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Minimally Invasive Video-Assisted Parathyroidectomy Versus Open Minimally Invasive Parathyroidectomy for a Solitary Parathyroid Adenoma: A Prospective, Randomized, Blinded Trial

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Abstract

Background: A variety of minimally invasive parathyroidectomy (MIP) techniques have been currently introduced to surgical management of primary hyperparathyroidism (pHPT) caused by a solitary parathyroid adenoma. This study aimed at comparing the video-assisted MIP (MIVAP) and open MIP (OMIP) in a prospective, randomized, blinded trial.

Materials and Methods: Among 84 consecutive pHPT patients referred for surgery, 60 individuals with concordant localization of parathyroid adenoma on ultrasound and subtraction Tc^{99m}-MIBI scintigraphy were found eligible for MIP under general anesthesia and were randomized to two groups (n = 30 each): MIVAP and OMIP. An intraoperative intact parathyroid hormone (iPTH) assay was routinely used in both groups to determine the cure. Primary end-points were the success rate in achieving the cure from hyperparathyroid state and hypocalcemia rate. Secondary end-points were operating time, scar length, pain intensity assessed by the visual-analogue scale, analgesia request rate, analgesic consumption, quality of life within 7 postoperative days (SF-36), cosmetic satisfaction, duration of postoperative hospitalization, and cost-effectiveness analysis.

Results: All patients were cured. In 2 patients, an intraoperative iPTH assay revealed a need for further exploration: in one MIVAP patient, subtotal parathyroidectomy for parathyroid hyperplasia was performed with the video-assisted approach, and in an OMIP patient, the approach was converted to unilateral neck exploration with the final diagnosis of double adenoma. MIVAP versus OMIP patients were characterized by similar operative time (44.2 ± 18.9 vs. 49.7 ± 15.9 minutes; $P = 0.22$), transient hypocalcemia rate (3 vs. 3 individuals; $P = 1.0$), lower pain intensity at 4, 8, 12, and 24 hours after surgery (24.9 ± 6.1 vs. 32.2 ± 4.6; 26.4 ± 4.5 vs. 32.0 ± 4.0; 19.6 ± 4.9 vs. 25.4 ± 3.8; 15.5 ± 5.5 vs. 20.4 ± 4.7 points, respectively; $P < 0.001$), lower analgesia request rate (63.3% vs. 90%; $P = 0.01$), lower analgesic consumption (51.6 ± 46.4 mg vs. 121.6 ± 50.3 mg of ketoprofen; $P < 0.001$), better physical functioning aspect and bodily pain aspect of the quality of life on early recovery (88.4 ± 6.9 vs. 84.6 ± 4.7 and 90.3 ± 4.7 vs. 87.5 ± 5.8; $P = 0.02$ and $P = 0.003$, respectively), shorter scar length (17.2 ± 2.2 mm vs. 30.8 ± 4.0 mm; $P < 0.001$), and higher cosmetic satisfaction rate at 1 month after surgery (85.4 ± 12.4% vs. 77.4 ± 9.7%;

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$P = 0.006$). Cosmetic satisfaction was increasing with time, and there were no significant differences at 6 months postoperatively. MIVAP was more expensive (US$1,150 ± 63.4 vs. 1,015 ± 61.8; $P < 0.001$) while the mean hospital stay was similar (28 ± 10.1 vs. 31.1 ± 9.7 hours; $P = 0.22$). Differences in serum calcium values and iPTH during 6 months of follow-up were nonsignificant. Transient laryngeal nerve palsy appeared in one OMIP patient ($P = 0.31$). There was no other morbidity or mortality.

Conclusions: Both MIVAP and OMIP offer a valuable approach for solitary parathyroid adenoma with a similar excellent success rate and a minimal morbidity rate. Routine use of the intraoperative iPTH assay is essential in both approaches to avoid surgical failures of overlooked multiglandular disease. The advantages of MIVAP include easier recognition of recurrent laryngeal nerve (RLN), lower pain intensity within 24 hours following surgery, lower analgesia request rate, lower analgesic consumption, shorter scar length, better physical functioning and bodily pain aspects of the quality of life on early recovery, and higher early cosmetic satisfaction rate. However, these advantages are achieved at higher costs because of endoscopic tool involvement.

