Worldwide Trends in the Surgical Treatment of Primary Hyperparathyroidism in the Era of Minimally Invasive Parathyroidectomy

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**Hypothesis:** Minimally invasive surgery for primary hyperparathyroidism has become an accepted part of endocrine surgical practice worldwide.

**Design:** Survey of members of the International Association of Endocrine Surgeons.

**Setting:** Clinical practice of endocrine surgeons worldwide.

**Main Outcome Measures:** Numbers of parathyroid procedures performed, types of minimally invasive procedures undertaken, and techniques used to ensure completeness of removal of hyperfunctioning parathyroid tissue as reported by the survey respondents.

**Results:** Of 160 surveys completed, 95 (59%) indicate that the surgeons currently perform minimally invasive parathyroidectomy and use this technique on average for 44% of patients with primary hyperparathyroidism. The most common approach is the focused technique with a small incision, either central or lateral (92% [87 respondents]), followed by a video-assisted technique (22% [21 respondents]), and a true endoscopic technique with gas insufflation (12% [11 respondents]). Techniques used to ensure completeness of resection include the quick intraoperative intact parathyroid hormone assay (68% [65 respondents]), a same-day intact parathyroid hormone assay (17% [16 respondents]), and the nuclear probe (14% [13 respondents]). The number of parathyroidectomies performed worldwide increased from 1727 in 1980 to 6977 in 2000 with the average number per surgeon increasing from 23 in 1980 to 45 in 2000. Geographically, 20 (59%) of 34 surveys from the Americas report the use of minimally invasive parathyroidectomy, 23 (56%) of 41 from the Australasian region, and 34 (49%) of 69 from Europe or the Middle East.

**Conclusions:** The number of parathyroidectomies performed for primary hyperparathyroidism has increased worldwide over the past 20 years. More than half of the surgeons responding to the survey perform minimally invasive parathyroidectomy, with the most using the focused small-incision technique.


SURGERY FOR primary hyperparathyroidism seems to be on the increase for many reasons. It is recognized that parathyroidectomy benefits patients who have symptoms that include fatigue, bone pain, osteoporosis, muscle weakness, nephrolithiasis, abdominal symptoms, and mental status changes. There is also mounting evidence pointing to improved cardiovascular status and control of diabetes mellitus postoperatively, even asymptomatic patients have been shown to have improved function and sense of wellness following parathyroidectomy. Despite controversy over the natural history of primary hyperparathyroidism, the cost and frequency of nonoperative follow-up lends weight to the argument for definitive surgical management of primary hyperparathyroidism at diagnosis when cure rates of 95% or better can be expected. For these reasons parathyroidectomy is recommended, even for asymptomatic patients.

Added to these reasons has been the introduction of minimally invasive approaches to parathyroid surgery. Many techniques have been reported, including a full endoscopic approach with gas insufflation, video-assisted approaches, and the direct-focused approach using a small cervical incision. The use of various techniques to ensure completeness of removal of all abnormal parathyroid tissue, including intraoperative measurement of quick intraoperative intact para-
thyroid hormone (PTH) assay\textsuperscript{22} and the intraoperative nuclear probe\textsuperscript{26} has allowed early discharge from the hospital. Indeed, parathyroid surgery is being promoted as a 1-day-only local anesthetic procedure\textsuperscript{27}. A 1999 "Editorial" in the New England Journal of Medicine recommended parathyroidectomy for almost all patients based on the dual view that "most patients with primary hyperparathyroidism probably have symptoms\textsuperscript{28(p1032)}" and that changes in surgical technique have made "surgical treatment simpler and faster than in the past.\textsuperscript{28(p1032)}"

Against this background, we felt that it would be useful to ascertain current practice among endocrine surgeons worldwide in relation to both the numbers of parathyroid procedures being performed as well as the use of minimally invasive parathyroidectomy (MIP) to determine whether the procedure had become an accepted part of endocrine surgical practice.

