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

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**Principal Investigator:** Marco Falcone MD, Urologist, SC UROLOGIA Presidio

Molinette – Città della Salute e della Scienza di Torino

**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 ≤ 3. Penile tumour with inguinal lymphadenectomy indication, according to EAU 2019 guidelines. Written informed consent.

**Exclusion Criteria:**

Age of patients > 80, CCI ≥ 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,
derhiscence 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:

Continuos data were analysed using analysis of covariance and categorical data were compared using a chi^2 test.
Bibliography


