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Randomised controlled trial of in- versus out-patient management of benign hemithyroidectomy

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ABSTRACT

INTRODUCTION. Outpatient (OPT) thyroid surgery is increasing, with patient selection being pivotal for safety. While numerous studies exist, most are retrospective and encompass both benign and malignant cases.
METHODS. We conducted a randomised clinical trial on patients undergoing hemithyroidectomy for benign thyroid disease. Participants were assigned to OPT or inpatient groups. We collected data on complications, failure to discharge on surgery day, post-operative pain, nausea, sleep quality and patient satisfaction.

RESULTS. Among 97 patients, 27.5% (14/51) in the OPT group could not be discharged on the day of surgery due to minor complications, primarily nausea (36%) and neck swelling (29%). No reoperations were needed. Though OPT patients exhibited a higher rate of minor complications (29%), they reported less post-operative nausea, better sleep and a faster return to normal activity.

CONCLUSIONS. Discharge on the day of surgery is not always possible with OPT thyroid surgery. However, our findings suggest that OPT hemithyroidectomy for benign cases can be both safe and feasible for a selected group of patients.

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Throughout the past century, the prevalence of outpatient (OPT) surgery has seen a significant rise. Advances in surgical and anaesthetic techniques have transformed procedures that once demanded days of inpatient (IPT) care into feasible OPT procedures [1]. This shift enhances resource utilisation while offering cost benefits. For instance, when thyroid procedures are conducted in an OPT setting, a documented 10-30% cost reduction is achieved [2]. However, paramount to these advantages is ensuring that patient safety is not compromised.

Historically, hemithyroidectomy was approached as an IPT procedure. This was largely due to the risk of potentially life-threatening post-operative haemorrhage, hypocalcaemia and paralysis of the recurrent laryngeal nerve (RLN) [3]. However, the occurrence of these risks is rare in hemithyroidectomies, rendering this procedure potentially safe as OPT [4].

Several studies have shown an increase in OPT thyroid surgery in recent decades, with the majority of studies agreeing that careful preoperative patient selection is crucial [5, 6]. In 2013, the American Thyroid Association suggested eligibility criteria for OPT thyroid surgery [5], and OPT thyroidectomy has become common in many US hospitals [7]. Europe, however, has embraced this trend more gradually [6]. Despite the global increase in OPT, many surgeons still abstain from performing hemithyroidectomy as an OPT procedure due to safety concerns. As healthcare systems and cultures differ, it is essential to perform trials investigating the applicability and safety of hemithyroidectomy in a European context.

We conducted a randomised clinical trial with patients undergoing hemithyroidectomy for benign thyroid disease, allocating them to either an IPT or OPT procedure. Our primary objective was to assess the rate of discharge failures in an OPT setting, defined as conversion to IPT or readmission within 24 hours, and to evaluate the complications leading to failure, especially post-operative haemorrhage. Furthermore, we aimed to evaluate patient-related outcome measures at the level of post-operative pain, nausea and, finally, acceptance of and satisfaction with the IPT or OPT procedures.

METHODS

This randomised, parallel group, non-inferiority study was approved by the local regional ethical committee (-495) and registered with clinicaltrials.gov (NCT02891252). The inclusion and exclusion criteria are listed in **Table 1**. Hemithyroidectomies were performed by seven experienced thyroid surgeons using Kocher's incision, Nerve Integrity Monitor and standardised closure techniques. Choice of surgical instruments, including LigaSure and Surgicel, was at the surgeon's discretion. Drains were placed if necessary, converting OPT to IPT.

TABLE 1 Inclusion and exclusion criteria, and outcome measures.

