA) in suspicious cases.

Furthermore Wade and co-workers at the Roswell Park Cancer Institute, using a “clearing technique”, found that 44% of perianal, perirectal and pericolonic lymph node metastases were <5 mm in diameter [4], which couldn't be detected by usual diagnostic tools.

Thus in recent years Sentinel Lymph Node Biopsy (SLNB) and fluorodeoxyglucose-Positron Emission Tomography (PET-CT scan) have been introduced in clinical practice to better stage inguinal nodes [5].

SLNB was firstly proposed in 2000 by John Spratt, who suggested that prophylactic groin dissection is not required but it could be curative in many cases for enlarged nodes or in the presence of a positive sentinel node biopsy [6]. Otherwise he didn't reported patients studied with this technique.

Since 2001 SLNB was applied in patients affected by anal cancer providing inguinal staging and permitting a better planning of radiotherapy planes [7]. Since then several studies [8-20] and 2 reviews [21-22] were published in international Literature. All reports agree that SLNB biopsy is a feasible and effective method for defining the inguinal node status in these patients. Moreover it may help to detect occult inguinal metastatic disease, in order to select patients to submit to inguinal radiotherapy.

Based on these results De Nardi and Coll [23] proposed a selective approach: node-positive patients could be selected for inguinal node irradiation while node-negative patients could take advantage of inguinal sparing irradiation, thus avoiding toxic side effects, such small bowel injury, soft tissue injury, femur head's osteonecrosis, neurogenic bladder and others, which were reported to be as high as 33%, with 15% of patients requiring major medical or surgical intervention [24].

Otherwise Gretschel [15] suggested that SLNB is mainly indicated in T1 and T2 tumours and it is not recommendable for larger (T3-T4) tumours, considering the high incidence of inguinal metastases (MTS), and in patients with prior surgical manipulation in the anal or inguinal region.

Mistrangelo et al. [25] stratified patients for T stage observing inguinal MTS in 14.3% of T1 and T2 patients, 35.3% of T3 and 25% of T4 ones. Considering overall data published in Literature on SLNB, inguinal MTS are found in 26.2% of all patients (45/172): 22.2% of T1; 17.3% of T2; 38.5% of T3 and 28.6% of T4 patients. Despite the low number of patients studied with this technique, these data suggest that inguinal SLNB is indicated for all patients affected by anal cancer.

Later de Jong and Coll reduced the value of staging squamous cell carcinoma of the anal margin and canal using the sentinel node procedure in a prospective study with long term follow up [26] considering the possible occurrence of False Negative (FN) cases.

On the contrary Mistrangelo et al. [25]. Evidenced, after a review of the Literature, that only 6/163 (3.7%) lymph nodes negative at immunochemistry after SLNB developed inguinal MTS after a medium follow up of 27.3 months (range 5-50 months). Considering these data a FN rate of 3.7% should be considered as acceptable for patients affected by anal cancer.

Literature's data reporting the results of inguinal SLNB in patients affected by anal cancer were recently resumed in two papers reporting a review of the technique [27-28]. Noorani and Coll [27] identified 17 studies, containing 270 patients studied with SLNB. The detection

rate varied from 47% to 100%, and the presence of nodal metastases from 0 to 44%. Complications varied from 0% to 59% and FN ranged from 0% to 18.5% of cases. Tehranian and Coll [28] reviewed 16 studies including 323 patients in their meta-analysis. Pooled inguinal detection rate was 86.2% (73.4%-93.4%). For studies using both blue dye and radiotracer it was 90.1% and for studies using radiotracer alone was 72.4%. Pooled sensitivity was 90%.

Conclusions

Up to date SLNB technique in the detection of inguinal metastases in patients affected by anal cancer should be considered as a standard of care. FNA has been proposed in the work up of inguinal node staging in all anal cancer guidelines [29] even if nowadays no study has been published on this topic. All data were modulated by experience in patients affected by penile and vulvar cancer.

Moreover in a recent review Qiu and Chen [30] concluded that a consensus has been reached that SLNB is much more sensitive than PET-CT scan for detecting small lymph node metastasis, therefore FDG PET and PET-CT scan cannot replace SLNB for the evaluation of early stage regional lymphatic tumor dissemination in patients affected by various malignancies.

As suggested by De Nardi and Coll [23] the best staging of these patients with SLNB permits a new individualized and tailored approach to anal cancer based on the results of these exams in order to select patients to be submitted to inguinal radiotherapy, avoiding morbidity associated to this treatment in patients negative for inguinal MTS.

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