Bilateral neck exploration has become a gold standard for primary hyperparathyroidism (pHPT) with excellent results of more than a 95% cure rate and minimal morbidity in the hands of an experienced endocrine surgeon.[1,2,3] However, most cases of pHPT caused by a single parathyroid adenoma (80%) require removal of only one hyperfunctioning gland to achieve the cure. Progress in localization studies, including parathyroid subtraction scintigraphy and high-resolution ultrasonography, has led to the birth of a new concept in parathyroid surgery called the minimally invasive parathyroidectomy (MIP). Initially, the idea was directed at a unilateral exploration of the side of the neck harboring the parathyroid adenoma revealed by preoperative imaging techniques.[4] Introduction of the rapid intact parathyroid hormone (iPTH) assay into clinical practice allowed for narrowing unilateral neck exploration to a focused approach for parathyroid adenoma with no need for exploring the other unilateral parathyroid gland, as the assay itself could have confirmed the cure if an adequate intraoperative iPTH serum level drop was obtained.[5] Since then, few different techniques of targeted parathyroidectomy have been introduced,[6] including radio-guided parathyroidectomy,[7,8] endoscopic parathyroidectomy,[9] minimally invasive video-assisted parathyroidectomy (MIVAP) using central[10,11] or lateral access to the neck,[12] as well as open minimally invasive parathyroidectomy (OMIP).[13,14,15] In theory, less invasive operations should be associated with similar cure rates as bilateral neck exploration but with lower morbidity, shorter hospital stay, and better recovery. Data indicating the benefits of minimally invasive parathyroidectomy are based so far on large retrospective series with only few prospective randomized trials, including a comparison of bilateral neck exploration versus MIVAP,[16] bilateral versus unilateral neck exploration,[17] bilateral neck exploration versus MIP under local anesthesia,[18] and MIVAP under general versus local anesthesia.[19] The question as to which approach is the best for pHPT is still under investigation, with growing evidence pointing to beneficiary outcomes of MIP.[20] The forthcoming question requiring an answer is what procedure is the best among various MIP techniques for the management of pHPT.

To date, no blinded, prospective, randomized trial has been published that would compare MIVAP with OMIP in the treatment of pHPT caused by a single parathyroid adenoma. Therefore, the present study was designed with the focus on the impact of the surgical technique on success rate and incidence of postoperative hypocalcemia as primary end points and postoperative pain intensity, analgesic consumption, cosmetic satisfaction, quality of life within the early recovery period, and cost-effectiveness as secondary end points.

MATERIAL AND METHODS

Patient Selection

Eighty-four patients with pHPT were referred to the Department of Endocrine Surgery, Third Chair of General Surgery, Jagiellonian University College of Medicine in Kraków, Poland, for first-time surgery between December 2002 and December 2004. Of this group, 63 patients meeting the inclusion criteria were found to be eligible for MIP. Inclusion criteria were diagnosis of pHPT confirmed by biochemical evaluation (increased serum calcium of more than 2.6 mmol/l and serum iPTH level of more than 65 pg/ml), a single parathyroid gland disease (concurrent localization with high-resolution ultrasound of the neck and ^{99m}Tc-MIBI subtraction scintigraphy), a parathyroid adenoma not exceeding 30 mm in the largest diameter,

Table 1.
Characteristics of patients included in the study

	MIVAP (n = 30)	OMIP (n = 30)	Reference range	*P*
Age (years)	59.1 ± 12.4	61.5 ± 11.9	–	0.44[a]
Gender ratio (M:F)	4:26	5:25	–	0.71[b]
Total serum calcium (mmol/L)	3.03 ± 0.14	3.02 ± 0.1	2.15–2.6	0.78[a]
iPTH (pg/ml)	282.5 ± 121.7	289.1 ± 118.7	12–65	0.82[a]
Alkaline phosphatase (IU/l)	142.9 ± 30.3	146.1 ± 27.7	30–260	0.66[a]
Creatinine (μmol/l)	82.3 ± 18.0	86.3 ± 10.5	60–120	0.30[a]

MIVAP: minimally invasive video-assisted parathyroidectomy; OMIP: open minimally invasive parathyroidectomy; iPTH: intact parathyroid hormone.

Values are represented as mean ± SD.

[a] *t*–test.

[b] χ^2–test.

no previous neck surgery, and absence of nodular goiter requiring one-step thyroid surgery. Subtraction scintigraphy of the neck and mediastinum with 60 MBq ^{99m}Tc and 250 MBq ^{99m}Tc–MIBI (Orbiter; Siemens, Erlangen, Germany) was performed in all the patients before referral for surgery. High-resolution Doppler ultrasound of the neck with 12-MHz linear array transducer (Logiq 7; GE, Solingen, Germany) was performed during an outpatient visit prior to admission by an endocrine surgeon experienced in parathyroid ultrasound imaging (MB) who was blinded to the sestamibi scintigraphy results. Exclusion criteria were a familial history of pHPT (MEN 1, MEN 2, hereditary pHPT), negative (n = 2) or discordant (n = 7) localization studies, suspicion of multiglandular disease (n = 4), extracervical ectopy, parathyroid cancer, concomitant goiter larger than 30 ml of volume (n = 8), pregnancy or lactation, age below 18 years, high-risk patients American Society of Anesthesiology (ASA) grade 4, emergency surgery for hypercalcemic crisis, and inability to comply with the scheduled follow-up. Three eligible patients refused their consent to undergo MIP in favor of conventional bilateral cervical exploration and were excluded. Finally, 60 patients (52 women and 8 men) who signed informed consent forms and represented 95% of all eligible individuals encountered throughout the study period were randomized with the sealed envelope method (1:1) to two groups equal in size (n = 30): MIVAP and OMIP. Characteristic data of both groups are presented in Table 1. The flow chart summarizing the study design is presented in Fig. 1. The study was approved by the Bioethics Committee of the Jagiellonian University.

