

# Annual Report 2009

Scandinavian Quality Register for Thyroid and Parathyroid Surgery

Editor A.Bergenfz

©Anders Bergenfelz

Printed by Media-Tryck, Lund 2010

ISBN 978-91-978553-2-7

# Contents

1. Participating Units	5
2. Coverage	6
3. Quality/Validity	6
4. Reporting	7
5. Feedback	7
6. Quality improvement	7
7. Results (2008)	9
Thyroid	9
Primary Hyperparathyroidism	23
Secondary hyperparathyroidism	37
8. Extended analyses	40
Graves' Disease 2004-2008	40
Primary hyperparathyroidism 2004-2008	47
9. Conclusions	57
Thyroid	57
Parathyroid	57
10. Actions in response to the results (thyroid and parathyroid)	59



# 1. Participating Units

(as of September 1st, 2009)

Sweden:

Department of Surgery, Lund University Hospital  
Department of Surgery, Helsingborg Hospital  
Department of Surgery, Central Hospital, Kristianstad  
Department of Surgery, Halmstad County Hospital  
Department of Surgery, Växjö County Hospital  
Department of Surgery, Ljungby Hospital  
Department of Surgery, Falu Hospital  
Department of Surgery, Uppsala University Hospital  
Department of Otorhinolaryngology, Lund University Hospital  
Department of Surgery, Sunderby Hospital  
Department of Surgery, Karolinska University Hospital, Solna  
Department of Surgery, Västerås Central Hospital  
Department of Surgery, Sahlgrenska University Hospital, Gothenburg  
Department of Surgery, Ryhov County Hospital, Jönköping  
Department of Surgery, Norrland University Hospital, Umeå  
Department of Surgery, Nyköping Hospital  
Department of Surgery, Älvsborg Northern Hospital  
Department of Surgery, Karlstad Hospital  
Department of Surgery, Sundsvall County Hospital  
Department of Surgery, Östersund County Hospital  
Department of Surgery, Örebro University Hospital  
Department of Otorhinolaryngology, Örebro University Hospital  
Department of Surgery, Gävle County Hospital  
Department of Otorhinolaryngology, Karlstad County Hospital  
Department of Surgery, Kungälv Hospital  
Department of Surgery, Borås Hospital  
Department of Surgery, Skövde Hospital  
Department of Otorhinolaryngology, Skövde Hospital  
Department of Surgery, Varberg Hospital  
The Departments of Surgery and Otorhinolaryngology, Ystad Hospital  
Department of Otorhinolaryngology, Blekinge Hospital, Karlskrona  
Department of Surgery, Blekinge Hospital, Karlskrona  
Department of Surgery, Västervik Hospital  
Department of Surgery, Danderyd Hospital

## Other Departments in Scandinavia Using the Same Platform

Denmark:

Department of Surgery, Randers Central Hospital  
Centre for Endocrine Neck Surgery, Ear Nose and Throat Department F, Odense University Hospital  
Department of Surgery, Århus University Hospital  
Department of Surgery, Aabenraa Hospital  
Department of Surgery, Viborg Hospital  
Department of Surgery, Herning Regional Hospital

Norway:

Haukeland University Hospital, Bergen

## 2. Coverage

(as of 1 September 2009)

Coverage in Sweden (based on the 2008 figures from the Epidemiological Division of the Swedish National Board of Health and Welfare) currently corresponds to 76.3% of all units performing thyroid surgical procedures, and 87.1% of units performing parathyroid surgery.

Participating units performed 88.4% of all thyroid surgical procedures and 95.9% of parathyroid surgical procedures. *Major efforts have been made to inform non-participating clinics and departments and the degree of coverage has increased during the year.*

## 3. Quality/Validity

A decision to conduct an audit of the data as an external control was taken during 2005 and this work was initiated in 2006. The audit comprised in part a check that all of the operations performed in these fields were registered and that the registered data was correct (using random sample checks). It is mandatory for all of the registered participating clinics to assist with data validation. The person appointed by the Board to carry out the audit was Professor Staffan Smeds, Linköping, who has a good knowledge of the subject field. The results of the audit were provided to the departments visited and to the Register Board.

Two participating clinics were visited during 2008. The results revealed good data quality. The numbers of patients who were not registered and those erroneously registered were less than 5%.

## 4. Reporting

The participating clinics registered data continuously throughout the year. Data registration was schematically subdivided into three data blocks.

*Block I* comprised basic data, preoperative data, surgery itself and the hospitalisation period until discharge. For data to be able to be saved (including patient data) registration of all data up until the time of discharge from the hospital was required.

*Block II* comprised data from the first follow-up visit following surgery (< 6 weeks postoperative), including histology.

*Block III* comprised long-term follow-up data (6-12 months postoperative).

All patients with complications in the form of hypoparathyroidism or nerve damage must be followed-up beyond 6 months. In addition all patients with primary and secondary hyperparathyroidism must be followed-up beyond 6 months due to the possibility of disease recurrence.

To support both the individual clinics and the administrator, the data register has a function that allows patients with incomplete follow-up data beyond 6 months to be listed.

## 5. Feedback

Online standard reports with graphics can be generated by both the central register administrator and the participating clinics. There are six standard report formats in total: all thyroid patients, thyroid bilateral procedures, Graves' disease, thyroid cancer, primary HPT and secondary HPT.

Standard reports can be selected for different time periods for aggregate data compared with that from individual clinics. Gender-specific, as well as age-specific data can be generated.

Additional statistics can be processed by importing data from Excel files. In the data register there are relevant variables (that are mandatory in order to save individual entries) for the degree of disease severity, the type of disease and known variables for the degree of difficulty of the surgical procedure, which enables a case-mix for individual clinics to be managed using multivariate analyses. In addition, factors described in the literature and those identified in the data register as "confounders" can be taken into account.

The annual report, based on SAS programmed univariate and multivariate analyses as well as graphics, is presented at the annual user meeting and can be viewed on the website, from where it can also be downloaded. In addition, following translation into English, the annual report is also printed and distributed to all of the participating clinics. Presentations at national and international meetings, as well as publications, can be accessed via the register's website after login. Reprints of scientific publications are distributed to the participating clinics.

## 6. Quality improvement

The register was initiated in 2004, which was a pilot year. Database functionalities were tested, bugs corrected and the variables to be included were reappraised. The first year of full operation was 2005.

The number of entries in the register has now reached the point where longitudinal analyses can be performed and in this annual report, an analysis of the development over the last 5 years of the surgi-

cal treatment of primary hyperparathyroidism (pHPT) is followed with a focus on the implementation of new techniques and the results of surgical treatment. Data from the register has previously been presented at a number of both national and international meetings showing that preoperative localisation examinations are performed relatively frequently prior to surgery, but despite this the majority of patients undergo conventional bilateral neck surgery. Longitudinal analyses currently demonstrate that this trend has been broken. An increasing number of patients undergo limited parathyroid exploration (unilateral or minimally invasive operations).

## **Nerve injury in conjunction with thyroid procedures**

During Surgical Week in Stockholm a symposium was held, which was instigated due to the register, on the subject of nerve injury and neural monitoring during thyroid surgery. During the year a number of clinics have introduced EMG monitoring of nerve functioning during thyroid procedures to reduce the risk of complications. In addition, a number of clinics have implemented routine postoperative vocal cord examination in order to reliably follow-up their results.

The Board has also assembled a multidisciplinary group, which will embark on an initiative in 2010 to, if possible achieve a consensus, and national guidelines, on the examination of vocal cord function by laryngoscopy pre and postoperatively in conjunction with thyroid and parathyroid surgery. Recommendations concerning intra-operative nerve monitoring using EMG will also be discussed.

It is of importance in this context that individual clinics are easily able to access their own data online, in the form of text and graphics, and that they therefore have the possibility to compare the results they achieve with aggregate data from the register. This function consequently means that they will be able to follow-up their own results locally and monitor whether the measures implemented give the desired results.

## **Accuracy of preoperative diagnostics in thyroid cancer**

Results from the register have demonstrated that up to 20% of patients who are diagnosed as having cancer as their main diagnosis following thyroid surgery, are not diagnosed preoperatively. Either cytological examination has not been carried out or assessed to be benign. These results precipitated a detailed survey of participating clinics regarding "missed" patient cases.

The results of the survey were presented in conjunction with the 2007 user meeting. Misinterpreted cytology was found to only contribute to preoperatively "missed" cancer diagnoses to a small degree, and only half of the cases had a histological stage of T1 (i.e. small tumours). Ultrasound guided puncture had been used on relatively few patients.

The Board therefore took the initiative in organising a multidisciplinary symposium in conjunction with the Swedish Society of Medicine Annual General Meeting in Gothenburg on 28 November 2008, in collaboration with the Swedish Association of Endocrine Surgeons: "*Can we improve the quality of the investigation of thyroid nodules*".

The Board will follow-up this symposium with an article in the medical press during 2009. In addition the Swedish Association of Pathology and Cytology have been contacted to discuss the standardisation of cytological results from FNA of thyroid nodules, in the form of the categorisation/grading of results in a similar way to the manner that is well established for breast cytology.

Within the southern healthcare region in 2007, guidelines were established for the diagnosis of thyroid nodules. In these guidelines the importance of representative preoperative cytology prior to thyroid surgery is emphasised, as well as the role of ultrasound in the diagnosis of thyroid cancer.



# 7. Results (2008)

The results below have been obtained from the 2008 data.

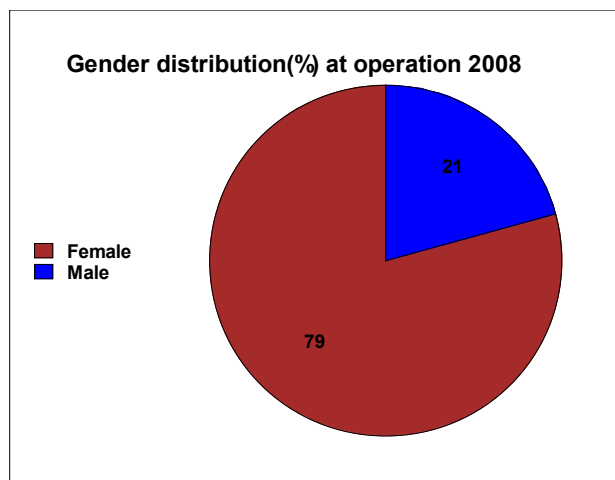
It is important to note in this context that the analysis of the data is based on procedures registered up to and including 10 August 2008. The deadline for the registration of all data from 2008 (including 6 month follow-ups) is 1 October 2009. Based on the experience of previous years it is estimated therefore that there will be more registrations to come before the final date.

## Thyroid

### Gender and breakdown by age

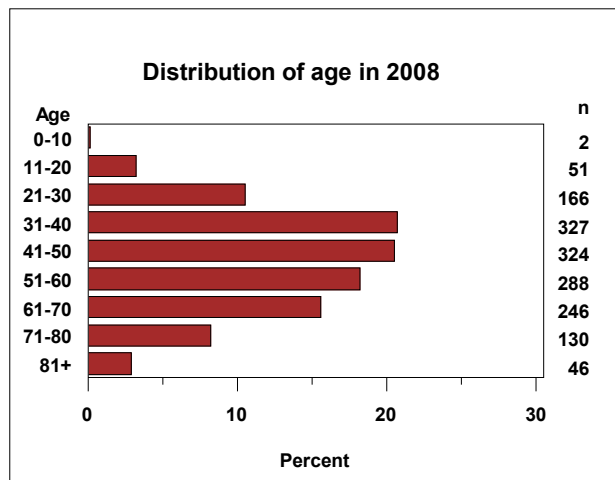
During the year 1580 procedures were registered. Females were, as expected, predominant, comprising approximately 79% of the patients. The female predominance was however slightly less for patients over 60 years of age.

#### Gender distribution for thyroid surgery

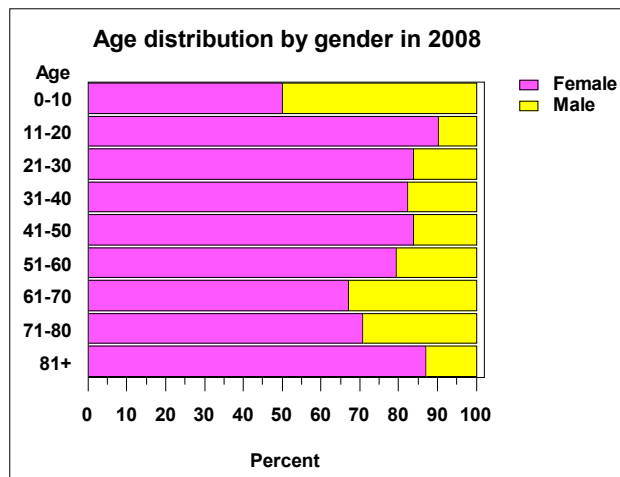


Thyroid operations were mainly performed on patients younger than 60 years of age, with only around 27% of patients being over 60 years old at the time of surgery, and barely 11% of patients being older than 70 years of age. Moreover, 3% were younger than 20 years of age at the time of surgery.

## Age distribution for thyroid surgery



## Age and gender distribution for thyroid surgery



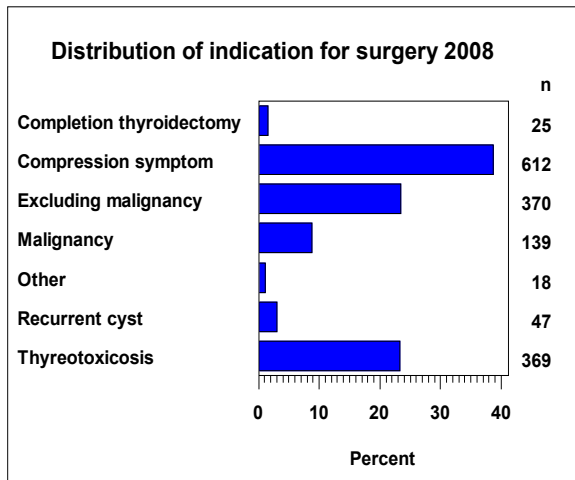
## Intrathoracic goitre and prior thyroid surgery

Intrathoracic goitre was registered for 139 patients (8.7%) and was mainly seen in older patients. 133 patients (8.4%) had previously undergone thyroid surgery. The proportion of patients who had previously undergone thyroid surgery increased markedly with age.

## Indication for surgery

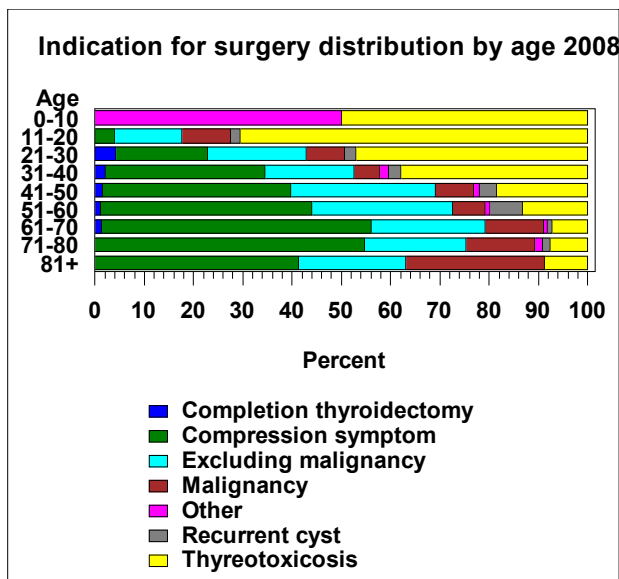
The preoperative indications for thyroid surgery were primarily malignancies (8.8%), to exclude malignancies (23.4%), compression symptoms (38.7%) and thyreotoxicosis (23.4%).

