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Sentinel Lymph Node Biopsy in Endometrial Cancer

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Abstract

The definition of "sentinel" lymph nodes today has found wide application in clinical practice for complex examination and treatment of patients with cancer of the uterine body. Further research in this direction will help to optimize intraoperative staging of tumors. They will also allow avoiding extended surgeries and limiting themselves only to the removal of sentinel lymph nodes in the early stages of the disease. And vice versa, to expand the scope of the operation if lymphogenous metastases are detected outside the zone removed by standard lymph node dissection. The definition of SLN is sufficient to identify patients at high risk of recurrent EC and to plan adjuvant therapy.

Key words: Endometrial cancer • Lymph nodes • Sentinental lymph node • Biopsy • Prognosis • Prognostic factors

Introduction

Endometrial cancer (EC) is today the most common gynecologic oncopathology in developed countries, accounting for 60,050 new cases in the US in 2021, causing death in 10,470 cases [1]. According to the statistical data provided by the Registry National Cancer Center in the Republic of Moldova, in 2021 the incidence of endometrial cancer was 420 cases, the mortality being 92 cases [2].According to statistical data, in the Republic of Moldova, over 77.0% of cases are diagnosed in the early stages (stages I and II), with a high rate of 5-year survival [1]. As a result of a detailed analysis, we can observe that 5-year survival results vary within limits stage I and constitutes in stage IA – 91-95%, and in stage IB – 80-65% [1, 2]. Survival at 5 years in stage II constituted 50.6% [5].

The increasing incidence of CE drives the need early detection of this disease, but also of the indication an adequate treatment, arising from the biological nature and molecular of CE. Surgery remains the key treatment method for CE today. The status of the lymph nodes is the most important prognostic factor for this pathology. It has been determined that the lymph nodes determine the risks of EC recurrence [1], and the results of the global rate of 5-year survival in nodal involvement pelvic or para-aortic lymphatics constitute 44-52% [1].

In the GOG-33 study, the surgical pathological characteristics of 621 patients with CE stage I. All patients underwent primary surgery in the volume of hysterectomy total abdominal, bilateral salpingo-oophorectomy, pelvic and paraaortic lymphadenectomy. The factors of multiple prognosis, especially grade and depth invasion, contributes to the occurrence of metastases in the pelvic and para-aortic lymph nodes (Table 1).

A series of retrospective studies indicate the important prognostic and therapeutic role of retroperitoneal staging [3], which does not coincide with the results of the prospective study in which they are examined the role of hysterectomy with or without lymphadenectomy in early CE, which also showed an increase in incidence surgical complications without improving oncological results [4].

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Therefore, the sentinel lymph node study (SNL), which is found between performing a standard lymphadenectomy and leaving the lymph nodes retroperitoneal without any morphological examination, is an acceptable and very promising procedure, which has the efficacy of retroperitoneal lymphadenectomy in identifying patients with positive lymph nodes, while minimizing the risk of complications surgical.

This is especially appropriate for female patients from the older age group or in patients with metabolic syndrome, in which the benefit of performing a actual lymphadenectomy has not yet been established [5].

Results of 2 retrospective multicenter studies presented, which compared systemic lymphadenectomy and removal GLS, have demonstrated safety, feasibility, accuracy and oncologic efficacy of the last procedure in both low-risk and high-risk EC patients. A promising direction in the treatment of patients with CE is the determination of the "sentinel" lymph nodes (GLS), that is, the lymph nodes that are the first in the way of the lymphatic flow from the area affected by tumor and are the first to be affected by tumor cells which migrates with the lymphatic flow. According to the existing concept, if the sentinel lymph node is not affected by metastasis, then all other regional lymph nodes are intact [3].

Another direction to optimize the treatment of EC patients in clinical stage I currently consists in studying the prognostic parameters of lymphogenous metastasis in these patients. According to ESGO consensus data, ESMO, ESTRO (2014), indications for lymphodissection in the case of clinical stage I endometrial cancer are determined by the risk assessed depending on the results preoperative examination, including depth of invasion and degree of tumor differentiation. But this model has several limitations, especially in patients with intermediate risk of lymphogenous metastasis.

Adequate surgical staging is now recognized by most oncologists as the standard for differentiated CE treatment moderate and weak, as well

Table 1: The clinic-pathological factors of prognosis of metastases in the pelvic and para-aortic lymph nodes.