Anesthesia

Both the MIVAP and OMIP procedures were performed under general anesthesia. Two anesthesiologists involved in the study followed a strict protocol including premedication with IV midazolam and anesthesia induction with fentanyl, thiopental, and pancuronium at the body-mass-dependent dose. After endotracheal intubation, all patients were put on mechanical ventilation (sevoflurane and oxygen mixture). In the course of the operation, all patients received an IV infusion of Ringer's solution (15 ml/kg). To prevent postoperative vomiting, IV metoclopramide was administered prior to awakening.

Surgical Technique

The MIVAP procedure was performed according to the Miccoli technique with a 1.5-cm horizontal skin incision 2 cm above the sternal notch.[10,11,19] Having dissected but not divided the strap muscles in midline, a working space was created by retraction of the unilateral thyroid lobe medially and the strap muscles laterally. The parathyroid adenoma was located, dissected, and removed employing the video-assisted approach and instruments designed for parathyroid and thyroid surgery (Karl-Storz, Tutlingen, Germany) and sent for frozen-section examination. The remaining ipsilateral parathyroid gland was electively not exposed. The study protocol defined extending the MIVAP-targeted exploration to video-assisted unilateral neck exploration in cases of an inadequate decrease in the serum iPTH level at both 10 and 20 minutes postexcision. In cases of intraoperative demonstration of a normally appearing second parathyroid gland on the operated side or unsuccessful video-assisted unilateral cervical exploration, the study protocol required extending the video-assisted exploration to the opposite side of the neck and then converting the procedure to conventional bilateral neck exploration if the cure was not achieved with the video-assisted approach.

The OMIP procedure was an open, targeted operation for parathyroid adenoma removal. We employed the

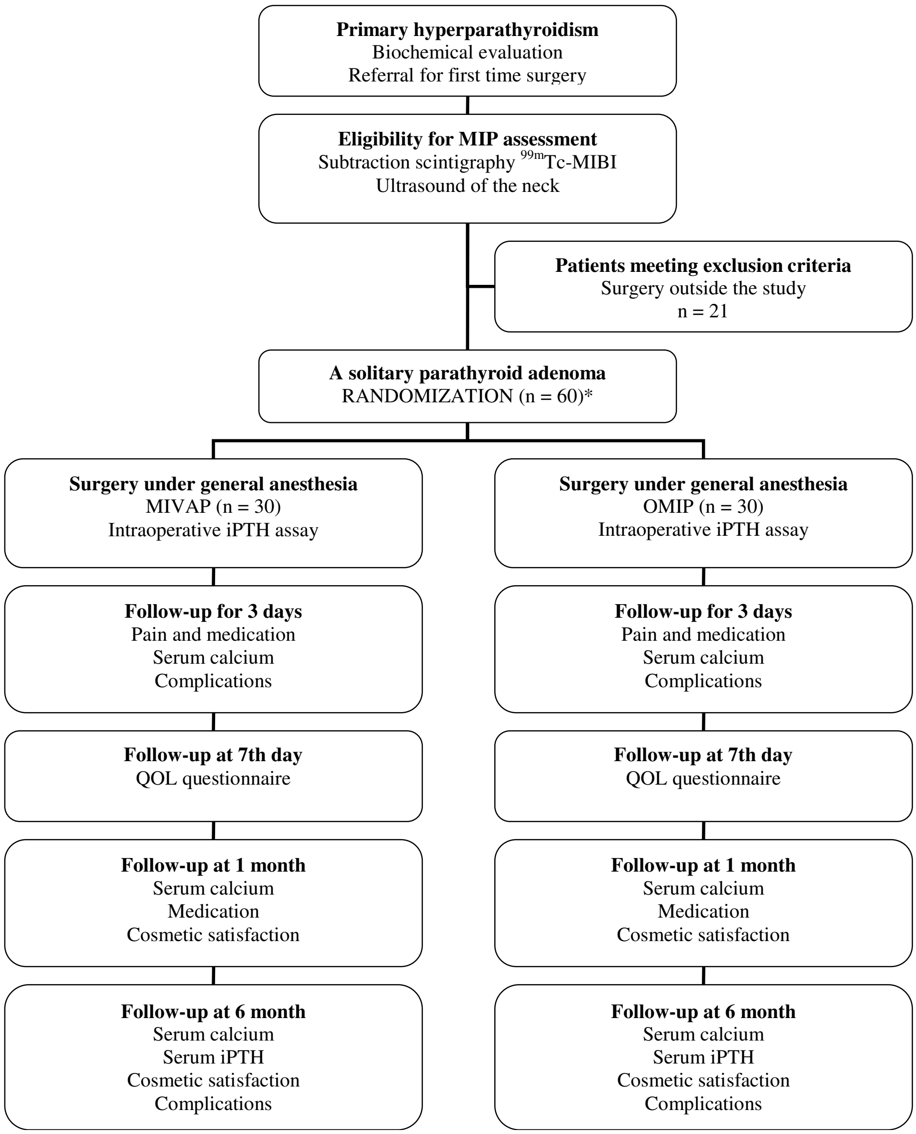

Figure 1. Flow chart summarizing the study on minimally invasive video-assisted parathyroidectomy (MIVAP) versus open minimally invasive parathyroidectomy (OMIP) for a single parathyroid adenoma: a prospective, randomized, blinded trial (asterisks: 3 eligible patients refused their consent).