## Indication for surgery



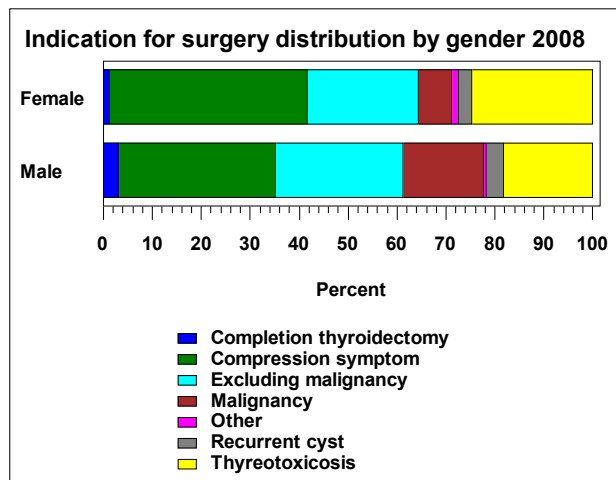
Thyreotoxicosis was a major reason for surgery among younger patients, while operations for compression symptoms increased with age, as did operations for malignancy.

## Age distribution and indication for surgery



In men, an indication of thyroid cancer comprised a relatively large portion of the total number of operations.

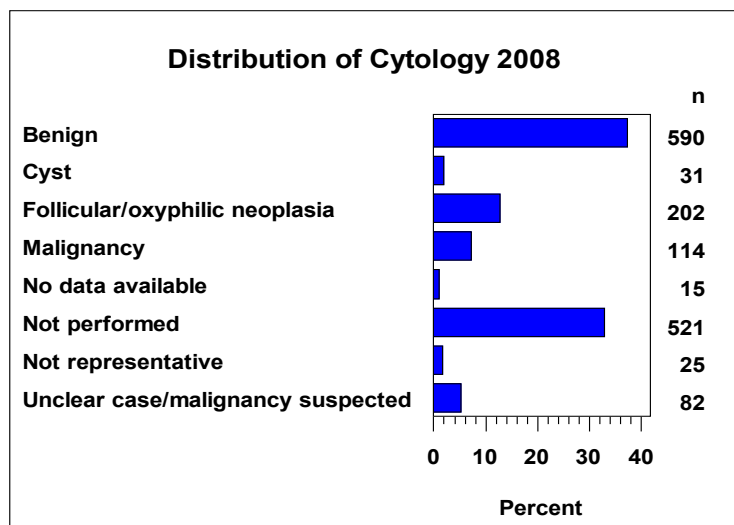
## Gender and indication for surgery



## Preoperative cytology

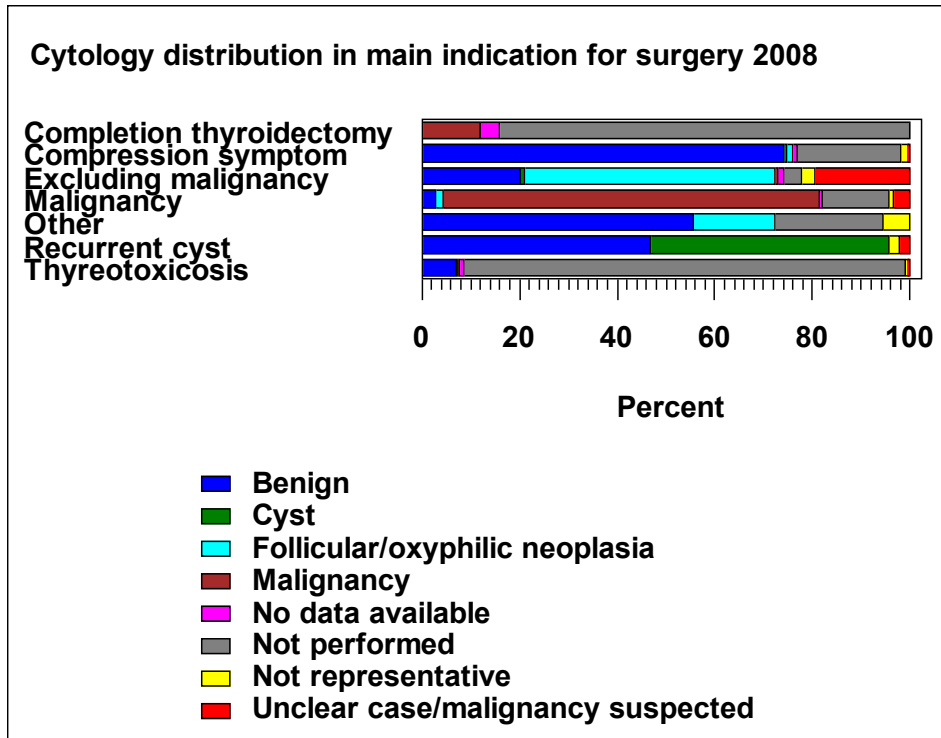
Preoperative cytology was not carried out prior to 521 operations (33%) and was not representative in 25 cases (1.6% of all FNAs performed). This result is somewhat of an improvement compared to the data registered for 2007 (38.6% and 2.5%, respectively).

## Preoperative cytology results



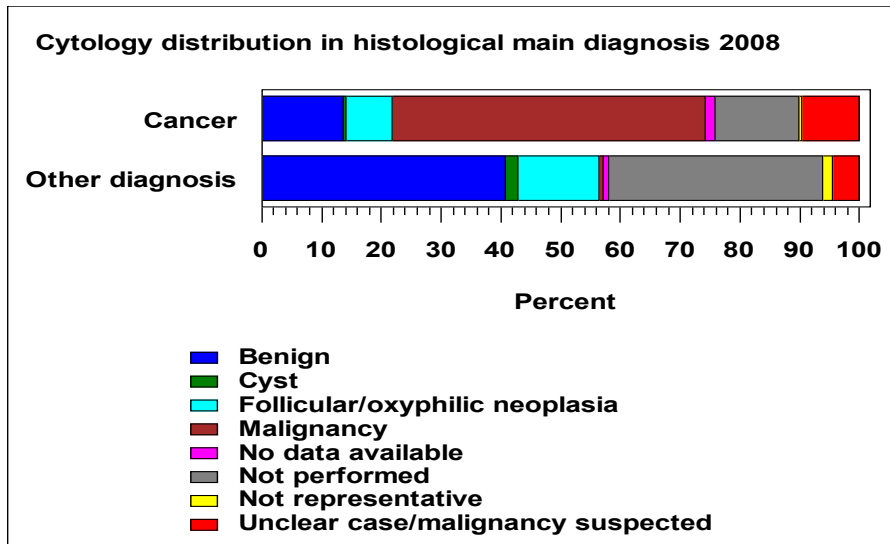
It is noteworthy that preoperative cytology was not carried out for a relatively large portion of patients who underwent surgery for compression symptoms.

Cytology results and indication for surgery



Of those patients who were diagnosed *postoperatively* with thyroid cancer as their main histological diagnosis, a relatively large portion had not undergone preoperative cytology, or alternatively, their cytological samples were assessed to be benign. Obvious changes compared to the results from 2007 cannot yet be assessed.

Results of cytology for cancer and other diagnoses

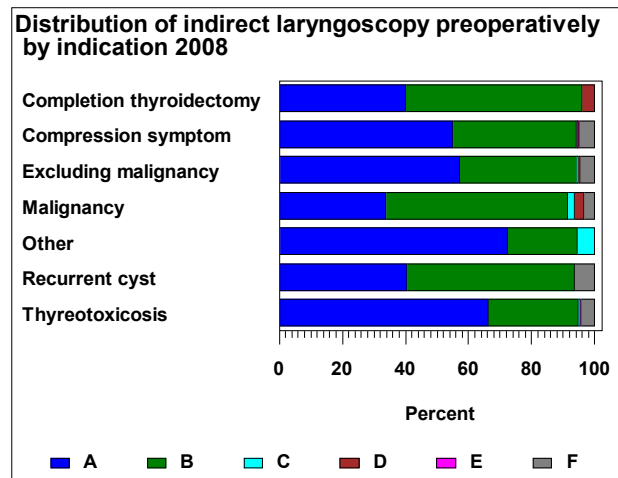


## Preoperative vocal cord evaluation

Preoperative evaluation of vocal cord function was carried out for 55.8% of all patients, but performance of this evaluation varied greatly between participating clinics.

It is noteworthy that even if patients had a prior history of thyroid surgery, or if the indication for surgery was thyroid cancer, there were significant numbers of patients who did not undergo preoperative laryngoscopy.

### Preoperative laryngoscopy in relation to indication for surgery



A=Not performed

B=Normal

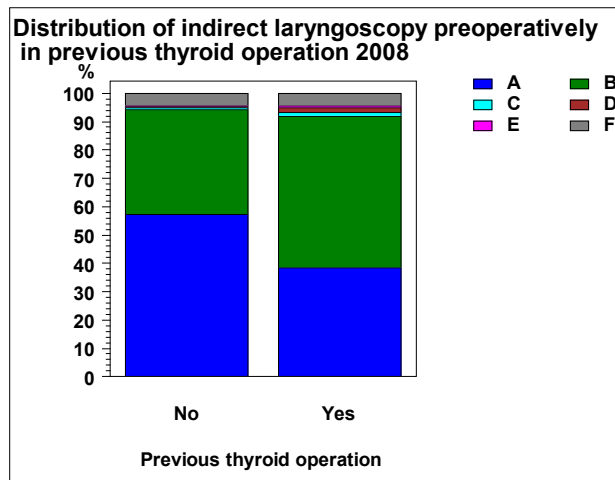
C=Paresis of the left recurrent laryngeal nerve

D=Paresis of the right recurrent laryngeal nerve

E=Bilateral paresis of the recurrent laryngeal nerve

F=No data available

## Preoperative laryngoscopy and previous history of thyroid surgery

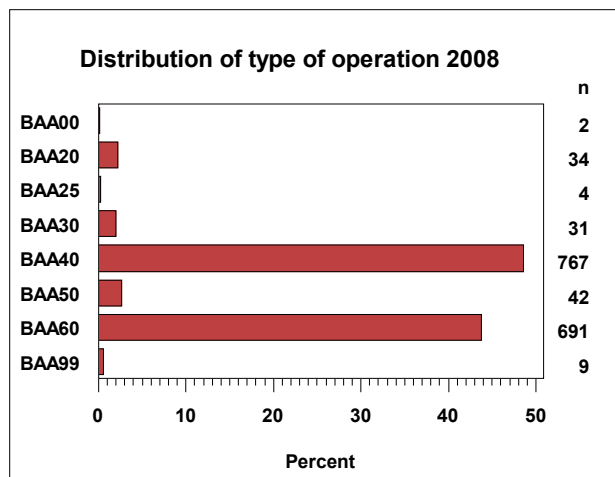


## Thyroid surgical procedures

The procedures performed were mainly lobectomy (48.5%) and total thyroidectomy (43.7%).

Compared to data from 2007 there was a decrease in the number of patients who underwent hemithyroidectomy and an increase in the number of patients who underwent total thyroidectomy (52% and 39%, respectively).

## Type of thyroid procedure



BAA00=Biopsy of thyroid gland, BAA00

BAA05=Exploration of thyroid gland, BAA05

BAA20=Unilateral resection of thyroid gland, BAA20

BAA25=Bilateral resection of thyroid gland, BAA25

BAA30=Isthmus resection of thyroid gland, BAA30

BAA40=Unilateral lobectomy of thyroid gland, BAA40

BAA50=Lobectomy and resection of contralateral lobe of thyroid gland, BAA50

BAA60=Thyroidectomy, BAA60

BAA99=Other operation on thyroid gland, BAA99

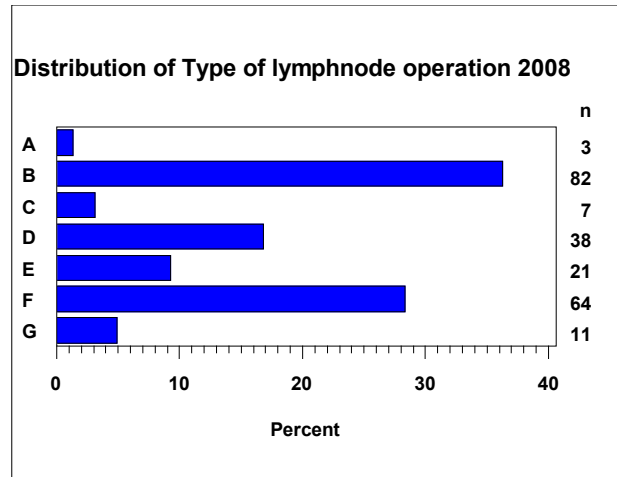
## Lymph node surgery in conjunction with thyroid procedures

Lymph node surgery was performed in conjunction with 226 thyroid procedures (14.3%).

The type of procedure is detailed below.

A total of 141 procedures (62.4%) were “compartment-oriented”. This is an increase compared to the data from 2007 (13.3% compared to 45.5%).

### Type of lymph node procedure



A=Bilateral lateral lymph node dissection, PJD51

B=Central lymph node dissection, PJD41

C=Central lymph node dissection, PJD41, and bilateral lateral lymph node dissection, PJD51

D=Central lymph node dissection, PJD41, and one-sided lateral lymph node dissection, PJD51

E=Exploration of lymph nodes (incl biopsy), PJD10

F=Exstirpation of lymph nodes, PJD41

G=One-sided lateral lymph node dissection, PJD51

## General complications

Postoperative bleeding resulted in emergency re-operation being required for 36 patients (2.3%). In addition, infections that required treatment were reported for 25 patients (1.6%).

## Definitive main diagnosis

Definitive histological diagnoses were primarily nodular goitre (48.7%), Graves' disease (16.6%), benign adenoma (12.4%) and cancer (12.8%).



## Definitive main histological diagnosis

	Number	Percent
Nodular goitre T-96 M-71640	748	48.7
Graves' disease T-96 D-2193	255	16.6
Follicular adenoma T-96 M-83300	171	11.1
Papillary cancer T-96 M- 82603	145	9.4
Lymphocytic thyroiditis, Hashimoto T-96 M-45810	46	3.0
Other diagnosis	37	2.4
Follicular cancer T-96 M- 83303	23	1.5
Oxyphilic adenoma T-96 M- 82900	18	1.2
Thyroid normal T-96 M-00110	17	1.1
Benign tumour UNS T-96 M- 80000	13	0.8
Anaplastic cancer T-96 M- 80123	9	0.6
Medullary cancer T-9605 M-85103	8	0.5
Chronic fibrotic thyroiditis, Riedel T96 M-45000	6	0.4
Oxyphilic cancer T-96 M- 82903	6	0.4
Thyroid nothing malignant T-96 M-0945	6	0.4
C-cell hyperplasia T- 9605 M- 72000	5	0.3
Cyst, ductus thyreoglossus T-96-M-26500	3	0.2
Follicular tumour with uncertain malignant potential	3	0.2
Malignant tumour UNS T-96 M-80003	3	0.2
Lymphoma T-96 M- 95903	2	0.1
Metastasis from cancer UNS T-96- M-80106	2	0.1
Parathyroid normal	2	0.1
Poorly differentiated thyroid cancer	2	0.1
Subacute thyroiditis, de Quervain T-96 M-44000	2	0.1
Clear-cell adenoma T-96 M- 83100	1	0.1
Lymph node metastasis anaplastic cancer T-O82 M-80126	1	0.1
Lymph node metastasis papillary cancer T-082 M-82606	1	0.1
Metastasis from malignant tumour UNS T-96 M-80006	1	0.1
Oxyphilic tumour with uncertain malignant potential	1	0.1
Total	1580	100

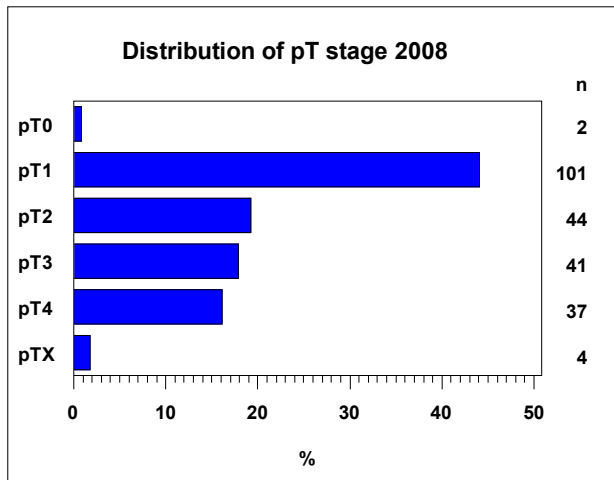
## Cancer

A total of 229 patients had thyroid cancer (14.5%) according to the definitive main histological diagnosis.

