

Randomized clinical trial comparing regional and general anaesthesia in minimally invasive video-assisted parathyroidectomy

P. Miccoli¹, L. Barellini¹, J. M. Monchik², R. Rago¹ and P. F. Berti¹

¹Department of Surgery, Ospedale Santa Chiara, University of Pisa, Pisa, Italy and ²Division of Endocrine Surgery, Rhode Island Hospital, Brown University, Providence, Rhode Island, USA

Correspondence to: Dr P. Miccoli, Department of Surgery, Ospedale Santa Chiara, Via Roma 67, 56126 Pisa, Italy (e-mail: p.miccoli@dc.med.unipi.it)

Background: This randomized clinical trial was performed in a single institution to compare the results of minimally invasive video-assisted parathyroidectomy (MIVAP) conducted under regional anaesthesia (RA) or general anaesthesia (GA).

Methods: Fifty-one patients undergoing MIVAP for primary hyperparathyroidism were assigned randomly to either RA (26 patients) or GA (25). RA involved a bilateral deep cervical block, and local infiltration of the incision site with a mixture of 0.25 per cent lignocaine and 0.15 per cent bupivacaine. GA was induced by intravenous administration of propofol, remifentanyl and rocuronium bromide.

Results: The two groups were matched for age, sex, adenoma size, and preoperative serum calcium and parathyroid hormone levels. The interval from skin incision to closure was similar in the two groups (27.6 and 25.8 min for RA and GA respectively), whereas the total operating time (from induction of anaesthesia to return to the ward) was significantly lower with RA (72.1 versus 90.2 min; $P = 0.001$). The postoperative requirement for pain medication, measured in terms of amount of ketorolac administered at the request of the patient, was significantly lower in the RA group (28.5 versus 80 mg/day; $P < 0.001$).

Conclusion: MIVAP performed under RA was associated with a shorter overall operating time and a reduced need for postoperative pain relief.

Paper accepted 28 February 2005

Published online 1 June 2005 in Wiley InterScience (www.bjs.co.uk). DOI: 10.1002/bjs.5048

Introduction

Parathyroidectomy is the only curative treatment for primary hyperparathyroidism (PHPT), but the surgical approach is controversial¹⁻³. Bilateral neck exploration with resection of enlarged parathyroid glands is the 'gold standard' procedure and is associated with a 95 per cent cure rate in experienced hands³. Despite these good results, minimally invasive surgical procedures for the treatment of PHPT have become increasingly adopted⁴⁻⁷. A selective approach with unilateral exploration has been advocated, based on preoperative localization of an enlarged gland by ultrasonography and in some cases ^{99m}Tc-labelled sestamibi scan (STS). Intraoperative monitoring of parathyroid hormone (PTH) levels is also generally used to minimize the risk of missing multiglandular disease⁸⁻¹¹. Minimally invasive video-assisted parathyroidectomy (MIVAP) is a new technique that has rates of cure and an incidence of

complications similar to those of the conventional bilateral approach^{6,12,13}, but has a distinct advantage in terms of better cosmetic outcome and pain reduction.

Although locoregional anaesthesia has not been used previously for endoscopic operations, it has been used for minimally invasive open procedures^{7,8,14,15}. MIVAP with regional anaesthesia (RA) was introduced in the authors' institutions in July 2002. The present randomized clinical trial was designed to compare use of RA and general anaesthesia (GA) in MIVAP.

Patients and methods

Between July 2002 and October 2003, 96 patients with PHPT were referred for surgery, but only 67 (70 per cent) were eligible for MIVAP. Eligibility criteria were: a non-familial form of hyperparathyroidism, preoperative localization of a single enlarged parathyroid gland by

ultrasonography, confirmed where possible by STS, no previous thyroid or parathyroid surgery, no previous neck irradiation, and no suspicion of thyroiditis or malignancy. Only 51 patients (44 women and seven men) gave informed consent to take part in the study, which was approved by the local ethics committee. The low rate of consent was mainly related to refusal to undergo operation under RA. Patients were randomly allocated to MIVAP under either RA or GA. Preoperative symptoms and signs were recorded. Endpoints of this study were the consumption of analgesic drugs, calculated as milligrams of ketorolac administered during the first 24 h after operation, and total operating time (interval between induction of anaesthesia and return to the ward).