technique described by Irvin and modified by Udelsmann.[3,13-15] A 2- to 3-cm-long abbreviated Kocher skin incision was made 2 cm above the sternal notch in most patients. For superior or retroesophageal parathyroid adenomas, a higher incision was made along the anterior border of the ipsilateral sternocleidomastoid muscle. After dissecting but not dividing the strap muscles from the lateral aspect, the thyroid lobe was mobilized, the parathyroid adenoma identified, dissected, removed, weighed, and sent for frozen-section examination. The remaining ipsilateral parathyroid gland was electively not exposed. The study protocol dictated a conversion from OMIP to unilateral neck exploration in cases of an inadequate decrease in serum iPTH level at both 10 and 20 minutes postexcision. In cases of intraoperative demonstration of a normally appearing second parathyroid gland on the operated side or of unsuccessful unilateral neck exploration, the study protocol required a conversion to bilateral neck exploration. In cases of conversion, patients were analyzed according to their initial group assignment in order to respect the intention-to-treat rule. Wound drainage was not used in either the MIVAP or OMIP technique in favor of loose wound closure.

Quick iPTH Assay

An intraoperative quick iPTH assay (STAT-Intraoperative-iPTH-Assay, Future Diagnostics, Wijchen, The Netherlands) was routinely used. The following peripheral venous serum samples were analyzed: preoperative baseline (before tracheal intubation), preexcision (after dissection of the adenoma but before its removal), and 10 minutes postexcision. The Miami criterion was used to determine the cure (an iPTH drop of 50% or more from the highest of either preoperative baseline or preexcision level at 10 minutes after gland excision.[21,22] In cases with an inadequate iPTH decrease at 10 minutes post-excision, an additional estimation was made at 20 minutes to clarify the situation before the conversion was considered.

Histopathology

Intraoperative frozen sections were routinely used in both groups to determine the underlying pathology of pHPT: parathyroid adenoma or hyperplasia according to the conventional histological criteria.

Intraoperative Evaluation

The following parameters were recorded during surgery: operative time (skin incision to skin closure), location of parathyroid adenoma (right/left, inferior/superior), time for adenoma localization, intraoperative exposition of the recurrent laryngeal nerve (RLN), time for adenoma excision, weight of the removed parathyroid adenoma, intraoperative serum iPTH levels, iPTH decrease rate, histological findings in frozen sections, time until results of frozen-section analysis and quick iPTH assay where available, incidence of multiglandular disease, and conversion rate.

Postoperative Follow-Up

Neither patients nor nurses knew the relevant group assignment. The lower part of the neck was covered with an opaque, large, and air-permeable but water-resistant dressing to conceal the length of the scar for the initial 7 days following surgery. An overnight hospital stay was mandatory for all patients.

For adequate evaluation of biochemical hypocalcemia, blood samples were analyzed at 24, 48, and 72 hours postoperatively (during hospital stay and after discharge on morning outpatient visits). Episodes of symptomatic hypocalcemia were also recorded. Indirect laryngoscopy was mandatory on the 2nd day postoperatively, being performed by an independent ear, nose and throat (ENT) specialist to assess the RLN morbidity. In cases of recurrent nerve palsy, an additional ENT examination was scheduled at 1 and 6 months following surgery.

Oral calcium (calcium 300, 3–12 tablets in 3 divided doses; Polfa Kutno, Poland) was administered in cases of reported symptoms of hypocalcemia and/or decreased serum calcium below 2.0 mmol/l. Vitamin D metabolites (Alphadiol, 1 μg/day; GlaxoSmithKline) were given orally in cases of decreased serum calcium below 1.8 mmol/l. Doses of calcium and vitamin D metabolites, as well as duration of supplementation, were recorded. Pain intensity was assessed using the visual analogue scale (VAS) at 4, 8, 12, and 24 hours following surgery. Nurse-controlled analgesia rate (NCA) on the patient's request, as well as analgesic consumption, were recorded for 24 hours following surgery. Ketoprofen was used as a painkiller, the dose being 50 mg administered on demand (not more frequently than every 4 hours). Each patient was given a standard quality-of-life questionnaire on the 7th postoperative day. A generic instrument, the Medical Outcomes Trusts Short Form 36 Health Survey (SF-36) was employed.[23] The results were tabulated and scored according to the instruction manual provided by the Medical Outcome Trust.[24] Using simple questions that the individuals scored from 1 to 6, the SF-36 allows for achieving reproducible measures of wellness and the lack of wellness for a variety of conditions and populations. The instrument consists of 36 items categorized into the following 9 domains covering physical, psychological, and social aspects of health status: physical functioning, social functioning, role limitations due to physical problems, social functioning, bodily pain, general mental health, role limitations due to emotional problems, vitality, and general health perceptions. The number of questions that contributed to each domain ranges from 2 to 10. Scores on all domains are standardized from 1 to 100, with the latter number representing optimal wellness. On follow-up visits at 1 and 6 months after surgery, the following data were recorded: serum calcium level, serum iPTH level, cosmetic satisfaction as assessed by VAS, scar length, and healing effects (estimated by a physician).