Pelvic lymph nodes	Grade I	Grade 2	Grade 3
Endometrium	0%	3%	0%
Invasion < 50%	3%	5%	9%
Invasion 50%	0%	9%	4%
Invasion > 50%	11%	19%	34%
Paraaortic lymph nodes	**Grade I**	**Grade 2**	**Grade 3**
Endometrium	0%	3%	0%
Invasion < 50%	1%	4%	4%
Invasion 50%	5%	0%	0%
Invasion > 50%	6%	14%	23%

as for adenocarcinoma with clear and serous cells. However, for CE highly differentiated these recommendations remain the subject of discussion with great variability in the intraoperative evaluation of retroperitoneal lymph nodes. Some patients are not surgically staged at all, some are staged limited to the discretion of the surgeon, and surgical staging standards vary from to institution to institution.

Objective

The aim of the research was to study the possibility of the use of a pharmaceutical preparation (PF) for the determination of sentinel lymph nodes and for optimizing the prognosis of the risk of lymphogenic metastasis in patients with endometrial cancer in the stage I.

Materials and Methods

The study included 15 patients with endometrial cancer in stage I (mean age: 57 ± 9.8 years) who received surgical treatment in the extirpation volume of the uterus with appendages with pelvic lymphadenectomy in the framework Surgical Gynecology Department of the NOVAMED Polyvalent Hospital. The diagnosis was histologically verified in all patients at the preoperative stage. The stage of the disease was determined according to the FIGO and TNM systems edition 7. On based on a comprehensive examination, all patients have were subjected to a physical status assessment according to the ASA classification: patients with endometrial cancer belonged class III according to the ASA, taking into account severe concomitant diseases, such as metabolic syndrome with severe obesity (BMI ≥ 40), mild hypertension controlled, undercompensated diabetes. To all the patient's lymph nodes were detected sentinel using the pharmaceutical preparation indigo carmine. The study was carried out successively at the preoperative stage. The finished pharmaceutical preparation (PF) was injected into the cervix - in 4 points, at 3, 6, 9 and 12 o'clock of the conventional dial, the administered dose being 5 ml.

Results

The analysis of patients with endometrial cancer by risk groups draws attention to the prevalence of low and intermediate risk among them, of 50% and 39%, respectively, that is, these are the patients in whom the usefulness of lymphadenectomy is questionable. In women from the low-risk group, adenocarcinomas predominated with an average degree of differentiation - 11 (55.0±11.41%) and low - 6 (30.0±10.51%) cases.

From a morphological point of view, the histotype of endometrial tumors was represented by endometrial adenocarcinoma (n = 15), predominating tumors with a moderate degree of differentiation in 61%. In this work, the degree of differentiation of endometrial cancer in different oncological risk groups was studied. In the patients from the group with increased oncological risk, adenocarcinomas with an average degree of differentiation predominated - 2 cases. In the intermediate risk group, adenocarcinomas predominated with a medium degree of differentiation - 8 and high - 2 cases. In the low-risk group, adenocarcinomas predominated with a medium degree of differentiation - 2 and high - 1 case. The use of PF staining in the pelvis and abdominal cavity in cases of endometrial cancer made it possible to identify sentinel lymph nodes in 8 (97.2%) patients, 12 GLS being identified. At the same time, bilateral accumulation of PF in the case of intraoperative detection was identified in 2 (33%) patients, unilateral accumulation in 12 (63.8%) patients, and in 1 patient GLS were not detected, but in this one it was detected a macroscopic metastatic lesion of the pelvic lymph nodes. Most often, GLS were located along the course of the internal iliac vessels – 12 (35.5%), along the course of the external iliac vessels – 2 (18.7%), along the course of the vessels common iliac – 1 (16.6%), and unique GLS were located in the area of the obturator fossa, bifurcation of the aorta and iliac arteries (Figures 1 and 2).

In patients with endometrial cancer, on postoperative histological examination of the removed tissues, metastases were detected in the GLS in all cases

