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Risk of nodal involvement and therapeutic strategy in endometrial and cervical cancers

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Key words: Uterine Cervical Neoplasms; Endometrial Neoplasms; Lymph Nodes; Lymph Node Excision; Antineoplastic Protocols

The treatment of endometrial and cervical cancer depends on the risk of nodal involvement. The mini-invasive surgery has changed the strategy.
Concerning endometrial cancer, surgery is the first treatment: 80% of apparent FIGO Stage I disease. The risk of nodal involvement is higher with more than 50% of myometrial involvement, High FIGO Grade, lymph vascular space involvement and non endometrioid histology. There is no indication of pelvic lymphadenectomy in IAG12 FIGO stages (randomized studies, PORTEC 1 and 2). There is an indication of para-aortic lymphadenectomy (+/- pelvic lymphadenectomy) in IBG23 FIGO stages or more (and in non endometrioid histology) or in case of lymph vascular space involvement. In these last cases, lymphadenectomy is for tailoring adjuvant treatment.
Concerning cervical cancer, the fertility of young women could be preserved but only in case of less than 2 cm disease without lymph vascular space involvement and pelvic involved lymph nodes. For less than 4 cm cervical cancer, pelvic lymphadenectomy by mini-invasive approach could select high-risk patients with pelvic involved lymph nodes. In these last cases, concomitant chemoradiation is indicated. For locally advanced cervical disease (>=4cm), para-aortic lymphadenectomy by laparoscopic extraperitoneal approach could define the superior limit of concomitant chemoradiation even in case of negative FDG-PET.
Actually, lymphadenectomy is usually one of the most important procedures for the treatment of endometrial and cervical cancers. Sentinel lymph nodes could be the procedure of the future.

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Sentinel lymph nodes in cervical cancer: standards and perspectives

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Key words: Uterine Cervical Neoplasms; Sentinel Lymph Node Biopsy; Lymph Nodes; Neoplasm Staging; Antineoplastic Protocols; Gynecologic Surgical Procedures

Lymph node status is one of the main prognostic factors in cervical cancer. Surgical staging performs better than imaging to predict its involvement, and is therefore essential in the management of cervical cancer. Although surgery and radiotherapy offer similar survival rates in early stages, radical hysterectomy with bilateral pelvic lymphadenectomy is more often performed in France. However, less than 20% of patients will present lymph node involvement (mostly a single micrometastasis) and nodal staging is associated with a significant morbidity, including lymphatic complications, with a risk of lymphedema up to 20%.
Sentinel Lymph Node Biopsy. The Sentinel Lymph Node (SLN) biopsy is a diagnostic method whose purpose is to assess the locoregional lymph node status of a solid tumor by performing a targeted sampling rather than a complete lymphadenectomy: the status of SLNs would be representative of regional and downstream nodes. This procedure, which is validated in breast cancer, has been developing for several years in early cervical cancer, to reduce perioperative morbidity of lymphadenectomy, but also to improve staging by the identification of aberrant drainage area and by nodal ultrastaging.
The SN procedure can be performed with an isotopic, a colored, or a combined (isotopic+colored) technique. Radioactive tracer is injected into the four cardinal points of the uterine cervix on the day before or on the day of surgery. A lymphoscintigraphy is performed on the day of surgery to detect hot nodes preoperatively. At the beginning of surgical procedure, patent blue is injected under anesthesia into the four cardinal points of the uterine cervix. Colored and/or hot channels and sentinel nodes are detected before and after the opening of pelvic sidewall, using an endoscopic probe and the colored detection. As the technique is still under assessment, a complete pelvic lymphadenectomy is then performed.
The SLN biopsy is a feasible technique, which can be performed easily by laparoscopy. The detection rate of SLNs is high (70%-100%) and the main factors improving the detection are the combined technique, small tumor size, the absence of prior radio or chemotherapy, the absence of prior cone biopsy and young age.
The SLN technique is associated with an excellent diagnostic value (92% with a combined technique) and the false negative rates reported in the literature are less than 10%. Nevertheless, unilateral detection, large tumor size and parametrial involvement are associated with a risk of false negatives.
The SLN procedure also aims at identifying unexpected lymphatic drainage territories, which are not systematically sampled and which might constitute a source of recurrence.
Finally, the analysis of few nodes permits nodal ultrastaging to detect micrometastases.
Sentinel lymph node biopsy in early cervical cancer aims to improve lymph node staging of cervical cancer but also to tailor the therapeutic strategy. If the feasibility and diagnostic value of this technique are now accepted, the results of ongoing clinical trials are expected to measure the impact on morbidity and survival of the technique.