Cost-effectiveness analysis was performed using an official in-hospital price list for medical procedures. The costs included (in US dollars): $15 for ultrasonography, $102 for sestamibi scintigraphy, $90 for an intraoperative iPTH assay, $15 for frozen section examination, $3/minutes for anesthesia, $3minutes for operating theater use, $3/minutes for videoscopic equipment, and $60/day of hospital stay.

The sample size was estimated based on the principle of detecting a 10% difference in the success rate, hypocalcemia rate, and pain intensity, with an 80% probability at $P < 0.05$. Statistical analysis was based on the χ^2-test and Student's *t*–tests. A commercially available statistical package (STATISTICA; Stat-Soft, Kraków, Poland) was used. All data were entered onto a dedicated spreadsheet by a blinded medical assistant (Microsoft Excel 2002; Microsoft Corporation, San Jose, CA) and analyzed by a statistician.

RESULTS

Among 84 consecutive pHPT patients referred for surgery throughout the study period, 63 (75%) individuals were found eligible for MIP. Three patients refused their consent to participate in the study, and finally, 60 patients with the preoperative diagnosis of a solitary parathyroid adenoma representing 95% of the eligible individuals were included. Preoperative clinical and biochemical data were similar between both groups (Table 1). Four patients in the MIVAP group and 5 in the OMIP group were considered asymptomatic ($P = 0.71$).

Including the 24 excluded patients operated on outside the study (unilateral or bilateral neck exploration with a quick iPTH assay), the real incidence of multiglandular disease within the study period was 7.1% (5 cases of parathyroid hyperplasia and 1 case of double adenoma). Four of these cases were correctly identified in the course of preoperative evaluation (excluded patients), but two were missed, and the diagnosis of multiglandular disease was made intraoperatively. Concordant results of Doppler ultrasound and ^{99m}Tc-MIBI subtraction scintigraphy had the cumulative sensitivity of 92.4% (Doppler ultrasound vs. ^{99m}Tc-MIBI subtraction scintigraphy alone: 89.7% vs. 87.0%, respectively), and positive predictive value of 93.6% (Doppler ultrasound vs. ^{99m}Tc-MIBI subtraction scintigraphy alone: 92.1% vs. 90.5%, respectively).

Twenty-nine MIVAP and 29 OMIP patients had solitary parathyroid adenomas; one patient in each group had multiglandular disease (Table 2). Localization and mean weight of parathyroid adenomas were similar between both groups (Table 3). In 1 MIVAP patient and 2 OMIP patients, the parathyroid adenoma weighed less than 500 mg. All patients included in the study were cured, and none suffered from persistent disease at 6 months of follow-up (Table 4). Mean time for adenoma localization was significantly shorter in the MIVAP group compared with the OMIP group (9.3 ± 5.1 vs. 11.3 ± 2.6 minutes, respectively; $P = 0.05$). The following intraoperative data were found not to differ significantly between groups: mean operating time, number of visualized RLNs, mean time for quick iPTH assay, and mean time for frozen-section results (details in Table 3). However, the quick iPTH assay result was available twice as fast as the frozen-section result in both groups (11.5 ± 1.3 vs. 24.1 ± 4.7 minutes; $P < 0.001$). Moreover, frozen-section examination after a single gland excision was found not to be helpful in diagnosing multiglandular disease in the two cases reported within the study. Transient postoperative symptomatic versus asymptomatic hypocalcemia was present in 1 versus 2 MIVAP and 2 versus 1 OMIP patients, respectively ($P = 0.55$). Mean calcium intake for 30 days following surgery was 0.67 ± 0.23 g per day versus 0.75 ± 0.26 g per day (MIVAP vs. OMIP, respectively; $P = 0.26$). Mean serum calcium levels were within the reference range and were not significantly different between groups either at 24, 48, and 72 hours postoperatively or at 1 and 6 months following surgery (data not shown). Mean serum iPTH levels were within the reference range and similar in both groups at 6 months postoperatively: 46.5 ± 9.4 vs. 45.1 ± 7.6 pg/ml (MIVAP vs. OMIP, respectively; $P = 0.52$).

A routine employment of intraoperative quick iPTH assay prevented 2 cases of persistent postoperative hyperparathyroidism (1 case in each group). One false negative case and two true negative cases were observed (all were clarified correctly with an additional serum estimation at 20 minutes postexcision). The following predictive assay values were found: sensitivity 98.3%, specificity 100%, positive predictive value 100%, negative predictive value 66.6%, and overall accuracy 98.3%. Pain assessed by VAS was significantly lower at 4, 8, 12, and 24 hours postoperatively in MIVAP versus OMIP patients, respectively ($P < 0.001$). The difference in pain intensity varied from 17.5% at 8 hours to 24% at 24 hours after the operation. Analgesia request rate was significantly lower in MIVAP versus OMIP patients (19 vs. 27 individuals, respectively; $P = 0.007$). Mean analgesic consumption was also lower among MIVAP compared with OMIP patients (51.6 ± 46.4 mg vs. 121.6 ± 50.3 mg of ketoprofen, respectively; $P < 0.001$). Quality of life assessed by the SF-36 questionnaire on the 7th postoperative day was similar between the groups except for a significantly better physical functioning aspect among MIVAP versus OMIP patients (88.4 ± 6.9 vs. 84.6 ± 4.7, respectively; $P = 0.008$) and bodily pain aspect (90.3 ± 4.7 vs. 86.5 ± 4.9, respectively; $P = 0.003$). Details are presented in Table 4. Mean scar length was significantly shorter in MIVAP versus OMIP patients (17.2 ± 2.2 vs. 30.8 vs. 4.0 mm; respectively; $P < 0.001$). Cosmetic satisfaction assessed by VAS at 1 month postoperatively was significantly higher in MIVAP versus OMIP patients (85.4 ± 12.4 vs. 77.4 ± 9.7, respectively; $P = 0.006$). This difference became nonsignificant between both groups at 6 months postoperatively ($P = 0.16$). Satisfaction was increasing with time after the operation in both MIVAP and OMIP patients ($P = 0.006$ and $P = 0.002$), not being dependent on gender. Details are presented in Table 4.

