Original Article

Post-Thyroidectomy Hemorrhage: Time, Place, Risk, and the Surgeon

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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ABSTRACT

Purpose: Post-thyroidectomy hemorrhage has been conducted on re-operated reactive hemorrhage usually occurred within 24 hours. We investigated all hemorrhages including reoperated or not and also secondary hemorrhages occurred after discharge.

Methods: We retrospectively reviewed 16,701 patients from 1999 to 2019 and investigated the risk factors and time patterns of post-thyroidectomy hemorrhagic events.

Results: The annual incidence of hemorrhage decreased from 1.7% to 0.1%. The risk factors included age ≥ 55 years, male sex, body weight ≥ 60 kg, larger thyroid specimens, and advanced stage (stage III or IV). The type of surgery and body mass index showed no significant associations with the hemorrhagic events. Ligation methods were associated with a greater incidence of hemorrhagic events than energy devices (0.6% vs. 0.3%), but they were not independent predictive factors (odds ratio [OR]=1.5; $P=0.157$). The OR was high for surgeons' experience < 3.5 years (OR=1.8), age ≥ 55 years (OR=1.8), weight ≥ 60 kg (OR=1.9), and aggressive tumor stage (OR=4.8). The highest OR was observed for Surgeon X's procedures (OR=9.6). Extremely severe airway obstruction was observed in 17% of the patients and one patient did not survive. Most of the hemorrhagic events occurred during hospitalization, but 13% of the events occurred at home after discharge, or in the dialysis chamber of another hospital.

Conclusion: Post-thyroidectomy hemorrhagic events are life-threatening complications that can occur at unexpected times and places. Delicate hemostasis and careful monitoring even after normal discharge constitute the best approach to prevent these events. Moreover, we do not recommend routine outpatient-based thyroidectomy.

Keywords: Thyroidectomy; Hemorrhage; Hematoma; Risk factors; Surgeons

INTRODUCTION

Hemorrhage and hematoma are life-threatening and unpredictable complications after thyroid and neck surgery (1-3). The reported rate of subsequent hemostatic reoperations was 0–9.1% (4-6). Cardiac arrests or deaths have also been reported in rare instances (7,8). There have been many advances in surgical procedures with respect to endoscopic thyroidectomy procedures, energy devices, and hemostatic agents. Compared to benign diseases, a drastic increase has been observed in thyroid cancer over the last few decades. We were

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able to respond to these complications more appropriately through several authors' efforts and valuable surgical tips (8-13). Rates of hemorrhage or other complications decreased dramatically, but these complications were not eliminated completely (14).

Hemorrhage in general surgery can be classified into three categories: 1) primary (within the operative field), 2) reactive (within 24 hours), and 3) secondary (7-10 days postoperatively) (15-18). Several studies have been conducted mostly on post-thyroidectomy reactive hemorrhage of reoperation occurred within 24 hours (5). Quick and accurate judgment and timely treatment are important. We have experienced two instances of secondary bleeding at 7 days and at 10 days after the initial surgery, respectively. These were life-threatening hemorrhages that occurred at home and in the dialysis chamber. We have also experienced two pseudo-hemorrhages that were misdiagnosed as hemorrhages. Such misdiagnosis may lead to incorrect treatment.

It is necessary to identify risk factors that may cause hemorrhage or hematoma and to prevent them in an active and appropriate manner. Some studies have determined the methods to distinguish hemorrhage from hematoma in cases of primary and reactive hemorrhage (9). However, data regarding delayed secondary hemorrhage and pseudo-hemorrhage have rarely and never been reported. We evaluated all types of hemorrhagic events, such as hemorrhage, hematoma, pseudo-hemorrhage, and abscess after initial surgery, as well as reoperated or not, and hemorrhagic events occurring in the hospital or after discharge.

