NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of minimally invasive video-assisted thyroidectomy/parathyroidectomy

If the thyroid or parathyroid glands are overactive or enlarged, or if cancer is suspected, it may be necessary to remove all or part of them. Minimally invasive video-assisted thyroidectomy removes the thyroid or parathyroid through 'keyhole surgery' using specially designed instruments.

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this interventional procedure (IP) overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This IP overview was prepared in December 2013 and updated in June 2014.

Procedure name

- Minimally invasive video-assisted thyroidectomy/parathyroidectomy (MIVAT/P)

Specialist societies

- British Association of Endocrine and Thyroid Surgeons
- British Association of Head and Neck Oncologists.

Description

Indications and current treatment

Hyperthyroidism

Hyperthyroidism causes symptoms such as anxiety, weight loss, breathlessness, tiredness, and eye problems. The overactive thyroid is usually enlarged and clearly visible (goitre). The most common cause of hyperthyroidism is Graves' Disease, an autoimmune disease where antibodies stimulate the thyroid cells to secrete excess thyroid hormone. Other causes include toxic adenoma and toxic multinodular goitre.

First line treatment for hyperthyroidism includes medication to reduce the production of thyroxine or radioiodine treatment. Radioiodine treatment involves taking a drink or a capsule that contains radioactive iodine. The radioactivity concentrates in the thyroid gland and destroys some of the thyroid tissue. Surgery to remove part or all of the thyroid gland is also an option.

Thyroid cancer

Thyroid cancer usually develops slowly and the most common first sign is a small, painless lump in the neck. Other symptoms include hoarseness, swollen lymph nodes in the neck, difficulty swallowing or breathing, and pain in the throat or neck. The most common types of thyroid cancer are papillary and follicular thyroid cancer.

The most common treatment for thyroid cancer is surgery to remove all, or part of, the thyroid gland. This is sometimes followed by radioactive iodine treatment or radiotherapy.

Hyperparathyroidism

Hyperparathyroidism occurs when an excess of parathyroid hormone is released by the parathyroid glands in the neck. It generally leads to high levels of calcium in the blood. Symptoms and signs include tiredness, depression, confusion, constipation, polydipsia, polyuria, the development of kidney stones, bone pain and fractures. The most common cause of primary hyperparathyroidism is a single adenoma. Other causes include hyperplasia affecting more than 1 parathyroid gland and rarely, cancer. Secondary hyperparathyroidism can also occur, resulting from conditions such as kidney disease, vitamin D deficiency and gut malabsorption.

Patients with mild hyperparathyroidism may not need active treatment, but will be regularly monitored. More severe hyperparathyroidism is usually treated by surgery to remove the abnormal parathyroid gland or glands.

Conventional open thyroidectomy or parathyroidectomy is done through an incision across the base of the neck. Endoscopic techniques have been developed that use smaller incisions, with the aim of reducing postoperative pain and improving cosmesis.

What the procedure involves

Minimally invasive video-assisted thyroidectomy/parathyroidectomy uses a smaller incision than conventional surgery, with an endoscope to improve

visualisation. The potential benefits are reduced postoperative pain, reduced complications, and improved cosmesis.

The procedure is usually done with the patient under general anaesthesia. The patient's neck is less extended than it needs to be for conventional open surgery. A small incision is made above the sternal notch. The operative space is maintained using external retraction: gas insufflation is not used. An endoscope is inserted through the incision and dissection of the thyroid lobe(s) or parathyroid gland(s) is carried out. Care is taken to identify and preserve the recurrent laryngeal nerve.

An alternative technique for minimally invasive video-assisted parathyroidectomy uses a lateral approach via an incision at the anterior edge of the sternocleidomastoid muscle. A space is dissected between the ipsilateral thyroid lobe, the carotid artery and the internal jugular vein to allow insertion of an endoscope.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to minimally invasive video-assisted thyroidectomy/parathyroidectomy. Searches were conducted of the following databases, covering the period from their commencement to 30 April 2014: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts, the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with benign or malignant thyroid or parathyroid disease.
Intervention/test	Minimally invasive video-assisted thyroidectomy/parathyroidectomy.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This Interventional Procedures (IP) overview is based on approximately 2300 patients treated by minimally invasive video-assisted thyroidectomy from 1 systematic review, 1 randomised trial, 5 non-randomised comparative studies and 3 case series[1–10] and approximately 1180 patients treated by minimally invasive video-assisted parathyroidectomy from 3 randomised controlled trials (RCTs), 3 non-randomised comparative studies, 2 case series and 1 case report[11–19].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction tables (tables 2a and 2b) have been listed in appendix A.