An overnight hospital stay was mandatory, and mean hospitalization length was similar between groups ($P = 0.22$). Cost-effectiveness analysis revealed that

Table 2.
Details regarding conversions and complications noted during the study

Patient no.	Randomized	Operated	Histology	Comments
7	OMIP	OMIP	Adenoma	Transient recurrent laryngeal nerve palsy, withdrawal at 1 month after surgery.
24	MIVAP	VA-BNE	Four parathyroid glands chief cells hyperplasia	Preoperative serum calcium 2.87 mmol/l, serum iPTH 241 pg/ml. Ultrasound: 8 × 5 × 5 mm adenoma (148 mg) of the left superior gland. MIBI — left-sided uptake. Serum iPTH 223 pg/mt at 10 minutes and 237 pg/ml at 20 minutes postexcision (frozen section positive). Conversion to video-assisted left-sided exploration–excision of 5 × 5 × 5 mm (96 mg) left inferior parathyroid gland (positive frozen section). Serum iPTH 176 pg/ml at 10 minutes and 169 pg/ml at 20 minutes. Suspicion of 4-gland disease. Conversion to video-assisted right-sided exploration with 2 parathyroid glands identified: 4 × 4 × 4 mm (54 mg) and 3 × 3 × 3 mm (29 mg), subtotal parathyroidectomy completed (positive frozen section) with video-assisted approach. Serum iPTH 41 pg/ml at 10 minutes and 27 pg/ml at 20 minutes. No morbidity. Cure confirmed at 6 month follow-up.
53	OMIP	UNE	Double adenoma	Preoperative serum calcium 3.19 mmol/l, serum iPTH 421 pg/ml. Ultrasound: 17 × 12 × 11 mm adenoma of the right superior gland (1.54 g). MIBI—right-sided uptake. Serum iPTH 289 pg/ml at 10 minutes and 321 pg/ml at 20 minutes postexcision. Conversion to right-sided UNE. A13 × 11 × 7 mm second adenoma within the upper pole of the thymus (685 mg). Serum iPTH 69 pg/ml at 10 minutes and 33 pg/ml at 20 minutes postexcision. No morbidity. Cure confirmed at 6-month follow-up.

OMIP: open minimally invasive parathyroidectomy; iPTH: intact parathyroid hormone; MIVAP: minimally invasive video-assisted parathyroidectomy; VA-BNE: video-assisted bilateral neck exploration; UNE: unilateral neck exploration.

Table 3.
Intraoperative data

	MIVAP (n = 30)	OMIP (n = 30)	*P*
Localization of the adenoma:[a] RSPG / RIPG / LSPG / LIPG	6 / 7 / 7/ 9	6 / 8 / 7 / 8	0.13[c]
Operating time (minutes)	44.16 ± 18.89	49.66 ± 15.91	0.22[b]
Time for adenoma localization (minutes)	9.3 ± 5.1	11.3 ± 2.6	0.05[b]
RLN exposition (number)	26	22	0.19[c]
Time for adenoma excision (minutes)	9.4 ± 2.4	9.0 ± 2.3	0.50[b]
Time for quick iPTH assay (minutes)	11.5 ± 1.3	11.5 ± 1.2	1.0[b]
Time for frozen section (minutes)	23.9 ± 4.6	24.6 ± 4.9	0.56[b]
Adenoma weight (g)	1.98 ± 1.43	2.29 ± 1.27	0.38[b]

MIVAP: minimally invasive video-assisted parathyroidectomy; OMIP: open minimally invasive parathyroidectomy; RSPG: right superior parathyroid gland; RIPG: right inferior parathyroid gland; LSPG: left superior parathyroid gland; LIPG: left inferior parathyroid gland; RLN: recurrent laryngeal nerve; iPTH: intact parathyroid hormone.

Values are expressed as mean ± SD.

[a]In two patients, multiglandular disease was revealed.

[b]*t*-test.

[c]χ^2-test.

