Routine outpatient thyroid surgery cannot be recommended

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ABSTRACT

INTRODUCTION: More than 1,100 thyroid operations are performed annually in Denmark. The major concern regarding outpatient thyroid surgery (OTS) is post-thyroidectomy bleeding (PTB), which may cause compression of the trachea and compromise respiration. We aimed to explore the incidence of PTB and the exact timespan from surgery to PTB, and to identify risk factors for PTB in order to discuss whether OTS can be considered safe.

METHODS: Data from the Ear-Nose-Throat Department, Aarhus University Hospital, covering the period from January 2001 to August 2013 were collected from the THYRKIR database, and the medical records of patients with PTB were reviewed.

RESULTS: A total of 42 (2.8%) patients were re-operated due to PTB. Multivariate logistic regression analysis identified male gender (odds ratio (OR) = 1.85) and thyrotoxicosis (OR = 2.68) as risk factors for PTB. PTB occurred within 6 h of surgery in 63% of cases, between 6 and 24 h in 25% of cases, and more than 24 h after surgery in 13% of cases. One patient required urgent reoperation due to acute respiratory insufficiency.

CONCLUSION: Although a rare event, PTB is potentially life-threatening, and unselected routine OTS cannot be considered safe. Until more studies have been conducted on the selection of patients suitable for OTS, we recommend, as a minimum, that patients are observed for at least 6 h after surgery and subsequently stay at a nearby hospital hotel until discharge 16 to 24 h postoperatively.

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TRIAL REGISTRATION: The study was approved by the Danish Data Protection Agency (1-16-02-170-14).

More than 1,100 thyroid operations are performed at Danish ear-nose-throat departments annually, and the number is increasing [1]. Traditionally, thyroid surgery is performed as an inpatient procedure. In order to increase health-care productivity, some centres have experimented with outpatient thyroid surgery (OTS) [2, 3]. Initial studies show favourable patient acceptance and financial benefits compared with inpatient surgery [2].

Complications to thyroid surgery include recurrent laryngeal nerve injury, hypothyroidism, hypoparathyroidism, infection and haemorrhage. Post-thyroidectomy bleeding (PTB) (**Figure 1**) and hypocalcaemia are the complications that cause most concern when considering the safety of OTS. However, acute post-operative hypocalcaemia is almost exclusively an issue after total thyroidectomy, which only comprised 19% (223/1,159) of thyroid surgery patients in 2013. Hence, the major obstacle for converting a significant number of thyroid surgeries into an outpatient regimen is PTB, which may cause compression of the trachea and compromise respiration [4].

The aims of the study were to examine the incidence of and risk factors for PTB in patients treated at our department. Furthermore, we aimed to explore the exact timespan from surgery to acknowledgement of haemorrhage. Finally, on the basis of our results and previous studies, we discussed whether OTS may be considered safe.

METHODS

The study was based on data reported prospectively by thyroid surgeons to the THYRKIR Database. Only patients treated at the Ear-Nose-Throat Department, Aarhus University Hospital, from January 2001 to August 2013, were included.

The patients were divided into two groups. Group I consisted of patients with PTB requiring surgical reoperation. Patients undergoing thyroid surgery who did not require reoperation for haemorrhage were included in Group II.

The following clinical and demographic data were available from the THYRKIR Database: age, gender, previous thyroid surgery, histology, extent of surgery, neck dissection, thyrotoxicosis, use of drainage, weight of gland, bleeding during surgery and intrathoracal involvement. The timespan from surgery to onset of haemorrhage was added in January 2005.

The medical records of patients in Group I were reviewed and additional data were obtained: amount of bleeding during re-operation, initial symptoms of haematoma, the use of anti-platelet or anti-coagulant medication, and the timespan from surgery to acknowledgement of haemorrhage.

Patients taking anti-platelet and anti-coagulant medication were advised to pause this medication at least three days prior to operation.

