European Journal of Obstetrics & Gynecology and Reproductive Biology 224 (2018) 29–32

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Full length article

The safety and feasibility of minimally invasive sentinel lymph node staging using indocyanine green in the management of endometrial cancer

Alberto A. Mendivil[a], Lisa N. Abaid[a], John V. Brown III[a], Kristina M. Mori[a], Tiffany L. Beck[a], Howard D. Epstein[b], John P. Micha[a], Bram H. Goldstein[a,*]

[a] Gynecologic Oncology Associates, Hoag Memorial Hospital Cancer Center, Newport Beach, CA 92663, United States
[b] Hoag Hospital, Department of Pathology, Newport Beach, CA 92663, United States

ARTICLE INFO

Article history:
Received 17 October 2017
Received in revised form 23 February 2018
Accepted 26 February 2018
Available online xxx

Keywords:
Endometrial cancer
Disease staging
Sentinel lymph node mapping
Indocyanine green

ABSTRACT

Objectives: The purpose of this study was to report on the feasibility of laparoscopic sentinel lymph node (SLN) staging using indocyanine green (ICG) in the management of endometrial cancer.

Study design: We retrospectively evaluated the charts of presumed, clinical stage I endometrial cancer patients who underwent robotic-assisted surgery that incorporated mapping with ICG and SLN dissection from January 2016 until February 2017. Patient demographics, operative characteristics (e.g., complications, lymph node counts) and pathology data were evaluated.

Results: There were 87 patients who were included in the study. A total of 370 lymph nodes were removed, of which 245 were SLNs; unilateral and bilateral mapping of the SLNs was achieved in 84 (96.5%) and 71 (81.6%) of subjects, respectively. There were 10 (11.5%) patients who had metastatic disease identified within 22 (5.9%) of the total (n = 370) lymph nodes extracted, 19 (7.7%) of which were sentinel lymph nodes. We did not observe any intraoperative complications.

Conclusion: The results from our study suggest that minimally invasive SLN staging using ICG is a feasible procedure that is potentially effective at detecting metastases, which may ultimately attenuate the incidence of surgical morbidity.

Introduction

Endometrial cancer is the most frequently diagnosed gynecologic malignancy in the United States, accounting for an estimated 61,380 cases in 2017 [1]. The majority of endometrial patients are diagnosed with early stage disease, which coincides with a favorable outcome, in contrast to high risk subtypes that exhibit a proclivity for recurrent disease [2].

Traditionally, endometrial cancer is managed with hysterectomy and bilateral salpingo-oophorectomy; and when indicated, lymphadenectomy is utilized to further characterize the disease and determine the manner in which adjuvant therapy should be rendered [3–5]. Nevertheless, the data from randomized, controlled studies ascribing the utility of lymphadenectomy to survival improvements have been inconclusive [6] and increased risk for surgical morbidity (e.g., lymphedema, lymphocyst formation and neurologic injury) is concerning [7,8].

A sentinel lymph node biopsy encompasses the selective extraction of lymph nodes identified after a tracer dye (e.g., indocyanine green (ICG), technetium and patent blue) has been injected within or adjacent to the primary neoplasm [4,9–11]. The diagnostic technique safely facilitates the exclusive removal of nodal tissue directly implicated in the primary tumor's route of dissemination [9,12,13]. Sentinel lymph node mapping has since been incorporated into the National Comprehensive Cancer Network guidelines [14] for the treatment of endometrial cancer and recently evaluated in a large, multi-center, cohort study [15].

Despite the reported benefit of sentinel lymph node mapping in staging endometrial cancer, this procedure has not been conclusively investigated, particularly with ICG [5,16]. Hence, the primary objective of the current evaluation was to assess the feasibility of minimally invasive sentinel lymph node mapping using ICG in a population of presumed, clinical, early stage endometrial cancer patients.

* Corresponding author at: Gynecologic Oncology Associates, 35 Hospital Road, Suite 507, Newport Beach, CA 92663, United States.
E-mail address: bram@gynoncology.com (B.H. Goldstein).

https://doi.org/10.1016/j.ejogrb.2018.02.027
0301-2115/

Materials and methods

Study inclusionary and exclusionary criteria

We retrospectively reviewed the charts of presumed, clinical stage I endometrial cancer patients (in accordance with a physical exam, preoperative CT imaging and intraoperative assessment) who underwent robotic-assisted surgery that incorporated a staging procedure by a single group of gynecologic oncologists from January 2016 until February 2017. The patients' relevant demographic, operative and pathologic data were evaluated. An institutional review board approved this study prior to the retrieval of any patient chart data.

Endometrial cancer patients who underwent a cervical injection of ICG and sentinel lymph node mapping, followed by a pelvic lymphadenectomy, with or without a *para*-aortic lymphadenectomy, were considered for study participation. Conversely, the exclusionary criteria included patients with extra-uterine disease, treatment via an open or conventional laparoscopic procedure, a history of hysterectomy, retroperitoneal surgery or lymphadenectomy, and subjects on whom ICG mapping was not performed (e.g., the procedure was contraindicated or unavailable).

