



The impact of unplanned reoperations in head and neck cancer surgery on survival



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ABSTRACT

Objectives: Unplanned reoperation causes physical and psychological stress in patients and it costs more in terms of medical, economic and social resource. The purpose of the study was to evaluate the incidence, risk factors and clinical significance of unplanned reoperation (any unscheduled surgery within 30 days from the initial surgery) in patients who had undergone head and neck cancer (HNC) surgery.

Materials and methods: A total of 574 consecutive patients who had received surgery for HNC with or without flap reconstruction from 2010 to 2015 were analyzed. Clinical and biochemical characteristics, cause of unplanned reoperation, cancer subsites, and previous treatment history were compared between unplanned reoperation group (n = 60) and control group (n = 514). Multivariable analyses were performed to identify risk factors for unplanned reoperation. Clinical significance was evaluated by multivariable survival analyses using Cox proportional hazard model.

Results: Overall rate of unplanned reoperation was 10.5%. Flap complication (40.0%) was the most common cause, followed by infection (16.7%), necrosis (11.7%), and bleeding (8.3%). Higher N (N2) classification, long operation time and previous treatment before surgery were identified as risk factors for unplanned reoperation. Based on multivariable survival analyses, recurrence-free survival was significantly decreased in unplanned reoperation group (Hazard ratio = 1.85, 95% confidence interval [1.23–2.80]), but not overall survival.

Conclusion: Unplanned reoperation significantly decreased recurrence-free survival in patients with HNC surgery. Thus, careful surgical/ perioperative management is needed to reduce unplanned reoperation in HNC patients with advanced nodal disease, long operation time or previous treatment history.

Introduction

The head and neck area is comprised of complex anatomical structure in close association with respiration, swallowing, speaking and appearance. Thus, head and neck cancer (HNC) surgery is frequently combined with reconstructive surgery. Surgical ablation of tumors is still one of the main treatment options for HNC. It plays an independent role in early stage HNC [1]. Along with non-surgical treatment modalities, surgical ablation has been used for advanced stage HNC [1]. Most HNCs are diagnosed in the elderly and they are associated with habitual smoking, alcohol drinking and malnutrition [2–4]. These factors might result in various treatment-related complications in HNC patients [2–5]. In addition, tumor stage, duration of operation time, and comorbidities are also significant factors for post-operative complications after major surgery for HNC [6]. Previous treatments of cancer and time between initial treatment and salvage

surgery have been reported to be significant risk factors for surgical complications [7]. It has been demonstrated that major risk factors for surgical site infection after HNC surgery include cancer subsite of oral cavity, tracheostomy, and previous radiation therapy [8].

During the perioperative period, patients who suffer from surgical complications may undergo unplanned reoperation. Several studies have reported that unplanned reoperation or readmission could be associated with cancer recurrence and mortality in colorectal cancer and brain tumor [9–12]. Recent studies have also reported that surgical stress could promote cancer recurrence and metastasis [13–15]. Unplanned reoperation, not anticipated by caregivers or patients, could cause physical and psychological stress in patients and it also costs more in terms of medical, economic, and social resources [16,17]. Moreover, it might delay adjuvant treatments in a multidisciplinary cancer care. Therefore, unplanned reoperation over primary surgery might have negative effects on oncological outcomes in HNC.

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Despite this clinical assumption, few studies have reported events of unplanned reoperation linked to worse oncological outcomes in HNC. Thus, the purpose of this study was to evaluate the incidence and risk factors of unplanned reoperation in patients who had undergone HNC surgery, and identify the potential clinical significance of unplanned reoperation and prognosis of HNC patients.

Materials and methods

Study patients

All HNC patients were enrolled prospectively into our HNC registry. They submitted written informed consent for use of their clinical and biological data. The study protocol was approved by our Institutional Review Board (Protocol No. 2010-05-090, 2015-06-132, [ClinicalTrials.gov](https://www.clinicaltrials.gov/ct2/show/study/NCT02546895) NCT02546895). From registered HNC patients, we included those who had undergone curative surgery for HNC between 2010 and 2015. To establish more homogeneous study group, we excluded the cases with salivary gland cancer and para-nasal sinus/nasal cavity cancer, leaving oral cavity, oro- and hypo-pharynx and larynx cancer patients. This specific study focused on unplanned reoperation, and it was approved by our Institutional Review Board again before data collection. These patients were assigned into two groups: (1) control group (n = 514, 89.5%) and (2) unplanned reoperation group (n = 60, 10.5%). All the patients were followed up more than 2 years in cases without recurrence or deaths.