MATERIALS AND METHODS

Our two institutions (Chonnam National University Hospital and Hwasun Hospital) performed 19,256 endocrine surgeries from 1971 to 2019. We focused on the last 20 years (1999 to 2019) and enrolled 16,701 patients after excluding those who underwent non-thyroid endocrine surgeries and those with unclear medical records. We retrospectively reviewed the electronic medical records to search for the missing patient data and for information regarding the contents of the intubation tubes, additional drains, and recently re-operated patients after the initial surgery.

Hemorrhage was defined as clear bleeding from an artery or vein or an oozing area on the muscle or on the trachea. Hematoma was defined as having collection of blood or clot without definite bleeding foci. There were 36 hemorrhages and 31 hematomas. But there were grey zone patients which it is not clear whether to define hemorrhage or hematoma. Five of hematoma patients re-classified as hemorrhage for the following reasons: persistent or repeated hemorrhagic events occurred even-though careful hemostasis. Finally, we classified the patients into those with hemorrhage (41 patients) and those with hematoma (26 patients). We carried out 16 observations without reoperation (34.0%), 14 operation under local anesthesia (29.8%), and 37 operation under general anesthesia (78.7%). We also included patients with pseudo-hemorrhage and abscess. In two patients, pseudo-hemorrhage had been misdiagnosed as true hemorrhage. They were also included in this study. These pseudo-hemorrhages exhibited symptoms of airway obstruction that were very similar to the symptoms of hemorrhage. They were included to determine the reason for misdiagnosis. We classified the patients into two groups for further analysis: hemorrhagic group (n=74) and non-hemorrhagic group (n=16,627).

Thirty-one surgeons performed the surgeries during the 49-year period and seven operators performed the surgeries during the present study period (1999–2019). There have been many changes in surgical skills, ligation devices, and sealing materials over the last 20 years. We started using energy devices in endoscopic (2003), in robotic (2010), and in open thyroidectomy (2012). Before their introduction, classic ligations were used to seal the vessels, various hemostatic agents in the liquid or solid form (19) were applied, and drainage tubes were optionally inserted.

The time from leaving the operation room to the detection of hemorrhagic events by the doctor or the nurse was reviewed. If the discovery of a hemorrhagic event by the nurse was earlier than that by the doctor, the former was selected to calculate the time to the onset of hemorrhage. To determine the exact timing of the event, detailed history was obtained about every event that occurred at home, while driving, or in the dialysis chamber in another hospital.

We reviewed the incidence, risk factors, pattern of occupied layers, time to the onset of event, and the place where the hemorrhagic events occurred. We also evaluated the cases of pseudo-hemorrhage and abscess. Among patient-related factors, we analyzed factors such as age, sex, height, body weight, body mass index (BMI), comorbidities, extent of surgery, pathology or tumor, node, metastasis (TNM) staging, specimen weight, hospital stay, and complications. Furthermore, surgeon-related factors such as operations performed by each surgeon, experience of each surgeon, operation procedure, operation time, and energy devices were analyzed. We enrolled all patients with hemorrhage and hematoma irrespective of whether they underwent reoperation. We also included patients with secondary bleeding that occurred after discharge. This study was approved by the International Review Board of Chonnam National University Hospital (CNUH-2020-299), and a waiver of informed consent was also approved.

We used the t-test to compare continuous variables and the chi-squared test for categorical variables. Receiver operating characteristic (ROC) curve analysis was used to determine the optimal cut-off value and compare the diagnostic performance. We used proportional hazards models for the relative risk to assess the simultaneous effects of various risk factors. Kaplan-Meier curve with log-rank test was adopted to analyze the time to the onset of hemorrhagic event and stratification according to various risk factors. Results were analyzed using IBM SPSS Statistics 26.0 (IBM Corp., Armonk, NY, USA). Statistical significance was set at a P value <0.05. An odds ratio (OR) >1.0 indicated the risk factors for hemorrhagic event.

