

Sentinel LYMPHO Node Mapping in Uterine Cancer on SPECT- CT an Experiment of the Nuclear Medicine Department Of Saint Antoine Hospital of Paris

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Abstract: The lymph node status is an important prognostic factor and a major criterion of decision uterine cancer's treatment. Its evaluation by the sentinel lymph node technique has greatly improved support but requires a good understanding of the mechanisms of cancer spread. The objective of this study was to determine the different location sites of sentinel node in cancers of the cervix in the early stages of the classification of FIGO. The exploration was performed in 42 patients with a mean age of 38 years (standard deviation of 9 years), whose preoperative MRI showed no suspect lymph node. The most representative class was that between [30-40] years. The Ib1 stage of FIGO classification was the most frequent with 64, 28%, Followed by IA1 stage with 21.1%. A combined analysis of planar and sectional image helped to recover 152 sentinel nodes. Pelvic location (internal iliac, external iliac, common iliac and sacred pre) was found in 87,5% against 12,5% extra pelvic location (aortic). Statistically significant associations were noted between different locations site: external iliac and common iliac (P = 0.002), external iliac and Aortic (P = 0.009), common iliac and Aortic (P = 0.0001). Among the sentinel nodes found on imaging, 81% were confirmed positive on histology. Sentinel lymph nodes of extra pelvic location were found histologically positive in 36.84% of cases against 24.8% in sentinel nodes pelvic location. The way of hypogastric dissemination was the most important (44%). Our results show that systematic lymphadenectomy realized in early stages are not always timely, and targeted analysis of nodes requires a use of sentinel lymph node technique with careful exploration of all nodal areas as well as a precise description of the topography of the ganglion. These results explain the deficiencies of treatment in systematic lymphadenectomy and show the value of a treatment adapted to a good mapping of the sentinel node.

Keywords: cartography - cervical cancer- sentinel lymph node –SPECT/CT

1. Introduction

Knowledge of lymph node status in the treatment of uterine cancers is an important prognostic factor. It remains a diagnostic criterion in lymph node staging, enables to adapt the surgery and guide adjuvant treatments [17 , 3].

This non-surgical nodal assessment which is essential in the treatment of uterine cancers has long been made by lymphography, CT or MRI [1] . However, MRI and CT appeared to be the most efficient but have moderate sensitivities due to the fact that they do not enable the detection of lymph node metastases that are not associated with an increase in the size of lymph nodes. [2] Anatomical imaging criteria CT or MRI are based on the size and morphology of the lymph nodes. Now, more than half of involved nodes are less than 1cm and 29% of unharmed nodes were larger than 1 cm [9, 10].

It is recognized that an increased lymph node volume may simply be inflammatory and a small ganglion under 1cm may contain metastatic localization [2,10] . So despite the introduction of these imaging techniques, pelvic lymphadenectomy + / _ para-aortic have always been considered as the gold standard for establishing the nodal status but are not without complications. The dissections are sometimes interspersed with lymphocele and lymphedema of the lower limbs , nervous and persistent vascular disorders, etc ... but also a risk of recurrence when the reached node is located in a territory not concerned by this act . [1,17]

With the advent of the sentinel lymph node (SLN), lymph node assessment had better results.

This technique consists of locating within the anatomical drainage territory the first relay node which is most likely to be invaded by tumor cells. Logic suggests that this technique limits unnecessary lymphadenectomy, reduce operating time, prevents many of their complications and significantly reduces the morbidity associated with surgery. [6]

Although interesting, the sentinel node procedure requires good accuracy of nodal sites, and therefore a good understanding of the lymphatic drainage of the uterus.

The objective of this article is to determine the different sites of the sentinel lymph node localization in cervical cancer in the early stages of the FIGO classification.

2. Patients and methods:

2.1. Patients

This is a prospective study from August 2014 to December 2015 evaluating the different sites of localization of sentinel nodes in patients received in the nuclear medicine department of St. Antoine of Paris hospital for pre-surgical assessment cancer of the cervix.