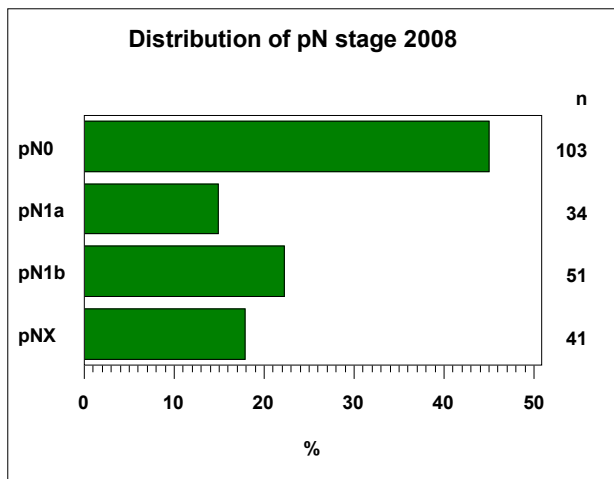
The pTNM stage for the patients with thyroid cancer is detailed below.

Compared to the data from 2007 the portion of patients with stage pT1 had increased from 34% to 44%. In contrast, those with stage pT2 had decreased from 27% to 19%.

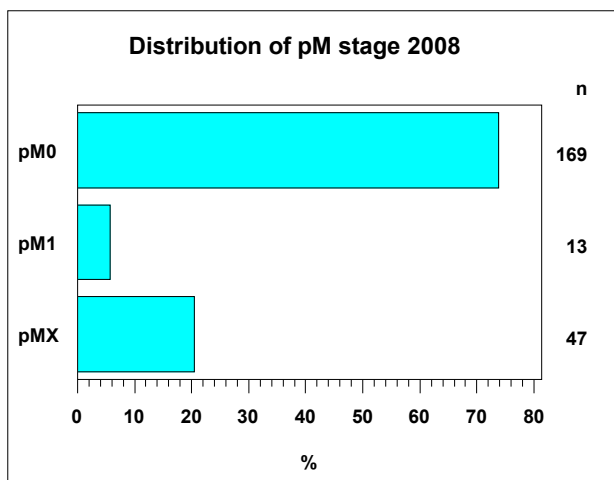
### pT stage



### pN stage



### pM stage



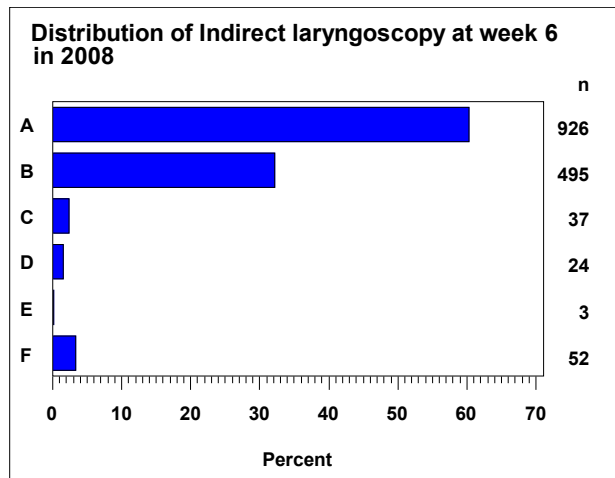
## Operation-specific complications (up to 6 weeks postoperatively)

### Nerve paresis

Postoperative vocal cord evaluation was carried out for 58.6% of all patients, with missing information for 3.3% (the 2007 figures were 51.6% and 1.6%, respectively).

Postoperative vocal cord paralysis was documented for 4.1% of patients following surgery; right side paralysis of the recurrent laryngeal nerve in 37 patients (2.3%), left side paralysis of the recurrent laryngeal nerve in 24 patients (1.5%) and bilateral paralysis in 3 patients.

### Laryngoscopy 6 weeks postoperatively



A=Not performed

B=Normal

C=Paresis of the left recurrent laryngeal nerve

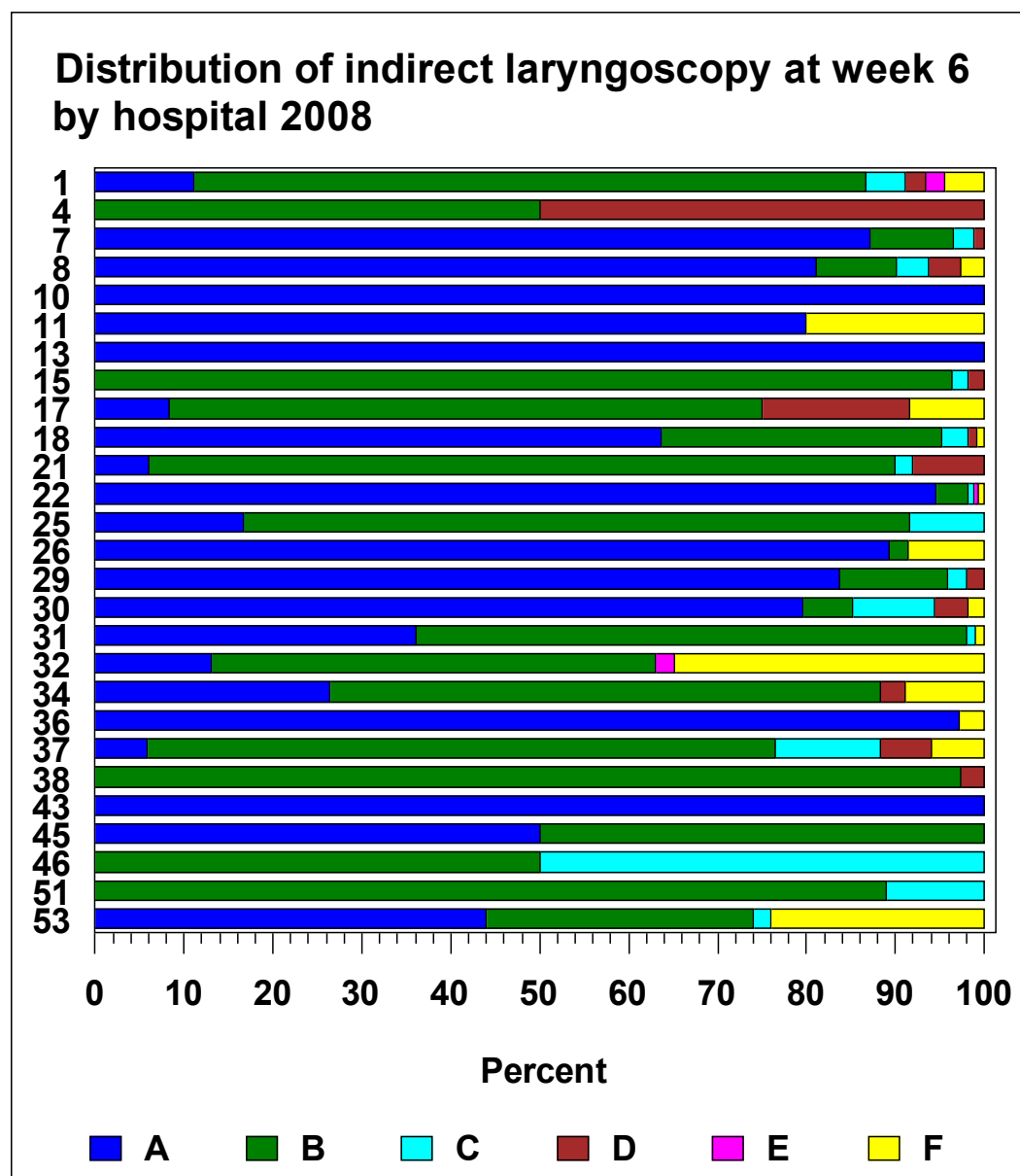
D=Paresis of the right recurrent laryngeal nerve

E=Bilateral paresis of the recurrent laryngeal nerve

F=No data available

The numbers of postoperative vocal cord evaluations carried out and their outcomes can be seen to vary greatly for the participating clinics.

Vocal cord evaluation at the first postoperative follow-up visit

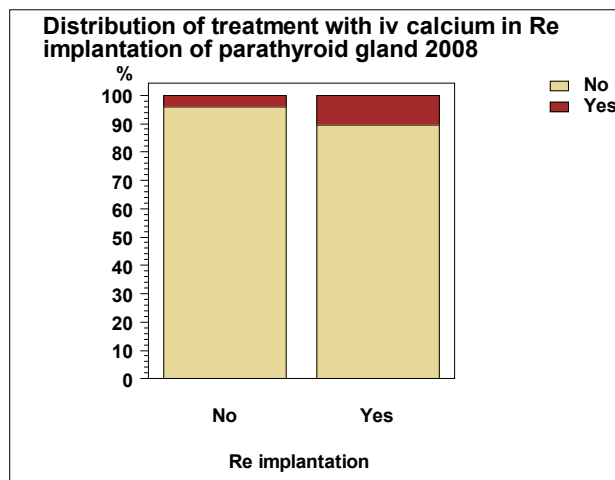
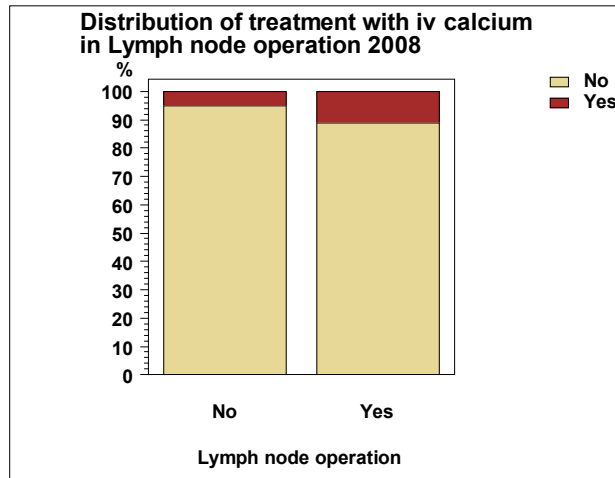


- A=Not performed
- B=Normal
- C=Paresis of the left recurrent laryngeal nerve
- D=Paresis of the right recurrent laryngeal nerve
- E=Bilateral paresis of the recurrent laryngeal nerve
- F=No data available

## Hypocalcaemia (bilateral thyroid surgery)

Following bilateral thyroid surgery (n=737), 46 patients (6.2%) received i.v. calcium treatment while hospitalised.

The risk increased somewhat for patients who underwent lymph node dissection and auto-transplantation of parathyroid tissue.



At the first postoperative follow-up visit after 1-6 weeks, 112 patients (15.2%) received oral calcium treatment and 56 patients (7.6%) were given a vitamin D analogue therapy.

## Operation-specific complications (6 months postoperatively)

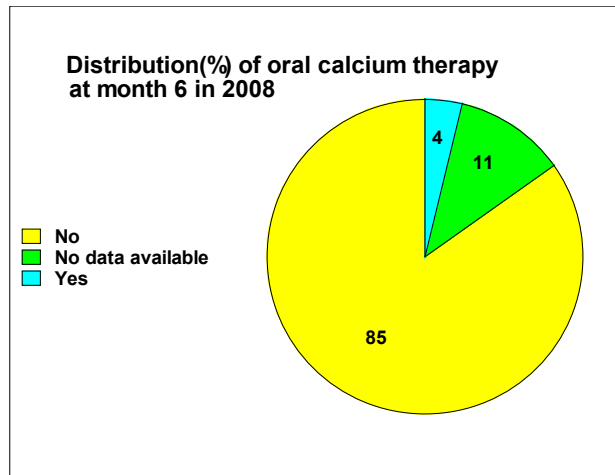
### Nerve paresis

At the 6 month postoperative follow-up visit unilateral paralysis of the recurrent laryngeal nerve was reported in 8 of 1467 patients examined (0.5%). Data was missing, however, for 72 patients and 41 patients had not yet been followed-up. This means that the above figure should definitely be considered to be a minimum frequency for postoperative vocal cord paralysis. From past experience, it is relatively unusual to see nerve restitution after 6 months.

## Hypocalcaemia (bilateral thyroid surgery)

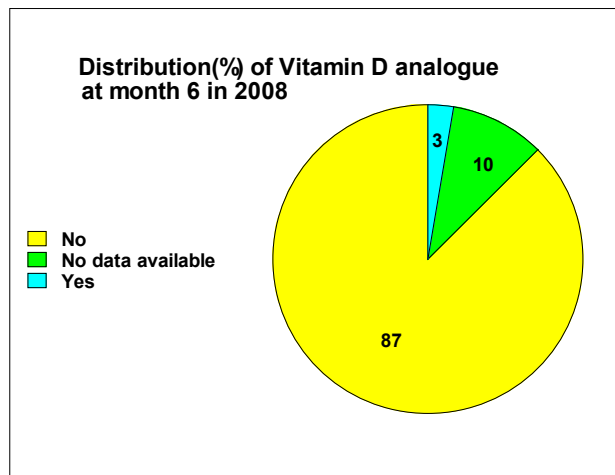
After 6 months 27 patients were treated with oral calcium (4.3%). However, data is not yet available for 29 patients and 28 patients who were given calcium treatment at the first follow-up visit and remain to be followed. Therefore, in the worst case scenario, 7.5% of patients were receiving oral calcium treatment after 6 months, with the true figure likely to be somewhere in between.

### Oral calcium 6 months postoperatively



At the 6 month follow-up visit there were still 19 patients (2.6%) being treated with vitamin D analogue therapy and data is not available for 71 patients. Twenty patients, who were treated with vitamin D at the first follow-up visit, remained to be followed, which means the worst case scenario is that 5.3% of patients at this time-point are being treated with vitamin D, with the true figure somewhere in between. From past experience, the treatment can often be assumed to be chronic at this time-point.

### Vitamin D therapy 6 months postoperatively

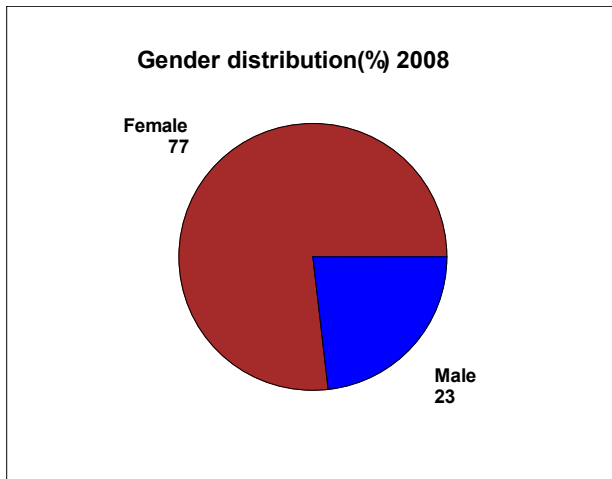


# Primary Hyperparathyroidism

## Gender; distribution by age

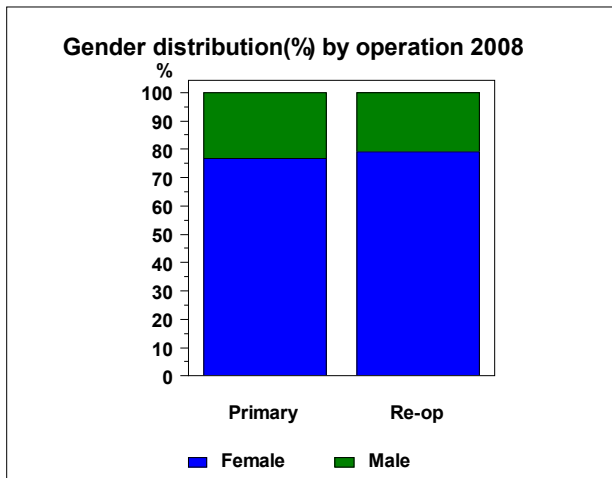
During 2008 there were 725 operations registered. Patients operated for primary hyperparathyroidism are mainly older women. The median age was 62 years, but actual ages ranged from 14 to 92 years.