**MATERIALS AND METHODS**

A survey was mailed to all 326 members of the International Association of Endocrine Surgeons listed in the 2000 membership directory. Mail, facsimile, and e-mail were the available methods of response. The survey questions included the following:

1. How many parathyroid operations overall did you perform in the last 12 months?
2. Do you perform minimally invasive/minimal access/endoscopic parathyroidectomy?
3. If "yes," what percentage of all your parathyroid operations is currently performed by this technique?
4. Which technique do you currently use?
5. Which technique do you use to ensure adequate removal of all abnormal parathyroid tissue?
7. Any other comments?

Specific choices were given for each question as well as the opportunity to note techniques not listed. Respondents were also asked to indicate whether their data were absolute or estimated. The survey was anonymous, although most respondents provided a return address or facsimile number imprint that was used to determine the region of practice, that is, the Americas, the Australasian region, or Europe and the Middle East.

**RESULTS**

Of the 326 surveys mailed, 177 were returned. Of those, 17 were marked “return to sender,” or the surgeon was no longer in practice and, therefore, did not complete the survey, leaving 160 surveys (49%) for analysis. Two respondents indicated that they had replied on behalf of a surgical department rather than as an individual, marginally affecting the estimate of the average numbers of procedures performed per surgeon. Within that group of respondents, 95 surgeons or groups (59%) indicated that MIP was performed in their center. Calculated on the basis of individual surgeons, 101 (61%) of 166 perform MIP. Those surgeons who performed MIP did so for 44% of all patients undergoing parathyroidectomy for primary hyperparathyroidism.

Minimally invasive techniques used are summarized in Table 1. The endoscopic mammary approach was not reported as being performed by any responding endocrine surgeon. The focused technique using a small cervical incision was reported as being used by 87 surgeons (92%). Of these, 54 surgeons (62%) performed the procedure through a central incision and 52 surgeons (60%) used a lateral incision, with some using both approaches. Clearly many surgeons use or have used a variety of techniques as the percentages, when summed, total more than 100%. In relation to the "Comments" section, one group used hypnosis instead of general anesthesia for outpatient parathyroidectomy. Several cited local anesthesia as a less invasive method, with either a focused small-incision approach or formal 4-gland exploratory surgery. Thoracoscopic parathyroidectomy was mentioned for ectopic mediastinal parathyroid adenomas. Some surgeons reserve MIP for patients undergoing another operation or for patients with high general risk under anesthesia. Comments also included having commenced MIP using an endoscopic technique but having now changed to the focused small-incision technique.

To assure complete removal of hyperfunctioning parathyroid glands during MIP, surgeons used various techniques as summarized in Table 2. Four surgeons commented on using methylene blue injection. Other comments included the use of macroscopic appearance or "good judgment" and several surgeons pointed out the ability to monitor postoperative calcium and PTH levels.

Several comments addressed factors influencing the number of MIPs performed. For example, only symptomatic patients were referred for surgery in some areas. Similarly, routine calcium level screening was not performed in all areas. One surgeon pointed out that in India, with a goiter rate of 50% to 70%, patients with primary hyperparathyroidism frequently required concomi-
tant thyroidectomy, thus, obviating MIP. Some surgeons had “cost-benefit concerns” for using MIP. Referral patterns had changed as well, with referrals going to a “new endocrine surgeon in town,” or going from all surgical units to a single unit managing hyperparathyroidism. Several centers were running their own pilot series or prospective randomized studies, after which they hoped to embrace MIP. Although many surgeons reported a trend over the last 2 to 5 years of increasing MIP, others, such as survey respondent 83, did not. Survey respondent 83 commented: “Concerning MIP, I don’t really see the point . . . even elderly patients can be operated on with minimal risk and a good cosmetic result via a 5- to 6-cm centrally placed neck incision. . . .”

