Cost-analysis of minimally invasive surgery and conventional neck exploration for primary hyperparathyroidism

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Abstract

Objective To obtain knowledge on cost-relations between minimally invasive adenomectomy and conventional neck exploration in patients with primary hyperparathyroidism.

Summary background data Imaging modalities and measurement of perioperative parathormone concentration facilitate successful minimally invasive adenomectomy. As a result reduction in operative time and admission days may be anticipated together with potential reduction in costs.

Methods Prospectively, 164 consecutive patients with biochemically proven primary hyperparathyroidism were enrolled. Because of variation in imaging protocol over time, 126 patients underwent ultrasonography and computed tomography; in 38 patients ultrasonography was the sole modality. Data were collected from the first preoperative surgical consultation to discharge from follow-up. Costs were calculated by multiplying patients' resources by unit costs. To obtain insight in the effect of changing appreciable variables multiple sensitivity analyses were performed.

Overall 123 patients were selected for minimally invasive adenomectomy, 41 for conventional neck exploration. Mean costs for minimally invasive adenomectomy were calculated to be € 1288 +/- 431 (mean, +/- SD) and for conventional neck exploration € 2106 +/- 1070. Sensitivity analyses showed that an increase in total average costs of 63%, an increase in operative time to 272 minutes, prolongation of admission with 2.5 days, or a failure rate of 54% in the minimally invasive adenomectomy group would result in a break-even point with equal costs of both alternatives.

Conclusion Minimally invasive adenomectomy, including preoperative imaging is less expensive than conventional neck exploration in the treatment of primary hyperparathyroidism.

Introduction

For many years conventional neck exploration (CNE) has been the gold standard in the surgical treatment of primary hyperparathyroidism (pHPT), but with the advent of minimally invasive surgery, this pre-eminence has been questioned. As primary hyperparathyroidism is caused by a solitary adenoma in the vast majority of cases, CNE involves unnecessarily extensive exploration of normal parathyroid glands and prolonged operating time. Several authors have recommended unilateral neck exploration for that reason [1 2], and moreover, direct adenomectomy can now be performed with promising results [3 4 5].
Recently, we have introduced a technique of direct, minimally invasive adenomectomy (MIA) based on preoperative localization studies by ultrasonography (US) and spiral computed tomography scanning (CT) [6].
The results of this approach in our first 110 patients led us to conclude that MIA is a safe and effective alternative to CNE and may replace CNE in approximately two thirds of patients with pHPT [7].
Given current limited resources, it is of vital importance to obtain knowledge on cost-relations between these two alternatives. The current study contains a prospective cost-analysis of 164 consecutive patients undergoing CNE or MIA for primary hyperparathyroidism. In addition, we have performed sensitivity analyses to obtain an impression of the effect of changes in particular variables, for example operative time and admission time.

Methods

Patients

Between October 1994 and July 2000, 164 patients with biochemically proven primary hyperparathyroidism were enrolled in this study. Previous (para)thyroid surgery, familial hyperparathyroidism and multiple endocrine neoplasia syndrome were considered criteria for exclusion. After informed consent had been obtained for MIA, when this was thought to be possible, the patient was scheduled for preoperative imaging using US and CT. If the test results unequivocally indicated solitary disease the patient was advised to undergo MIA. On the other hand, if test results were equivocal or indicated multiglandular disease the patient was advised to undergo CNE. Surgery took place during a regular hospital admission and patients were discharged after surgery when they were able to look after themselves unaided and only needed oral analgesics for pain management.

Protocol

In this study four sub-groups are identified on basis of a) variation of preoperative imaging protocols over time b) the introduction of a perioperative parathormone (PTH) assay in late 1998. In the first series of 65 patients (October 1994 - March 1997) both US and CT were performed as preoperative localization studies. In the second series (April 1997 - October 1998, 45 patients) US was used alone unless its results were inconclusive, when CT was added. Because initial imaging with US produced inferior results [7] we reintroduced both modalities in the routine as preoperative work-up since then (November 1998 - July 2000, 54 patients). As we have described elsewhere, we started in June 1998 to use a perioperative PTH assay to predict the success of surgery for primary hyperparathyroidism, after the assay had been shown to agree fully with both conventional PTH assays and postoperative serum calcium measurements in over 100 patients [8].