Clinical and pathological variables

Demographic and surgical variables included age, body mass index (BMI), number of sentinel lymph nodes mapped and location, and intra-operative complications. Pathology data encompassed tumor histology, stage, grade, number of regional pelvic/para-aortic lymph nodes resected and the presence of metastatic disease.

Surgical procedure

The surgery was conducted via the da Vinci Xi® (Intuitive Surgical; Sunnyvale, CA). Initially, the abdominal cavity was entered, whereupon the round ligament on the right side as well as the peritoneum lateral to the infundibulo-pelvic ligament were divided. Prior to the placement of the manipulator, 4 mL of ICG (Akorn Pharmaceuticals; Lake Forest, CA) was infiltrated in the cervix at the 3 and 9 o'clock position [15,17], submucosally and deep within the cervical stroma; thereafter, the peritoneal cavity was inspected, pelvic washings were examined, and the fluorescent imaging was initiated within approximately 20 min [14]. The various nodal regions (e.g., obturator, external iliac, presacral) of interest were evaluated and then developed, whereupon the sentinel lymph nodes were identified via the Firefly near infrared camera (Intuitive Surgical; Sunnyvale, CA).

In addition to detecting the sentinel lymph nodes, when indicated (e.g., the nodes were grossly abnormal, no lymphatic tissue was encountered or the SLN mapping was unsuccessful), a pelvic lymphadenectomy comprising the resection of the common, external, internal iliac and obturator nodes at the level of the inguinal ligament was performed. In select patients who were at high risk (e.g., myometrial invasion >50%, positive pelvic lymph nodes, or adnexal involvement) for having *para*-aortic node metastases, a *para*-aortic lymph node resection incorporated the removal of nodal tissue adherent to the aorta and vena cava and proximal to the renal vessels. Following the lymph node excision, the tissue was extracted vaginally via the ENDOPOUCH® (Ethicon *endo*-surgery; New Brunswick, NJ) specimen retrieval bag, and submitted for frozen section.

Pathologic evaluation

Excised lymph nodes were submitted for frozen section. Intraoperative frozen section was periodically utilized to assess suspicious nodes, determine the risk of nodal metastasis and for consideration to perform a lymph node dissection. Ultra-staging was not performed because the procedure does not impact the upstaging of disease.

Statistical analyses

Statistical analyses were conducted using MedCalc statistical software for biomedical research (version 9.5.1 for Windows). The initial data analysis preceded a descriptive statistical approach. Additional evaluation comprised nominal estimates and 95% confidence intervals.

Results

Patient demographic and clinical characteristics

From January 2016 until February 2017, we reviewed 241 available endometrial cancer patient charts, of whom 87 underwent a robotic-assisted sentinel lymph node biopsy procedure; the median operative time was 110 min (range, 73–210), of which approximately 25 min constituted the sentinel lymph node mapping component of the procedure. In this group, the median age was 61.5 years (range, 27–84) and BMI was 32.9 kg/m^2 (range, 18.2–54.5).

In the study population, 32 (36.8%) possessed high grade histology (grade 3 endometrioid or non-endometrioid histology). The patients' median tumor size was 3.5 cm (range, 0.9–9.5) and 73 (83.9%) subjects had a tumor >2 cm; also 40 (45.9%) study participants had >50% myometrial invasion. The patients' demographic and pathologic characteristics are listed in Table 1.

Lymph nodes removed

Pelvic lymph nodes were resected in all of the study patients, whereas a *para*-aortic lymphadenectomy was performed on 8 (9.2%) of subjects. In terms of total pelvic and para-aortic lymph nodes, 370 and 43 were removed, respectively. There were no observed intra-operative complications.

Table 1
Patients' demographic and pathologic characteristics (N = 87).

Median age	61.5 years (range, 27–84)
Body Mass Index	32.9 kg/m^2 (range, 18.2–54.5)
Pathologic FIGO stage	
IA	44 (50.6)
IB	24 (27.6)
II	8 (9.2)
IIIA	5 (5.7)
IIIC1	6 (6.9)
Histological type and grade	
Endometrioid	
Grade 1	41 (47.1)
Grade 2	15 (17.2)
Grade 3	13 (14.9)
Mixed	6 (6.8)
Carcinosarcoma	4 (4.6)
Serous	4 (4.6)
Adenosarcoma	2 (2.2)
Clear cell	1 (1.1)
Mucinous	1 (1.1)
Endometrial stromal sarcoma	1 (1.1)
Myometrial invasion	
≥50%	40 (45.9)
<50%	29 (33.3)
None	17 (20.8)
Lymphovascular space invasion	
Yes	25 (28.7)
No	62 (71.3)