Treatments for head and neck cancer

All enrolled patients with primary and recurrent HNC had received surgery for curative intent with or without flap reconstruction. Surgery for the primary tumor was performed to resect all gross tumors with adequate tumor-free safety margins. Type of neck dissection (comprehensive or selective) for regional lymph nodes was based on tumor extent. Reconstruction of surgical defects was performed using skin grafts, local, regional, or free flaps according to defect characteristics and the decision of surgeons.

During the study period, three-dimensional conformal radiation therapy (RT) and intensity modulated RT were used. Radiation dose fractionations (1.8, 2.0, 2.2, or 2.4 Gy per fraction) were used to deliver 66–72 Gy over 6–8 weeks. With three-dimensional conformal RT technique, 70–72 Gy was applied to the target volume by 1.8 or 2.0 Gy per fraction. Simultaneous integrated boost was incorporated into intensity modulated RT technique, with 66.0–69.4 Gy of gross tumor volume by 2.2 or 2.4 Gy per fraction, or 60.0 Gy of clinical target volume by 2.0 Gy per fraction. Concurrent chemoradiation included cisplatin-based chemotherapy every three weeks during RT periods. Dose of cisplatin (60–100 mg/m²) was individualized based on patient tolerance and tumor characteristics.

Unplanned reoperation

Unplanned reoperation was defined as any unscheduled surgery within 30 days from the initial or salvage surgery for HNC [18,19]. All unplanned reoperations (including surgical management for wound infection, necrosis, fistula, reconstructed flap complication, and chyle leak) were performed under general anesthesia. Secondary resection for oncological safety was excluded from analyses, because it may reflect tumor-related factor, but not surgery-related complications.

A clinical decision to reoperation was made by intra-department discussion among responsible physicians and surgeons. Except emergent cases, such as bleeding or airway obstruction, patients who had surgical complications were managed initially with medical treatments (appropriate antibiotics) and active wound care (curettage, drainage, disinfection or dressing) for at least one week. If complications did not improve with conservative management, reoperation was performed to

correct such complications for patients.

One reason for unplanned reoperation was wound adhesion in the anterior vocal cord that caused respiratory difficulty after laryngeal cancer resection. Other reasons included acute myocardial infarction and cerebrovascular events which required emergent surgical intervention to restore blood flow.

Statistical analyses

Clinical and biochemical data of baseline characteristics (age, gender, body mass index), American Society of Anesthesiologists (ASA) Physical Status Classification System score [20,21], hemoglobin, albumin, underlying disease, operation time, use of flap reconstruction and duration of hospital stay were collected. HNC subsites were oral cavity, larynx and oro-/hypo-pharynx. Tumor staging was defined based on American Joint Committee on Cancer (7th edition) TNM staging manual [13]. Continuous variables were analyzed by Mann-Whitney *U* test, while categorical variables were compared with Chi-square test or Fisher's exact test.

To identify risk factors for unplanned reoperation, clinical factors were evaluated by a logistic regression analysis (univariable and multivariable analysis). In addition, the clinical significance of unplanned reoperation (prognosis) was evaluated Cox proportional hazard model for survivals (recurrence-free and overall survival). A multivariable Cox proportional hazard model was reconstructed using a backward selection to eliminate nonsignificant variables. In addition, collinearity among variables was examined measuring variance inflation factor. All variables in a multivariable model had variance inflation factors of less than 4, suggesting that collinearity among variables was not significant. Statistical package of R and SPSS for Windows ver. 20.0 (SPSS Inc., Chicago, IL, USA) were used for statistical analyses.

Results

Comparison of clinical variables between unplanned reoperation and control group

During the study period in our cohort, the incidence of unplanned reoperation in HNC surgery was 10.5% (60/574). The most common cause of unplanned reoperation was reconstruction flap related complication (n = 24, 40.0%), followed by wound infection (n = 10, 16.7%), necrosis (n = 7, 11.7%), bleeding (n = 5, 8.3%), and fistula (n = 4, 6.7%) (Table 1).

Age, gender, ASA score, body mass index, hemoglobin, albumin, presence of diabetes or hypertension was not significantly different between the two groups (Table 2). Interestingly, the proportion of non-smokers (51.7%) in the unplanned reoperation group was higher than that (29.8%) in the control group. However, the proportion of current smokers in the control group (45.5%) was more common than that (31.7%) in the unplanned reoperation group (*P* = 0.003). Current-

Table 1
Causes of unplanned reoperation within 30 days in head and neck cancer surgery (n = 60).

Causes	No. (%)
Reconstructed flap complications	24 (40.0)
Infection	10 (16.7)
Necrosis	7 (11.7)
Bleeding	5 (8.3)
Fistula	4 (6.7)
Flap donor site complications	3 (5.0)
Chyle leak	3 (5.0)
Wound adhesion	2 (3.3)
Others ^a	2 (3.3)

^a Managements for cardiovascular and cerebrovascular events.

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