Data collection

For the purpose of this cost analysis resources of 164 patients were prospectively measured. Resources before inclusion were not included as these were considered to be equal for all patients with primary hyperparathyroidism (i.e. diagnostic procedures for the diagnosis of primary hyperparathyroidism).
Data were collected from the first (preoperative) surgical consultation at the outpatient department to discharge from follow-up and counted for all 164 patients.
It was expected that all patients would receive regular intravenous anesthesia and be monitored on a normal ward postoperatively. Nevertheless, we recorded type of anesthesia and level of care (i.e. intensive care, medium care or normal care).

Procedures and measurement of resources

As the result of both operations is the same, we chose to perform a cost-minimisation-analysis [9]. A hospital-perspective was taken, since it is unlikely to expect differences in societal costs. The following parameters were identified as appreciable units and counted for each patient;

Before admission:

1 preoperative consultation (including laboratory testing)

2 imaging strategy (ultrasonography, computed tomography, nuclear mapping)

Admission:

3 total time in operating theatre (minutes), operation time (minutes) defined as the time between skin incision and - closure, time on recovery ward (minutes)

4 number of days in hospital

5 perioperative parathormone assay

6 in-hospital complications: conversion in CNE, reexploration, and miscella-

neous costs due to failed surgery, bleeding or infection, vocal cord paralysis, clinical hypocalcemia
7 laboratory tests

After discharge
8 number of postoperative consultations (outpatient department, emergency room)
9 late post-operative complications (described under 6)
10 miscellaneous costs due to recurrent disease (list 1-10)

Calculation of costs

Costs were calculated by multiplying patients' resources by unit costs [10]. The costs of materials and anesthesia, considered equal in both groups and based on average consumption, were provided by the department of financial administration of the University Medical Center Utrecht (The Netherlands), based upon 1999 guidelines.
Costs for nursing and medical personnel were calculated using the bottom-up principle [11]. According to this principle costs are calculated based on actual consumed time and resources. Based on personnel salaries and wages (1999 guideline) costs were calculated per time unit (minute) and multiplied by actual consumed time during operation and recovery time.
Costs for hospital days and outpatient consultations were calculated according to the guidelines of the Dutch Ministry of Health, Welfare and Sports issued in 1999 [12] and include all relevant overhead costs of administration and management, other hospital departments (cleaning, maintenance) and housing. General overhead costs were not used, since these figures are inaccurate and not generally representative on account of inter-hospital variability in financial systems. Costs of PTH assays and other laboratory tests were provided by laboratory administration of the University Medical Center Utrecht (The Netherlands). In cases of clinical hypocalcemia patients were treated with oral calcium (CalciumSandoz®) and alfacalcidol (Etalpha tablets®). Average retail prices for medication in the Netherlands were used [13].
All costs were calculated in Euro's (€). The official exchange rate at January 15, 2001 was 1€ = 0,9439 US Dollar.

Outcome assessment

The clinically most relevant outcome of surgical intervention in pHPT is failure or success, defined respectively as postoperative serum calcium concentrations above or below 2.60 mmol/L.

Sensitivity analysis

Sensitivity analyses give insight into the effects of change of an important variable on total average costs. Variables were identified to be important if their costs were appreciable in relation to the total costs and if they were liable to significant change (for example operative time or admission time). We chose to perform a so-called threshold analysis of each variable. This analysis uses the basic assumption that total average costs are equal in both alternatives. Then, the percentage in change of the variable is calculated. This gives insight into the degree of change, which is required to eliminate differences in costs.

The following four variables were identified:

1. Operating time. Individual variation in personal skills and experience influences operating time.
2. Admission days. Duration of admission varies between different reported studies. We calculated (a) how long an MIA patient's admission could be prolonged to bring the costs up to those of CNE and (b) the effect on CNE costs of reducing admission to one day.
3. Failure rate. Failure rate varies in MIA and CNE with individual experience.
4. Imaging. Conventional exploration can be done safely and effectively without preoperative imaging. For comparative purposes we therefore also calculated total average costs in MIA with all imaging costs charged to MIA.

Finally, we performed a fifth sensitivity analysis based upon the assumption that PTH assay can be performed in all future patients with primary hyperparathyroidism. Consequently, surgical failure will be identified within one hour after surgery and this will result in immediate re-exploration without the additional costs of secondary admission, imaging and laboratory tests. We calculated the costs of MIA and CNE if PTH assay was performed in all cases.