- Inclusion criteria : cervical cancer at early stages (< IA1 at Stage de FIGO). No suspect lymph node on preoperative MRI.
- Exclusion criteria : No sentinel node identified.

2.2 . Methods

2.2.1 . injection protocol

Four injections of 0.1 to 0.2 mL of Nanocis * are carried to the four corners of the cervix (at 3, 6 , 9 and 12 hours) with a needle of 21 Gauge at a depth of a few millimeters by the gynecologist surgeon in the nuclear medicine department. (Fig.1).

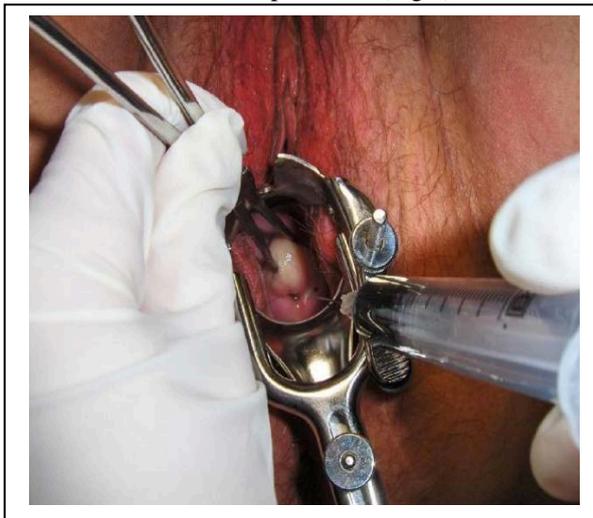


Figure 1: Injection method of the radiotracer

2.2.2. Images acquisitions

The acquisition of scintigraphic images was performed one to two hours after injection. The Scintigraphy was performed by a hybrid gamma camera, dual head, equipped with a high resolution collimator with parallel holes, low energy Symbia T2 (Siemens *). The acquisition spectrometric window focused on the photoelectric peak of 99mTc (140 keV) corresponding to the peak energy of the gamma radiation. The total examination time was 30 minutes (planar: ten minutes SPECT / CT: 20 minutes).

2.2.2.1. Planar acquisitions.

A planar static acquisition (matrix 256 * 256) centered on the abdominal and pelvic region was conducted during 600 seconds with the patient supine, the arms raised.

2.2.2.2. SPECT / CT acquisitions.

A second acquisition was performed immediately after in SPECT / CT, the patient maintaining the same position between the two acquisitions.

2.2.3. Interpretation of scintigraphic data

Visual analysis of planar images and SPECT / CT identified the number, location and laterality of lymph node bindings, corresponding to hyperactivity homes visually above the background noise.

2.2.4 Data analysis

Data were collected in the Excel table. A descriptive and statistical analysis was carried out with the XLSTAT 2016 version 1.8 software.

The value of p <0.05 was selected as the positivity threshold.

3. Results

3.1 Clinical aspects:

Patients meeting the inclusion criteria were the number of 42 and had an average age of 38 (27-72) with a standard deviation of 9 years. The most representative class was that between [30-40] years. The Ib1 stage of FIGO classification was the most frequent with 64, 28%, Followed by IA1 stage with 21.1%.

3.2 scintigraphic Aspects

In total 152 sentinel nodes were found by a combined analysis of the planar image and the sectional (eg Figure 2).

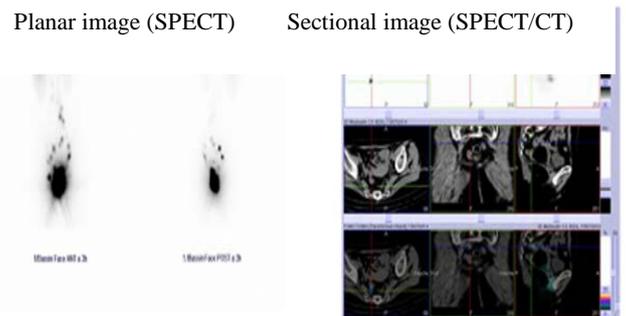


Figure 2: A combined analysis of planar and sectional image

3.2.1 Distribution of nodes according to their location site

Pelvic location (internal iliac, external iliac, common iliac and pre-sacral) was found in 87, 5% against 12, 5% extra pelvic location (aortic) as shown in Table I.

