Increase in presentations and procedure rates for hyperparathyroidism in Northern Sydney and New South Wales

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ABSTRACT

Objective: To examine changes in presentation of primary hyperparathyroidism and rates of parathyroidectomy in Northern Sydney (the Northern Sydney Area Heath Service) and New South Wales (NSW).

Design: Retrospective case series January 1962 – December 2001 and audit of the NSW Department of Health inpatient database (1993–1999).

Setting: University of Sydney Endocrine Surgical Unit, Royal North Shore Hospital.

Participants: 1613 patients undergoing parathyroidectomy during the study period.

Main outcome measures: Age-standardised parathyroidectomy rates and indications for surgical intervention.

Results: The age-standardised rates of parathyroidectomy for primary hyperparathyroidism in women have increased significantly in Northern Sydney from 0.14 cases per 100 000 in 1976 to 7.7 cases per 100 000 in 1996 ($P < 0.001$). In NSW there has been an increase in parathyroidectomy rates in women from 5.1 cases per 100 000 in 1993 to 12.3 cases per 100 000 in 1998 ($P < 0.001$). Osteoporosis was the most common overall indication for surgery in Northern Sydney, accounting for 27% of all cases. The proportion of cases presenting with osteoporosis increased significantly from 4% in 1962–1980 to 34% over the past decade ($P < 0.001$).

Conclusions: The rate of parathyroidectomy procedures has increased markedly in Northern Sydney and in NSW. The investigation of osteoporosis has led to the diagnosis of primary hyperparathyroidism in an increasing proportion of cases and has contributed to the growing surgical referral rates.

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PRIMARY HYPERPARATHYROIDISM is now recognised as a relatively common endocrinopathy for which surgery remains the most successful primary therapy.[1] Surgical success rates exceeding 95% have been consistently achieved by appropriately experienced surgeons.[2,3] The incidence and prevalence of the disease varies with the population being studied and the frequency of measurement of serum calcium level. Commonly quoted annual incidence rates vary from 25–28 cases per 100 000 population to as low as 2.2 per 100 000.[4-6]

We reported previously that the number of patients referred for parathyroidectomy had "increased virtually exponentially" over the past three decades. This trend has continued, with the predicted annual caseload of parathyroidectomies for 2002 exceeding by three times the number performed only three years ago.[7,8]

The reasons why a single unit would see such a dramatic rise in referrals for a surgical procedure may include:

- changing geographic referral patterns;
- changes in operative technique facilitating easier surgery;
- increased awareness of the disease by the medical community;
- improved diagnostic capability;
- changing indications for referral for surgery; or
- a true increase in presentations.

We examined local changes in presentation of hyperparathyroidism, and quantified changes in the rates of parathyroidectomy throughout Northern Sydney (the Northern Sydney Area Health Service) and the whole of New South Wales (NSW).

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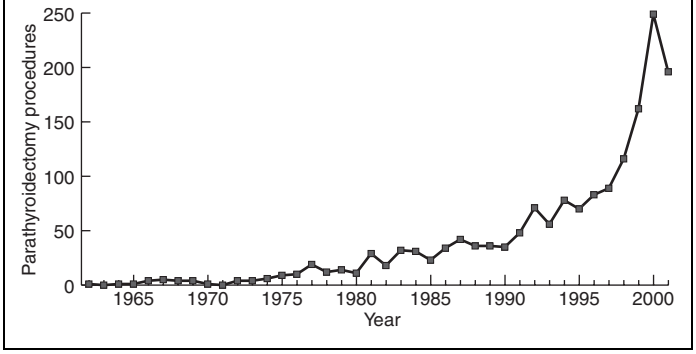
METHODS

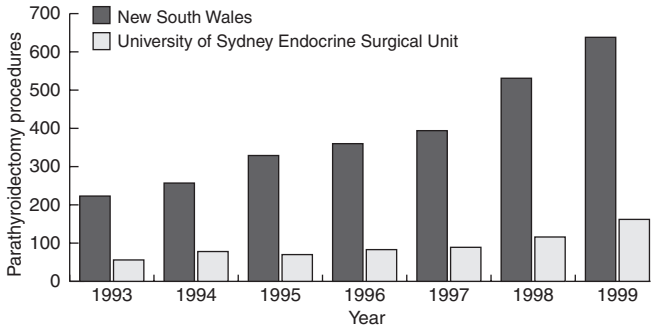
Parathyroidectomies in Northern Sydney

All patients undergoing parathyroid surgery in the University of Sydney Endocrine Surgical Unit from January 1962 until December 2001 were included. All thyroid, parathyroid and adrenal procedures performed within the unit have been recorded in a database established in 1957. The first documented parathyroidectomy was performed in 1962. Specific information obtained included presentation, indications for surgery and operative technique. The indication for surgery was documented and recorded in the database at the time of the initial surgical consultation, and refers to the principal presenting feature which led to the diagnosis of hyperparathyroidism (see Box 6 [*page 249*] for definition of terms).