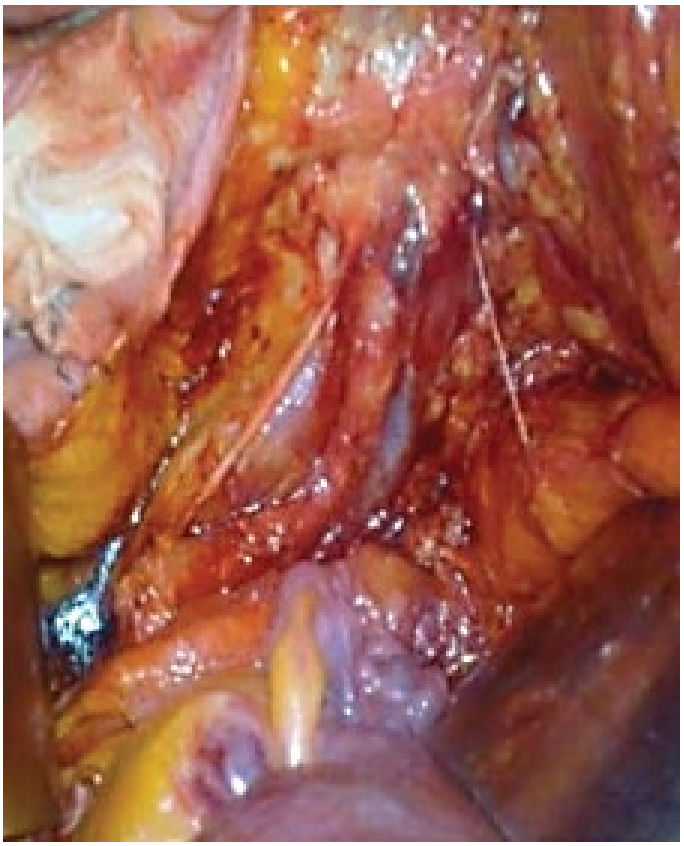

Figure 1: GLS situated in external iliac vessels.

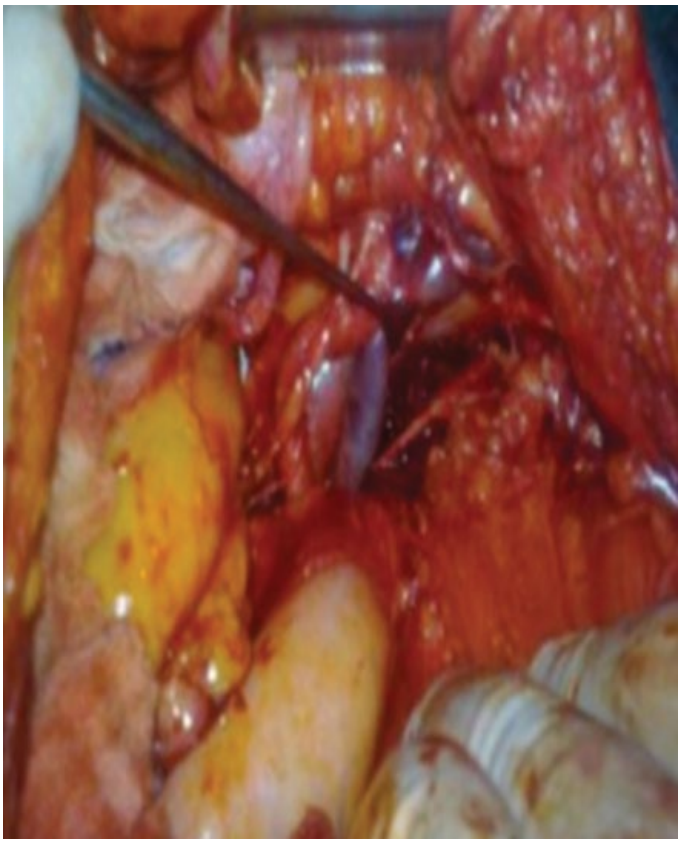

Figure 2: GLS situated in common iliac vessels.

Conclusion

The sentinel lymph node detection method complements the current trends in modern invasive surgery of uterine cancer and has found wide application in clinical practice as a component of a comprehensive examination and treatment of patients with endometrial cancer. Further research in this direction will help to optimize the staging of regional tumor dissemination and, respectively, to choose an appropriate treatment [1, 4].

They will also allow to avoid extensive surgical interventions, limiting themselves only to the removal of sentinel lymph nodes in the early stages of the disease. And, on the contrary, to expand the volume of the intervention or to complete the treatment with chemotherapy or radiotherapy if lymphogenic metastases are detected outside the distant area by standard lymphadenectomy. Thus, if we recognize that systemic lymphadenectomy has only a diagnostic role, then the detection of GLS for the identification of patients at high risk of CE recurrence and the planning of adjuvant therapy is sufficient.

This can be achieved with a lower incidence of surgical complications compared to lymphadenectomy and the long-term consequences of adjuvant therapy which is not always indicated.

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