Statistical analyses were performed using the χ^2-

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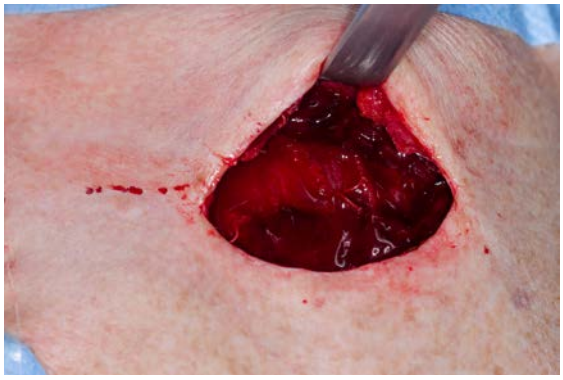
FIGURE 1

Post-thyroidectomy haemorrhage.



and the Fisher's exact test to compare categorical variables. Student's t-test and the Kruskal-Wallis test were used to compare continuous variables between the two groups. Multivariate logistic regression analysis was used on statistically significant risk factors for PTB found in the univariate analyses.

Trial registration: The study was approved by the Danish Data Protection Agency (1-16-02-170-14).

RESULTS

Incidence

During the study period, 1,404 patients underwent partial or complete thyroidectomy at our department. Among these, 108 patients underwent thyroid surgery twice. Thus, the total number of thyroid operations was 1,512. A total of 42 patients (2.8%) had PTB requiring surgical reoperation. Three patients experienced haemorrhage twice.

The number of thyroidectomies increased and the PTB rate decreased significantly during the study period from an annual average of 78 operations in the 2001-2008 period and a PTB rate of 3.9% (24/624) to 178 annual surgeries and a PTB rate of 2.0% (18/888) in the 2009-August 2013 period (p = 0.034, χ^2). The median hospitalisation time was three days (range: 2-16 days) for patients with haemorrhage, and two days (range: 1-90 days) for patients without haemorrhage (p < 0.001, Kruskal-Wallis).

Risk factors

The clinical characteristics of patients with and without PTB are shown in **Table 1**.

In univariate analyses, male gender (odds ratio (OR) = 1.85, 95% confidence interval (CI): 1.00-3.28), thyrotoxicosis (OR = 2.68, 95% CI: 1.24-5.83) and the use of drainage (OR = 4.45, 95% CI: 1.12-38.44) were found to be statistically significantly associated with a higher frequency of haemorrhage. Using multivariate logistic regression analysis on these three variables, male gender and thyrotoxicosis remained significantly associated with an increased risk of haemorrhage (p = 0.019 and p = 0.021, respectively), while the use of drainage was insignificant (p = 0.067).

Bilateral procedures and a higher weight of the excised gland tended to be more common among patients with haemorrhage, but did not reach statistical significance (p = 0.082 and p = 0.073, χ^2 and Kruskal-Wallis, respectively).

Onset of symptoms

Table 2 shows the clinical characteristics of the patients with PTB. The median timespan from surgery to onset of symptoms of haemorrhage was 2 h (range: < 1-96 h). The majority of patients presented with symptoms within the first 6 h (63%), whereas 25% and 13% of patients developed haematoma 6 to 24 h and more than 24 h after surgery, respectively. The median blood loss during reoperation was 300 ml (range: 15-2,000 ml) (only registered in twelve patients).

No statistically significant differences in clinical characteristics were found between the patients with PTB who were recognised less than 6 h after surgery and those in whom haemorrhage occurred more than 6 h after surgery.

Biochemical coagulation data were abnormal in 18% (7/40) of patients with PTB. A total of eight (19%) patients with PTB took anti-platelet medication daily. Six of these patients had paused their anti-platelet medication 3-7 days prior to surgery, while two patients had not paused this medication despite receiving instruction to do so.

Two (5%) patients with PTB had paused their anticoagulant medication (warfarin) 4 and 5 days prior to surgery and both patients were given low molecular weight heparin until the night before surgery. One of these patients had a haemorrhage 92 h after surgery.

In the vast majority of cases, the first signs of PTB were neck swelling and/or haemorrhage from the cicatrice (Table 2). One patient required urgent reoperation due to haematoma-induced respiratory failure. No patients died from complications to thyroid surgery during the study period.