### Gender distribution



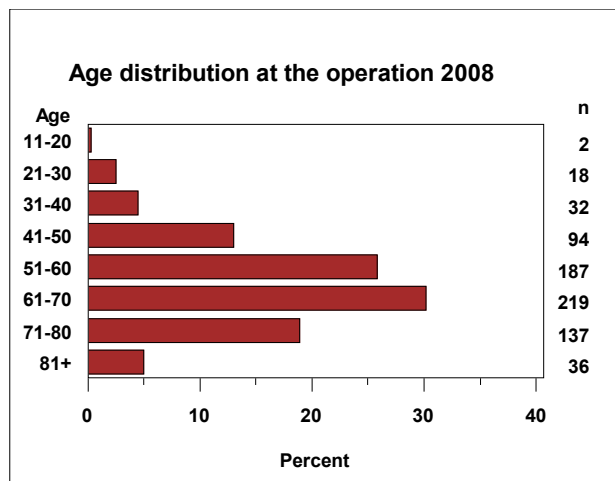
For re-operations the female predominance was somewhat further accentuated.

### Age distribution for primary procedure and re-operation



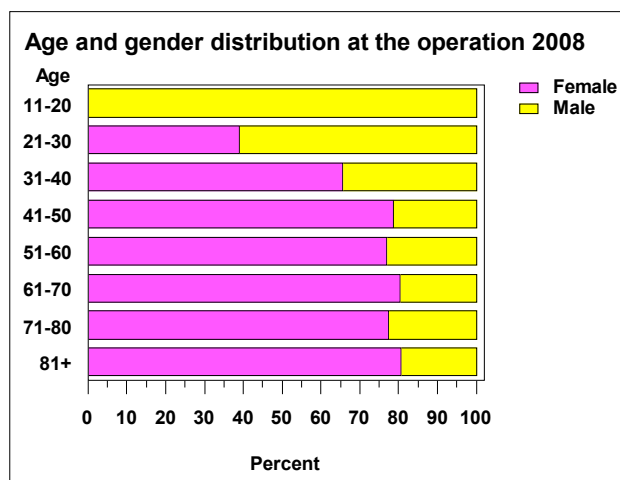
The age distribution is markedly skewed. It is noteworthy that only 7.2 percent of patients were younger than 40 years old when their operations were carried out. In contrast 23.9% of the patients were over 70 years old, and 9.9% were over 80 years old, when their operations were carried out (in other words there were almost equal numbers of patients who were younger than 40 years old at the time of surgery as there were those who were over 80 years old).

## Age distribution



Interestingly, there is a male predominance in the young ( $\leq 30$  years old).

## Age and gender distribution



## Type of procedure and heritability

Of all patients, 687 had surgery for the first time and 38 patients (5.2%) were re-operated for primary HPT. There were 10 patients with hereditary disease.

## Preoperative Serum Calcium

The majority of patients had surgery for mild or moderate hypercalcaemia. The median preoperative serum calcium (total) value was 2.77 mmol/l (range 2.24 to 4.40 mmol/l).

There were 16 patients (2.1%) who had a calcium level less than 2.50 mmol/l and 80 patients (10.5%) who had levels equal to or higher than 3.00 mmol/l.



## Preoperative localisation examination

A preoperative localisation examination was performed for 570 patients (78.7%).

The two most common examinations were sestamibi scintigraphy, performed for 456 patients (62.8%) and ultrasound examination, performed for 441 patients (60.8%). The results of the examinations, compared with the findings of the operations and definitive histology, are documented in the following section.

### Results of Sestamibi scintigraphy

	Number	Percent
Sestamibi scintigraphy	108	23.7
Negative/inconclusive preop. examination		
True preop. localisation of solitary adenoma (TP)	304	66.7
Correct position of one pathologic gland, but multiglandular disease not predicted	7	1.6
False preop. localisation of solitary adenoma (FP)	33	7.2
True preop. prediction of multiglandular disease	3	0.6
False prediction of multiglandular disease in solitary adenoma	1	0.2

A solitary focus (a suspected solitary adenoma) was seen in 344 patients (75.4%). However, 7 of these patients (1.6%) were found to be suffering from multiglandular disease and in 33 patients (7.2%) the examination was found to be false positive for correct localisation. The sensitivity for correctly localising a solitary adenoma was therefore only 66.7%. In 23.7% of examinations the outcomes were completely negative.

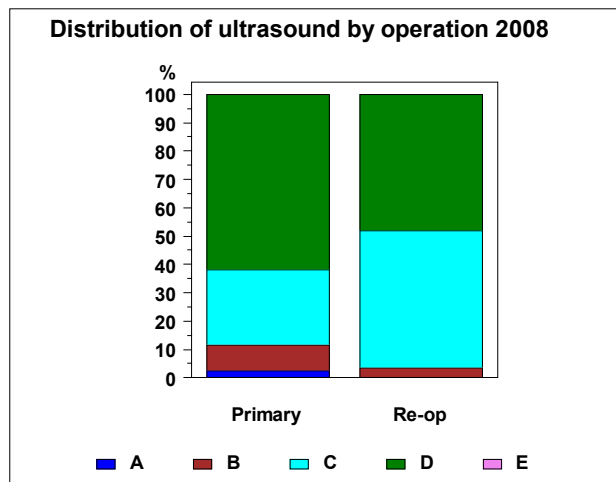
### Results of ultrasound examination

	Number	Percent
Ultrasound	10	2.3
Correct position of one pathologic gland, but multiglandular disease not predicted		
Negative/inconclusive preop. examination	124	28.1
True preop. localisation of solitary adenoma (TP)	268	60.8
False preop. localisation of solitary adenoma (FP)	38	8.6
True preop. prediction of multiglandular disease	1	0.2

A solitary focus (a suspected solitary adenoma) was seen in 316 patients (71.7%). Of these patients there were 10 (2.3 %) who were found to be suffering from multiglandular disease and in 38 patients (8.6 %) the examination was found to be false positive for correct localisation. The sensitivity for correctly localising a solitary adenoma was therefore 60.8 %. The examination was negative in 28.1% of cases.

The accuracy of the ultrasound examination was less for re-operations and when prior thyroid surgery had been performed.

Results of ultrasound examinations for primary procedures and for re-operation



A=Correct position of one pathologic gland, but multiglandular disease not predicted

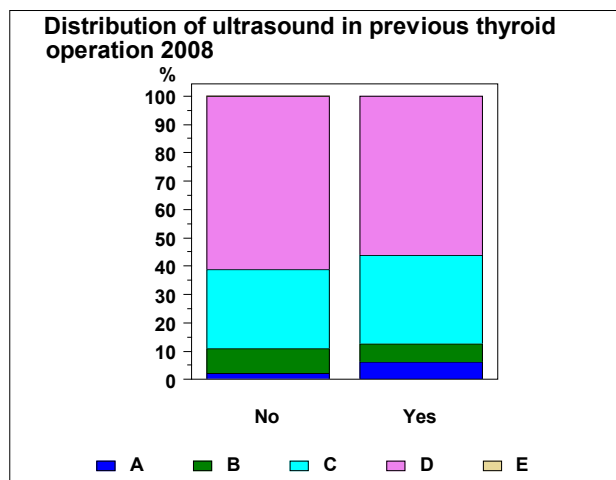
B=False preop. localisation of solitary adenoma (FP)

C=Negative/inconclusive preop. examination

D=True preop. localisation of solitary adenoma (TP)

E=True preop. prediction of multiglandular disease

Ultrasound examination when undergoing thyroid surgery



A=Correct position of one pathologic gland, but multiglandular disease not predicted

B=False preop. localisation of solitary adenoma (FP)

C=Negative/inconclusive preop. examination

D=True preop. localisation of solitary adenoma (TP)

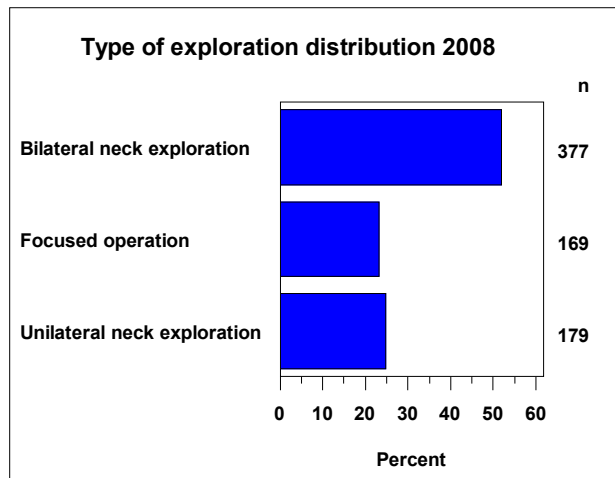
E=True preop. prediction of multiglandular disease

## Type of operation

Classic bilateral neck exploration was the predominant surgical procedure (52%).

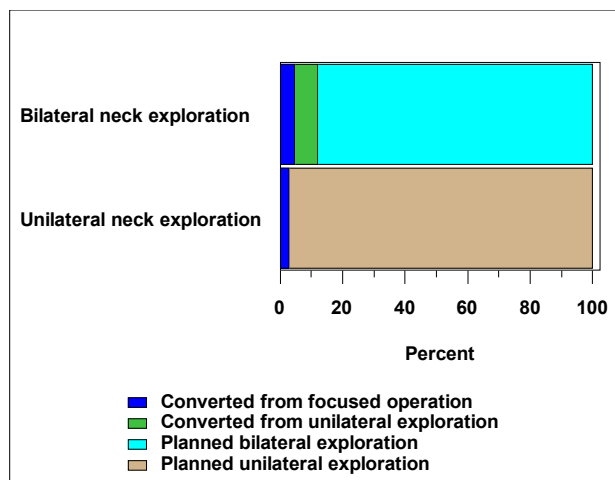
Focused surgery was performed in 23.3% of cases and unilateral exploration in 24.7% of all operations. Concomitant thyroid surgery was performed for 49 patients (6.8%) and thymus surgery was performed in 61 cases (8.4%). Re-implantation of parathyroid tissue was performed in 3% of the procedures.

## Type of parathyroid exploration



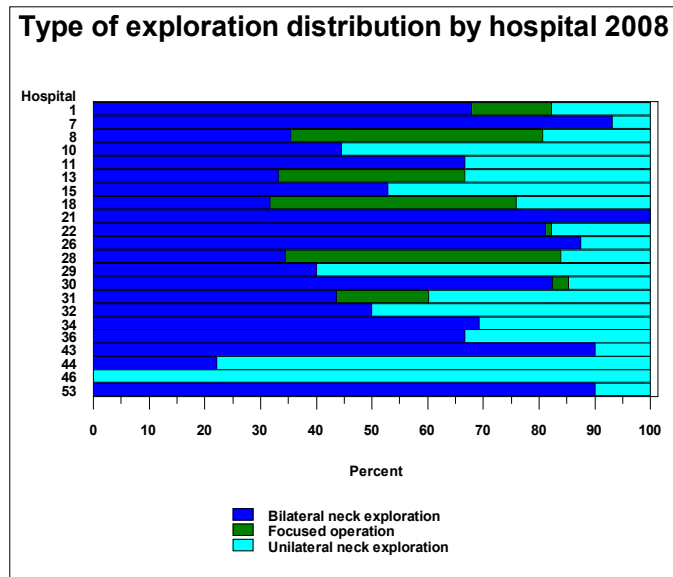
For an overwhelming majority of the patients who underwent bilateral neck exploration this was also the scheduled procedure.

## Reason for bilateral neck exploration



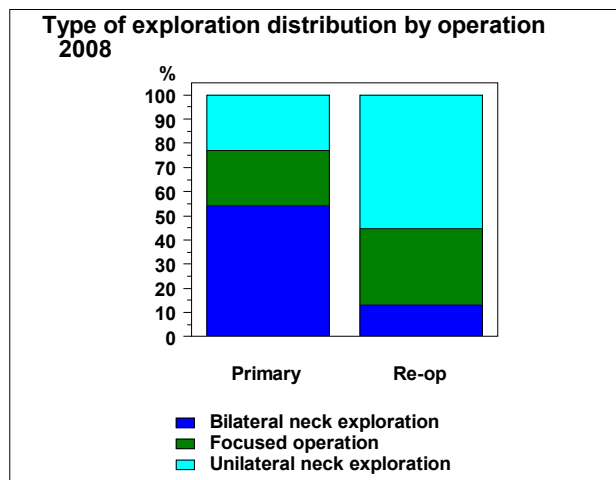
There was a great deal of variation in surgical strategy between the participating clinics.

## Type of parathyroid exploration at the participating clinics



For re-operations only a minor fraction of patients underwent a bilateral neck exploration.

## Type of parathyroid operation



## Intraoperative determination of PTH

Intraoperative PTH (iOPTH) was used for 225 patients (31%) and in general was seen to have high sensitivity and specificity, with false positive findings (FP) for solitary adenoma of 2.7%.

## Results of intraoperative PTH

Intraoperative PTH	Number	Percent
Incorrect. Persistent HPT in spite of “adequate” decline in ioPTH (FP)	6	2.7
Correct ioPTH (TP)	214	95.1
Misleading. Insufficient decline in ioPTH in spite of “adequate” operation (FN)	5	2.2

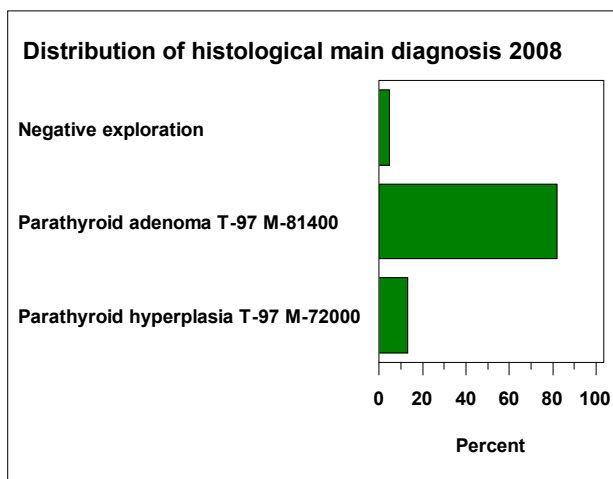
## Complications during hospitalisation

Postoperative bleeding with re-operation was reported in ten cases (1.4%), while infected wounds requiring treatment were noted for three patients (0.4%).

## Definitive histological investigation

Solitary parathyroid adenoma was reported for 82.1% of all patients. Hyperplasia occurred in 13.2% and in 4.7% of surgeries, the outcome of investigation was negative.

## Histological diagnosis



The median gland weight was 0.57 grams, with a broad range (50 mg to 50 grams).

## Specific postoperative complications within six weeks of operation

### Results of laryngoscopy

Indirect laryngoscopy (< 6 weeks from the time of operation)	Number	Percent
Normal	186	26.35
Not performed	499	70.68
Paresis of the right recurrent laryngeal nerve	3	0.42
No data available	14	1.98
Paresis of the left recurrent laryngeal nerve	4	0.57
Total	706	100.00

Vocal cord examinations were not performed on 499 patients (70.7%). Unilateral vocal cord paralysis affected seven patients (1%).

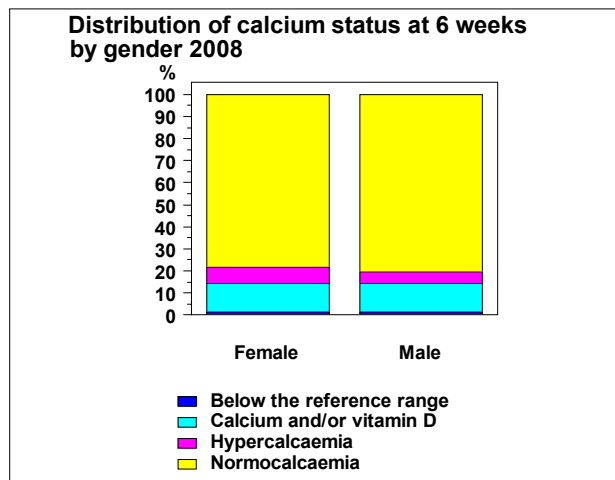
### Postoperative calcium status within six weeks of operation

A total of 11 patients (1.7%) were re-operated within six weeks of the primary surgical procedure. At the first postoperative follow-up 12.2% of the patients were given medical treatment for hypocalcaemia. Persistent hypercalcaemia was noted for 6.4% of patients.