RESULTS

1. Incidence of hemorrhagic events

The annual number and the incidence of hemorrhagic events among 16,701 patients between 1999 and 2019 at two institutions are depicted in **Fig. 1**. The annual number of included patients increased from 229 to 1,380 till 2011 and then steadily decreased to 717 cases in 2017. The decreased number of annual cases might be attributed to the controversy regarding overdiagnosis or overtreatment (20). The number of annual cases exhibited an increase again since 2018.

Altogether, 74 patients (0.44%) suffered from hemorrhagic events. These included 41 with hemorrhages (0.25%), 26 with hematomas (0.16%), five with abscesses (0.02%), and two

Fig. 1. Trends of the annual cases and the incidences of hemorrhagic events.

with pseudo-hemorrhages (0.01%). There were two cases of pseudo-hemorrhage in 2009 and 2013, respectively and five abscesses for three consecutive years since 2017. Although the incidence of hemorrhage significantly decreased from 1.7% to 0.1%, the incidence of hematoma remained constant (0.1%–0.4%) and the incidence of abscess increased from 2017 to 2019 (Fig. 1).

2. Patient factors related to hemorrhagic events

We divided the patients into the hemorrhagic group and the non-hemorrhagic group (Table 1). The age of the patients showed a normal distribution and the mean age was greater in the hemorrhagic group (52.0 vs. 47.6 years, $P=0.002$). The proportion of patients aged over 55 years was greater in the hemorrhagic group (0.6% vs. 0.4%, $P=0.047$). The number of male patients and the number of patients with body weight above 60 kg were greater in the hemorrhagic group ($P=0.009$ and $P=0.024$, respectively).

We categorized the extent of surgery into following groups: 4,241 (25.9%) patients who underwent procedures less than total thyroidectomy; 9,041 (55.2%) patients who underwent total thyroidectomy; and 1,129 (6.9%) who underwent surgery extended to the tracheoesophageal or the lateral neck compartment. There were 838 (5.1%) reoperations due to recurrence and 1,134 (6.9%) endoscopic or robotic surgeries. No differences were observed in the type of surgery between the hemorrhagic and the non-hemorrhagic group ($P=0.088$). The duration of the initial operation also showed no difference between the groups (131 vs. 125 minutes, $P=0.224$).

The mean weight of the thyroid specimens was greater (20.4 vs. 17.0 g, $P=0.003$) in the hemorrhagic group. The number of patients with advanced tumor stage (stage III or IV patients) was significantly greater in the hemorrhagic group (5.1%) when than the number of patients with early-stage (0.9%) or benign tumors (0.8%, $P=0.002$).