DISCUSSION

Incidence of post-thyroidectomy bleeding

The incidence of PTB varies greatly between studies (0.03-4.2%) (**Table 3**) [1-13]. However, most studies find incidence rates below 2%, and our PTB of 2.8% seems relatively high. Godballe et al [1] found an overall haem-

TABLE 1

Clinical characterisation of patients with (Group I) and without (Group II) post-thyroidectomy haemorrhage and calculated odds ratios for potential risk factors for post-thyroidectomy haemorrhage

Variable	Group I (n = 42)	Group II (n = 1,470)	OR (95% CI)	p-value
Age at operation, yrs, mean (95% CI)	55.8 (51.6-60.1)	53.2 (52.4-54.0)	–	0.279[a]
Sex, n (%)			1.85 (1.00-3.28)	0.044*[,b]
Male	17 (41)	361 (27)		
Female	25 (59)	1,001 (73)		
Previous thyroid surgery, n (%)	4 (10)	157 (12)	0.81 (0.21-2.28)	1.000[c]
Histology, n (%)			1.29 (0.61-2.77)	0.499[b]
Benign	34 (81)	978 (77)		
Malignant	8 (19)	301 (23)		
Extent of surgery, n (%)			0.57 (0.30-1.08)	0.082[b]
Unilateral	29 (69)	1,084 (80)		
Bilateral	13 (31)	271 (20)		
Neck dissection performed, n (%)	3 (7)	140 (10)	0.67 (0.13-2.14)	0.794[c]
Thyrotoxicosis[d], n (%)	7 (18)	58 (7)	2.68 (1.24-5.83)	0.012*[,b]
Use of drainage, n (%)	38 (95)	577 (81)	4.45 (1.12-38.44)	0.021*[,c]
Weight of excised gland, g, mean (95% CI)	44 (8-548)	33 (1-1,250)	–	0.073[e]
Bleeding during surgery, ml, mean (95% CI)	50 (10-1,600)	40 (2-4,500)	–	0.086[e]
Intrathoracal involvement, n (%)[f]	9 (21)	260 (19)	1.15 (0.56-2.37)	0.706[b]

CI = confidence interval, OR = odds ratio.
*) $p < 0.05$, i.e. statistically significant.
a) Student's t-test; b) χ^2-test; c) Fisher's exact test; d) Use of anti-thyroid medication prior to surgery; e) Kruskal-Wallis test; f) Because of the structure of the database, patients without intrathoracal involvement also includes patients without this information (n = 77).

orrhage frequency of 4.2% in a national Danish study, with a wide variation between individual departments. In the present study, the frequency of haemorrhage may have been influenced by the fact that patients with thyrotoxicosis, malignancy, intrathoracal involvement, extensive surgery and previous thyroid surgery are relatively frequent at our department. The PTB rate decreased significantly (from 3.9% to 2.0%) as the number of surgeries rose over time.

Risk factors for post-thyroidectomy bleeding

A multivariate analysis identified two statistically significant risk factors for PTB: male gender and thyrotoxicosis. Previous studies have also found male gender and thyrotoxicosis to be associated with an increased risk of PTB [1, 4, 6, 13]. In the univariate analysis, the use of drainage was significantly associated with an increased risk of haemorrhage. Most likely, drainage was used more often in patients with large or thyrotoxic glands, and drainage is a quasi-variable for other factors associated with increased risk of haemorrhage and not a real risk factor. A Cochrane meta-analysis found no significant influence of the use of drainage on the frequency of PTB [14].

Previous studies have identified other risk factors for PTB including higher age [1, 6], malignant histology [1], bilateral surgery [1,4], extent of resection (total or near-total thyroidectomy) [4], previous thyroid surgery [4, 5] and size of dominant nodule [5]. However, in other large studies no risk factors for PTB were found [7, 9, 12, 15]. Although an increased risk of haemorrhage after surgery in other organs has been found in patients taking anti-coagulant medication [16], previous studies on thyroid surgery have not identified any such association [9, 12].

TABLE 2

Characteristics of 42 patients with post-thyroidectomy haemorrhage.

	% (n/N)
First sign of haematoma	
Neck swelling/secretion from the cicatrice	95 (37/39)
Dyspnoea	3 (1/39)
Excessive bleeding from drain	3 (1/39)
Anti-platelet medication	21 (8/39)
Anti-coagulative medication	5 (2/39)
Time from surgery to onset of haemorrhage, h	
< 6	63 (25/40)
6-24	25 (10/40)
> 24	13 (5/40)

Onset of symptoms

We found that the majority (63%) of haemorrhages requiring reoperation occurred within 6 h after surgery, which is similar to the findings in most other studies (Table 3) [4, 5, 9, 10, 12]. However, some studies found that a considerable proportion (18-90%) of patients had on-

TABLE 3

Studies in the time from surgery to onset of post-thyroidectomy bleeding and recommendations concerning outpatient thyroid surgery[a].