Finally, the surgeons were asked to include the number of parathyroidectomies performed over the past 20 years in increments of 5 years. The total number of parathyroidectomies increased from 1727 in 1980 to 6977 in 2000 (Figure). Given that fact, when looked at for each individual surgeon, this increase was almost universal, with only a small minority reporting a decrease in the number of parathyroidectomies performed over the decades. Since many surgeons were not in practice during this entire interval, averages were calculated. In 1980, 76 of the responding surgeons were already in practice. By 2000, 155 of the responding surgeons were still in practice. The average number of parathyroidectomies performed in 1980 by the surgeons reporting was 22.7. The average number of parathyroidectomies performed increased to 24.6 in 1985, 28.8 in 1990, 34.1 in 1995, and 45.0 in 2000.

Of 177 surveys returned, 34 were from the Americas, 41 from the Australasian regions, 68 from Europe or the Middle East, and 34 were unidentifiable as to region of the world. Of 34 surveys from the Americas, 20 (59%) performed MIP and 14 (41%) did not. In the Australasian region, 23 (56%) of 41 performed MIP and 18 (44%) did not. In Europe and the Middle East, 34 (50%) of 68 performed MIP, and the other 50% did not. The difference in the number of MIPs by region was not statistically significant (P=.99).

This study has confirmed that the rate of parathyroid surgery seems to be increasing worldwide. Not only has this occurred across the group as a whole but also, on an individual basis, with most of the actively practicing surgeons reporting a progressive increase in MIPs being performed. We have previously reported an exponential increase in parathyroidectomy for primary hyperparathyroidism in our own state of New South Wales, Australia,1,2 and similar marked increases have been reported in other centers such as Madrid, Spain.30 Whether this increase is because of an increasing incidence of primary hyperparathyroidism, the greater use of routine testing of blood calcium levels, or simply because of more patients being referred for parathyroidectomy remains unclear. Although some major referral centers in the United States have reported a constant number of parathyroidectomies over the years, they already maintain a high number of parathyroid operations.31 The very few surgeons in this study who reported decreasing numbers commented on either a slowdown in practice because of pending retirement or on changing referral patterns, such as “a new endocrine surgeon in town.” It is highly likely that part of the increase seen in parathyroid surgery relates to the introduction of MIP, with the perception by referring physicians that parathyroid surgery is much quicker, simpler, and safer than in the past. This was certainly the view expressed by Utiger in the New England Journal of Medicine editorial, in which parathyroidectomy was universally recommended based on the view that “most patients with primary hyperparathyroidism probably have symptoms”28(p1032) and that changes in surgical technique have made “surgical treatment simpler and faster than in the past.”

This study has demonstrated that most endocrine surgeons undertake MIP for just under half their patients who are initially seen with primary hyperparathyroidism. Presumably, the other half have contraindications to a minimally invasive approach such as the presence of a multinodular goiter, familial disease, or the absence of confident preoperative localization. The key to successful MIP is careful patient selection, with avoidance of those patients who are likely to have multiglandular disease,32 as well as confident preoperative localization with techniques such as sestamibi nuclear scanning33 or ultrasonography. A concordant result with these modalities affords the most reliable preoperative localization of parathyroid adenomas.34 In our own unit, if the sestamibi nuclear scan and ultrasound are not concordant, patients undergo open bilateral neck exploratory surgery.

The earliest reports of MIP described the use of true endoscopic18-20 and video-assisted techniques.21-23 Although it is accepted that these techniques provide excellent visualization of the anatomical structures, they can be time consuming and are associated with a steep learning curve. Many surgeons commented on having started using these techniques and having shifted to the focused small-incision techniques more recently. This study has demonstrated that most (87 respondents or 92%) of endocrine surgeons prefer to use the focused small-incision technique with a small cervical incision placed either centrally or laterally. We prefer a 2-cm lateral incision placed directly over the presumed site of the
adenoma as directed by the preoperative localization studies. The adenoma can then be retrieved through the incision with more than a 97% success rate, even without the use of the intraoperative PTH assay. We draw intraoperative PTH levels but monitor them routinely postoperatively, obtaining results prior to discharging the patient on the day of surgery. If the quick PTH assay fails to show a decrease in PTH level and the calcium level fails to normalize, the patient undergoes an open exploratory procedure the next day. Those advocating a central small-incision point to the ability to surgically excise the small hole is necessarily restricted.