Inclusion criteria
Age between 18 and 70 yrs, both included Normal OPT criteria of the hospital: ASA ≤ 2 An adult person should be able to stay with patient on the night of surgery Euthyroid Normal function of vocal cords preoperatively Living within a 30-km radius or a 45-min. drive from the hospital Fluent in spoken and written Danish
Exclusion criteria
Suspicion of malignancy Previous thyroid or other major neck surgery Intrathoracic thyroid gland Former treatment with radioactive iodine Anticoagulation treatment: low-dose acetylsalicylic acid adenosine diphosphate receptor inhibitors were accepted, if paused pre-operatively 3 and 7 days, respectively Any deviation from this was up to the surgeon and was registered
Outcome measures
Primary:
Percentage of patients who were converted to IPT and/or readmitted < 24 hrs are < 20% in the OPT group
Secondary:
Patient acceptance to OPT procedure from patient satisfactory questionnaire Difference in post-operative haemorrhage Difference in mean level of NRS pain scores at rest based on measurements at 2 a.m. and 8 p.m. on POD0 and at 8 a.m. and 8 p.m. on POD 1 Difference in mean level of NRS pain scores during swallowing of saliva based on measurements at 2 a.m. and 8 p.m. on POD0 and at 8 a.m. and 8 p.m. on POD 1 Difference in mean levels of NRS nausea at 2 h, 8 p.m. (POD 0) and at 8 a.m. and 8 p.m. (POD1) Difference in NRS-rated quality of sleep and level of tiredness at 8 a.m. on POD1

ASA = American Society of Anesthesiologists classification; IPT = inpatient; NRS = numeric rating scale; OPT = outpatient; POD = post-operative day.

Preoperative medication included oral celecoxib 200 mg and paracetamol 1,000 mg. Anaesthesia was standardised using propofol and remifentanil infusions. Dexamethasone 16 mg, administered intravenously (i.v), was used for both pain and as anti-emetic prophylaxis, together with ondansetron i.v. 4 mg. Post-operatively, patients were transferred to the post-anaesthesia care unit (PACU) and received i.v. oxycodone as needed for pain. In the ward, standard observation and pain relief were provided. Discharge followed the department's OPT criteria, with the doctor in charge assessing each patient. All patients were observed for a minimum of six hours and had a fibreoptic laryngoscopy prior to discharge.

Primary and secondary outcomes are described in Table 1. Patient-related outcome measures (PROM) were registered by the patients using a numeric rating scale (NRS 0-10), including pain, nausea, sleep and fatigue. Vomiting episodes and opioid administration were noted at the PACU. Additional PROMs included NRS-rated satisfaction and days until patients could resume normal activity (questionnaire in the supplementary material https://content.ugeskriftet.dk/sites/default/files/2023-11/a06230377-supplementary.pdf). Complications were

registered retrospectively from the patient's medical records. OPT were defined as discharge on the day of surgery. Failures were defined as OPT converted into IPT or re-admission within 24 hours. Complications were categorised as either minor or major.

Preoperative and perioperative data were recorded, including gender, age, indication for surgery, vocal cord function, anticoagulation use, thyroid-stimulating hormone (TSH), thyroxine (T_4), gland weight, perioperative bleeding, LigaSure use, Surgicel use, surgery time and anaesthesia time.

The power calculation was based on a 20% limit of non-inferiority between the IPT and OPT groups .A total of 86 patients (43 in each group) were required to ensure sufficient power. Block randomisation with a 4:1 female-to-male ratio was used. Randomisation lists were kept in sealed opaque envelopes. Neither patients nor surgeons were blinded during the study. Data were analysed using SPSS version 28.0, with χ^2 test for dichotomous parameters and Student's t-test for continuous parameters. Pearson's correlation was applied across all parameters, considering r values < 0.40 as low or no correlation. Both IPT and OPT groups were analysed as intention to treat.

Trial registration: ClinicalTrials.gov Identifier: NCT02891252

RESULTS

Between May 2016 and November 2021, 97 patients were included (80 women and 17 men); 46 in the IPT and 51 in the OPT group (**Table 2**). Indications for surgery were most often compressive symptoms (48%) and, following the Danish guidelines, if indeterminate cytology or nodule growth was present (16%) (Table 2). No strong correlations were found using Pearson's correlation. No differences were observed in patient demographics or perioperative characteristics (Table 2).

TABLE 2 Patient and perioperative characteristics.