Table 1. Patient characteristics and surgeon-related factors

Patients	All patients (n=16,701)	Hemorrhagic events (n=74)	No hemorrhagic events (n=16,627)	P value
Age (yr)	47.6±12.5	52.0±11.6	47.6±12.5	0.002
<55	11,700 (71.2)	45 (0.4)	11,655 (99.6)	0.047
≥55	4,725 (28.8)	29 (0.6)	4,696 (99.4)	
Sex				
Female	13,154 (80.1)	51 (0.4)	13,103 (99.6)	0.016
Male	3,278 (19.9)	23 (0.7)	3,255 (99.3)	
Physical status				
Height (cm)	169.7±7.5	160.9±8.4	159.7±7.5	0.178
Body weight (kg)	60.3±10.0	63.0±11.9	60.2±10.0	0.024
<60 kg	3157 (51.9)	25 (0.8)	3,132 (99.2)	
≥60 kg	2928 (48.1)	44 (1.5)	2,884 (98.5)	0.009
Body mass index (kg/m ²)	23.6±3.3	24.2±3.4	23.6±3.3	0.122
Surgical extent				0.088
Less than TT	4,241 (25.9)	15 (0.4)	4,226 (99.6)	0.147
TT±CND	9,041 (55.2)	47 (0.5)	8,994 (99.5)	0.458
Extended TT±LND	1,129 (6.9)	7 (0.6)	1,122 (99.4)	0.498
Reoperation	838 (5.1)	5 (0.6)	833 (99.4)	0.604
Endoscopic or robotic	1,134 (6.9)	0	1,134 (100.0)	
Operation time (min)				
Mean±standard deviation	125±46	131±41	125±46	0.224
Median (range)	115 (25–645)	120 (65–275)	115 (25–645)	0.073
Postoperative hospital stay (day)				
Median (range)	2.0 (0–117)	6.0 (2–35)	2.0 (0–117)	0.000
Thyroid specimen (g)				
Median (range)	17.0 (2–600)	20.4 (3–140)	17.0 (2–600)	0.003
TNM staging, 8th edition				
Benign disease*	871 (12.2)	7 (0.8)	864 (99.2)	0.689
Stage I, II	6,162 (86.4)	54 (0.9)	6,108 (99.1)	0.272
Stage III, IV	99 (1.4)	5 (5.1)	94 (94.9)	0.002
Instrument				
Classic ligation	8,359 (51.5)	48 (0.6)	8,311 (99.4)	0.021
Energy devices	7,867 (48.5)	26 (0.3)	7,841 (99.7)	
Surgeons				
Surgeon 1	2,201 (13.2)	8 (0.4)	2,193 (99.6)	0.546
Surgeon 2	3,447 (20.6)	13 (0.4)	3,434 (99.6)	0.513
Surgeon X	632 (3.8)	11 (1.7)	621 (98.3)	0.000
Surgeon 3	6,027 (36.1)	21 (0.3)	6,006 (99.7)	0.166
Surgeon 4	3,119 (18.7)	14 (0.4)	3,105 (99.6)	0.957
Surgeon 5	806 (4.8)	4 (0.5)	802 (99.5)	0.782
Surgeon 6	469 (2.8)	3 (0.6)	466 (99.4)	0.466
Surgeons' experience (yr)				
Median (range)	9.0 (0–32)	5.0 (0–31)	9.0 (0–32)	0.000
<3.5	3,834 (23.6)	33 (0.9)	3,801 (99.1)	0.000
≥3.5	12,419 (76.4)	41 (0.3)	12,378 (99.7)	

Data are presented as number (percentage) not otherwise specified.

TT = total thyroidectomy; CND = central neck dissection; LND = lateral neck dissection; TNM = tumor, node, metastasis.

*Benign diseases included parathyroid surgery.

The risk factors for hemorrhagic events included age above 55 years, male sex, body weight above 60 kg, larger thyroid specimen, and advanced stage (stage III or IV). On the other hand, there was no statistically significant difference in the type of surgery, operation time, and BMI (24.2 vs. 23.6 kg/m², P=0.122).

3. Energy devices and surgeon-related factors

Our institutions started using energy devices in endoscopic thyroidectomy since May 2003 and in open thyroidectomy since May 2012. During the last 20 years (1999–2019); 7,867

(48.5%) patients were operated upon using energy devices and 8,359 (51.5%) were operated upon using classic cut and ligation method with tie materials. The number of hemorrhagic events associated with the classic ligation methods was higher than that associated with energy devices (0.6% vs. 0.3%, $P=0.021$). However, since the success of the ligation method is highly dependent on the surgeon's skill and experience, we performed multivariate logistic regression analysis to determine whether it was an independent predictive factor for hemorrhagic events.

Thirty-one operators performed endocrine surgeries at two institutions for over 49 years, and seven operators performed the surgeries during the present study period (1999–2019). A greater number of hemorrhagic events were associated with procedures performed by Surgeon X (1.7% vs. 0.3%–0.6%). This incidence was three to 5 times higher ($P=0.000$) than the incidence associated with procedures performed by other surgeons. The other six surgeons experienced an incidence of 0.3%–0.6% with no significant difference in the incidence of hemorrhagic events among them.