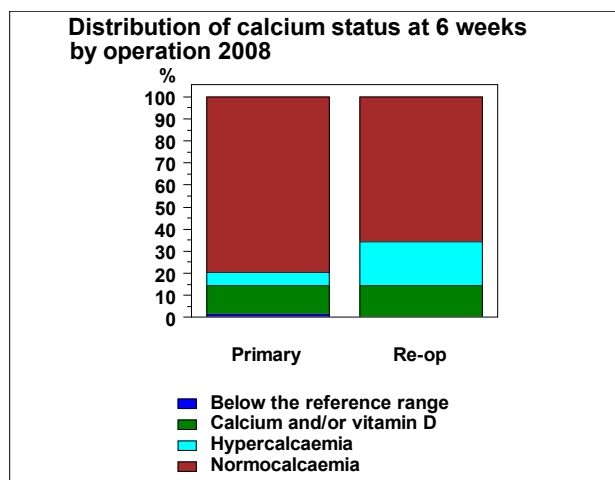
Only minor differences due to gender were recorded. In contrast, the results were markedly worse for patients who had surgery because of hereditary disease and for re-operation. Patients with a histological diagnosis of hyperplasia had an increased risk both of persistent disease and of requiring medical treatment for hypocalcaemia.

Calcium status < 6 weeks from the time of operation	Number	Percent
Normocalcaemia	518	73.37
Hypercalcaemia (spontaneous)	45	6.37
Calcium below the reference range without treatment (regarded as asymptomatic)	10	1.42
No data available	47	6.66
Treatment with calcium and/or vitamin D analogue therapy	86	12.18
Total	706	100.00

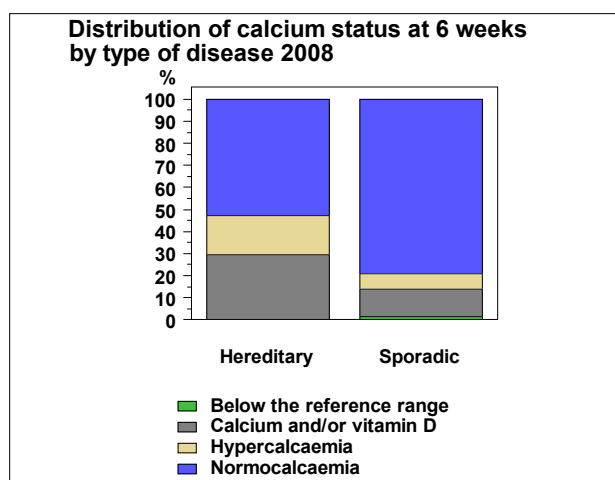
## Gender and calcium status 6 weeks postoperatively



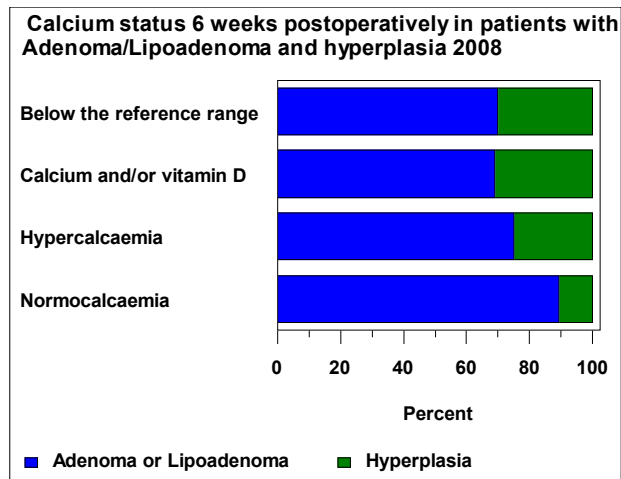
## Calcium status 6 weeks postoperatively, primary procedure versus re-operation



## Calcium status 6 weeks postoperatively, sporadic versus hereditary disease

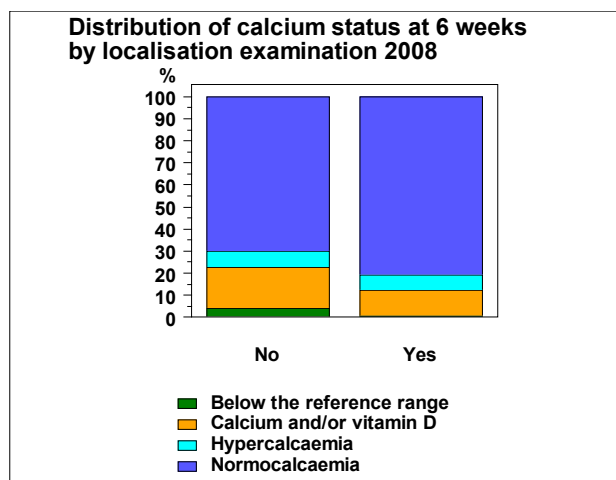


## Histological diagnosis and calcium status 6 weeks postoperatively



The use of new techniques also affected the outcome after surgery. Thus, the use of preoperative localisation examination reduced the risk of requiring medical treatment for hypocalcaemia.

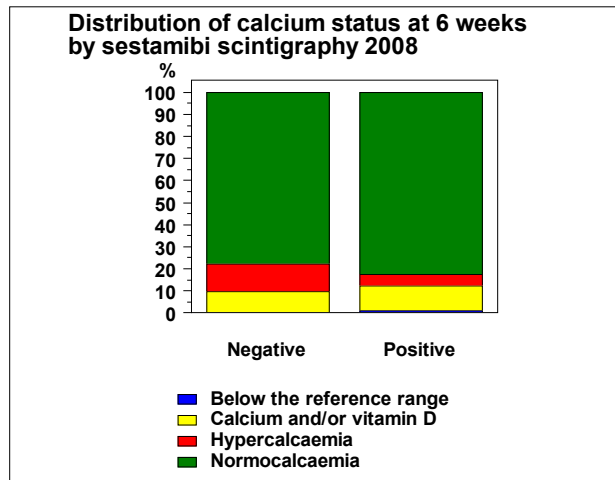
## Preoperative localisation examination and calcium status 6 weeks postoperatively



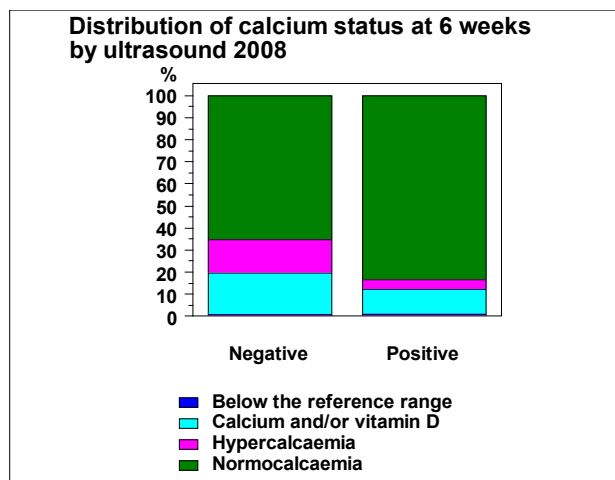
The results of the examinations themselves also had a large impact on the surgical outcomes, both for sestamibi scintigraphy and for ultrasound examinations. Therefore, for both types of examination, the risks of persistent disease increased markedly when the gland was not preoperatively localised.



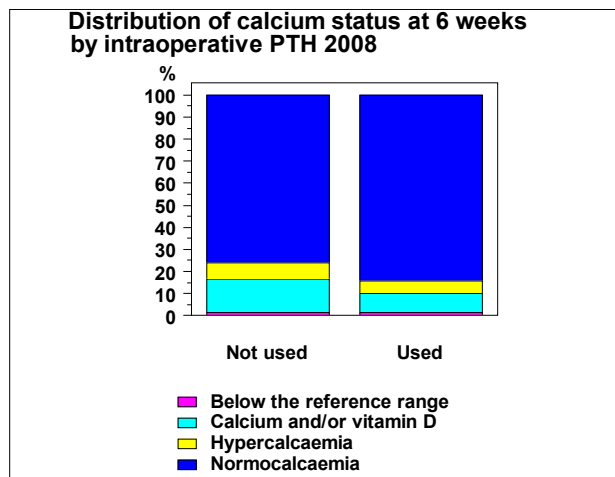
### Results of Sestamibi scintigraphy and calcium status 6 weeks postoperatively



### Results of ultrasound examination and calcium status 6 weeks postoperatively



### Intraoperative PTH and calcium status 6 weeks postoperatively



Intraoperative PTH reduced the risks both of persistent hypercalcaemia and of hypocalcaemia requiring medical treatment and thus meant that a larger proportion of patients postoperatively had strict normocalcaemia.

## Specific complications (6 months postoperatively)

At the 6 month follow-up, 4 patients (0.5%) were reported to be suffering from vocal cord paralysis. Data is however lacking for two patients who were diagnosed with paralysis at the first follow-up visit, which means in worst case a frequency of nerve injury of 0.7%.

## Calcium status 6 months after surgery

At the 6 month follow-up, hypercalcaemia was reported for a further eight patients who were re-operated.

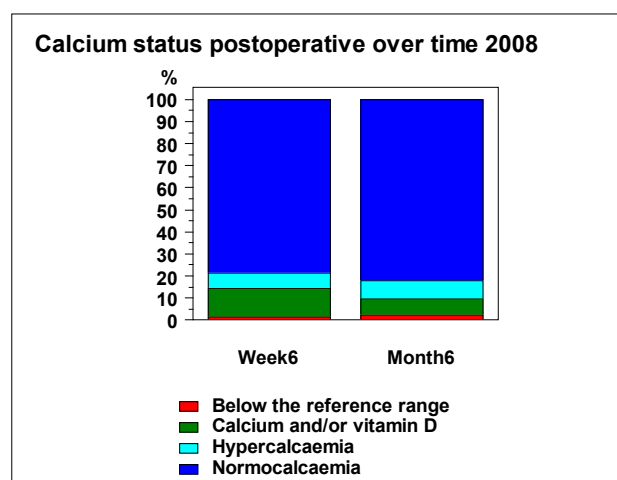
Calcium status 6 months postoperatively

Calcium status at 6 months postoperatively	Number	Percent
Missing	173	23.86
Normocalcaemia	311	42.90
No data available	174	24.00
Hypercalcaemia (spontaneous)	32	4.41
Calcium below the reference range without treatment (regarded as asymptomatic)	8	1.10
Treatment with calcium and/or vitamin D analogue therapy	27	3.72
Total	725	100.00

Data is still lacking for 174 patients (24%) and 173 patients are still to be followed-up. Extreme caution should therefore be adopted in interpreting the 6 month data and it is difficult to draw more definitive conclusions.

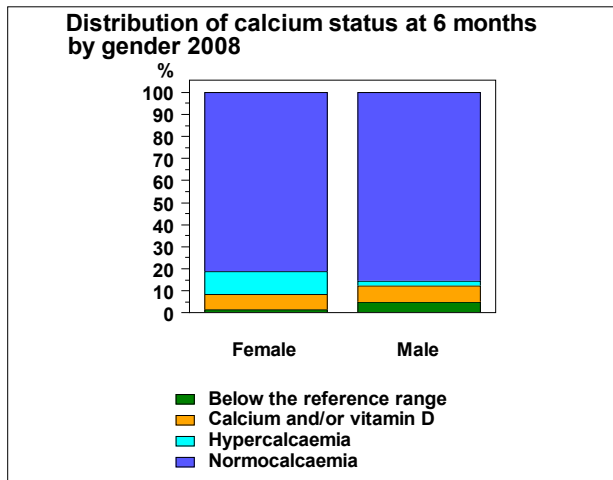
Of the 378 patients who have been followed-up, 311 (82.3%) appear to have normocalcaemia, 32 patients (8.5%) have hypercalcaemia and 27 patients (7.1%) were receiving medical treatment with calcium and/or vitamin D analogue.

## Time course for postoperative calcium status

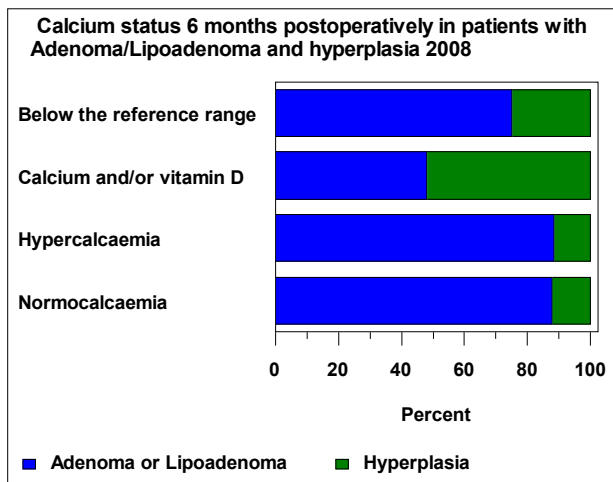


Women comprised a higher proportion of patients with persistent hypercalcaemia, but there were no obvious age-dependent differences. Patients with hyperplasia had, above all, an increased risk of hypocalcaemia, which was also true for patients with hereditary disease. Patients who underwent re-operation had a clearly increased risk of both persistent disease and risk of requiring medical treatment for hypocalcaemia after 6 months.

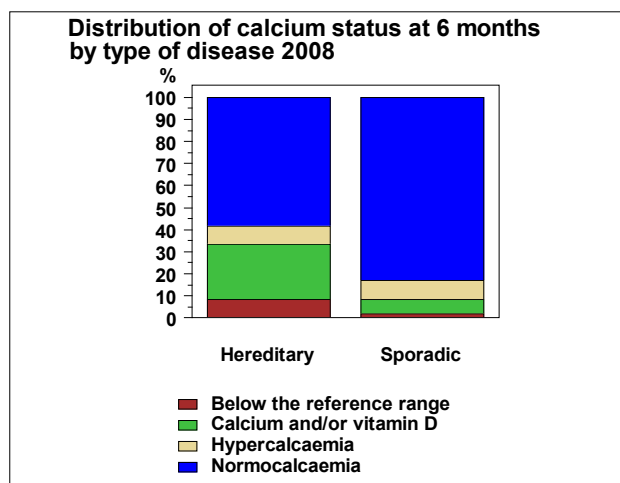
## Gender and calcium status 6 months postoperatively



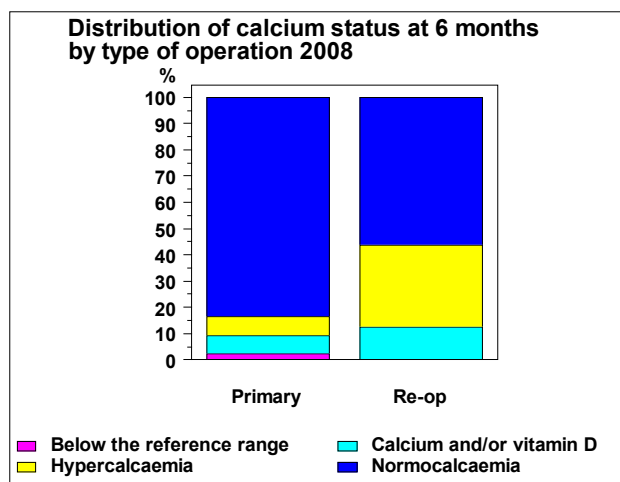
## Calcium status and histological diagnosis 6 months postoperatively



Calcium status after 6 months, sporadic versus hereditary disease



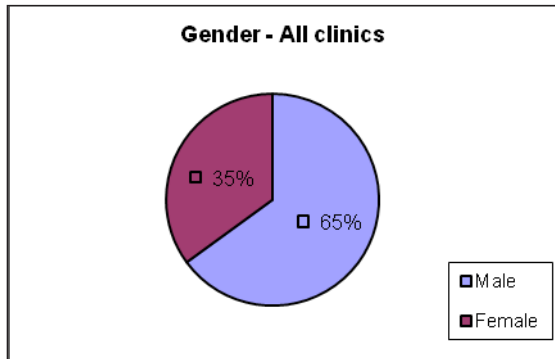
Calcium status 6 months, primary procedure versus re-operation



# Secondary hyperparathyroidism

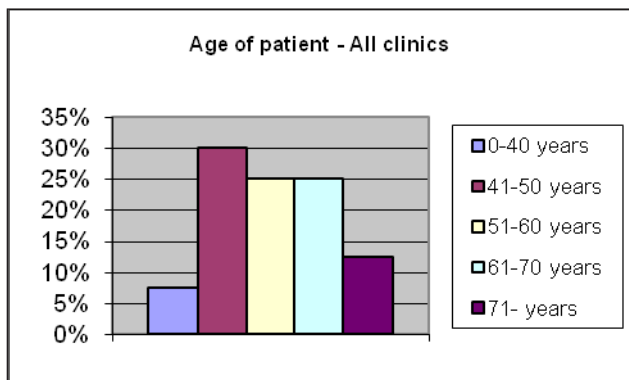
During the year there were 40 patients who were operated for secondary HPT. Of these patients almost two thirds were male.