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Sentinel lymph nodes in endometrial carcinoma: The 2010 French standards and options

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Key words: Endometrial Neoplasms; Sentinel Lymph Node Biopsy; Early Detection of Cancer; Diagnostic Techniques and Procedures

Every year about 6400 new cases of endometrial cancer are diagnosed in the UK, 81500 in the European Union, and 40100 in North America. Histological type and grade of endometrial cancer, and depth of myometrial invasion, are prognostic factors in the early stage disease; however, the prognostic relevance of assessing lymph-node status by lymphadenectomy is debated. For patients with early stage endometrial cancer, randomized trials and a meta-analysis have shown that pelvic lymphadenectomy has no effect on overall or recurrence-free survival, and leads to a higher incidence of early and late complications. However, these trials did not take into account the contribution of sentinel lymph-node (SLN) biopsy in reducing the risk of surgical complications and improving staging. Moreover, when lymph-node status is unknown, indications for adjuvant therapies are based on pathological features of surgical specimens of the primary tumor, exposing some patients to overtreatment or undertreatment. In a meta-analysis of various techniques to assess lymph-node status in endometrial cancer, Selman and colleagues (1) showed that SLN biopsy was more accurate than MRI and CT scan. So far, only a few retrospective series have studied SLN biopsy, and these have had small sample sizes, used various injection sites, and reported detection rates of 45–94% and false-negative rates of 0–33%, justifying further prospective validation.
In the only multicenter prospective trial including 125 eligible patients, no complications occurred after injection of technetium colloid and no anaphylactic reactions were noted after patent blue injection. No surgical complications were reported during SLN biopsy, including procedures that involved conversion to open surgery. At least one SLN was detected in 111 of the 125 eligible patients. Nineteen of 111 (17%) had pelvic-lymph-node metastases. Five of 111 patients (5%) had an associated SLN in the para-aortic area. Considering the hemi pelvis as the unit of analysis, NPV was 100% (95% CI 95–100) and sensitivity 100% (63–100). Considering the patient as the unit of analysis, three patients had false-negative results (two had metastatic nodes in the contralateral pelvic area and one in the para-aortic area), giving an NPV of 97% (95% CI 91–99) and sensitivity of 84% (62–95). Immunohistochemistry and serial sectioning

detected metastases undiagnosed by conventional histology in 9 of 111 (8%) patients with detected SLNs, representing 9 of 19 patients (47%) with metastases. SLN biopsy upstaged 10% of patients with low-risk and 15% of those with intermediate-risk endometrial cancer. Therefore, SLN biopsy with cervical dual labeling could be a trade-off between systematic lymphadenectomy and no dissection at all in patients with endometrial cancer of low or intermediate risk and SLN biopsy could provide important data to tailor adjuvant therapy.

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Multimodality imaging for volume definition in pelvic radiotherapy

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Key words: Pelvic Neoplasms; Diagnostic Imaging; Positron-Emission Tomography; Tomography, X-Ray Computed; Radiotherapy Planning, Computer-Assisted; Magnetic Resonance Imaging; Radiotherapy

Pelvic lymph node involvement is an adverse prognostic factor in gynecologic cancers, namely in cervix and endometrium carcinomas. The knowledge of nodal status that could be assessed before treatment by either standard or metabolic imaging or by surgery is important for defining the best strategy. Indeed, preoperative prediction of positive nodes can allow better selection of the primary treatment modality. Computed tomography (CT) and magnetic resonance imaging (MRI) are routinely used for nodal assessment and positron emission tomography (PET) combined with CT seems to be promising in this regard (1).

For pelvic radiotherapy, it is well known that the risk of toxicity is correlated to irradiated volume, total dose, and its fractionation, and combined chemotherapy. Post-treatment morbidity of multimodality therapy and radiotherapy in postoperative setting is substantially higher than radical surgery or radiation alone (2).

Radiotherapy planning in pelvic tumors

Radiotherapy planning volume definition is still mainly based on CT images. Depending on the strategy, target definition, target volumes and organ sparing could significantly vary. When RT is indicated after the surgery, the clinical target volume (CTV) includes the anatomic nodal areas with a significant risk of organ at risk (OAR) exposure. Conversely, when radiotherapy is planned as an exclusive therapy or in the preoperative setting, the CTV is defined according to the gross tumor volume (GTV), which is defined using CT combined or not to other imaging modalities. The lymphatic nodes are generally included in the CTV. To deliver lower doses to the OAR, GTV definition and planning should rely more on metabolic imaging considering the higher specificity that reaches 97-98%. Thus, new tools using metabolic imaging and elastic fusion may help to increase the benefit/risk ratio of pelvic radiotherapy +/- brachytherapy (3).

Multimodality image fusion for radiotherapy planning

Multimodality image registration and fusion have a key role in routine diagnosis, staging, restaging, and the assessment of response to treatment and surgery of malignant disease. The complementarity between anatomic (CT and MR imaging) and molecular (SPECT and PET) imaging modalities is well established and the role of fusion imaging widely recognized as a central piece of the general tree of clinical decision making. Multimodality fusion for radiotherapy planning has been used increasingly during the last years for several cancers (3, 4). The use of new compounds, new PET technology (PET/MRI) and new generation of high technology of linear accelerators are promising for the next 10 years of evolution.

In gynecologic cancers, radiation therapy planning may benefit from advances of multimodality imaging to define target volumes and insure better sparing of OAR when radiotherapy is involved as primary treatment or in the post operative setting (5). We will discuss several cases that highlight these issues and show perspectives in pelvic radiotherapy.

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