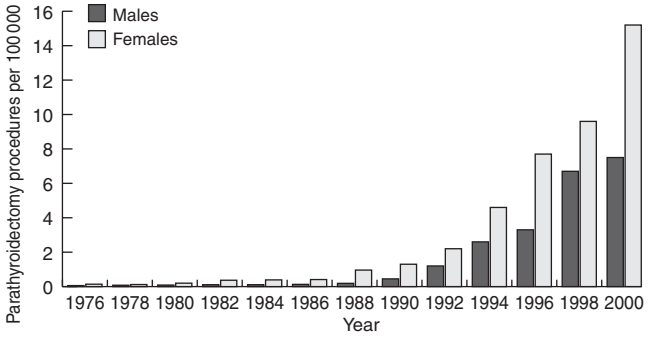
1: Annual number of parathyroidectomy procedures performed in Northern Sydney (University of Sydney Endocrine Surgical Unit), 1962–2001



2: Annual number of parathyroidectomy procedures for NSW and Northern Sydney (University of Sydney Endocrine Surgical Unit), 1993–1999



3: Age-standardised parathyroidectomy rate for Northern Sydney (University of Sydney Endocrine Surgical Unit), by sex, 1976–2000



Parathyroidectomies in New South Wales

Data on the number of parathyroid procedures performed in NSW were obtained from the Inpatient Statistical Collection Online System (ISCOS) for the period January 1993 to December 1999. This database, which was established by the NSW Department of Health in 1993, provides a record of all admissions and procedures performed within the various State Area Health Services.

Age-standardised parathyroidectomy rates

Population statistics for Northern Sydney and NSW were obtained from the *Northern Sydney Area Health Service Annual Report 1999* and the Australian Bureau of Statistics, respectively.[9,10]

Age-standardised parathyroidectomy rates were calculated for men and women in NSW for 1993–1999, using the direct method.[11] Age-standardised parathyroidectomy rates for Northern Sydney were similarly calculated for the period 1976–2000.

Statistical analysis

An exact test based on the Poisson distribution was used to compare age-standardised parathyroidectomy rates. Comparisons between the numbers of patients presenting with osteoporosis and asymptomatic disease were performed using Fisher's exact test.[12] Statistical analysis and age-standardised procedure rate calculations were performed using the STATA software package.[13]

RESULTS

Parathyroidectomies in Northern Sydney and NSW

In the 39-year period from January 1962 to December 2001, 1613 parathyroidectomies were performed in the University of Sydney Endocrine Surgical Unit. Of these, 1506 were performed for primary hyperparathyroidism and 107 for secondary or tertiary hyperparathyroidism. Box 1 shows the number of parathyroid procedures performed in the unit per year for all indications from January 1962 to December 2001. The annual number of procedures has continued to rise markedly throughout the study period.

The number of parathyroidectomy procedures performed per year also increased markedly in NSW in 1993–1999 (Box 2). The proportion of parathyroidectomy procedures performed in the University of Sydney Endocrine Surgical Unit has remained relatively constant, at between 20% and 30% of the total State caseload for this period (Box 2).

Age-standardised parathyroidectomy rates in Northern Sydney and NSW

The age-standardised rates of parathyroidectomy in Northern Sydney for men and women between 1976 and 2000 are shown in Box 3, and the rates for the years 1976, 1986 and 1996 are compared in Box 4. Rates in women have increased significantly in Northern Sydney from 0.14 cases per 100 000 in 1976 to 7.7 cases per 100 000 in 1996 ($P < 0.001$).

Age-standardised parathyroidectomy rates for NSW for 1993–1999 are shown in Box 5. There has been a significant increase in parathyroidectomy rates in both sexes in this time. The age-standardised procedure rate in women across NSW was 5.1 per 100 000 in 1993, rising to a peak of 12.3 per 100 000 in 1998 ($P < 0.001$). There was also a significant increase in parathyroidectomy rates in men in NSW, rising from 2.1 per 100 000 in 1993 to 4.7 per 100 000 in 1998 ($P < 0.001$).