## Gender distribution



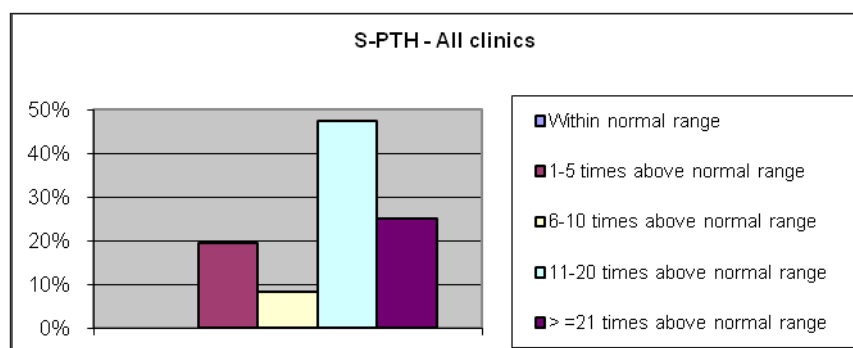
Only 3 patients (7.5%) were under 40 years of age at the time of surgery. Five patients (12.5%) were over 70 years of age.

## Age distribution



The vast majority of patients had pronounced secondary HPT: almost 72% had a preoperative PTH value more than 10 times higher than the reference value. In addition 65% of the patients had symptoms of secondary HPT.

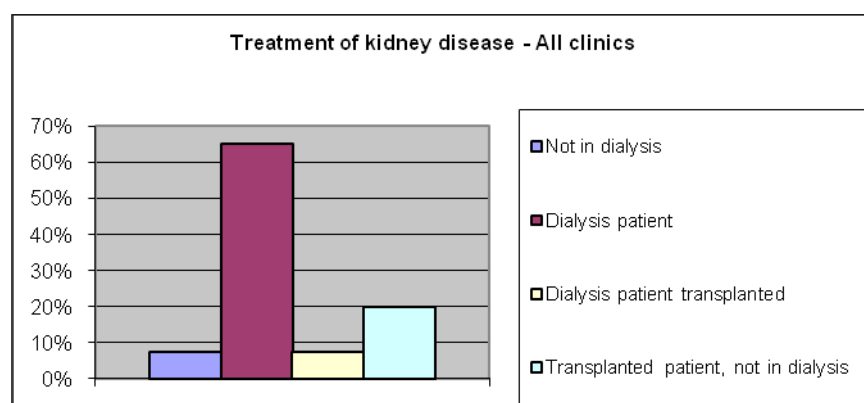
## PTH values in relation to the normal interval



The median concentration of serum calcium (total) was 2.62 mmol/l (range 2.12 mmol/l to 3.24 mmol/l).

Just over 34% had previously undergone renal transplantation and 30% of the patients had a functioning transplant.

## Renal disease



## Type of procedure

Total and subtotal operations were performed to approximately the same extent. Thymus resection was carried out for 14 patients (35%). Re-implantation of parathyroid tissue was performed in 43 % of the cases.

Primary operations represented 90% of the procedures. The type of operation is detailed below.

Parathyroid operation		
Biopsy of parathyroid gland, BBA10	0	0,00 %
Exploration of parathyroid gland, BBA20	2	5,00 %
Extirpation of parathyroid gland, BBA30	2	5,00 %
Subtotal parathyroidectomy, BBA40	19	47,50%
Parathyroidectomy, BBA50	17	42,50%
Other operation on parathyroid gland, BBA99	0	0,00 %

## Follow-up at 6 weeks

### Complications

There were no instances of re-bleeding or nerve paralysis registered and neither were there any serious complications. One patient was treated for a postoperative wound infection.

### Histological examination

The average weight of excised parathyroid tissue was 1.65 grams (range 0.24 grams to 7.44 grams).

### Calcium status 6 weeks postoperatively

Calcium status (< 6 weeks from the time of operation)		
No data available	1	2,50 %
Calcium below the reference range without treatment (regarded as asymptomatic)	2	5,00 %
Normocalcaemia, without treatment with calcium and/or vitamin D analogue	7	17,50%
Treatment with calcium and/or vitamin D analogue therapy	26	65,00%
Hypercalcaemia (spontaneous)	4	10,00%

Thus, 5% of the patients were taking calcium and/or vitamin D analogue at the first follow-up visit. Spontaneous hypercalcaemia was reported for 10% of patients.

## Follow-up after 6 months

Data is missing for 9 patients and so the results should be interpreted with caution.

### Calcium status 6 months postoperatively

Calcium status		
No data available	4	14,81%
Calcium below the reference range without treatment (regarded as asymptomatic)	0	0,00 %
Normocalcaemia, without treatment with calcium and/or vitamin D analogue	2	7,41 %
Treatment with calcium and/or vitamin D analogue	18	66,67%
Hypercalcaemia	3	11,11%

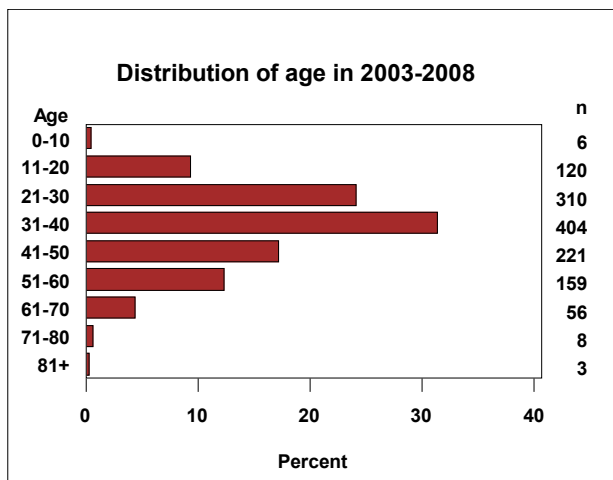
## 8. Extended analyses

### Graves' Disease 2004-2008

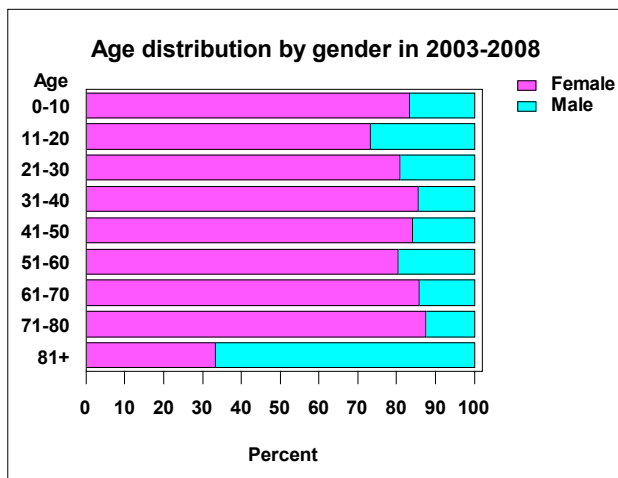
#### Gender and breakdown by age

During the period 2004-2008 there were 1287 patients registered who were surgically treated for Graves' disease. Almost 10% of these patients were younger than 20 years old and there was a strong female predominance. The median age was 35 years, with a range of 7-84 years.

#### Age distribution



#### Age distribution by gender

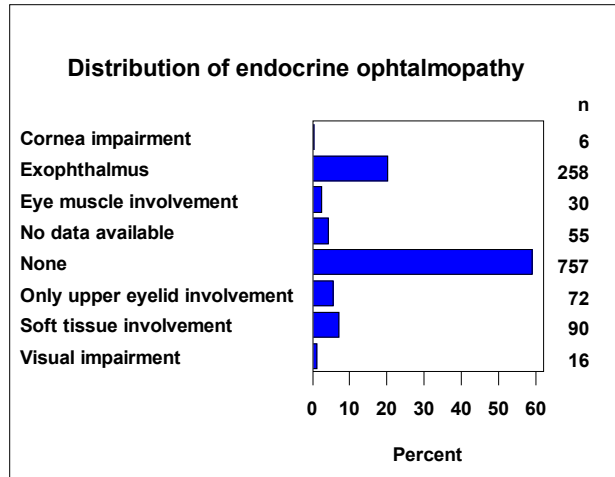




## Endocrine ophthalmopathy

Clinical indications of ophthalmic symptoms were present in 530 patients (41.2%) and the most commonly reported symptom was exophthalmus.

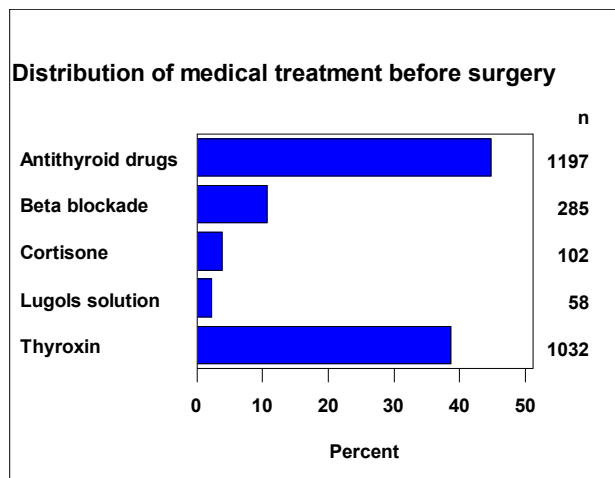
### Endocrine ophthalmopathy



## Medical treatment prior to surgery

Virtually all patients received medical treatment prior to surgery.

### Medical treatment prior to surgery



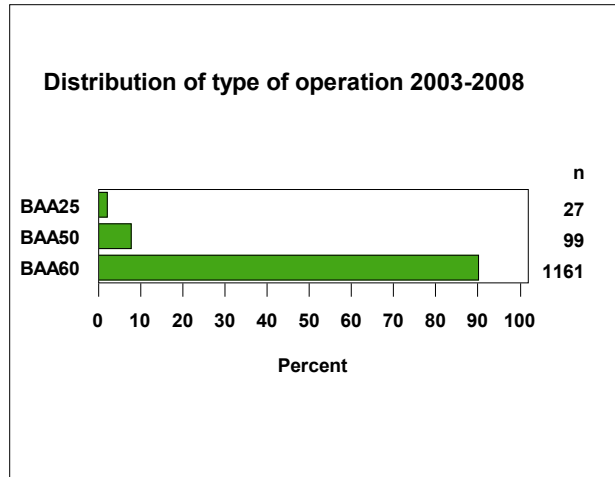
The most commonly used treatment before surgery was the combination of antithyroid drugs and thyroxin sometimes alone or in combination with beta blockers. For 89 patients (6.9%) pre-treatment was with antithyroid drug alone.

Medical treatment	n	%
Antithyroid drugs and Thyroxin	820	63.71
Beta blockade, Antithyroid drugs, and Thyroxin	110	8.55
Antithyroid drugs	89	6.92
Beta blockade and Antithyroid drugs	61	4.74
Antithyroid drugs, Thyroxin, and Cortisone	34	2.64
Beta blockade, Antithyroid drugs, Thyroxin, and Cortisone	30	2.33
Beta blockade, Antithyroid drugs, and Cortisone	20	1.55
Beta blockade	19	1.48
Thyroxin	18	1.40
All missing	16	1.24
Beta blockade and Lugol's solution	12	0.93
Antithyroid drugs, Thyroxin, Lugol's solution	9	0.70
Beta blockade, Antithyroid drugs, and Lugol's solution	9	0.70
Antithyroid drugs and Lugol's solution	6	0.47
Beta blockade, Lugol's solution and Cortisone	6	0.47
Beta blockade and Cortisone	5	0.39
Lugol's solution	4	0.31
Beta blockade, Antithyroid drugs, Thyroxin and Lugol's solution	4	0.31
Beta blockade, Antithyroid drugs, Lugol's solution and Cortisone	4	0.31
Beta blockade and Thyroxin	3	0.23
No medications	3	0.23
Beta blockade, Antithyroid drugs, Thyroxin, Lugol's solution and Cortisone	1	0.08
Beta blockade, Thyroxin, and Lugol's solution	1	0.08
Thyroxin and Lugol's solution	1	0.08
Thyroxin and Cortisone	1	0.08
Lugol's solution and Cortisone	1	0.08

## Type of operation

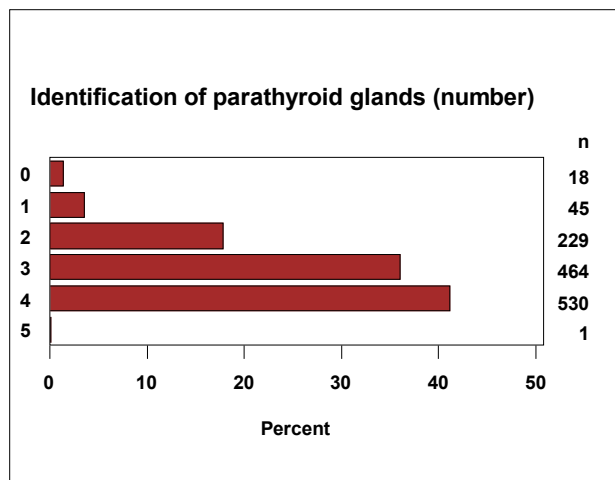
Just over 90% of the patients underwent total thyroidectomy for their condition. Bilateral subtotal thyroid resection was rare.

### Type of operation



Two or more parathyroid glands were identified in 95.1% of patients during the procedure. No parathyroid glands were identified in 18 patients (0.9%). Auto-transplantation was performed during 32% of the operations.

### Parathyroid glands identified



## Immediate complications

In conjunction with the surgical procedures, the recurrent laryngeal nerves were identified bilaterally in 98.1% of patients. These nerves were not identified in 0.8% of cases. Only in two instances was nerve injury suspected during the surgical procedure.

The risk of immediate complications associated with hospitalisation was relatively low.

Re-bleeding associated with surgery was registered for 27 patients (2.1%) and infections requiring treatment were registered for 15 patients (1.2%).

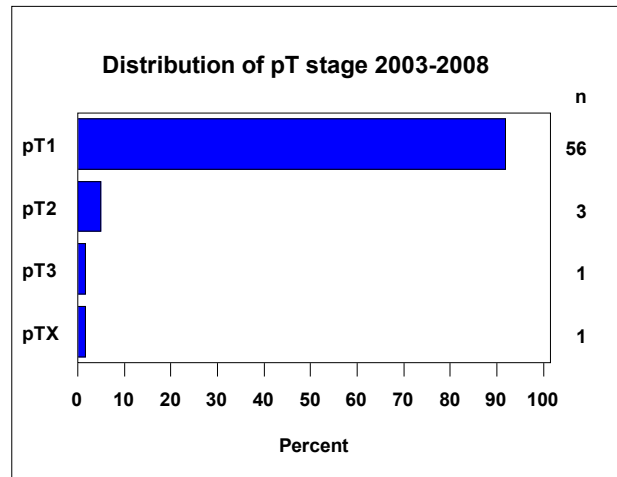
Ninety two patients (7.2%) required i.v. treatment with calcium because of severe hypocalcaemia during hospitalisation.

