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Real time indocyanin green near infrared lymphangiography for the reduction of drainage volume after neck dissection

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ABSTRACT

Background: To investigate the role of indocyanine green (ICG) lymphangiography in the reduction of drainage after neck dissection.

Methods: Patients with oral cavity squamous cell carcinoma were randomized into Group A (study group) and Group B (control). In the study group, upon the completion of neck dissection, a total of 2.5 mg of ICG was injected submucosally at the four quadrants around the tumour. Another 2.5 mg of ICG was injected subdermally in the groin bilaterally. The neck was screened using Near Infrared fluorescence. The presence of lymphatic leakage was noted and plicated with silk stitches. The total drainage volume of post-operative day 1, day 2 and the total accumulated volume until drain removal was measured.

Results: Twenty-two patients (Group A, n = 12; Group B, n = 10) were recruited. All patients in Group A had at least one site of lymphatic leakage identified. One patient in Group B developed chylous fistula and was excluded from analysis. The mean total drain output for day 1 and 2 after surgery, as well as the mean total output before drain removal, were significantly lower in Group A (22.4 ml vs. 86.2 ml [p = .02]; 14.2 ml vs. 72.8 ml [p = .02]; and 58.4 ml vs. 392 ml [p = .01], respectively), allowing earlier drain removal (2.2 days vs. 7.2 days, p = .02).

Conclusions: Intra-operative ICG lymphangiography is useful in the reduction of drainage volume after neck dissection for caners in the head and neck region.

Introduction

Neck dissection is an integral part of the surgical treatment for cancers in the head and neck region. The presence of lymph node metastasis, especially those with extra-capsular spread, is shown to have a negative impact on the survival outcome after treatment, warranting aggressive therapeutic neck dissection followed by adjuvant chemoradiation. On the other hand, in patients with clinically N0 necks, elective selective neck dissections are frequently performed for better staging of the cervical nodal status [1].

Among the various complications of cervical lymphadenectomy, seroma and chyle fistula formation has received much attention [2]. Various local strategies [3,4] and systemic administration of pharmacological agents [5,6] have been studied, with various efficacy as well as adverse events associated with each method.

Since the first human test using indocyanine green (ICG) in 1957, its applications in hepatology, cardiology, urology and ophthalmology are well established. Recently, improving photometric detection of ICG opens the door to real time intra-operative angiography and lymphoscintigraphy. The current study investigates the potential role of using ICG fluorescence imaging in minimizing the risk of seroma and chyle fistula after neck dissection.

Patients and methods

The study was approved by the Institutional Review Board of the University of Hong Kong and the Hospital Authority, Hong Kong West Cluster. Between 2016 and 2017, consecutive patients with squamous cell carcinoma (SCC) in the head and neck region who required modified radical neck dissection (mRND) for the treatment of cytologically proven metastatic cervical lymph nodes were recruited. Patients with previous radiotherapy or surgery to the neck, as well as those with known allergy to ICG were excluded from the study. These patients were then randomized into the two arms of investigation, the study group with mRND performed followed by ICG lymphangiography (Group A), and the control group with mRND performed only without lymphangiography (Group B).

All the operations were performed by the same surgeon who had

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more than 10 years of experience specialized in head and neck surgery, using standardized techniques via the McFee skin incisions.

Preparation and injection of ICG solution

For patients who were randomized into Group A, ICG (25 mg per vial, Pulsion Medical System [Munich, Germany]) was prepared by resuspending in 10 ml of sterile water to yield a 2.5 mg/ml solution. Upon the completion of neck dissection, 0.25 ml of ICG solution was injected submucosally at each of the four quadrants around the tumour (i.e. 2.5 mg injected in total around the primary tumour). In addition, 1.0 ml of ICG solution was injected subdermally at each side of the groin bilaterally (i.e. total 5.0 mg injected in the groin region).