Localization studies

Preoperative localization was performed by ultrasonography. Although most patients were referred with a scan performed elsewhere, ultrasonography was repeated at this institution in all patients by a radiographer with expertise in thyroid and parathyroid pathology. With the patient in the supine position and the neck hyperextended, multiple transverse and sagittal images were obtained using a 7.5-MHz probe and a Toshiba SAL 650 scanner (Toshiba Medical Systems Europe, Zoetermeer, The Netherlands). Parathyroid adenoma was characterized by a hypoechoic nodule with a partial vascular ring and increased vascular flow within the lesion demonstrated by colour Doppler sonography. It was possible to identify significant thyroid disease and the precise relationship between the adenoma and surrounding structures by ultrasonography.

Most patients had already undergone STS before referral to the surgeon. In this procedure, some 15–18 mCi ^{99m}Tc -labelled sestamibi was injected intravenously followed by pinhole collimation over the thyroid bed and superior mediastinum in an anterior projection immediately after injection and 2 h later.

Only a positive localization of an abnormal parathyroid gland by ultrasonography was considered mandatory. Any patient in whom the results of ultrasonography and STS were not concordant was excluded from the study. Some patients also underwent single-photon emission computed tomography.

Anaesthesia

RA was performed in the operating room by an anaesthesiologist, as described by Lo Gerfo *et al.*^{14,15}. It generally comprised a bilateral deep cervical block, associated with infiltration of the upper thyroid pedicle and

local infiltration along the line of incision. Approximately 20 ml of a mixture of 0.25 per cent lignocaine and 0.15 per cent bupivacaine was used on each side to obtain a bilateral block; the same amount was used on one side to achieve a unilateral block. Some 10–15 ml was used to infiltrate the incision site and the operative field. A bilateral block was preferred so that bilateral exploration could be performed if an adenoma was not found on the first side. Remifentanyl was used to provide mild intravenous sedation. GA was induced by intravenous administration of propofol and remifentanyl in addition to rocuronium bromide.

Surgical technique

All patients underwent MIVAP⁶ performed by the same surgeon. A 15-mm skin incision was made 2 cm above the sternal notch and the cervical midline was divided. The operative field was maintained by external retraction with a gasless technique. A 5-mm 30° scope and 2-mm surgical instruments were inserted through the incision. The operation involved a unilateral focused approach based on the preoperative localization. The enlarged parathyroid gland was removed after identification of the recurrent laryngeal nerve. The duration of the surgical procedure and the total time elapsed until the patient returned to the ward were recorded. Three hours after completion of the procedure, patients in the RA group were able to drink and stand up. The morning after operation a blood sample was withdrawn to check the serum calcium level and patients were then discharged.

Analgesic drugs (ketorolac and morphine) were administered in the postoperative period only when requested by the patient. The total amount administered in the first 24 h after surgery was noted.

PHPT was considered to be persistent if levels of calcium and PTH did not return to normal within 6 months. Recurrent PHPT was diagnosed if serum levels of calcium and PHT became raised more than 6 months after surgery.

Quick parathyroid hormone assay

Serum PTH levels were measured in the operating room in all patients by an endocrinologist using a two-site immunochemiluminometric method (Quick-IntraoperativeTM Intact PTH assay; Nichols Institute Diagnostic, San Juan Capistrano, California, USA). Levels were measured before induction of anaesthesia (basal), when the parathyroid gland had been localized (manipulation), and 5 and 10 min after removal of the abnormal gland. Hyperparathyroidism was considered to

have been corrected when a 50 per cent fall in PTH from the highest basal or manipulation value was registered at 5 or 10 min after resection of the enlarged parathyroid gland(s).

