Available online at www.sciencedirect.com

SCIENCE DIRECT®

Gynecologic Oncology 97 (2005) 588–595

Gynecologic Oncology

www.elsevier.com/locate/ygyno

Sentinel node detection in cervical cancer with ^{99m}Tc-phytate

Lucas B. Silva[a], Agnaldo L. Silva-Filho[a,*], Paulo Traiman[d], Sérgio A. Triginelli[a], Carla Flávia de Lima[e], Cristiano Ferrari Siqueira[e], Adelanir Barroso[f], Telma Maria F.F. Rossi[g], Moises Salgado Pedrosa[c], Dairton Miranda[c], José Renan Cunha Melo[b]

[a]*Department of Obstetrics and Gynecology, Federal University of Minas Gerais, Avenida Pasteur, 89/1310, Santa Efigênia 30150 290, Belo Horizonte, MG, Brazil*

[b]*Department of Surgery, Federal University of Minas Gerais, Belo Horizonte, MG, Brazil*

[c]*Department of Pathology, Federal University of Minas Gerais, Belo Horizonte, MG, Brazil*

[d]*Department of Obstetrics and Gynecology, Paulista State University, Botucatu, SP, Brazil*

[e]*Ecograf Nuclear Medicine SA, Belo Horizonte, MG, Brazil*

[f]*Nuclear MedCenter SA, Belo Horizonte, MG, Brazil*

[g]*Gynecologic Oncology Unit, Mario Penna Hospital, Belo Horizonte, MG, Brazil*

Received 24 November 2004
Available online 17 March 2005

Abstract

Objectives. The aim of this study was to investigate the feasibility of sentinel lymph node (SLN) identification using radioisotopic lymphatic mapping with technetium-99 m-labeled phytate in patients undergoing radical hysterectomy with pelvic lymphadenectomy for treatment of early cervical cancer.

Methods. Between July 2001 and February 2003, 56 patients with cervical cancer FIGO stage I (n = 53) or stage II (n = 3) underwent sentinel lymph node detection with preoperative lymphoscintigraphy (^{99m}Tc-labeled phytate injected into the uterine cervix, at 3, 6, 9, and 12 o'clock, at a dose of 55–74 MBq in a volume of 0.8 ml) and intraoperative lymphatic mapping with a handheld gamma probe. Radical hysterectomy was aborted in three cases because parametrial invasion was found intraoperatively and we performed only sentinel node resection. The remaining 53 patients underwent radical hysterectomy with complete pelvic lymphadenectomy. Sentinel nodes were detected using a handheld gamma-probe and removed for pathological assessment during the abdominal radical hysterectomy and pelvic lymphadenectomy.

Results. One or more sentinel nodes were detected in 52 out of 56 eligible patients (92.8%). A total of 120 SLNs were detected by lymphoscintigraphy (mean 2.27 nodes per patient) and intraoperatively by gamma probe. Forty-four percent of SLNs were found in the external iliac area, 39% in the obturator region, 8.3% in interiliac region, and 6.7% in the common iliac area. Unilateral sentinel nodes were found in thirty-one patients (59%). The remaining 21 patients (41%) had bilateral sentinel nodes. Microscopic nodal metastases were confirmed in 17 (32%) cases. In 10 of these patients, only SLNs had metastases. The 98 sentinel nodes that were negative on hematoxylin and eosin were submitted to cytokeratin immunohistochemical analysis. Five (5.1%) micrometastases were identified with this technique. The sensitivity of the sentinel node was 82.3% (CI 95% = 56.6–96.2) and the negative predictive value was 92.1% (CI 95% = 78.6–98.3). The accuracy of sentinel node in predicting the lymph node status was 94.2%.

Conclusion. Preoperative lymphoscintigraphy and intraoperative lymphatic mapping with ^{99m}Tc-labeled phytate are effective in identifying sentinel nodes in patients undergoing radical hysterectomy and to select women in whom lymph node dissection can be avoided.

Keywords: Cervical cancer; Sentinel lymph node; Gamma probe; ^{99m}Tc-fitato; Lymphoscintigraphy; Lymphatic mapping

* Corresponding author. Fax: +55 31 3296 5490.
E-mail address: agsilvaf@terra.com.br (A.L. Silva-Filho).