Table I: Distribution of nodes according to their location site

Topography	SIZE
external iliac	73
internal iliac	18
common iliac	35
Sacral	7
Aortic	19

3.2.2 Correlation between GS localization site

No correlation > 0.6 was observed between the various locations of the nodes as shown in Pearson correlation matrix.

3.2.3 statistical link between sites

Statistically significant links were noted between different locations site: external iliac and common iliac (P = 0.002), external iliac and Aortic (P = 0.009), common iliac and Aortic (P = 0.0001) Table II.

NB : REI= Right external Iliac. LEI= Left external Iliac. CI= Common iliac. II= internal iliac

3.3 histological aspects:

Among the sentinel nodes found on imaging, 81% were confirmed positive histology.

Sentinel lymph nodes of extra pelvic location (Aortic) were found histologically positive in 36.84 % of cases against 24.8 % in SLN pelvic location as shown in Tables III and IV.

Table III: Distribution of nodes according to the pelvic floor and histological aspect

Floor	Histological aspect	
	Positif	Negatif
Pelvic	32	97
Extra pelvic	7	12

Tableau IV: Distribution of nodes according to their topography and histological aspect

Topography	Histological aspect		Size
	Positif	Negatif	
external iliac	15	58	73
Internal iliac	4	14	18
Common iliac	11	24	35
Sacral	2	5	7
Aortic	7	12	19

3.4 Distribution of SLN in the way of dissemination

The way of dissemination hypogastric was the most frequent with 44% of cases (Figure 3)

Table II : statistical link between sites

Sites	REI	LEI	II	Sacral	CI	Aortic
REI	0	0,323	1,000	0,141	0,002	0,009
LEI	0,323	0	0,422	0,836	0,436	0,202
II	1,000	0,422	0	0,062	0,425	0,963
sacral	0,141	0,836	0,062	0	0,095	0,924
CI	0,002	0,436	0,425	0,095	0	0,0001
Aortic	0,009	0,202	0,963	0,924	0,0001	0

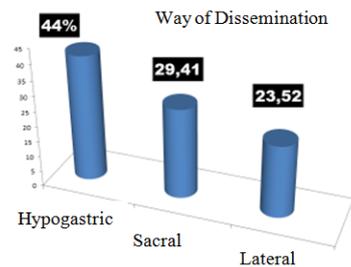


Figure 3: Distribution of nodes according to their way dissemination

4. Discussion: In this study we looked at the topography of sentinel nodes and their histological types in women followed for cancer of the uterus in the early stages of FIGO. The objective was to

determine the different site of location possible of the SLN.

The uterine cancers consisting of two major entities that are, endometrial cancer and cervical cancer, our study looked mainly to cervical cancer. The latter being considered as the cancer of the woman [16], which explains the age of our study population whose average was 38 years, comparable to that found in Corner's study that was 38 years (30- 72). [8] However, this average is much higher in the study of Mathevet and al. where it was between 45-50 years, [16] and in the senticol 1 study where it was 44.4 years (\pm 13.6) [4].

The description of the lymphatic drainage area is not uniform. French authors usually refer to the descriptions of Rouvière [22] while those Anglo-Saxon use classification Plentyl and Friedman [20, 21] which appoints the nodes based on the nearest anatomical structure. [12,19]

The topography determination was made through a combination of planar images and those in section for better location accuracy. Thus a total of 152 nodes, 87, 5% were pelvic location and 12.5% of extra pelvic location. Pelvic locations were distributed as follows: internal iliac (13.53%), external iliac (54.88%), common iliac (26.31%) and pré-sacral (5.26%). As for the extra pelvic locations, they were exclusively para-aortic. These results are consistent with those of certain authors. According studies of Bénot [7] Lecuru [14] and Wuntakal [24], the SLN in cervical cancer are found in 80-86% of cases in the external iliac territories, ilio-obturator or in inter iliac, otherwise, pelvic. In contrast, other studies have found higher pelvic proportions but still moving in the same direction as our results.