The experience of all surgeons since starting endocrine surgery was reviewed. The median experience was 9.0 (0–32) years. ROC curve analysis was performed to determine the optimal cut-off value, which was 3.5 years of experience (area under the curve [AUC]=0.621). Surgeons with experience below 3.5 years were associated with 3 times greater risk of hemorrhagic events than more experienced surgeons (0.9% vs. 0.3%, $P=0.000$).

4. Predictive factors for post-thyroidectomy hemorrhagic events

The patient-related risk factors for hemorrhagic events such as age, sex, body weight, tumor stage, and the surgeon-related risk factors such as ligation methods, surgery done by Surgeon X, and surgeons' experience were analyzed with Cox regression analysis and arranged in the order of OR and P value (**Table 2**). Surgeons' experience and operations performed by each surgeon were inter-dependent. Hence, Cox regression analysis was turned away from each other.

Classic ligation methods (OR=1.2; $P=0.456$) and male sex (OR=1.5; $P=0.157$) were not independent predictive factors for post-thyroidectomy hemorrhagic events. The odds ratio was significantly high for experience below 3.5 years (OR=1.8; 95% confidence interval [CI]=1.0–3.0), age above 55 years (OR=1.8; 95% CI=1.1–3.1), body weight above 60 kg (OR=1.9; 95% CI=1.1–3.3), and advanced tumor stage (OR=4.8; 95% CI=1.7–13.2). Unfortunately, the association between Surgeon X's procedures and hemorrhagic events was significantly high (OR=9.6; 95% CI=4.6–20.4) (**Table 2**).

5. Pseudo-hemorrhage and abscess

We performed further analysis after classifying the events into pseudo-hemorrhage, hemorrhage, hematoma, and abscess according to the time of onset (**Table 3**).

Table 2. Predictive factors for post-thyroidectomy hemorrhagic events

Factors	OR	95% CI	P value
Classic ligation vs. energy devices	1.216	0.728–2.030	0.456
Male sex	1.530	0.848–2.758	0.157
Surgeons' experience <3.5 year	1.778	1.043–3.030	0.034
Age ≥55 years	1.812	1.059–3.100	0.030
Body weight ≥60 kg	1.857	1.051–3.282	0.033
Stage III and IV	4.795	1.744–13.185	0.002
Procedures by Surgeon X	9.629	4.552–20.373	0.000

OR = odds ratio; CI = confidence interval.

Table 3. Differences among types of hemorrhagic events (n=74)

Patients	Pseudo-hemorrhage (n=2)	Hemorrhage (n=41)	Hematoma (n=26)	Abscess (n=5)
Body weight (kg)				
Mean±standard deviation	91.5±4.9	61.5±9.3	63.3±11.7	60.5±18.8
Surgeon's carrier (yr)				
Median (range)	3.5 (3–4)	5.0 (0–26)	4.0 (0–31)	13.0 (9–14)
Time to the onset (hr)				
Median (range)	1.0 (0.8–1.2)	8.2 (0.1–274.8)	16.0 (7.9–183.5)	91.9 (48.0–376.1)
Hospital stay (day)				
Median (range)	5 (4–6)	5 (3–35)	5 (2–17)	19 (3–30)
Place of onset				
Recovery room	0 (0.0)	3 (7.3)	0 (0.0)	0 (0.0)
Ward	2 (100.0)	31 (75.6)	24 (92.3)	2 (40.0)
After discharge	0 (0.0)	7 (17.1)	2 (7.7)	3 (60.0)

Data are presented as number (percentage) not otherwise specified.