Statistical analysis

Costs are presented as means with their standard deviation. For normally distributed, continuous data the Student's t-test was used to detect statistically significant differences between groups. Not normally distributed data were represented as medians with their interquartile ranges (IQR). We used the Mann-Whitney U-test to test differences between medians. A chi-square statistic was used to test independence between two categories of data. If an expected value of one of the categories was less than five, we used a Fisher-exact test. A p value of <0.05 was considered statistically significant.

Results

Patients

Resources were recorded for 123 patients in the MIA group, 41 in the CNE group. Patients' characteristics are listed in **Table 1**. All patients underwent US, and 126 patients additionally CT. Two patients underwent (on their own request) additional sestamibi-technetium99m scintigraphy (Sestamibi scintigraphy) after inconclusive US and CT to exclude the possibility of mediastinal adenoma. All patients were treated in normal hospital setting. No differences were recorded in the type of anesthesia and intensity of care.

Minimally invasive adenomectomy group (123);
Minimally invasive adenomectomy was immediately successful in 113 patients (92%), as judged by postoperative normocalcemia, recorded on the first postoperative day. Because the localized adenoma could not be found during initial exploration, MIA was converted to CNE in four patients resulting in postoperative normocalcemia. In the period before the implementation of PTH assay to our protocol, three patients displayed persistent hypercalcemia in the postoperative period and underwent successful reexploration at a later stage. Perioperative PTH assay identified three 'potential failures' after which immediate re-exploration followed, which resulted in resection of the causative adenoma.
Initial success, defined as postoperative normocalcemia at the first postoperative day was thus recorded in 120 patients (98%) (113 immediate successes + 4 converted MIA + 3 immediate re-explorations).

Conventional Neck Exploration group (44);
Two (5%) failures were recorded after conventional exploration. The first patient displayed persistent hypercalcemia on the first postoperative day and was re-explored at a later stage, during which a third, initially missed adenoma was found in the retrosternal thymus. Perioperative PTH assay correctly predicted persistent hypercalcemia in the second patient after three normal parathyroid glands were identified but no adenoma could be localized in the neck. Additional Sestamibi scintigraphy localized the missing adenoma in the mediastinum, whence it was subsequently resected after median sternotomy.

Hence, the initial success rate (defined as postoperative normocalcemia (serum calcium between 2.20-2.60 mmol/L) on day one) was 98% (120/123) in MIA and 95% (42/44) in CNE (NS). Until today (median follow-up 41.5 months, IQR 22-52) no recurrent disease has been documented.

Table 1 Patient characteristics.

	MIA		CNE	
Patients (n)	123		41	
Age (years)	59		60	
Male / Female	37/86	(30/70%)	12/29	(29/71%)
Asymptomatic (n)	92	(75%)	29	(71%)
Symptoms (n)	31	(25%)	12	(29%)
Nephrolithiasis	17		8	
Bone pain	10		4	
Abdominal complaints	3		2	
Miscellaneous	12		4	
Serum calcium *				
Preoperative (mmol/L)	2.84	(2.35-3.60)	2.85	(2.50-3.88)
Postoperative (mmol/L)	2.25	(1.61-2.80)	2.29	(1.81-2.64)
Preoperative PTH † (pmol/L)	12.5	(4.9-180)	13.1	(9-234)

MIA minimally invasive adenomectomy.

CNE conventional neck exploration.

* Serum calcium normal 2.20-2.60 mmol/L.

† Preoperative PTH normal <8 pmol/L.

Resources and costs

Resources could be determined for all patients and are listed in **Table 2**.
The median operation time was 20 minutes (IQR 15-25) for MIA and 75 minutes (70-90) for CNE ($p<0.0005$). Median additional time in the operation room (time in the operation room minus exploration time) for preoperative and postoperative anesthetic care was 42 (36-50) minutes for MIA versus 40 (29-54) minutes for CNE. No significant difference ($p<0.808$) was measured in median recovery time between MIA (115 minutes) and CNE (117 minutes), whereas median admission was significantly shorter ($p<0.0005$) in MIA (2 days) versus CNE (3days).
Owing to surgical failure, vocal cord paralysis or clinically significant hypocalcemia, 30 additional consultations (15 in both groups, 12% MIA and 34% CNE) were necessary, 32 additional laboratory tests for serum calcium were performed, and 11 patients needed supplementary calcium. Failure after MIA resulted in re-exploration on the same day in three patients. Three other failures in the MIA group underwent re-exploration during a second admission. Two of them had additional Sestamibi scintigraphy before being re-explored. As a consequence, a total of 380 minutes of exploration time and 9 admission days were added to the MIA group. Two failures in the CNE group were responsible for 165 additional operative

Table 2 Measurement of resources.