Reference	Operations, n	Time period	Study design	PTB frequency, %
Burkey et al, 2001 [9]	13,817	1976-2000	Retrospective case-control, single institution	0.3
Abbas et al, 2001 [15]	1,268	1995-1999	Retrospective cohort, single institution	0.7
Materazzi et al, 2007 [3]	1,571	2001-2004	Retrospective cohort, single institution	0.6
Rosenbaum et al, 2008 [10]	1,050	1990-2007	Retrospective cohort, single institution	0.6
Leyre et al, 2008 [12]	6,830	1991-2006	Retrospective case-control, single institution	1.0
Lee et al, 2009 [17]	1,040	1998-2008	Retrospective cohort, single institution	1.0
Godballe et al, 2009 [1]	5,490	2001-2007	Prospective cohort, nationwide	4.2
Snyder et al, 2010 [2]	1,242	2003-2009	Retrospective cohort, single institution	0.4
Promberger et al, 2012 [4]	30,142	1979-2008	Retrospective cohort, single institution	1.7
Lang et al, 2012 [5]	3,086	1995-2011	Retrospective cohort, single institution	0.7
Dixon et al, 2014 [11]	4,140	1996-2013	Retrospective cohort, single institution	0.4
Stack et al, 2013 [7]	38,362 OTS 54,373 inpatient	2005-2010	Retrospective cohort, 175 departments	0.03 OTS, 1.88 inpatient
Present study	1,512	2001-2013	Prospective and retrospective, single institution	2.8

ASA = American Society of Anesthesiologists; OTS = outpatient thyroid surgery; PTB = post-thyroidectomy bleeding.
a) Outpatient thyroid surgery means discharge within 6 h of surgery.
b) ≤ 24 h.

set of symptoms of haematoma development later than 6 h after surgery [1, 2, 4, 5, 9-12, 15, 17]. The key question when considering OTS is if patients with haemorrhage occurring more than 6 h after surgery experience acute respiratory failure and thus require urgent reoperation. In the present study, only one patient was identified with acute respiratory distress (2 h after surgery). However, it is possible that more patients required urgent reoperation as this information was not clearly described in all medical records.

Burkey et al found that 50% of patients with haemorrhage after thyroid or parathyroid surgery presented with respiratory distress [9]. The timespan from surgery to onset of symptoms ranged from less than 1 h to 16 h. Dixon et al [11] reported two patients with PTB requiring urgent reoperation, both within a few hours after surgery. Promberger et al [4] found that 1.7% (9/519) of patients with PTB required urgent intervention due to acute respiratory problems. The median timespan from skin closure to onset of symptoms was significantly longer in these patients with acute respiratory failure than in other patients with PTB (330 versus 100 minutes, respectively).

Three of these nine patients died from respiratory

Time from surgery to onset of haemorrhage, %				
< 6 h	**6-24 h**	**> 24 h**	**Recommends OTS**	**Remarks**
43	38	19	No	42 patients with PTB were matched with 42 patients without PTB concerning age, gender, type of surgery and year of operation Both thyroid and parathyroid surgery Against OTS: no risk factors were found
10	50	40	Inconclusive, but caution with OTS	Both thyroid and parathyroid surgery Against OTS: no risk factors were identified Be aware of late PTB (90% of PTB after 6 h)
–	–	0	Same-day discharge in selected patients	Selection for same-day discharge from a cohort of 6,651 patients Criteria: primary neck surgery, euthyroid, gland size < 80 ml, no malignancies, or intra-thoracic goitre Social criteria: autonomy post-discharge, possession of a telephone, suitable living situation, and adequate home support Favouring same-day discharge: no PTB were diagnosed after 10 h of surgery Safe, effective, and favourable patient acceptance
66	17	17	Yes	Both thyroid and parathyroid surgery Recommends OTS if unilateral surgery and if anti-platelet and anti-coagulant medicine is not prescribed Recommends observation for 23 h if bilateral thyroidectomy Favouring OTS: potential for reduced hospital stay and financial benefits
53	37	10	No	Seventy patients with PTB were matched with 210 patients without PTB concerning age, gender, type of surgery, and year of operation Against OTS: no risk factors were identified Be aware of late PTB (47% of PTB after 6 h)
50	50	0	Inconclusive	Different clinical patterns between cases of superficial haemorrhage (ecchymosis) and deep haemorrhage (airway obstruction) can be used to quickly determine the diagnosis and severity
97[b]	3	No		Against PTB: be aware of late PTB
40	40	20	Yes	Selection criteria for OTS: unilateral surgery, age < 60, and ASA score < 3 Favouring OTS: favourable patient acceptance and the potential for substantial health-care cost savings
81	17	2	Same-day discharge in selected patients	Criteria for same-day discharge: unilateral surgery In 2 (0.4%) patients the bleeding occurred directly after removal of the Redon drain Favouring same-day discharge: no PTB after 20 h of surgery in selected patients Potential for economic benefits
73	27	0	No	Against PTB: be aware of late PTB (27% of PTB after 6 h)
39	39	22	Yes	Both thyroid and parathyroid surgery Favouring OTS: no acute airway obstruction caused by PTB occurred after 6 h of surgery
–	–	–	(Yes)	Defines “outpatient” as discharge within 24 h OTS were primarily hemi-thyroidectomy, female, and younger patients Favouring OTS: significantly cheaper than inpatient surgery
63	25	13	No	Against OTS: be aware of late PTB (38% of PTB after 6 h), no well-defined selection criteria