Table 4.
Postoperative follow-up of pain by visual analog score (VAS), analgesia request, complications, scar length, cosmetic satisfaction, quality of life (QOL) on recovery, and hospital stay and costs analysis

	MIVAP (n = 30)	OMIP (n = 30)	*P*
Success rate (%)	100	100	1.0[b]
Transient hypocalcemia (no.)	3	3	1.0[b]
Pain at 4 h (VAS)	24.9 ± 6.0	32.2 ± 4.6	<0.001[a]
Pain at 8 h (VAS)	26.4 ± 4.5	32.0 ± 4.8	<0.001[a]
Pain at 12 h (VAS)	19.5 ± 4.8	25.4 ± 3.8	<0.001[a]
Pain at 24 h (VAS)	15.5 ± 5.4	20.4 ± 4.7	<0.001[a]
Analgesia request 24 h (no.)	19	27	0.01[b]
Analgesic consumption 24 h (mg)	51.6 ± 46.4	121.6 ± 50.3	<0.001[a]
Transient RLN palsy (No)	0	1	0.31[b]
Scar length (mm)	17.2 ± 2.2	30.8 ± 4.0	<0.001[a]
Cosmetic satisfaction at 1 month (VAS)	85.4 ± 12.4	77.4 ± 9.7	0.006[a]
at 6 months	90.5 ± 10.3	87.5 ± 5.8	0.16[a]
Hospital stay (hours)	28.0 ± 10.1	31.1 ± 9.7	0.22[a]
QOL on 7th postoperative day			
Physical functioning	88.4 ± 6.9	84.6 ± 4.7	0.02[a]
Bodily pain	90.3 ± 4.7	86.5 ± 4.9	0.003[a]
Hospital stay cost ($US)			
Surgery alone	465 ± 39.7	350 ± 37.1	<0.001[a]
Total	1,150 ± 63.4	1,015 ± 61.8	<0.001[a]

Values are expressed as mean ± SD.

MIVAP: video-assisted minimally invasive parathyroidectomy; OMIP: open minimally invasive parathyroidectomy; RLN: recurrent laryngeal nerve.

[a] *t*-test.

[b] χ^2-test.

*Only significant differences are shown.

mean hospitalization costs were higher in the MIVAP group compared with the OMIP group for total hospital charges, but the difference was related to the higher costs of endoscopic tool involvement being independently charged $2 per minute of operation, with the mean difference amounting to $135 (Table 4).

There was no mortality, and morbidity included one case of transient RLN palsy in 1 OMIP patient, which disappeared completely at 1 month, and similar numbers of transient hypocalcemia cases in both groups (Table 4).

DISCUSSION

In recent years, surgical treatment of pHPT has been evolving gradually from the gold standard of bilateral neck exploration toward less-invasive surgical techniques directed toward removal of parathyroid adenoma. This trend has become possible with improved diagnostic accuracy, improved abilities to anatomically localize the involved glands, and intraoperative quantitative assurance as to when all hypersecreting glands have been removed.[13] Many different techniques of MIP are currently in use, but a comparison of these techniques in randomized clinical trials is still lacking. To address this issue, we attempted to carry out this trial comparing MIVAP and OMIP in patients with a preoperatively diagnosed solitary parathyroid adenoma. Preselection was necessary to have a fair comparison of exactly the same surgical task consisting of parathyroid adenoma removal by the two different techniques, video-assisted and open, via a small direct skin incision. Thus, this study was focused on direct comparison of two different surgical techniques in similar operations. Patients with a solitary parathyroid adenoma are well known to represent the largest and also easiest to treat subpopulation of pHPT patients who benefit most from MIP. The common fear of all endocrine surgeons performing MIP is to correctly identify patients with multiglandular disease to avoid an increase in persistent disease rate. The number of patients at danger of persistent disease has been considered to be significantly reduced with the observation made after introduction of the intraoperative iPTH assay to clinical practice, indicating that the incidence of multiglandular disease is lower in patients undergoing parathyroidectomy with a quick iPTH assay performed intraoperatively (5%–8%) compared with those undergoing bilateral neck exploration without a quick iPTH assay when diagnosis of multiglandular disease is based on enlarged morphology of glands rather than on their function (20–30%).[25,26] Conflicting data can be found in the literature regarding the results of MIP with or without an intraoperative iPTH assay.[27,28] In spite of the strict protocol of the present study (concordant results of high-resolution Doppler ultrasound and 99mTc-MIBI subtraction scintigraphy) that required that patients with other than a single-gland pathology be disqualified from the MIP group, 2 out of 6 cases of multiglandular disease were overlooked preoperatively. If not the intraoperative quick iPTH assay, which correctly identified those 2 patients (1 in each group) based on the Miami criterion employed in the study, 2 failures would have been possible.[22,29] The overall success rate in achieving the cure from the hyperparathyroid state was 100% in both groups. MIVAP was successfully used to explore the opposite side of the neck in a case of 4-gland parathyroid hyperplasia, where a subtotal parathyroidectomy was finally performed. In 1 OMIP patient with a double adenoma, the technique was converted to open unilateral neck exploration with an excellent result.