0090-8258/$ - see front matter © 2005 Elsevier Inc. All rights reserved.
doi:10.1016/j.ygyno.2005.02.014

Introduction

It has been proposed that many carcinomas spread lymphatically in an anatomically predictable manner. The concept of sentinel lymph node (SLN) was introduced in 1997 by Cabanas meaning the first lymph node receiving lymphatic drainage from the tumor [1]. It represents the initial site of tumor implantation and its pathologic evaluation should then predict the pathologic status of the remaining lymphatic basin. This hypothesis has proven to be true in melanoma and breast cancer, and is currently being studied in the treatment of others tumors, such as vulvar and cervical cancer [2–6]. The SLN can be identified either using peritumoral injection of a blue dye, which will visually color the first draining node, or by peritumoral injection of a radioactive tracer that spreads to the sentinel node and can be detected with a gamma probe. The possibility of reducing morbidity associated with surgical dissection while maintaining accurate tumor staging is one of the greatest advantages of the SLN approach in surgical oncology.

The single most important prognostic factor for patients with early cervical cancer is the presence of lymph node metastases, associated with recurrence and survival. In a study of 545 patients with negative pelvic lymph nodes, Delgado et al. found a 3-year disease-free survival of 85.6% compared with 74.4% in patients with positive nodes [7]. Five-year survival rates also significantly decreased with the number of involved pelvic nodes (62% for one node, 36% for two nodes, 20% for three or four nodes, and no survivors for five nodes or greater) [8]. The incidence of pelvic and para-aortic lymph node metastases ranges from 8.5% to 21.4% and from 5% to 10% for early stage disease, respectively [9].

Radical hysterectomy with pelvic and para-aortic lymphadenectomy remains the gold standard to assess the nodal status and for treatment of patients with early cervical cancer. If pelvic lymph nodes are positive for tumor metastasis, there is an indication for adjuvant chemo-irradiation. Apart from the morbidity related to radical hysterectomy alone, the combination of surgery and radiotherapy will be associated with more treatment-related complications including ureteral injury, radiation cystitis or proctitis, and bowel and urinary fistula [10]. If the lymph nodes do not show metastatic involvement, as shown by SLN procedure, more conservative surgical strategies can be done [11].

This paper shows a prospective double-center study to assess whether it was possible to detect sentinel nodes after preoperative intracervical injection of technetium-labeled phytate (^{99m}Tc-labelled phytate) in patients undergoing radical hysterectomy with pelvic lymphadenectomy for treatment of early cervical cancer. Phytate is 200–1000 nm in diameter, a larger particle than either colloidal albumin or sulfur colloid. Generally, larger particles have a tendency to stay in lymph nodes longer and tend to flow into secondary lymph nodes more slowly. This radiopharmaceutical has already proven to be useful in sentinel node mapping in melanoma, breast cancer, and vulvar cancer with results comparable to those previously described in the literature [12].

Patients and methods

Between July 2001 and February 2003, 56 patients (mean age 48 years, range 24–73) with histologically proven cervical cancer FIGO stage IA2 (n = 2), IB1 (n = 38), IB2 (n = 13), and IIA (n = 3) were referred to our department for radical hysterectomy. The study was approved by the institutional ethics committee. Patients with prior chemotherapy, pelvic radiotherapy, or prior retroperitoneal surgery were excluded. The mean size of the primary lesion was 3.3 cm (range 0.7–6 cm) and the most frequent histological type was squamous cell carcinoma (87.5%) followed by adenocarcinoma (10.5%). Clinical and pathologic characteristics of the study population are depicted in Table 1.

Preoperative lymphoscintigraphy

After assigned informed consent, all the patients were enrolled in an institutional lymphoscintigraphy trial. In the evening before surgery, the cervix was superficially infiltrated in each quadrant around the tumor at 3, 9, 6, and 12 o'clock positions with a dose of 0.8 ml of ^{99m}Tc-labelled phytate (IPEN, São Paulo-SP, Brazil) with an activity of 55–74 MBq with a 25-gauge needle (Fig. 1).

Table 1
Tumor and treatment characteristics

Characteristic	No. of patients	%
Histology		
Squamous	49	87.5
Adenocarcinoma	6	10.5
Undifferentiated	1	2
Stage		
IA2	2	3.6
IB1	38	67.9
IB2	13	23.2
IIA	3	5.3
Grade of differentiation		
G1	2	3.6
G2	40	71.4
G3	14	25
LVSI		
Present	12	21.4
Absent	44	79.6
Previous conization		
Yes	2	3.6
No	54	96.4
Surgical approach		
RAH + LAD	53	94.6
LAD	3	5.4

Note. LVSI, lymph vascular space invasion; RAH, radical abdominal hysterectomy; LAD, lymphadenectomy.