Changing presentation of hyperparathyroidism

The presenting symptoms leading to a diagnosis of hyperparathyroidism and parathyroidectomy at the University of Sydney Endocrine Surgical Unit are shown in Box 6. The most common symptom was "osteoporosis", accounting for 27% (429) of the total number

of parathyroidectomies performed. The next most common were "asymptomatic" disease (249) and renal calculi (248), both accounting for about 15% of the total number of cases. The proportion of patients presenting with osteoporosis versus asymptomatic disease was significantly different ($P < 0.001$).

In 1991–2001, osteoporosis and asymptomatic disease continued to be the most common presenting symptoms initiating referral for surgery. However, the most dramatic change has been in presentations for osteoporosis, with the proportion of patients with osteoporosis as the indication for surgery rising by an order of magnitude from 4% in 1962–1980 to 34% between 1991 and 2001. The proportion of patients presenting with osteoporosis in the period 1991–2001 was significantly higher than for the period 1981–1990 ($P < 0.001$).

Changes in operative technique

Before 1998, all parathyroidectomies were performed as open procedures, with bilateral neck exploration to identify parathyroid adenomas. Minimally invasive parathyroidectomy was introduced in our unit in May 1998. Two techniques have been utilised: an endoscopically assisted technique, and an image-directed minimal incision procedure.[8,14] In the study period there have been 217 minimally invasive parathyroidectomy procedures performed. Although the classical open parathyroidectomy remains the most commonly used technique, there has been an increase in the proportion of minimally invasive procedures performed, so that in the last 12 months of the study about a third of all parathyroidectomies were minimally invasive procedures.

DISCUSSION

There has been a striking increase in the number of patients with primary hyperparathyroidism referred for surgical management to the University of Sydney Endocrine Surgical Unit, particularly over the past decade. This increase has been mirrored in the whole of NSW. Thus, the increase in annual parathyroidectomy procedures in our unit does not appear to be simply a referral phenomenon, but rather to reflect a true statewide pattern of change. This is evidenced by the increases in the age-standardised parathyroidectomy rates, and by the proportion of the parathyroidectomies in NSW performed in the University of Sydney Endocrine Surgical Unit remaining relatively constant over this period. This increase in parathyroidectomies in NSW seems to contrast with trends elsewhere, with studies showing declines in the incidence of primary hyperparathyroidism and a stabilisation of parathyroidectomy rates. This decrease in incidence has been documented in a population-based study in Olmsted County, Minnesota, USA, where the rate decreased steadily from 1979 to 1992.[15] A Swedish study of cases of primary hyperparathyroidism treated surgically has shown a relatively constant rate of procedures between 1970 and 1984.[16]

Having accounted for the ageing of the population, the significant increase in presentations and rates of parathyroid surgery across NSW could be attributed to several factors.

- *A more aggressive management approach.* Both surgeons and endocrinologists are more likely to suggest surgical intervention because of its proven benefits in symptom control and increases in bone density.[17,18]
- *The frequency of calcium measurement.* This has clearly been shown to influence the apparent incidence of primary hyperparathyroidism.[15] Automated biochemical analysers were first introduced to Northern Sydney in 1971, and all requests for routine serum biochemistry analyses at Royal North Shore Hospital included calcium until June 1991. With the advent of newer systems for biochemical analysis, physicians are now required to specifically request serum calcium measurement. Data show that serum calcium measurements since the system has been computerised (the past three years) have been stable at about 14 000 requests per year. We believe that the frequency of measurement of calcium level, a major contributor to the increase in primary hyperparathyroidism incidence rates in the 1970s, is unlikely to have influenced the current rise in diagnosis of hyperparathyroidism and parathyroidectomy rate.
- *Investigation of osteoporosis.* This appears to have led to the identification of primary hyperparathyroidism in an increasing number of patients in Northern Sydney. Patients have approached their general practitioner for assessment of the risk of osteoporosis, or a fracture has initiated investigation of bone density. The awareness of the general population and physicians has been heightened by a recent media campaign in NSW about osteoporosis, and this is reflected in a trebling of the number of bone mineral density studies performed at Royal North Shore Hospital between 1995 and 1999. The low bone mineral

4: Age-standardised parathyroidectomy rate, by sex, in Northern Sydney

	Parathyroidectomies per 100 000 population		
Sex	1976	1986	1996
Male (95% CI)	0.06 (0–1.13)*	0.13 (0–1.04)*	3.3† (1.69–5.73)
Mean age (years) (95% CI)	62 (52–72)	54 (46–62)	56 (49–63)
Female (95% CI)	0.14 (0–1.07)*	0.41 (0.06–1.92)	7.7† (5.2–11)
Mean age (years) (95% CI)	43 (23–64)	56 (51–61)	62 (58–65)

* One-sided 97.5% CI.
† $P < 0.001$ for comparison of parathyroidectomy rate in 1996 to rate in 1976.