Another important issue is the accuracy of preoperative localization studies of a single parathyroid adenoma in patients living in an endemic goiter region.[30] The endocrine surgeon-performed ultrasound of the neck was more specific in this study than sestamibi scanning (89.7% vs. 87%) whereas in the series with the radiologist-performed ultrasound of the neck, the results were reported to be much worse (61% vs. 86%).[2] A similar phenomenon was also observed by other authors.[31] False positive localization occurs with sestamibi scans, as its uptake is related to mitochondria, which are also present in a great number in thyroid nodules, particularly follicular tumors. To avoid an increased rate of false positive results of sestamibi, ultrasound examination of the neck is mandatory in patients with pHPT and goiter.[3,8] The most important component of minimally invasive parathyroid surgery is a surgeon with experience in conventional parathyroid surgery, good understanding of the limits and drawbacks of the employed technical adjuncts, and sound clinical judgment.[20,32]

As one might expect, both MIVAP and OMIP involved a low incidence of transient postoperative hypocalcemia (10% in this series). This value is comparable to the incidence of 12% described by Bergenfelz *et al.*[17,18] for bilateral neck exploration in patients with a single parathyroid adenoma if only visualization of all 4 parathyroid glands is used instead of taking routine biopsies, the maneuver considered to increase postoperative hypocalcemia rate to 20%–25% after conventional neck exploration.[17,18] Also, the mean oral calcium intake was nonsignificantly different between both groups, indicating clearly that the technique of a parathyroid adenoma removal, either video-assisted or open technique, inflicts the same trauma to the healthy parathyroid tissue.

Both the MIVAP and OMIP techniques were safe. The only case of transient laryngeal nerve palsy occurred in the OMIP group (nonsignificant difference). Although in MIVAP patients 4 more RLNs were visualized in comparison to the OMIP group, this difference was nonsignificant. However, a profound evaluation of this complication would require a much larger series. In theory, the video-assisted technique provides for magnification of the dissected structures (8–10 times), allowing for easier recognition of the recurrent nerve. But even in the most experienced hands, such a complication occurs in about 1% of patients. It was reported recently that intraoperative use of neuromonitoring may decrease this morbidity 2-fold or even 3-fold compared with conventional surgery without neuromonitoring.[33]

Postoperative pain assessed by VAS was significantly lower in MIVAP versus OMIP patients at all evaluated time points within the initial 24 hours following surgery. The reason for this could not have been entirely related to the shorter skin incision in MIVAP versus OMIP patients (17.2 ± 2.2 vs. 30.8 vs. 4.0 mm; respectively; $P < 0.001$) and less tissue damage. In fact, postoperative pain is also caused by neck hyperextension, which is avoided in the video-assisted technique.[16] Mean differences in pain intensity varied from 17.5% at 8 hours postoperatively to 24% at 24 hours postoperatively. The benefit of lower postoperative pain in the MIVAP group was also confirmed by a lower analgesia request rate and reduced analgesic consumption. Although these observations were statistically significant, it would be interesting to know if such relatively small differences have any clinical significance. That point was addressed in the quality-of-life analysis made on the 7th postoperative day. The SF-36 revealed significant improvements in bodily pain and physical functioning aspects of quality of life, with other components being nonsignificant, which could imply a clinical significance of the observed diminished pain intensity in the MIVAP group. Moreover, MIVAP patients experienced significantly higher cosmetic satisfaction with their scar (the scar being significantly shorter than in the OMIP patients). This was true for 1 month after surgery, but the difference became nonsignificant at 6 months postoperatively. In both groups, cosmetic satisfaction tended to increase with time. No differences were observed in the mean length of hospitalization. Although an overnight hospital stay was mandatory due to the insurer's (National Health Fund) regulations associated with reimbursement, both procedures could have been successfully performed in the majority of noncomplicated cases as outpatient operations under local anesthesia.[13,15,19] Mean hospital stay costs were significantly higher in the MIVAP compared with the OMIP group, and the difference was related only to the charges for endoscopic tool involvement, as other components, including localization studies, were similar.

Both the MIVAP and OMIP operations can be performed under local anesthesia with the previously described additional benefits, including reduced total operating time (from induction of anesthesia to return to ward, but not skin incision to skin closure time) and diminished analgesic consumption postoperatively.[19] However, the routine use of general anesthesia in this study was a deliberate action to avoid variability arising from a relatively high rate of noneligibility for local anesthesia approaching 40% of patients and the conversion rates from local to general anesthesia described to appear in about 8% of eligible patients in some series.[14] Whether or not these differences in pain intensity, analgesic consumption, better quality of life during the early recovery period and improved early cosmetic satisfaction are sufficient to compensate for the additional costs of endoscopic tool involvement will depend on local circumstances—the healthcare system and the acceptance of improved cosmetic outcomes as the leading benefits of the video-assisted approach.

CONCLUSIONS

In conclusion, this study demonstrated that both MIVAP and OMIP operations offer a valuable approach to solitary parathyroid adenomas with a similar excellent success rate and minimal morbidity rate. Routine use of the intraoperative iPTH assay is essential in both approaches to avoid surgical failures of overlooked multiglandular disease. Advantages of MIVAP include an easier recognition of RLN, lower pain intensity within 24 hours following surgery, lower analgesia request rate, lower analgesic consumption, shorter scar length, better physical functioning and bodily pain aspects of the quality of life on early recovery, and higher early cosmetic satisfaction. However, these advantages are achieved at higher costs because of endoscopic tool involvement.

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