	IPT (n_I = 46)	OPT (n_O = 51)	All patients (N = 97)	p value[a]
Patients				
Age, mean (± SD), yrs	48.9 (± 9.9)	51.8 (± 11.3)	49.8 (± 10.7)	-
Gender, n (%):				
Female	38 (83)	42 (82)	80 (82)	-
Male	8 (17)	9 (18)	17 (18)	-
Indications for surgery, n (%):				
Compressive symptoms	22 (48)	25 (49)	47 (48)	-
Recommended by surgeon[b]	14 (30)	9 (18)	23 (24)	-
Perioperative				
Time spent of, mean (min.-max), min.:				
Surgery	98 (56-154)	95 (55-219)	98 (55-219)	0.91
Anaesthesia	133 (80-188)	128 (65-251)	130 (65-251)	0.54
Use of, n (%):				
LigaSure	25 (54)	22 (43)	47 (48)	0.28
Surgicel	28 (61)	39 (76)	67 (69)	0.07
Gland weight, mean (min.-max), g	31 (5-123)	41 (3-160)	36 (3-160)	0.08
Bleeding, mean (min.-max), ml	32.6 (2-147)	38.2 (5-490)	36 (2-490)	0.61

IPT = inpatient; OPT = outpatient; SD = standard deviation.
a) Student's t-test except for use of LigaSure and Surgicel calculated using χ^2 test.
b) According to the Danish National Recommendations or presence of indeterminate cytology/nodule growth.

Outcome

Overall, complications were reported for 11% of the IPT group and 29% of the OPT group (**Table 3**). We observed three major complications; all were RLN injuries; one definitive and two transient. In the OPT group, 14 patients (27.5%) were converted to the IPT procedure and therefore registered as failures. The majority of failures were due to nausea (36%) and neck swelling (29%). The rate of failures decreased as the study progressed (data not shown). Specifically, 64% of all failures occurred among the first 40 patients included, and 79% of all failures among the first 60 patients. After the inclusion of 80 patients, no additional failures were recorded. None of the patients in either group required reoperation or readmission.

TABLE 3 Post-operative complications and reason for failure in the outpatient surgery group. The values are n (%).

	IPT (n_I = 46)	OPT (n_O = 51)	All patients (N = 97)	OPT failures
Definitive RLN paresis	1 (20)	0	1 (5)	0
Transient RLN paresis	2 (40)	0	2 (10)	0
Wound bleeding	1 (20)	1 (7)	2 (10)	1 (7)
Nausea	0	6 (40)	6 (30)	5 (36)
Vertigo	1 (20)	1 (7)	2 (10)	1 (7)
Pain	0	1 (7)	1 (5)	1 (7)
Drain	0	1 (7)	1 (5)	1 (7)
Neck swelling	0	5 (33)	5 (25)	4 (29)
Total	5 (11)	15 (29)	20 (21)	13 (27)[a]

IPT = inpatient; OPT = outpatient; RLN = recurrent laryngeal nerve.
a) 1 failure attributed to misinformation by staff is not included in this table.

An unsuspected diagnosis of thyroid carcinoma was found in 12% (data not shown).

Overall, 72 patients (74.2%) handed in a complete PROM questionnaire; 69.6% (32/46) in the IPT and 78.4% (40/51) in the OPT group of whom six were failures.

No significant difference was observed in levels of nausea and pain in the two groups upon leaving the PACU (**Table 4**). However, at 8 PM on post-operative day 0 (POD0) and at 8 AM at POD1, the OPT group reported significantly less nausea than the IPT group. Additionally, the OPT group reported better sleep the first night. No other differences were observed.

TABLE 4 Post-operative measurements.