	MIA	CNE
Pre-admission phase		
Consultation	123	41
Ultrasonography	123	41
Computed tomography	90	36
MIBI	0	2
Admission phase		
Operative time (average in min)	20	70
Additional time in operation room (average in min)	42	40
Recovery time (average in min)	115	117
Hospital days (average in days)	2	3
Perioperative PTH assay	57	24
Laboratory tests	123	41
Post admission phase		
Consultation	138	56
Recurrent disease	0	0
Complications (miscellaneous)	0	0
Laboratory tests	136	55
Complications		
Conversion	4	0
Additional imaging US	2	0
CT	0	0
MIBI	2	2
Reexploration	6	2
Operative time (average in min)	63	83
Additional time in operation room (average in min)	43	45
Recovery time (average in min)	108	140
Hospital stay (average in days)	3	8.5
Perioperative PTH assay	4	2
Laboratory tests	3	2
Temporary hypocalcemia	5	6
Miscellaneous temporary vocal cord paralysis	2	1
Bleeding/infection	0	0

Data are given in numbers, unless stated otherwise.

Table 3 Cost of main resources (Euro's).

	MIA	CNE
Consultation	10,659	3,962
Imaging	19,311	8,824
Surgical supplies	13,070	4,357
Anesthetic supplies	5,582	1,861
Recovery room supplies	391	130
Personal operation cost	9,373	10,190
Personal perioperative period cost	7,010	2,264
Personal recovery cost	6,677	2,297
Hospital stays	75,878	42,960
Perioperative PTH assay	1,467	625
Laboratory tests	1,783	667
Additional cost of complications	7,203	8,177
Total costs from hospital perspective	*158,404*	*86,314*
Average cost per patient (+/- SD)	**1,288 +/- 431**	**2,106 +/-1070**

minutes and 17 extra days in hospital, 12 of these days being attributable to the patient who had sternotomy. Both these patients had US and Sestamibi scintigraphy in their work-up before reexploration.
Resources were multiplied by unit costs to obtain total costs. **Table 3** shows the costs for preoperative work-up, operation and admission costs, complications and postoperative follow-up for both groups. Mean total costs (+/- SD) were calculated to be € 1,288 +/- 431 for MIA and € 2,106 +/- 1070 for CNE ($p<0.0005$).

Sensitivity analyses

The analysis for MIA shows that an increase in average total costs of 63% would result in a break-even point for total hospital costs (**Table 4**).
The first sensitivity analysis revealed that operation time of MIA may increase (with 1460%) to 272 minutes before the costs of MIA equal those of CNE.
Similarly a prolongation of 2.5 days (225%) of admission time in MIA would equal total costs of both methods. If, theoretically, admission for CNE would be reduced to one day, total average cost would decrease to € 1,377 (7% more expensive than MIA).
From the third analysis it can be calculated that the maximum allowable failure rate for MIA is 54%. This is based on recorded resources of failed MIA and the calculation that the average costs for reexploration in MIA is € 1,491 per reexplo-

Table 4 Sensitivity analyses. Effects on total average costs in minimally invasive adenomectomy and conventional neck exploration after changing appreciable variables.

Analysis	Variable	Variation	Effect		
			%	€	in terms
BE	average MIA costs	increase by	+ 63	2,106	MIA cost equals to CNE cost
1	operating time	increase of 272 minutes in MIA	+ 1460	2,106	MIA cost equals to CNE cost
2	admission	increase of 2,5 days in MIA	+ 225	2,106	MIA cost equals to CNE cost
		reduction to 1 day in CNE	- 35	1,377	CNE cost reduces to 107 % of MIA cost
3	failure rate	67 failures in MIA	+ 54	2,106	MIA cost equals to CNE cost
4	imaging	CNE minus imaging costs	- 10	1,890	CNE cost reduces to 147 % of MIA cost
		imaging costs CNE allocated to MIA	+ 6	1,360	MIA cost increases with 6%; CNE cost 139 % of MIA
5	PTH assay	MIA plus PTH assay	- 4	1,242	MIA cost reduces with 4 %
		CNE plus PTH assay	- 6	1,977	CNE cost reduces with 6 %