Real time fluorescence imaging

Near infrared fluorescence (NIRF) imaging of the neck wound was then performed using the SPY Intraoperative Imaging System (Novadaq Technologies, Mississauga, Ontario, Canada). This device consists of a 3 W, 806-nm laser diode, and the system optics spread the laser output over a field 7.6-cm by 7.6-cm square at a distance of 30 cm, resulting in a maximal intensity of 30 mW/cm^2. The unit also contained 2 charge-coupled device video cameras sensitive to the near infrared region of the spectrum, each equipped with a different fixed focal length lens and iris. The hand-held device was covered with a sterile drape so that the surgeon could adjust its position in and out of the surgical field and to switch to various modes to facilitate the detection of lymph leakage. These included the SPY Mode (NIR fluorescence was displayed in gray scale), the PINPOINT Overlay Mode (combination of white light and the NIR fluorescence image, appearing as fluorescent green on top of a high-definition white-light image) as well as the Color-Segmented Fluorescence (CSF) Mode (the NIR fluorescent image was color-scaled, with red representing the highest degree of fluorescence and blue being the least). Video recordings taken during the procedure were stored for later review.

The presence and the location of lymphatic leakage were noted and recorded. The leak was then plicated with 5/O Silk stitches until no more leakage was detected.

Completion of surgery

For both groups of patients, two silicon, hubless BLAKE drains (Ethicon, US) were placed into the operative fields. The upper drain (Drain 1) was inserted to the level I and II region, while the lower drain (Drain 2) drained the level III–V region. The neck wounds were sutured in layers with 3/O Vicryl and 4/O Nylon stitches. No pressure dressings were applied.

Post-operative care

All the patients were nursed in the general ward after surgery. The volume of output of each drain was measured and recorded every 4 h. The drain fluid was sent to the laboratory for biochemical testing and the presence of chyle was noted. The incidence of chylous fistula was noted. The drains were removed when the total output of the drain was less than 10 mls per day. The neck was examined by portable ultrasound machine 1 week after drain removal and the presence of fluid collection in the field of neck dissection was noted.

Patients' data were prospectively collected and entered into the head and neck cancer database, at the Division of Head and Neck Surgery, Department of Surgery, Queen Mary Hospital, University of Hong Kong. Chi-square or Fisher's exact tests were used to compare categorical variables, and Student's T-test was employed to compare continuous variables. Data were analyzed with Statistical package for social sciences version 18.0 (SPSS, Inc., Chicago IL). A p-value of .05 or less was considered as significant.

Table 1
Patient demographics and tumour characteristics.

	Group A (ICG) (n = 12)	Group B (Control) (n = 10)	*P* – value
Sex			
Male (%)	10 (83.3)	8 (80)	*ns*
Female (%)	2 (16.7)	2 (20)	*ns*
Age (years)			
Mean	65.6	62.8	*ns*
Range	48–74	50–72	
BMI (kg/m^2)			
Mean	22.9	22.5	*ns*
Range	18.6–26.4	18.2–25.3	
Primary malignancy			
Tongue	9	8	*ns*
Buccal mucosa	2	2	*ns*
Floor of mouth	1	0	*ns*
T – classification[a]			
T1	6	6	*ns*
T2	3	3	*ns*
T3	1	1	*ns*
T4	2	0	*ns*
N – classification[a]			
N1	5	4	*ns*
N2	5	5	*ns*
N3	2	1	*ns*

[a] American Joint Committee on Cancer (AJCC) 7th edition.

Results

During the study period, a total of 22 consecutive patients with SCC of the head and neck region were recruited into the study. Table 1 showed the demographics and tumour characteristics of the study subjects. The mean age of our patients was 64.2 years (range 48–74 years). Their mean body BMI was 22.7 kg/m^2 (range 18.2–26.4 kg/m^2). After randomization, 12 patients were allocated into Group A and the rest into Group B.

All patients in Group A had at least one site of lymphatic leakage identified by real time NIR fluorescence study (Table 2). The mean time from ICG injection to the first detection of leakage was 8.4 min. The presence of leakage was detected using the SPY mode and the location of the leak was confirmed using the PINTPOINT Overlay mode (Fig. 1). The commonest site of the lymphatic leakage detected by NIR fluorescence was located at level IV region, followed by level II and I. All the leakage identified were controlled successfully by plication, which was

Table 2
Details of lymphatic leakage identified by intra-operative ICG.

	Group A (n = 12)
Time of first detection of ICG leakage (minutes)	
Mean	8.4
Range	5.2–10.6
Number of points of ICG leakage	
Mean	4.5
Range	3–6
Location of ICG leakage points	
Level I	5
Level II	14
Level III	4
Level IV	20
Level V	11
Time taken for identification and repair of leakage (minutes)	
Mean	16.4
Range	12.4–20.8

Abbreviations: ICG, indocyanine green.