Pseudo-hemorrhage was previously defined as disruption or opening of the wound although there was no hemorrhage. The symptoms of airway obstruction were very similar to those associated with hemorrhage. The 2 patients with pseudo-hemorrhage had body weights (88 and 95 kg) greater than the body weights of patients from the other groups (mean 91.5 kg, $P=0.038$). We assumed that short, wide, and deep neck on heavy patients was easier to mistake for true hemorrhage rather than on normal-weight patients with normal body weight. Moreover, the frequency of pseudo-hemorrhage was high among procedures performed by surgeons with lower amount of experience (below 3.5 years, $P=0.049$). In the first case, pseudo-hemorrhage occurred at 51 minutes after the operation due to rapid infusion of antacids (operated upon by surgeon 4). In the second case, it occurred at 70 minutes after the operation due to seizure attack in a patient with epilepsy (operated upon by Surgeon X) (**Table 3**). The surgeons misdiagnosed these cases as true hemorrhage and executed opening the wound and tracheal intubation in the ward. However, there was no hemorrhage and we removed the tube 1 or 2 hours later. The wound was sutured immediately.

We experienced five cases of postoperative abscess from 2017 to 2019. It was observed in the ward or in the outpatient unit at 2–15 days after the surgery (median: 3.8 days). These patients had undergone extended surgeries such as mediastinal or lateral neck dissection and tracheoesophageal resection. We administered antibiotics only once before the surgery in case of extended surgeries. However, it was increased to 2 days after the surgery in procedures more extensive than total thyroidectomy.

6. Time pattern of hemorrhagic events

The time to the onset of hemorrhagic events was analyzed using Mann-Whitney U test and Kaplan-Meier analysis. It was 8.2 hours for hemorrhages and 16.0 hours for hematomas. The time to the onset of hemorrhages was lower than the time to the onset of hematomas, but the difference was not statistically significant (log-rank $P=0.136$, **Fig. 2A**).

The time to the onset of pseudo-hemorrhage was below 1.0 hour and was significantly lower than that for other events. The median time to the onset of abscess was 91.9 hours and 60% of these events occurred after discharge. The time to the onset was significantly lower in pseudo-hemorrhage and significantly higher in abscess than in true hemorrhage or hematoma (log-rank $P=0.000$, **Fig. 2A**).

The time to locate the hemorrhagic focus was lowest in cases of arterial bleeding, followed by those of venous bleeding, bleeding of muscular origin, and isolated hematoma. However, the difference was not statistically significant (log-rank $P=0.401$, **Fig. 2B**). The time to the onset of a

Fig. 2. Time to the onset of hemorrhagic events after the initial surgery.

(A) The time to onset was 8.2 hours for hemorrhages and 16.0 hours for hematomas, but was not statistically different (Log-rank $P=0.136$). The time to onset of pseudo-hemorrhage was below 1.0 hour and was significantly lower. The median onset-time of the abscess was 91.9 hours and 60% of them have occurred after discharge. (B) The time to onset was lowest in cases of arterial bleeding, followed by those of venous bleeding, bleeding of muscular origin, and isolated hematoma. However, the difference was not statistically significant (log-rank $P=0.401$). (C) The time to the onset was the shortest in hemorrhages occupying both deep and superficial layers (mixed), followed by those involving deep layers and those involving superficial layers (log-rank $P=0.041$).

hemorrhagic event was the shortest in hemorrhages occupying both deep and superficial layers (combined), followed by those involving deep layers and those involving superficial layers, with statistically significant differences among these three groups (log-rank $P=0.041$, **Fig. 2C**).

7. Characteristics of hemorrhage and hematoma

The differences in bleeding foci, occupied layers, airway obstruction, and the place of onset of are depicted in **Fig. 3**. It describes the 67 patients including 41 hemorrhage and 26 hematoma patients, after excluding two pseudo-hemorrhage and five abscess patients. In the figure, the upper panels indicate hemorrhage, the middle panels indicate hematoma, and the lower panels indicate both events. Among hemorrhagic events, 34% of the events had arterial foci, 27% had venous foci, 27% had hemorrhagic foci of muscular origin, and 12% had unidentified bleeding foci. Among the total sample, 21% of the events had arterial foci, 17% had venous foci, 16% had hemorrhagic foci of muscular origin, and 46% had no obvious hemorrhagic foci (**Fig. 3C**).