Indeed, the senticol 1 study which covers 430 nodes [13] found in cancerous cervical stages IA1 to IB1 of the classification of FIGO had found less than 1% of extra pelvic location with over 99% of pelvic location. In this senticol 1 study [4], although the majority of SLN are often located in external iliac with (60.5%), so-called "unusual site" or "atypical" localizations are also noted with (19.6%) in common iliac (10.8%) in para-aortic (pelvic extra) and 6% in the parameter.

The Ouldmer study [19], a meta-analysis of the localization of sentinel lymph nodes in early stages had regained 95% of pelvic location against 5% extra pelvic location. Although found proportions differ in terms of number, pelvic predominance is always found.

As for the Martinez study [15], 3% have been regained in localization in the parameter and 3% in the para-aortic position. These so-called unusual drainage, affect 5 to 20% of nodal sites according to the Kushner study [11] and 6.7% according to Bournaud study [6] against 35.35% in our study. Of these 35.15% were confirmed histologically

positive, thus explaining relapses observed in the usual systematic lymphadenectomy (not concerning these areas, therefore incomplete). Therefore, it becomes obvious that the dissection must be adapted to the level of lymph node involvement without more nor less. According Brénot, nodal metastases are found in only 0-17% of cancers of cervix stage I [7]. Other authors [41-43] argue that the probability of pelvic lymph nodes in early stages of cervical cancer is less than 30%. So we can easily say that more than 70 to 80% of these patients do not benefit from this systematic pelvic lymphadenectomy formerly considered the standard treatment.

Lymph node dissemination is partly related to the stage of the cancer, but also to the lymphatic drainage system. Indeed, it is recognized that in most cases of cervical cancer drains first to the pelvic lymph nodes and only then that the extra pelvic lymph node metastases (para-aortic) may occur [19, 5, 23].

The anatomical rule wants the dissemination be done by node floor from step to step. But in fact, the drain depends on the cancer location site. The lymphatic drainage of the cervix is variable but the classic pattern described by Lecuru [12] is: Cervical drains into the lymph nodes in the upper part of the chains located in inner and below of the external iliac vein (trips injected in 40% of cases). The relay(s) located in the birth of the internal iliac artery seem to predominate (relay injected in 60% of cases). The nodes arranged along the initial portion of this artery are also a major drainage pathway. Direct routes, connecting the neck to the para-aortic territories seem rarer in the physiological state, even if the parameters clamping. [16]. This drainage explains the statistically significant link between the locations : common iliac and external iliac ($P = 0.008$), external iliac and Aortic ($P = 0.009$), common iliac and Aortic ($P = 0.0002$). These results in turn explain the way of classical dissemination in perfect agreement with those found in our study. However, it is noted that the invasion of the para-aortic nodes in cervical cancer is exceptional in the lack of metastasis of pelvic lymph nodes. Rouvière [22] had found that a manifold of the internal iliac pedicle could ascend directly to the origin of the common iliac artery at L5. He also admitted as theoretically possible that an anastomosis between cervical lymphatics and those of the endometrial can directly lead metastases L4 level through the pedicle ovarian lumbo.

5. Conclusion: Our results show that systematic lymphadenectomy realized early stage are not always timely, and targeted analysis of nodes requires a use of sentinel lymph node technique with careful exploration of all the lymph node

territories and a precise description of the their topography.

This diversity found in the location of the sentinel node, especially in so-called “unusual territories” can explain the under treatment of incomplete dissection leading to recurrence. Hence the necessity of good lymph node mapping before any treatment. Therefore, it is also necessary that the nuclear physician and gynecologist surgeon confers the anatomical description of the nodes.

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