failure (overall thyroidectomy mortality rate: 0.01% (3/30,142)). Schwartz et al [16] calculated that for every 100,000 thyroidectomies performed, 94 deaths secondary to post-operative bleeding could potentially be prevented by a 24-h hospitalisation compared with a 6-h observation.

Limitations

Our study carries several limitations. Some potential risk factors (anti-platelet and anti-coagulation medication, coagulation status) for PTB were not included in the THYRKIR Database and, due to the number of patients, they were only retrieved from the medical records of patients with PTB. Hence, no statistical calculations concerning these factors could be made and the relevance of these factors is largely uncertain. Moreover, the dataset in the THYRKIR Database was incomplete (for instance the use of anti-thyroid medication was only registered for 58% of the patients), which may bias our results on risk factors.

The number of patients with PTB is relatively low, especially when sub-stratifying into three categories on the basis of timespan from surgery to acknowledgement of haemorrhage. Thus, our recommendations concern-

ing the safety of outpatient thyroid surgery are primarily based on previous studies and to a much lesser extent on our findings in the present study.

Outpatient thyroidectomy

Hospitalisation for 24 h after thyroidectomy is recommended by most previous researchers [3, 4, 18]. Although some PTB present more than 24 h after surgery, no studies report cases with urgent reoperation for haematoma later than 16 h post-operatively [9]. Thus, late onset PTB seems to be safely managed subacutely. Infrequently, acute reoperation due to respiratory failure is required later than 6 h after surgery. Hence, we find that routine OTS cannot be recommended. However, it remains unexplored if patients requiring urgent reoperation have significant risk factors associated with PTB and if careful selection of low-risk patients is feasible.

Several authors report that OTS is safe in selected patients (Table 3) [2, 7, 10, 11, 19]. Rosenbaum et al [10] found that unilateral surgery was safely performed as OTS with discharge only 4 h post-operatively. Snyder et al [2] selected patients for OTS on the basis of co-morbidities and anticipated less extensive surgery. However, in the only prospective study performed, Godballe et al [1] did not recommend OTS due to the risk of late PTB.

The American Thyroid Association (ATA) has recently published a meta-analysis and consensus statement on the eligibility criteria for OTS [20]. They concluded that a variety of comorbidities (among others uncompensated cardiac or respiratory disease, dialysis-dependent renal failure, anti-coagulant or anti-platelet therapy, etc.) may be considered relative contraindications to OTS. The ATA also advises that inpatient care after thyroidectomy is favoured by social factors such as communication and language barriers, challenges in transportation and lack of family/friend support.

Thus, at present, it seems difficult to prepare precise guidelines for the selection of patients suitable for OTS based on scientifically supported criteria. However, both factors associated with an increased risk of PTB (male gender and thyrotoxicosis) as well as social factors are important to take into consideration.

CONCLUSION

In light of the fact that PTB infrequently develops more than 6 h after surgery (some with fatal outcome) and as risk factors associated with severe, sudden and late onset PTA are not well-described, routine OTS cannot be recommended. Selection criteria for OTS have previously been suggested, but additional research is warranted. As PTB requiring urgent reoperation can develop up to 16 h post-operatively, we recommend that patients undergoing thyroid surgery be observed for at least 16 h or, as a minimum, for 6 h followed by a stay at a nearby hospital hotel until clinical examination and discharge 16 to 24 h after surgery.

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