	IPT	OPT	p value[a]
Time until discharge, mean (± SD), hrs	22 (± 4.69)	10 (± 8.96)	< 0.001
Patient-related outcomes reported at PACU before leaving			
Pain at rest, mean (± SD), NRS value	1.78 (± 1.44)	1.58 (± 1.42)	0.82
Pain when coughing, mean (± SD), NRS value	2.22 (± 1.81)	2.38 (± 1.89)	0.69
Nausea, mean (± SD), NRS value	0.33 (± 0.75)	0.27 (± 0.84)	0.76
Vomit episodes, n	0	0	-
Morphine dose, mean (± SD), mg	4.6 (± 6.05)	4.1 (± 5.80)	0.69
Patient-related outcomes POD0			
At 8 p.m., mean (± SD), NRS value:			
Pain at rest	2.06 (± 1.65)	2.69 (± 2.07)	0.56
Pain when swallowing	2.28 (± 1.84)	3.12 (± 2.23)	0.31
Nausea	2.67 (± 3.65)	1.58 (± 2.84)	0.03
Patient-related outcomes POD1			
At 8 a.m., mean (± SD), NRS value:			
Pain at rest	2.11 (± 1.92)	2.00 (± 1.89)	0.87
Pain when swallowing	2.28 (± 2.20)	2.38 (± 1.91)	0.94
Nausea	1.06 (± 2.41)	0.31 (± 0.68)	0.001
Sleep	4.06 (± 2.75)	3.50 (± 2.59)	0.05
Fatigue	3.78 (± 2.91)	3.31 (± 2.48)	0.39
At 8 p.m., mean (± SD), NRS value:			
Pain at rest	2.11 (± 2.00)	1.78 (± 1.92)	0.66
Pain when swallowing	2.22 (± 2.10)	2.23 (± 2.07)	0.95
Nausea	0.50 (± 1.84)	0.27 (± 0.68)	0.06
Satisfaction, mean (± SD), NRS value			
Operation risk information	8.5 (± 3.06)	8.69 (± 3.06)	0.95
Complications risk information	7.61 (± 3.35)	7.85 (± 3.23)	0.63
Would you do the same again?	7.89 (± 3.21)	8.65 (± 3.56)	0.75
Total satisfaction	7.94 (± 2.83)	8.08 (± 3.33)	0.66
Restitution time, mean (± SD), days			
Until normal activity	9.44 (± 5.40)	5.92 (± 3.70)	0.01
Until resuming work	12.72 (± 7.67)	12.50 (± 6.94)	0.95

IPT = inpatient; NRS = numeric rating scale: 1-10 scale, lower is better; OPT = outpatient; PACU = post-operative care unit; POD = post-operative day; SD = standard deviation.
a) Student's t-test.

The OPT group reported significantly fewer days until resuming normal daily activity than the IPT group, 5.9 versus 9.4 days, respectively (Table 4). Both groups reported an equally high level of satisfaction.

DISCUSSION

This randomised study evaluated the feasibility of OPT hemithyroidectomy for benign conditions. A total of 27.5% of the OPT patients in this group failed to be discharged on the same day. However, no severe

haemorrhages or re-operations occurred. The OPT group experienced less post-operative nausea, better first-night sleep and fewer days until resuming normal activity. Patient satisfaction was similar in both groups with no single parameter correlating with complications or discharge failures.

Even though thyroid surgery is increasingly performed as OPT, most studies are retrospective [2, 8] and heterogeneous [2, 3]. By including only benign hemithyroidectomies, this study achieved a homogeneous cohort with a low risk of complications. Careful patient selection is universally agreed upon as essential for OPT thyroid surgery [5, 6], with factors such as proximity to skilled facilities, absence of major comorbidities and appropriate social settings considered [5, 6].

Changing routines may be challenging and are influenced by both cultural norms and distinctive geographical challenges. In Denmark, widespread rural regions and numerous islands, some lacking direct bridge connections, often translate into longer hospital commutes. This can delay crucial post-operative care, especially when winding roads or ferry routes are involved. Such challenges are less pronounced in urban areas with nearby healthcare facilities, making OPT more straightforward. In contrast, rural regions face inherent complexities due to these logistical challenges. Moreover, while OPT is becoming more common globally, its adoption in Denmark may potentially be influenced not just by habit and culture but also by these geographical and infrastructural considerations. In this study, resistance to discharging OPT patients decreased over time, indicating a learning curve for providers. Some neck swelling and mild complications like nausea are expected and may not require hospitalisation. Failure to discharge on the same day is inevitable in some cases, with observed failure rates ranging from 9% to 42% in studies involving only hemithyroidectomies [6]. It must be noted that some institutions discharge patients with drainage. At our department, we do not.

In this study, the average time to discharge for OPT was ten hours. Our protocol mandates a minimum six-hour interval between surgery and discharge, aligning with the practices of several other centres [5, 9-11]. Given the logistical concerns and considering patients' welfare, nighttime discharges are not feasible. To address this, patients participating in the project were typically scheduled as the first surgeries of the day, ensuring that they could be evaluated for discharge during the evening rounds.

Post-operative nausea and vomiting is a common challenge [9]. In this study, 36% of failures were due to nausea despite anti-emetic prophylaxis given as standard treatment. No significant difference in morphine use was found between OPT failures and the remaining OPT group. OPT patients reported less nausea than the IPT group. Neck swelling resulted in 28.6% (four out of 14) failures in our study. Neck swelling was assessed clinically without the use of ultrasound or other measures and decreased in the course of the study period. The doctor in charge was not instructed to evaluate both OPT and IPT patients equally regarding complications, and the higher complication rate in the OPT group may potentially be explained by not reporting minor problems, such as neck swelling, in our IPT patients.