Fig. 3. Bleeding foci, occupied layers, airway obstruction, and place of onset among 41 patients with hemorrhage and 16 patients with hematoma. The upper panels indicate hemorrhage, the middle panels indicate hematoma, and the lower panels indicate both events.

We have previously identified that a combined hematoma occupying both superficial and deep layers exhibits early onset and severe airway obstruction (**Fig. 2C**). Altogether, 42% of the hemorrhagic events, 4% of the hematomas, and 27% of both events showed occupation of both superficial and deep layers (**Fig. 3**).

In terms of symptoms related to airway obstruction, mild obstruction was defined as mild symptoms of airway obstruction that allowed immediate airway intubation without opening the wound. Severe obstruction was defined as more than two attempts of airway intubation or the need for opening the wound before intubation. Altogether, among the 67 patients of hemorrhagic patients, 28 (41.8%) patients complained of swelling without dyspnea, 5 (7.5%) complained of mild dyspnea, 20 (29.9%) complained of moderate dyspnea, and 4 (6.0%) complained of severe obstruction. Extremely severe airway obstruction was defined as significantly reduced oxygen saturation, cyanosis, or the need for cardiopulmonary resuscitation. Failure to provide proper treatment could lead to death. This situation was observed in 17.9% (12/67) of the cases and there was one mortality case in 2012.

Most of the events occurred in the wards (82.1%, 3/67) or in the recovery room (4.5%, 3/67). However, a significant proportion (13.4%, 9/67) of events occurred after discharge at home, on the road, or in the dialysis chamber of another hospital.

8. Specific underlying diseases and mortality

Some of the included patients had chronic renal failure, hemophilia B, acquired immunodeficiency syndrome, or natural killer/T-cell lymphoma. In a patient with hemophilia B, factor IX deficiency was confirmed after third hemostatic operation. The patient was stabilized after the fourth operation with transfusion and factor IX replacement.

A single death was reported among 74 patients (1.35%) with post-thyroidectomy hemorrhage in October 2012. The patient was a 70-year-old male with no specific underlying disease. Surgeon 1 and 5 co-operated him for about 4 hours through total thyroidectomy, left lateral dissection after ligation of the jugular vein, and proved to T3bN1b classic papillary cancer. He died in the intensive care unit at 30 days after the initial surgery.

DISCUSSION

From 1999 to 2019, the incidence of hemorrhage significantly decreased from 1.7% to 0.1%, but the incidence of hematoma remains constant within 0.1%–0.4% incidences, and the abscess was increased from 2017 to 2019. Rates of hemorrhage, or other complications such as hypoparathyroidism or voice change decreased dramatically, but these complications were not eliminated completely.

Among patient-related risk factors, age above 55 years, male sex, body weight above 60 kg, large thyroid, and advanced stages were independent risk factors for hemorrhagic events. However, unlike the results of some previous studies (5-7,21), the type of operation and BMI were not independent risk factors for hemorrhagic events. Since Asians weigh less than other races, we had to set new BMI standards and cut-off values. However, we could not find any inflection point in the ROC analysis (AUC=0.511). We cautiously assumed that this trend might persist in future studies, especially in studies involving Asian population. However, we await the results of further studies.

Other institutions reported a hemorrhage or hematoma incidence of 0.72% after endoscopic thyroidectomy. Age above 35 years, lateral compartment dissection, and main video trocar cavity were reported as the risk factors (22). However, there were no incidences of hemorrhage or hematoma in our institutions.

Among the surgery-related or surgeon-related factors, the incidence of hemorrhagic events associated with the classic ligation method was two times the incidence associated with the use of energy devices in the univariate analysis (0.6% vs. 0.3%, $P=0.021$). However, Cox regression analysis showed no differences between these ligation methods in terms of associated hemorrhagic events (OR=1.2; $P=0.456$).

Surgeons' volume had a considerable effect on the overall complication rate of thyroid surgery when compared with the hospital volume (18). Procedures performed by Surgeon X were associated with a nearly three to five times higher number of hemorrhagic events than

the procedures by other 6 surgeons who experienced a 0.3%–0.6% incidence of hemorrhagic events with no significant differences among them.