## Cancer

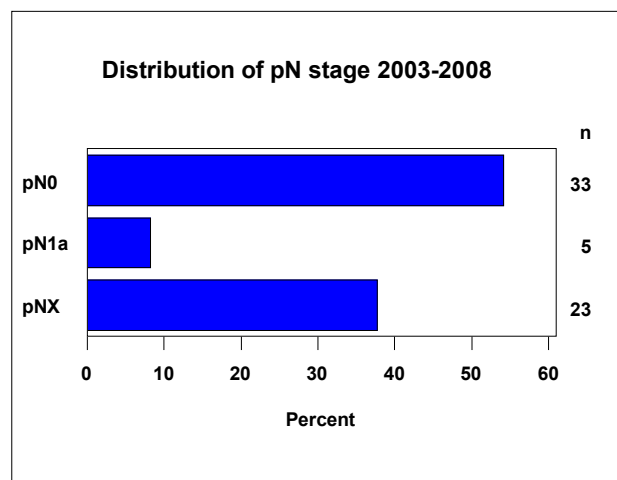
The histological examinations additionally identified papillary cancer in 58 patients (4.5%).

The vast majority of these patients presented with stage pT1, but more advanced stages were also seen. Lymph gland metastases were registered for 5 of the patients with thyroid cancer (8%).

### Papillary cancer pT stage for Graves' disease



### Papillary cancer pN stage for Graves' disease



### Laryngoscopy 6 weeks after surgery

Unilateral paresis of the recurrent laryngeal nerve occurred in 4% of the patients. Two patients experienced bilateral paresis. No laryngoscopy was performed on 60% of the patients.

## Laryngoscopy 6 weeks after surgery

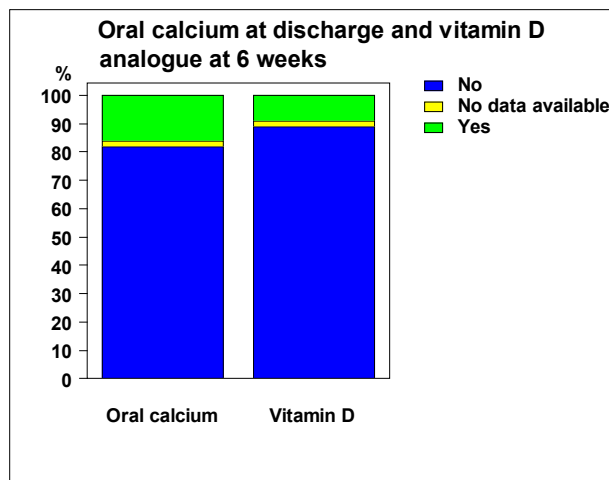
	Number	Percent
Indirect laryngoscopy (< 6 weeks from the time of operation)	426	33.36
Normal		
No data available	30	2.35
Not performed	768	60.14
Paresis of the right recurrent laryngeal nerve	20	1.57
Paresis of the left recurrent laryngeal nerve	31	2.43
Bilateral paresis of the recurrent laryngeal nerve	2	0.16
Total	1277	100.00

## Medical treatment for hypocalcaemia after 6 weeks

At the first follow-up there were 1013 patients (78.7%) who were not being treated for hypocalcaemia.

There were 118 patients (9.1%) who received treatment with vitamin D analogue, three quarters of these in combination with orally administered calcium. There were 116 patients (9%) who were receiving treatment with a fixed dose of orally administered calcium alone.

## Medical treatment with calcium and vitamin D analogue after 6 weeks



Multivariate analyses showed that calcium levels on the first day after surgery correlated strongly with orally administered calcium and vitamin D analogue treatment at 6 weeks ( $p < 0.0001$ ).

## Laryngoscopy after 6 months

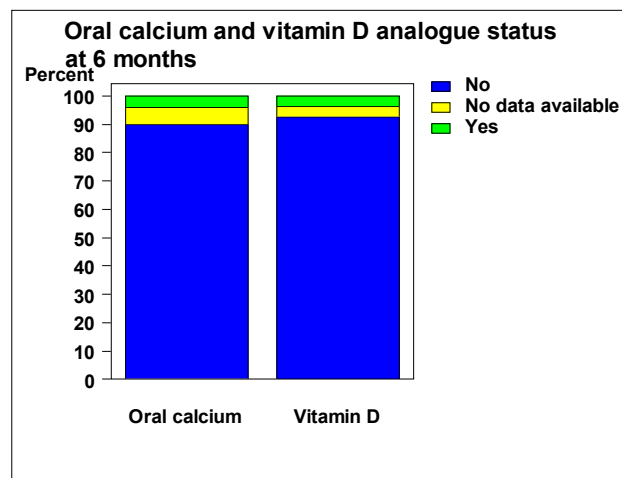
After 6 months unilateral paralysis was registered for 5 patients and bilateral paralysis for one patient. Data was missing or follow-up data not available for 16 patients with postoperative paresis. The frequency of nerve paresis after 6 months was therefore within the interval of 0.5 to 1.7%.

## Medical treatment for hypocalcaemia after 6 months

After 6 months there were 1113 patients (87.5%) who were not being treated for hypocalcaemia.

Fifty patients received treatment with vitamin D analogue (3.9%), two thirds of which were combined oral calcium treatment cases. There were 20 patients (1.5%) receiving treatment with a fixed dose of orally administered calcium alone. There are 27 patients, however, who have not been followed-up and data is missing for 20 patients who were initially treated for hypocalcaemia, so the true frequency is likely to be significantly higher.

### Medical treatment with calcium and vitamin D analogue after 6 months



# Primary hyperparathyroidism 2004-2008

## Changes in treatment and results over 5 years

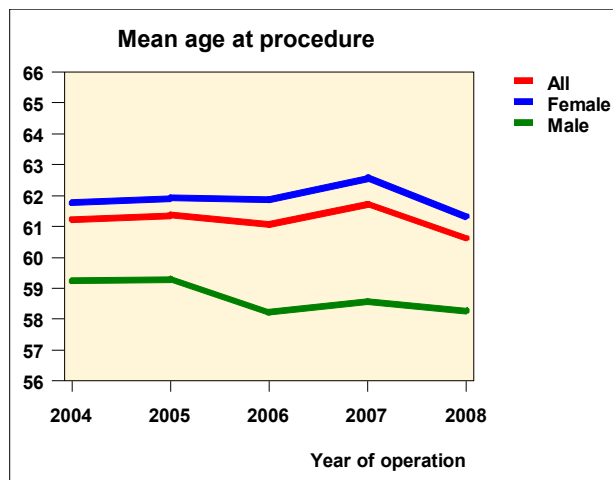
### General

During the 5 year period there were 3343 operations for primary hyperparathyroidism registered. The median age was 62 years, 78% of the patients were female and the preoperative mean value for total calcium was 2.82 mmol/l. There were 72% of the patients recorded as being symptomatic. It is also noteworthy that the number of patients who were re-operated during the analysed period was relatively stable, at around 5%.

### Changes over time in age, gender, and serum calcium

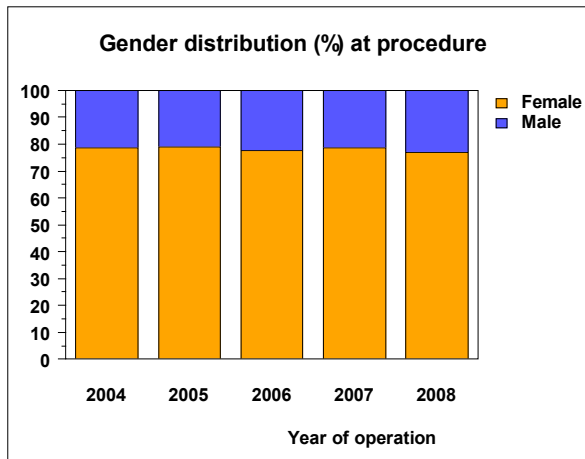
During the time-span there were no obvious differences observed in patient demographic parameters. Males were younger than females. The preoperative values for serum calcium (total) dropped somewhat, for both men and women, but not significantly.

### Age



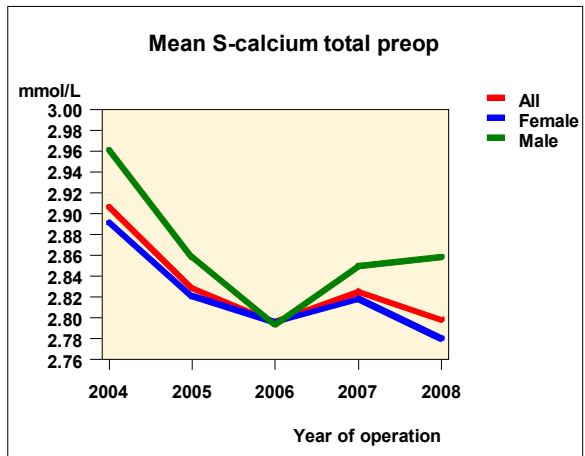
Not significant

## Gender



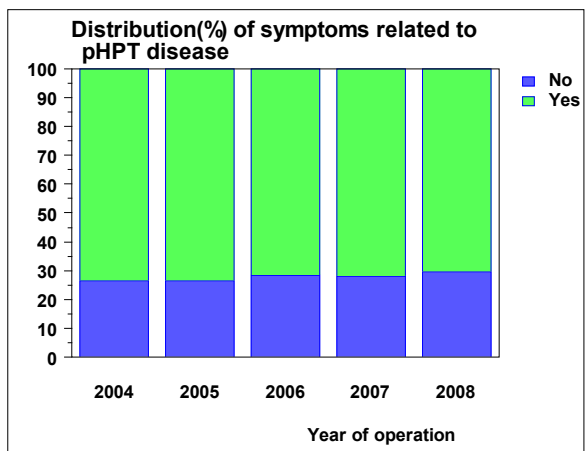
Not significant

## Total serum calcium (mmol/l)



$p = 0.36$

## Symptoms



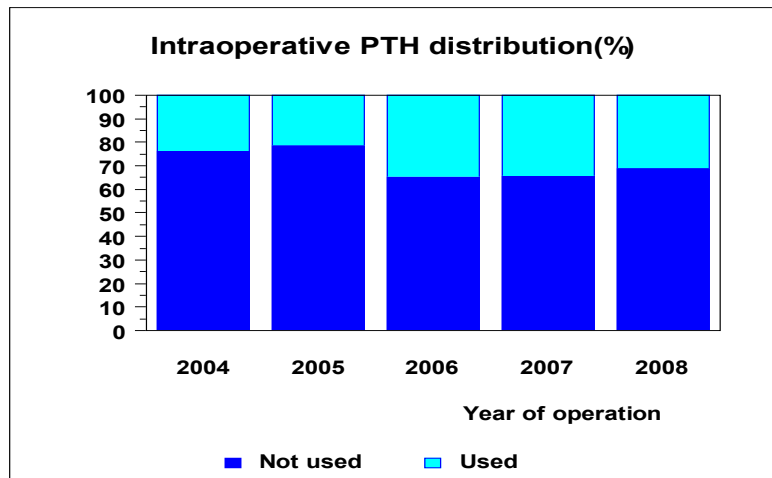
$p = 0.22$



## New techniques

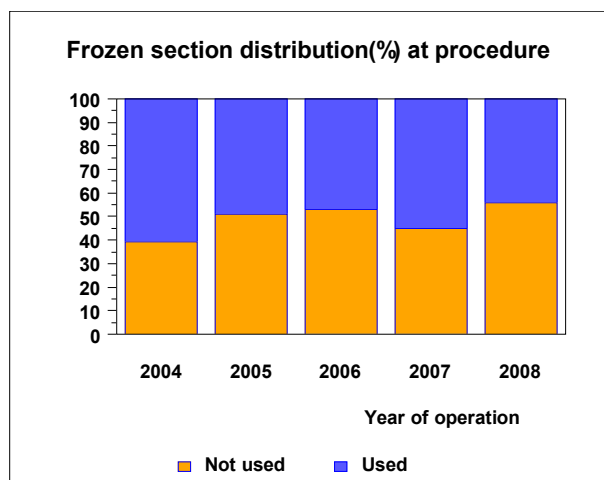
Use of intraoperative PTH increased during the period, mainly between 2005 and 2006, and after that stabilised at around 35% of operations performed. During this period the proportion of patients who were operated with frozen section examination was reduced.

### iOPTH



$p < 0.001$

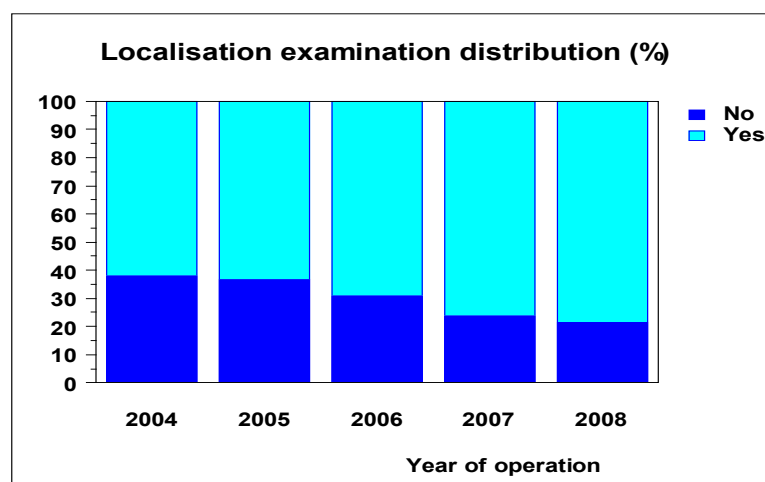
### Frozen section



$p < 0.001$

The use of preoperative localisation examinations successively increased over the period and is now used for around 80% of patients prior to surgery.

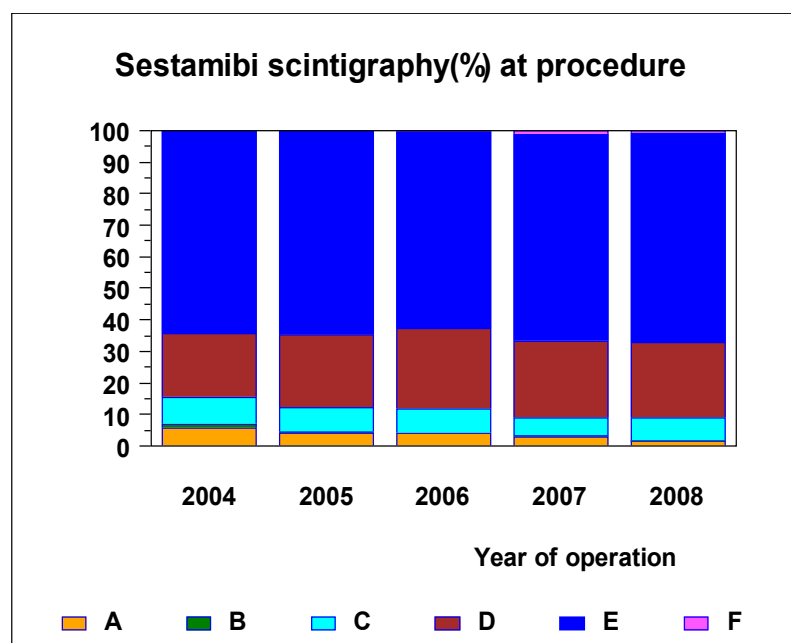
## Proportion of patients undergoing preoperative localisation examinations



$p < 0.001$

During the time-span, however, there were no obvious changes in sensitivity and specificity for the most common localisation examination methods, sestamibi scintigraphy and ultrasound.