Statistical analysis

Data were analysed using the non-parametric Mann-Whitney *U* test. Statview[®] software (SAS Institute, Cary, North Carolina, USA) was used for statistical analysis. $P < 0.050$ was considered statistically significant. The study was found to have sufficient power (0.90) after analysis of data for 40 patients, so recruitment was stopped at 51 subjects.

Results

The mean age of the 51 patients was 57.9 (range 24–77) years. Mean preoperative serum levels of calcium and PTH were 10.7 mg/dl and 37 pg/ml respectively. Twenty-six patients were randomized to RA and 25 to GA. The sex, age, preoperative serum levels of calcium and PTH, and size and location of the enlarged parathyroid glands were comparable between the two groups (Table 1). There was no difference in clinical signs and symptoms between groups.

In the LA group all but one patient had undergone ultrasonography before referral and STS had been performed in all but six patients. Ultrasonography and STS localized the enlarged parathyroid glands to the same site in all patients. Ultrasonography demonstrated ipsilateral thyroid nodules in five patients and multiple contralateral thyroid nodules in six. One patient was

diagnosed with Plummer's disease (with a 2-cm nodule) and an ipsilateral parathyroid adenoma. This patient underwent MIVAP and minimally invasive video-assisted ipsilateral hemithyroidectomy (MIVAT) under local anaesthesia through the same incision; the time taken for lobectomy was subtracted from the total operating time. This was the only exception to the protocol; the thyroid procedure was performed to demonstrate that lobectomy could also be carried out under RA.

In the GA group all but two patients had undergone ultrasonography before referral and an STS was available for all but one. In one of these patients the STS was initially reported as negative, but on review the film was considered positive, and the abnormal gland was localized during surgery to the site shown by ultrasonography. Bilateral thyroid nodules were diagnosed in three patients in whom the operation was accomplished with MIVAP.

The mean interval between skin incision and closure was 27.6 (range 12–60) min in the RA group and 25.8 (range 15–50) min in the GA group. The intraoperative PTH level dropped by at least 50 per cent after removal of the enlarged parathyroid gland in all patients (both groups). In the first patient operated on under RA in this experience, the parathyroid gland was situated in a very deep position with adhesions to the thyroid lobe. The operation was converted to a conventional procedure and completed under locoregional anaesthesia.

The mean overall operating time (the interval between induction of anaesthesia and return to the ward) was 72.1 (median 50) min in the RA group and 90.2 (median 70) min in the GA group ($P < 0.001$). This difference was accounted for by the very short time spent in the recovery room by patients in the RA group; these patients were transferred to the ward immediately, their Aldrete score being 10.

The mean dose of ketorolac administered in the first 24 h after surgery was 28.5 (median 30, range 0–90) mg in the RA group and 80 (median 30, range 10–90) mg in the GA group ($P < 0.001$). Two patients in the latter group complained of severe postoperative pain and administration of 6 mg morphine was necessary. No additional drugs were used in the RA group. After operation all patients in the RA group claimed that they had not suffered severe discomfort and would undergo such an operation under local anaesthesia again.

Mean follow-up was 20 (range 16–31) months. One patient in the RA group had transient recurrent laryngeal nerve paresis. No patient in either group developed hypocalcaemia. A persistent slight increase in PTH level occurred in 70-year-old woman in the RA group despite an intraoperative decrease of 50 per cent. However, her

Table 1 Comparison of demographic and preoperative variables in patients randomized to regional or general anaesthesia

	Regional anaesthesia (<i>n</i> = 26)	General anaesthesia (<i>n</i> = 25)
Sex ratio (F : M)	24 : 2	20 : 5
Age (years)*	58.2(10.4) (38–77)	57.5(10.4) (24–71)
Calcium (mg/dl)*	10.8(0.6) (10.0–12.3)	10.6(0.6) (9.9–12.4)
Parathyroid hormone (pg/ml)*	140(55) (78–354)	135(53) (71–332)
Mean size of adenoma (mm)	14 × 10	12.5 × 9
Location		
IR	15	12
IL	6	9
UR	4	3
UL	1	1

*Values are mean(s.d.) (range). IR, inferior right; IL, inferior left; UR, superior right; UL, superior left.