There are various ways to analyze a surgeon's ability for him/her to be considered a highly experienced specialized endocrine surgeon. These may include a large number of surgeries, lower complication rate, higher amount of experience, and lower recurrence rate. We investigated surgeons' experience with respect to the hemorrhagic events alone and the cut-off value was 3.5 years. The risk of hemorrhagic events associated with experience below 3.5 years was three times the risk associated with greater amount of experience (OR=1.77 in the Cox analysis).

Two cases of pseudo-hemorrhage occurred in 2009 and 2013 due to rapid infusion of antacids and epileptic seizure, respectively, immediately after arrival at the ward. The wounds were immediately opened at the bedside in the ward, but there was no hemorrhage. We deliberated about excluding these cases from the present study. However, we believed that discussion about these cases might help other surgeons prevent malpractices related to pseudo-hemorrhage.

There are many controversies regarding the use of antibiotics in endocrine surgery. We administered antibiotics only once before the surgery in procedures more extensive than total thyroidectomy. However, they were expanded to 2 days after the surgery in procedures more extensive than total thyroidectomy. It is important to operate delicately and to ensure appropriate asepsis (23), but we would like to conduct further research to determine if increased frequency of antibiotics can decrease the rate of post-thyroidectomy infection or abscess.

The median time to the onset was 8.2 hours for hemorrhage and 16.0 hours for hematoma, but late bleeding was also observed after normal discharge. Most of the studies have reported that bleeding occurs in the early postoperative period or during the hospital stay (7,11,24) and it could be delayed by approximately 2 to 7 days (7,10). Some authors reported very late hemorrhage, which occurred at 13 days postoperatively even after treatment with oral anticoagulants and low-molecular-weight heparin (2). We experienced two cases of delayed secondary hemorrhage on the seventh and on the tenth day after the operation, respectively. The former case involved a male patient who experienced extremely severe airway obstruction in the dialysis chamber in another hospital. After two failed attempts, intubation was possible after evacuation of the hematoma. The latter case involved a relatively healthy female patient who experienced severe airway obstruction at home. Subsequently, she collapsed in front of the reception desk of an adjacent hospital. Fortunately, airway intubation could be performed at 5 minutes after the onset of symptoms. After the airway was maintained, hemostasis was performed at our institution.

In the present study, 24% of the cases exhibited bleeding deep to the strap muscles, 34% showed bleeding superficial to the muscles, and 42% showed involvement of both the layers. The number of cases involving the superficial as well as the deep layers was greater than that reported in other studies. The pattern of involvement showed greater and statistically significant correlation with airway obstruction than the focus of hemorrhage or hematoma. This result was consistent with those of previous studies (5,9).

Some studies have reported that in selected cases, it is possible to discharge the patient on the day after the surgery on an outpatient basis without further hospitalization. However,

other studies do not recommend routine outpatient or same-day thyroidectomy (5,10). Similarly, we do not recommend routine outpatient thyroidectomy.

This study has several limitations. First, history of diabetes and hypertension was reviewed, but factors associated with hemorrhage such as antiplatelet therapy, anticoagulation agent, or topical hemostatic agent used in the surgical field were not reviewed. Second, pseudo-hemorrhage and abscess were included in this study, because these were important on analysis in event onset-time. We presumed that pseudo-hemorrhage means the false-positiveness on hemorrhage and abscess could develop if infection occurs while observing small hematoma. Finally, unlike previous western studies, analysis of benign diseases such as grave's disease or thyroiditis is a little lacking.

CONCLUSION

Although several risk factors for post-thyroidectomy hemorrhagic events were identified in this studies, the incidence is extremely low. We believe that it is impossible to predict the possibility of hemorrhagic events before or even after the surgery. Delicate and careful ligation as well as proper hemostasis in a surgery constitute the ideal approach even in a simple operation.

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