No post-operative haemorrhages occurred, and a recent systematic review supported the low risk in OPT hemithyroidectomies [12]. Surgery time did not differ between groups, suggesting that equally careful haemostasis was employed in the OPT and IPT groups. Patient satisfaction was generally high in the OPT group. While other studies have shown similar results [1, 6, 9], very few have addressed patient satisfaction, and none employed comparable measures.

The strength of this study lies in its randomisation, minimising confounding and selection, allocation and performance bias. However, weaknesses include the 74% return rate for PROM questionnaires, potentially introducing selection bias. The study deliberately employed non-validated questionnaires to enhance patient compliance. Our primary objective was to compare differences between the two groups rather than to obtain absolute scores for broader comparisons with other populations or studies. The study was not blinded and

objective criteria for assessing swelling were lacking. A further limitation of the study is that we did not track the number of patients who chose OPT surgery versus those who declined participation. Additionally, we did not record reasons why patients were deemed ineligible. Such data would have offered valuable insights.

CONCLUSIONS

This study did not demonstrate non-inferiority of OPT compared to IPT hemithyroidectomy. However, no serious complications or reoperations were observed. The failure rate was initially higher, suggesting a transgressive discharge process. Patient satisfaction was high, and no re-admittances were recorded. We suggest that hemithyroidectomy for benign indications is a feasible procedure in an OPT setting for a selected group of patients, given the mild complications and overall satisfaction.

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REFERENCES

1. Doran HE, England J, Palazzo F. Questionable safety of thyroid surgery with same day discharge. Ann R Coll Surg Engl. 2012;94(8):543-7. doi: 10.1308/003588412X13373405384576.
2. AlEssa M, Al-Angari SS, Jomah M et al. Safety and cost-effectiveness of outpatient thyroidectomy: a retrospective observational study. Saudi Med J. 2021;42(2):189-95. doi: 10.15537/smj.2021.2.25686.
3. Seybt MW, Terris DJ. Outpatient thyroidectomy: experience in over 200 patients. Laryngoscope. 2010;120(5):959-63. doi: 10.1002/lary.20866.
4. Rosenbaum MA, Haridas M, McHenry CR. Life-threatening neck hematoma complicating thyroid and parathyroid surgery. Am J Surg. 2008;195(3):339-43. doi: 10.1016/j.amjsurg.2007.12.008.
5. Terris DJ, Snyder S, Carneiro-Pla D et al. American Thyroid Association statement on outpatient thyroidectomy. Thyroid. 2013;23(10):1193-202. doi: 10.1089/thy.2013.0049.
6. Dulfer RR, de Valk KS, Gilissen F et al. Introduction of day care thyroid surgery in a Dutch non-academic hospital. Neth J Med. 2016;74(9):395-400.
7. McLaughlin EJ, Brant JA, Bur AM et al. Safety of outpatient thyroidectomy: review of the American College of Surgeons National Surgical Quality Improvement program. Laryngoscope. 2018;128(5):1249-54. doi: 10.1002/lary.26934.
8. Noel CW, Griffiths R, Siu J et al. A population&;based analysis of outpatient thyroidectomy: safe and under&;utilized. Laryngoscope. 2021;131(11):2625-33. doi: 10.1002/lary.29816.
9. Torfs A, Laureyns G, Lemkens P. Outpatient hemithyroidectomy: safety and feasibility. B-ENT. 2012;8(4):279-83.
10. Jeppesen K, Skjøt-Arkil H, Moos C, Nielsen SH. Outpatient hemithyroidectomy for benign thyroid disease. Dan Med J. 2020;67(10):A03200151.
11. Champault A, Vons C, Zilberman S et al. How to perform a thyroidectomy in an outpatient setting. Langenbeck's Arch Surg. 2009;394(5):897-902. doi: 10.1007/s00423-009-0527-3.
12. Jeppesen K, Moos C, Holm T et al. Risk of hematoma after hemithyroidectomy in an outpatient setting: a systematic review and meta-analysis. Eur Arch Otorhinolaryngol. 2022;279(8):3755-67. doi: 10.1007/s00405-022-07312-y.