Despite careful selection, the presence of multiglandular disease leading to failure of MIP remains a possibility. If outpatient or same-day surgery is to be performed, some technique should be used to ensure complete removal of all hyperfunctioning parathyroid tissue so that the patient may be discharged from the hospital “cured.” The development and modification of the chemiluminescent assay for the intact PTH level (quick PTH) allowed fast measurement of the PTH level without the use of radioisotopes. This is a highly accurate technique with a success rate of 95% to 98% and was demonstrated in our survey to be the technique of choice for 65 surgeons (68%). Although quick intraoperative intact PTH assay is the most frequently chosen modality to confirm cure with MIP, it is not readily available throughout the world and is expensive. It is also not accurate when it is needed most, that is, for patients with multiple abnormal parathyroid glands. As the alternative to same-day PTH measurement, using a series of routine laboratory tests still allows same-day discharge from the hospital but is significantly more cost-effective, and does require reoperation. Same-day PTH measurement is used by 17% of surgeons (16 respondents). It must be pointed out, however, that, provided patients are appropriately selected for an MIP, 97% of them will be cured with MIP even if no testing of any sort is performed.

The radioguided approach using a nuclear probe similar to that used for sentinel node biopsy met with initial enthusiasm because of the presumed increased ability to localize an adenoma as well as the ability to ensure complete removal by comparing the count in the adenoma with the background radioactivity. As this study has shown, enthusiasm for that technique has waned with only 13 surgeons (14%) still using the technique because of both the initial good results not being confirmed as well as the logistics of timing of the administration of sestamibi nuclear scanning on the morning of surgery.

In a previous systematic review of MIP published in the ARCHIVES in 2000, we questioned whether there

was sufficient evidence to justify the introduction of MIP into clinical practice. In conclusion, it would seem as if MIP has gained an acceptable place in the armamentarium of endocrine surgeons worldwide. Most surgeons are performing MIP in just fewer than 50% of patients. The focused small-incision technique with direct removal of the adenoma through a small cervical incision has come to be used by almost all surgeons performing MIP.
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Treatment and Outcome of Staphylococcus aureus Bacteremia: A Prospective Study of 278 Cases

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Background: Staphylococcus aureus bacteremia is still a serious problem, and the optimal treatment is under debate. Only a few studies concerning treatment are available.

Methods: The study population was all patients with a positive blood culture result for S aureus in Copenhagen County, Denmark, from May 1994 through April 1996. Of 278 patients with S aureus bacteremia, 186 were evaluated according to outcome in a prospective, observational follow-up study. The time above the minimum inhibitory concentration was estimated for dicloxacillin sodium for each treatment regimen and evaluated by logistic regression along with other potential risk factors.

Results: The following variables were statistically associated with death: the presence of an uneradicated focus (odds ratio [OR], 6.7; 95% confidence interval [CI], 2.1-21.0); the presence of septic shock (OR, 3.7; 95% CI, 1.5-9.1); the total daily dose of penicillinase-stable penicillin less than 4 g (OR, 3.7; 95% CI, 1.3-11.1); and age 60 years or older (OR, 2.4; 95% CI, 1.1-5.3). The following variables were significantly associated with recurrence: the total daily dose of penicillinase-stable penicillin less than 3 g (OR, 3.9; 95% CI, 1.6-10.0) and the presence of a secondary focus (OR, 3.2; 95% CI, 1.3-7.7). Among 153 patients with observation time longer than duration of treatment, this factor (duration of treatment, <14 days) was significantly related to mortality (OR, 0.84; 95% CI, 0.76-0.94).

Conclusions: Focus eradication and the dosing of penicillinase-stable penicillin are important to the outcome of S aureus bacteremia. We recommend treatment with at least 1 g of penicillinase-stable penicillin 4 times daily for longer than 14 days. (2002;162:25-32)

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