- 6 Miccoli P, Bendinelli C, Berti P, Vignali E, Pinchera A, Marcocci C. Video-assisted *versus* conventional parathyroidectomy in primary hyperparathyroidism: a prospective randomized study. *Surgery* 1999; **126**: 1117–1122.
- 7 Monchik JM, Barellini L, Langer P, Kahya A. Minimally invasive parathyroid surgery in 103 patients with local/regional anaesthesia, without exclusion criteria. *Surgery* 2002; **131**: 502–508.
- 8 Chen H, Sokoll LJ, Udelsman R. Outpatient minimally invasive parathyroidectomy: a combination of sestamibi–SPECT localization, cervical block anesthesia, and intraoperative parathyroid hormone assay. *Surgery* 1999; **126**: 1016–1021.
- 9 Lorenz K, Miccoli P, Monchik JM, Düren M, Dralle H. Minimally invasive video-assisted parathyroidectomy: a multiinstitutional study. *World J Surg* 2001; **25**: 704–707.
- 10 Dralle H, Lorenz K, Nguyen-Thanh P. Minimally invasive video-assisted parathyroidectomy – selective approach to localized single gland adenoma. *Langenbecks Arch Surg* 1999; **384**: 556–562.
- 11 Carneiro DM, Irvin GL III. Late parathyroid function after successful parathyroidectomy guided by intraoperative hormone assay (QPTH) compared with the standard bilateral neck exploration. *Surgery* 2000; **128**: 925–929.
- 12 Miccoli P, Berti P, Conte M, Raffaelli M, Materazzi G. Minimally invasive video-assisted parathyroidectomy: lesson learned from 137 cases. *J Am Coll Surg* 2000; **191**: 613–618.
- 13 Miccoli P, Monchik JM. Minimally invasive parathyroid surgery. *Surg Endosc* 2000; **14**: 987–990.
- 14 Lo Gerfo P. Bilateral neck exploration for parathyroidectomy under local anesthesia: a viable technique for patients with coexisting thyroid disease with or without sestamibi scanning. *Surgery* 1999; **126**: 1011–1015.
- 15 Ditkoff BA, Chabot J, Feind C, Lo Gerfo P. Parathyroid surgery using monitored anesthesia care as an alternative to general anesthesia. *Am J Surg* 1996; **172**: 698–700.
- 16 Utiger RD. Treatment of primary hyperparathyroidism. *N Engl J Med* 1999; **341**: 1301–1302.
- 17 Miura D, Wada N, Arici C, Morita E, Duh QJ, Clark OH. Does intraoperative quick parathyroid hormone assay improve the results of parathyroidectomy? *World J Surg* 2002; **26**: 926–930.
- 18 Dunhill TP. Exophthalmic goitre: partial thyroidectomy under local anaesthesia. *Intercolonial Medical Journal of Australia* 1907; **12**: 589–593.
- 19 Lorenz K, Phuong NT, Dralle H. Diversification of minimally invasive parathyroidectomy for primary hyperparathyroidism: minimally invasive video-assisted parathyroidectomy and minimally invasive open videoscopically magnified parathyroidectomy with local anesthesia. *World J Surg* 2002; **26**: 1066–1070.
- 20 Inabnet WB, Fulla Y, Richard B, Bonnichon P, Icard P, Chapuis Y. Unilateral neck exploration under local anesthesia: the procedure of choice for asymptomatic primary hyperparathyroidism. *Surgery* 1999; **126**: 1004–1009.