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Study protocol

Project title:

Surgical and oncological outcomes of the laparoscopic assisted radical inguinal

lymphadenectomy for cN1/N2 penile cancer: a prospective comparative study between

open and laparoscopic approach

Local Ethics Committee Approval n° 00025/2020 of date April 4, 2020

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Background and aims:

Penile cancer represents, to date, a rare oncological pathology (1/100000 males in

Europe). However, in tertiary reference centres, such as the SCU Urologia (Prof. P.

Gontero), the number of patients sent for this pathology is increasing.

Although for the main lesion (T) there are now consolidated standards of care,

increasingly aimed at a conservative "sexual sparing" approach where oncologically

possible, the management of loco-regional lymph nodes is still not completely standardized.

The European Guidelines (EAU) recommend bilateral inguinal radical lymphadenectomy

for cN1/N2 (palpable lymph nodes mono/bilaterally, but not fixed) or high-risk tumour (>

T1G2).

Lymph node management is the factor that most influences patient survival. For this

reason, this must be entrusted to highly specialized centres. Some recent trials have shown

that bilateral inguinal lymphadenectomy has a statistically significant superiority to

radiotherapy and clinical surveillance in cN1/N2 patients.

Despite this, inguinal lymphadenectomy has an important incidence of morbidity (up to

50% of cases) which often wrongly limits its indications.

Main complications are:

- Lymphocele
- Prolonged lymphatic drainage
- Skin necrosis
- Dehiscence of the surgical wound
- Edema of lower limbs and genitals

Only few studies have recently evaluated the oncological and functional results of inguinal

lymphadenectomy performed with minimally invasive techniques using video-laparoscopic instruments. First results seem to support minimally invasive approach, that

appears to have comparable oncological results and less post-operative morbidity.

However, evidences are still extremely limited, and no high-grade recommendations can

be made.

The aim of the present study is to prospectively compare oncological and functional

results of penile radical inguinal lymphadenectomy performed with an open versus video-

laparoscopic technique.

Study design:

Surgical, observational, prospective, monocentric study.

20 patients with indication for inguinal lymphadenectomy (according to EAU 2019

Guidelines - in case of primary lesion > pT1G2 or in case of lymph node disease cN1/N2)

will be enrolled.

Each patient will undergo treatment of the primary lesion and contextual inguinal

lymphadenectomy. The procedure will be performed in this way:

- Groin 1: open lymphadenectomy performed by a surgical team with extensive experience

in traditional surgery

- Groin 2: laparoscopic lymphadenectomy performed by a surgical team with extensive

experience in minimally invasive surgery

The results of these procedures will be prospectively collected and compared.

The main outcome will be the percentage of postoperative complications (lymphocele,

prolonged lymph drainage, necrosis of the skin, dehiscence of the surgical wound, edema

of lower limb, emergency admission from the ED, re-intervention/surgical revision).

Complications will be classified according to the international Clavien-Dindo

classification.

Additionally, secondary outcomes (number of lymph nodes, number of positive lymph

nodes, surgical time) will be evaluated.

After the operation, patients will attend a 24-month follow-up program, as reported in the

flow chart, functional results and patient satisfaction will be evaluated during the visits.

Statistical analysis:

The categorical variables will be described using frequency and percentage, and the

continuous variables will be described using median and interquartile range (IQR) value.

Differences between groups will be assessed by the Student independent t test or the

Mann-Whitney U test on the basis of their normal or not-normal distribution, respectively

(normality of variables' distribution will be tested by the Kolmogorov-Smirnov test).

Inclusion Criteria:

Age of patients [45-80], CCI \leq 3. Penile tumour with inguinal lymphadenectomy

indication, according to EAU 2019 guidelines. Written informed consent.

Exclusion Criteria:

Age of patients $>$ 80, CCI \geq 3. Patients with lymphatic disorders of lower limbs. Patients

with previous inguinal surgery/radiotherapy. Previous or concomitant diagnosis of other

tumours.

Study Endpoints**Primary endpoint:**

- Compare peri/postoperative complications of open VS video-laparoscopic lymphadenectomy

Secondary endpoint:

- Compare surgical time of procedures, number of lymph nodes removed, number of metastatic lymph nodes

Outcomes measures:

Complications: lymphocele, prolonged lymph drainage, necrosis of the skin,

dehiscence of the surgical wound, edema of lower limb, emergency admission from

the ED, surgical re-operation/revision. Stratification of complications according to the

international classification of Clavien-Dindo.

Secondary outcomes evaluation: surgical time of the procedures, number of lymph

nodes removed, number of lymph nodes that are metastatic.

Video – laparoscopic procedure learning curve analysis

Study planning:

Kick off of the project: April 2029

Expected date deadline: April 2023

Duration of the study (referring to the individual patient and including all phases: recruitment, treatment, follow-up): 24 months.

Statistical Analysis:

Continuous data were analysed using analysis of covariance and categorical data were compared using a χ^2 test .

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