## Sestamibi scintigraphy



$p = 0.37$  for true positive results for solitary parathyroid adenomas

A=Correct position of one pathologic gland, but multiglandular disease not predicted

B=False prediction of multiglandular disease in solitary adenoma

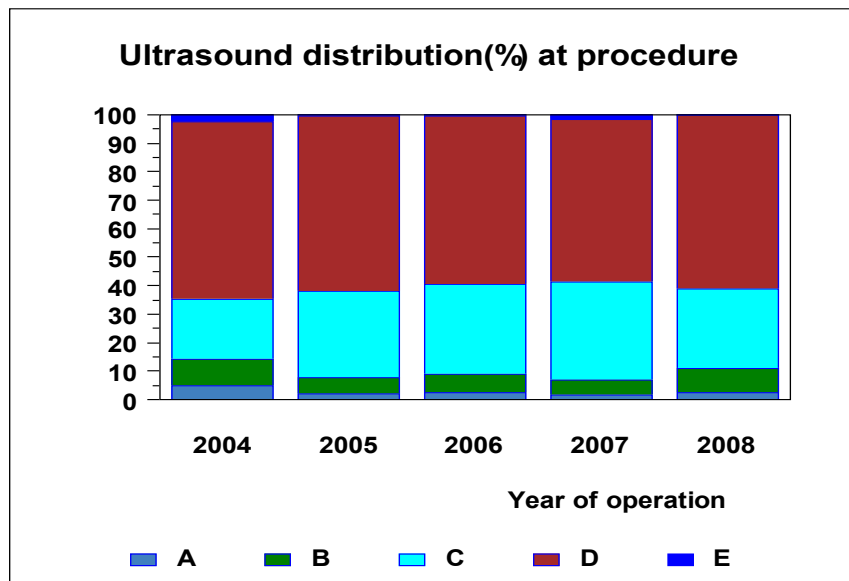
C=False preop. localisation of solitary adenoma (FP)

D=Negative/inconclusive preop. examination

E=True preop. localisation of solitary adenoma (TP)

F=True preop. prediction of multiglandular disease

## Ultrasound examination



$p=0.40$  for true positive results for solitary parathyroid adenomas

A=Correct position of one pathologic gland, but multiglandular disease not predicted

B=False preop. localisation of solitary adenoma (FP)

C=Negative/inconclusive preop. examination

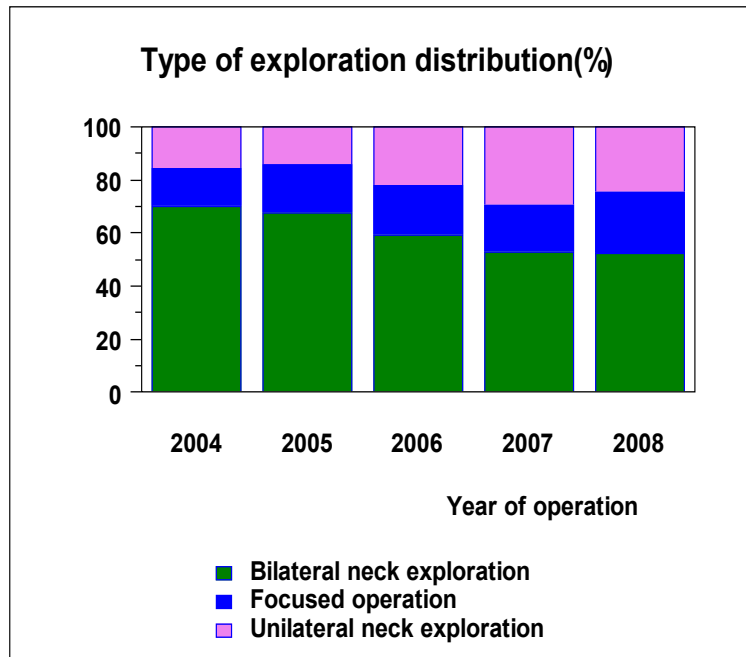
D=True preop. localisation of solitary adenoma (TP)

E=True preop. prediction of multiglandular disease

## Operation and immediate consequences

The proportion of patients who underwent limited parathyroid exploration increased during the time period, so that approximately 50% of the patients were operated either with a focused or unilateral procedure. The calcium values on the day after the procedure did not change during the period studied.

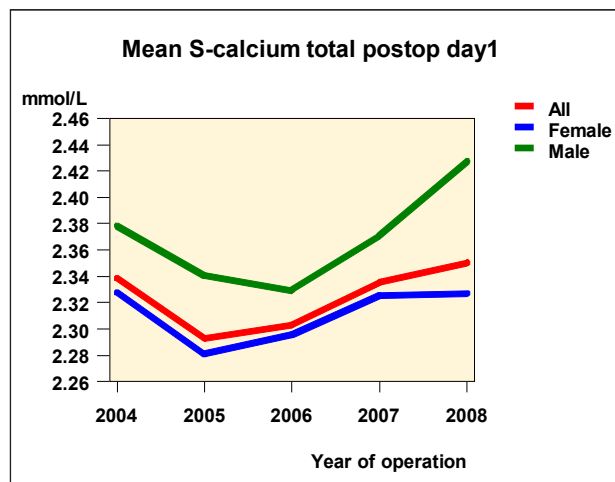
## Type of procedure



Type of exploration	2004	2005	2006	2007	2008
Bilateral neck exploration	69.7	67.5	59.2	52.6	52.0
Focused operation	14.7	18.3	18.5	17.8	23.3
Unilateral neck exploration	15.6	14.1	22.3	29.7	24.7

P<0.001

## Total calcium (mmol/l) day 1 postop.

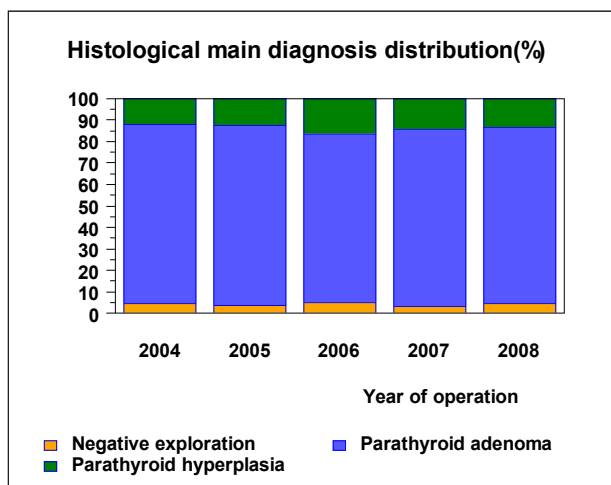


Gender	2004	2005	2006	2007	2008	(Random Coefficients Models) P value
All	2.34	2.29	2.30	2.34	2.35	0.6490
Female	2.33	2.28	2.30	2.33	2.33	.
Male	2.38	2.34	2.33	2.37	2.43	.

### Histological examination

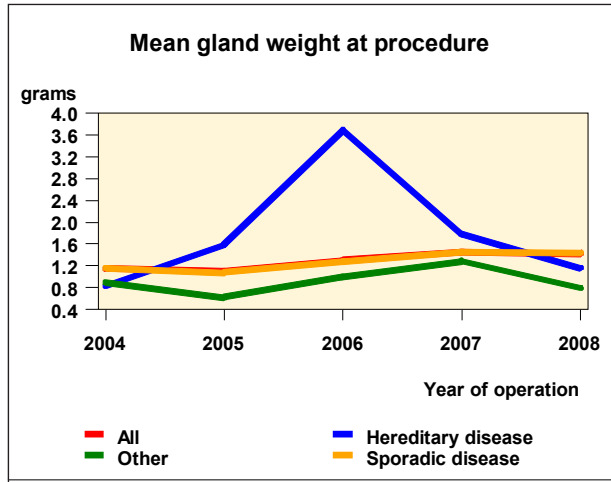
In contrast to literature reports, the increase in patient numbers has not led to a change in the distribution of diagnoses between patients with solitary adenoma and those with multiglandular disease. The proportion of patients with negative exploration results has not changed notably either. A trend can be seen, however, towards a reduction in the weight of the parathyroid tissue excised for sporadic disease, while the reverse has happened for hereditary disease during the time period studied.

### Histology



Histological main diagnosis	2004	2005	2006	2007	2008
Negative exploration	4.6	3.5	4.8	3.3	4.7
Parathyroid adenoma	83.5	84.2	78.8	82.3	82.1
Parathyroid hyperplasia	11.9	12.3	16.4	14.4	13.2

## Excised gland weight

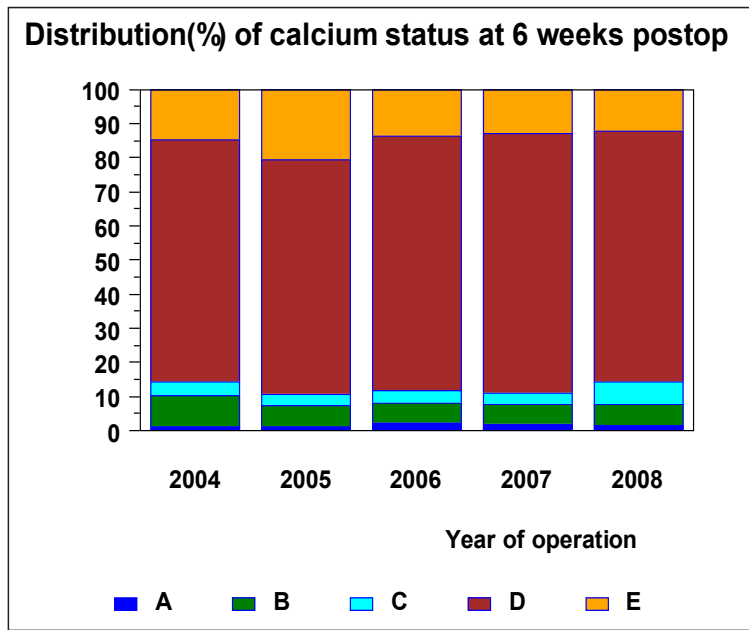


p= 0.95

## Calcium status at the first follow-up visit

The proportion of patients who had strict normocalcaemia at the first postoperative follow-up increased during the time period. The reasons for this were a combination of the fact that fewer patients received medical treatment for hypocalcaemia and that the proportion of patients with persistent disease also declined.

## Calcium status at the first postoperative follow-up check-up (< 6 weeks)



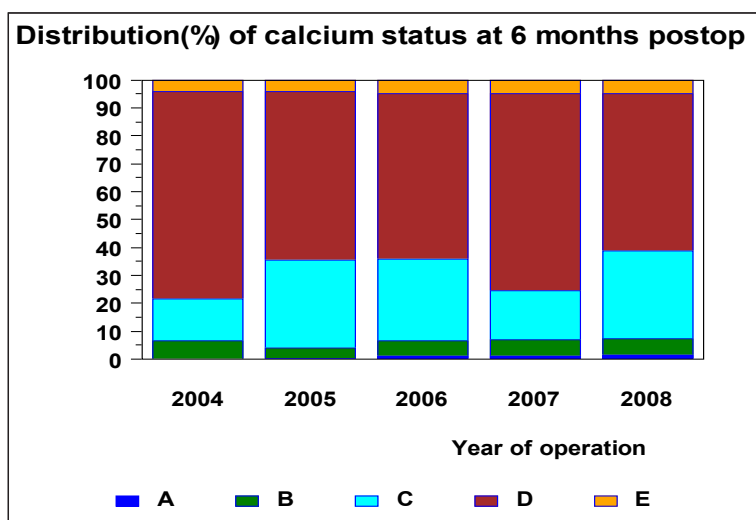
Calcium status at 6 weeks postop	2004	2005	2006	2007	2008
A = Calcium below the reference range without treatment	1.2	1.0	2.3	1.8	1.4
B = Hypercalcaemia (spontaneous)	9.2	6.3	5.7	6.0	6.4
C = No data available	3.7	3.3	3.9	3.2	6.7
D = Normocalcaemia	71.2	68.8	74.7	76.0	73.4
E = Treatment with calcium and/or vitamin D analogue therapy	14.7	20.6	13.5	13.0	12.2

	Number of patients with Normocalcaemia					
Normocalcaemia	2004	2005	2006	2007	2008	Cochran-Armitage Trend Test P-value
No	90	226	342	222	241	0.02
Yes	257	346	504	540	311	

### Calcium status after 6 months

A change in persistent disease after 6 months is difficult to comment on from the existing data. Instead there is an obvious increase in the number of patients who have not been followed-up after 6 months, probably due to more departments participating in the registry that have not previously had this follow-up routine.

### Calcium at 6 months



$p < 0.001$

- Normocalcaemia
- Patients not followed-up





# 9. Conclusions

## Thyroid

- The results show that a remarkably large number of patients with thyroid cancer underwent surgery in the absence of a malignant diagnosis being suspected or confirmed preoperatively. The sensitivity of cytology was below what is regarded as the standard in the literature. A significant proportion of patients, diagnosed with thyroid cancer, were initially operated only for compression symptoms.
- Papillary cancer was diagnosed to a somewhat greater extent than expected in operations for Graves' disease. The majority of cases were, however, stage pT1.
- Postoperative hypocalcaemia requiring oral treatment with calcium or vitamin D analogue occurred to an alarming extent, even as late as 6 months after surgery.
- Postoperative vocal cords paresis occurred somewhat more often than reported in the literature. The majority of injuries were however of short duration.
- Preoperative vocal cord examinations were not consistently routinely performed prior to thyroid surgery for patients with thyroid cancer, and not either for patients who had previously undergone a thyroid procedure.

## Parathyroid

- All of the preoperative localisation examinations used had a moderate sensitivity.
- During the period 2004-2008 the proportion of patients who underwent a preoperative localisation examination increased, as well as the proportion of patients undergoing focused parathyroidectomy or limited neck exploration. The preoperative values for serum calcium (total) decreased.
- There is a tendency towards a reduction of biochemically and medically treated hypocalcaemia during the time period 2004-2008, without an increase in the number of re-operations or patients with persistent disease. The proportions of patients with solitary parathyroid adenoma versus hyperplasia have not been affected either.
- The proportion of patients who have been cured is, however, somewhat lower and postoperative hypocalcaemia is more common than reported in the literature, especially for patients who undergo re-operation and have a hereditary form of the disease and/or multiglandular disease.
- With regard to new techniques, the use of intraoperative PTH would appear to improve the chances of cure, and conveys a reduced risk of being affected by postoperative hypocalcaemia.
- Localisation examination appear to reduce the risks of medically treated hypocalcaemia, at least in the short term.
- A localisation examination that is negative indicates a significantly higher risk of a poorer outcome following surgery.



## 10. Actions in response to the results (thyroid and parathyroid)

- A detailed survey has been carried out with regard to preoperative diagnostics (cytology and ultrasound investigation) for thyroid cancer. Collected data has been presented at both national and international meetings. Additional analyses will be carried out during 2009-2010 as part of a separate research/post-graduate project, with supervisors/co-supervisors who are also members of the steering committee of the registry.
- A multidisciplinary symposium on thyroid cancer diagnostics was held at the Swedish Medical Association 2008 National Convention. Articles for the medical press from this meeting are in manuscript.
- The Pathology Association in Sweden have been contacted with the aim to standardise/grade cytology results for thyroid investigations. Work on this project is ongoing.
- Local guidelines for the investigation of thyroid nodules have been formulated and distributed in the southern healthcare region.
- A detailed survey of the techniques used for preoperative localisation examinations for primary HPT was carried out during 2008. Statistical analysis of the factors that affect sensitivity and specificity will be carried out during 2009-2010.
- The relatively poor results that were seen following re-operation for primary HPT were discussed in conjunction with the workshop of the European Association of Endocrine Surgeons in Lund in March 2009 on modern surgical techniques for the treatment of primary HPT. Further discussions will be initiated in conjunction with the 2009 user meeting.
- An in-depth analysis will be carried out regarding the impact of modern surgical techniques, in particular ultrasound examination, sestamibi scintigraphy and intraoperative PTH, with regard to the possibilities of achieving a cure, as well as the risk of postoperative hypocalcaemia when operations are performed for primary HPT.
- The Steering Committee will discuss and issue invitations to separate symposia regarding the problem areas that have been identified.

Lund 4 September 2009

Anders Bergenfelz  
Register Administrator  
Scandinavian Quality Register for Thyroid and Parathyroid Surgery