BE = break-even.

ration, indicating that average total costs of MIA and CNE are equalized after 67 (67/123) failed MIA procedures.
Our fourth sensitivity analysis calculated costs of CNE in our series disregarding imaging costs. After deducting total imaging costs, the total average cost for CNE reduces to € 1,890 (reduction of 10%). If all imaging costs are then charged to MIA, costs in MIA rise to an average of € 1,360 (increase of 6%).
Finally, if PTH measurement would be used in every exploration, costs for MIA and CNE become € 1,242 and € 1,977 respectively; a further additional saving of 4 % and 6 % respectively.

Discussion

Conventional neck exploration was found to be more expensive than minimally invasive adenomectomy from a hospital point of view. Three dominant features of the minimally invasive technique that contribute towards the disparity in costs were identified. Firstly, since the exploration is limited to the diseased gland only, operative time is significantly shorter, but well comparable with reported [2 3] exploration times of 25-30 minutes in similar limited access parathyroid surgery.

Secondly, admission time is reduced from three to two days in favor of MIA. However, an admission time of three days, as we found in our study after bilateral exploration, is longer than the admission times of 1.4 to 1.9 days after comparable surgery reported in recent papers [14 15]. Therefore, we recalculated costs, using admission time as a variable in the sensitivity analysis. This showed that a reduction of stay to one day made costs compatible. However, if the assumption is made that admission time in CNE is reduced, it may also concomitantly be reduced in MIA, and thus lead to further cost reduction in the latter group. Furthermore, it should be realized that further cost reduction might be expected from MIA, when executed in day-care setting using intravenous sedation combined with the use of local anesthesia [2].
Thirdly preoperative imaging is a prerequisite to select patients for MIA, but we believe this is defensible because imaging in patients with primary hyperparathyroidism will result in identification of suitable patients for MIA, which is considered to be beneficial for patients with primary hyperparathyroidism. We agree with the statement that imaging is of no added value in first time CNE. Imaging consumed about 12 percent of the total budget in MIA (10 percent in CNE) but it resulted in MIA being performed in 75% (123/164). The fourth sensitivity analysis showed differences of 47 percent and 39 percent in costs between MIA and CNE after imaging costs were firstly denied in CNE and then allocated to MIA.
It is vital to realize that sensitivity analyses change only one variable at a time,

whereas in reality this is not the case. For example, if operative time is prolonged with four-and-half hours in MIA, admission time will probably increase as well.

The use of a perioperative parathormone assay as predictor of successful surgical treatment will facilitate 'delayed' conversion the same day when necessary during MIA or continuing exploration after CNE, resulting in limited additional work-up and need for secondary admissions for re-exploration. We calculated in our last sensitivity analysis that the use of perioperative parathormone assay results in an additional cost saving of 4 percent in MIA and 6 percent in CNE. However, even if we calculate total costs for failed MIA, using all records including those of failures before we began to use perioperative parathormone assay, it can be demonstrated that a maximum allowable failure rate of 54 percent in MIA will equalize costs with CNE. This is unlikely to occur and therefore we believe the outcomes of our results are robust.

We did not perform a randomized study. This does not necessarily vitiate the quality of our prospective comparison. Indeed, our groups are well comparable. Effectiveness for instance in terms of quality of life or morbidity and mortality is unlikely to differ between the two procedures. It is therefore completely justifiable to perform a cost-minimisation-analysis instead of a cost-effectiveness-analysis. However, if it had been recorded, post-operative pain might have been less in MIA patients, enhancing patient satisfaction and allowing them to resume normal life and return to work earlier. This would have counted in favor of MIA, and resulted in a larger cost difference from CNE. Furthermore, a hospital perspective was preferred over a societal perspective because societal costs are unlikely to differ between both alternatives.

In conclusion, minimally invasive adenomectomy is cheaper than conventional neck exploration for primary hyperparathyroidism. Given the present development of the standard use of perioperative PTH assay and the trend toward a shorter hospital stay after both procedures, we expect minimally invasive adenomectomy to be a safe, effective and cheap alternative to conventional neck exploration.

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