5: Age-standardised number of parathyroidectomies performed per 100 000 population per year in New South Wales, 1993–1999, by sex

	Parathyroidectomies performed per 100 000 population	
Year	Males (95% CI)	Females (95% CI)
1993	2.1 (1.6–2.7)	5.1 (4.3–5.9)
1994	2.8 (2.2–3.5)	5.5 (4.7–6.4)
1995	2.8 (2.2–3.4)	7.8* (6.9–8.9)
1996	2.9† (2.3–3.5)	8.7* (7.7–9.8)
1997	3.8* (3.1–4.5)	8.9* (7.9–10)
1998	4.7* (3.9–5.5)	12.3* (11–14)
1999	2.7 (2.2–3.3)	7.6* (6.7–8.6)

* $P < 0.001$ for comparison of parathyroidectomy rates to baseline rate in 1993.
† $P = 0.03$ for comparison of parathyroidectomy rates to baseline rate in 1993.

6: Parathyroidectomy procedures in the University of Sydney Endocrine Surgical Unit, by presenting condition, 1962–2001

Presentation	1962–1980	1981–1990	1991–2001	Total
Osteoporosis (bone mineral density > 2SD below age- and sex-matched controls, determined by osteodensitometry)	4 (4%)	25 (8%)*	400 (34%)*	429† (27%)
Asymptomatic (absence of any relevant symptoms)	5 (5%)	58 (18%)	186 (16%)	249† (15%)
Renal stones (radiologically documented presence of renal calculi)	42 (38%)	68 (21%)	138 (12%)	248 (15%)
Neuromuscular symptoms (muscle weakness, fatigue, lethargy or similar symptoms)	9 (8%)	38 (12%)	112 (9%)	159 (10%)
Neuropsychiatric symptoms (depression, insomnia, memory loss or similar symptoms)	9 (8%)	24 (8%)	113 (10%)	146 (9%)
Secondary/tertiary hyperparathyroidism	6 (5%)	29 (9%)	72 (6%)	107 (7%)
Incidental (a parathyroid tumour found incidentally during a thyroid procedure)	16 (15%)	22 (7%)	71 (6%)	109 (7%)
Other	8 (7%)	23 (7%)	29 (2%)	60 (4%)
Hypercalcaemic crisis (acute admission with severe hypercalcaemia, vomiting and dehydration)	4 (4%)	10 (3%)	39 (3%)	53 (3%)
Abdominal symptoms (abdominal pain, constipation, peptic ulceration, persistent nausea or vomiting)	7 (6%)	22 (7%)	24 (2%)	53 (3%)
Total	110	319	1184	1613 (100%)

* $P < 0.001$ for comparison of proportion of patients presenting with osteoporosis between the two time intervals.
† $P < 0.001$ for comparison of overall proportion of patients presenting with osteoporosis v asymptomatic disease.

density frequently found in patients with hyperparathyroidism has presumably triggered further investigation of serum calcium and parathyroid hormone levels.

■ *The role of minimal access surgery.* We previously expressed a rather guarded opinion of the role of minimal access surgery in the treatment of hyperparathyroidism.[7] However, this technique has become an effective and frequently performed procedure in our unit.[8] About a third of all parathyroidectomies performed in the last 12 months of our study were minimally invasive procedures, either endoscopically assisted parathyroidectomies or image-directed parathyroidectomies. The less invasive approach may be more attractive to referring physicians and patients alike. However, the procedure is still conducted under the auspices of the Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP–S) and must be part of a feasibility trial.[19] It is therefore unlikely that the increase in parathyroidectomy rates in NSW could be attributed to this change. In addition, within our unit, emphasis has been placed on the principle that the availability of minimally invasive parathyroidectomy should not alter the standard indications for surgery.

■ *A true increase in the prevalence of hyperparathyroidism?* This seems unlikely given that the underlying pathological process in 95% of cases is the development of a benign neoplasm. The only factor known to increase the incidence of parathyroid tumours is a history of irradiation at a young age, and there is no evidence that this has occurred in NSW.[20]

CONCLUSIONS

Parathyroidectomy is being performed more frequently in NSW. We believe that a major part of this increase is the result of the introduction of widespread informal screening for osteoporosis, with the ready availability of bone mineral density testing. If that is the case, then, as with other screening programs, the numbers of patients referred for parathyroid surgery should gradually plateau,[21] something that may indeed have started to happen in the past 12 months.

COMPETING INTERESTS

None identified.

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