Table 2a Summary of key efficacy and safety findings on minimally invasive video-assisted thyroidectomy

Abbreviations used: CI, confidence interval; CT, conventional thyroidectomy; IP, interventional procedures; MIVAT, minimally invasive video-assisted thyroidectomy; ns, not significant; OR, odds ratio; POSAS, Patient and Observer Assessment scale; PSAQ, Patient scar assessment questionnaire; RATT, robot-assisted transaxillary thyroidectomy; RCT, randomised controlled trial; SMD, standardised mean difference; TSH, thyroid-stimulating hormone; VAS, visual analogue scale)

Study details	Key efficacy findings	Key safety findings	Comments
Pisanu A (2013)[1] **Systematic review** International (studies from Italy, Egypt, Taiwan and Hungary) Search date: December 2012 Study population: RCTs comparing MIVAT with conventional thyroidectomy for thyroid nodular disease **n=581** (289 MIVAT versus 292 conventional thyroidectomy) patients (9 studies) Age: MIVAT: study mean ranged from 38 to 51.8; CT: study mean ranged from 37 to 52.1 years Sex: MIVAT: 80.3% (232/289) female, CT: 80.5% (235/292) female [calculated by IP analyst] Patient selection criteria: prospective RCTs written in English that compared characteristics and perioperative outcomes of adults undergoing MIVAT and CT for thyroid disease. Technique: MIVAT versus CT (MIVAT: total thyroidectomy in 150 patients and thyroid lobectomy in 139 patients; CT: total thyroidectomy in 148 patients and thyroid lobectomy in 144 patients) **Follow-up: mean 3.2 months** (range: 1-23 months) Conflict of interest/source of funding: none	Number of patients analysed: **581 (289 versus 292) although this varies for each outcome** **Conversion rate** (MIVAT to CT) was 0.033 (10 patients). This was because the recurrent laryngeal nerve could not be identified in 5 patients, bleeding in 1 patient, thyroid oversize in 1 case and follicular carcinoma at frozen section in 3 patients. **Mean postoperative satisfaction scores** (patients graded the cosmetic appearance of their wound on a scale from 0 to 10, with higher scores being better) [5 studies]:MIVAT: 9.0 , CT:6.8; 95% CI: -5.720 to -1.057 (significant heterogeneity Q=125.69, p<0.0001) **Operative time** Operative time was significantly shorter in favour of conventional surgery (7 studies) 75.2mins versus 59.2mins, SMD: 1.246, 95% CI: 0.227 to 2.266 (significant heterogeneity Q=113.88, p<0.0001). **Postoperative pain score** (measured on a 10-point VAS, with higher scores representing more severe pain) [5 studies] At 6hrs: MIVAT:2.28, CT:3.53; SMD=-0.659; 95% CI: -1.007 to -0.310 (no heterogeneity Q=1.423, p=0.490) At 24hrs: MIVAT:1.69, CT:3.39; SMD=-3.101; 95% CI: -4.840 to -1.361 (no heterogeneity Q=115.59, p<0.0001) At 48hrs: MIVAT:1.05, CT:2.45; SMD=-2.571; 95% CI: -4.247 to -0.896 (no heterogeneity Q=113.50, p<0.0001)	No mortality observed **Total morbidity rate (7 studies):** 0.1 MIVAT (29/289) versus 0.14 CT (42/292), OR 0.65, 95% CI 0.387 to 1.091 (no heterogeneity Q=4.994, p=0.544) **Transient inferior laryngeal nerve palsy rate (6 studies):** • MIVAT=4.8% • Conventional thyroidectomy=4.4% OR 1.086, 95% CI 0.496 to 2.375 (no heterogeneity Q=0.963, p=0.965) **Permanent inferior laryngeal nerve palsy rate:** • MIVAT=0.3% (1/289) • Conventional thyroidectomy=0% **Paralysis of the external branch of the superior laryngeal nerve:** • MIVAT=0% • Conventional thyroidectomy=2.0% (6/292) **Transient postoperative hypocalcaemia (5 studies):** • MIVAT=4.1% (12/289) • Conventional thyroidectomy=3.7% (11/292) OR 1.095, 95% CI 0.478 to 2.507 (no heterogeneity Q=1.063, p=0.900) **Postoperative haematoma**: 2 patients in the CT but the haematomas did not need surgical evacuation. No cases of permanent	**This study was identified during the update literature search at the time of consultation. It has replaced Lui 2011 (this study now appears in appendix A)** **Study design issues**: • The primary outcome measures were overall morbidity, recurrent laryngeal nerve palsy, postoperative hypocalcaemia and postoperative haematoma. **Study population issues**: • Studies comparing MIT without video assistance to CT were excluded. • 1 prospective study (Alesina et al) that was included in Lui 2011 was excluded here because it was not randomised. • 2 RCTs were excluded: 1 because it showed the preliminary results of another study and another because it did not include the outcomes of interest. **Other** • The inferior laryngeal nerve is the terminal branch of the recurrent laryngeal nerve.

Abbreviations used: CI, confidence interval; CT, conventional thyroidectomy; IP, interventional procedures; MIVAT, minimally invasive video-assisted thyroidectomy; ns, not significant; OR, odds ratio; POSAS, Patient and Observer Assessment scale; PSAQ, Patient scar assessment questionnaire; RATT, robot-assisted transaxillary thyroidectomy; RCT, randomised controlled trial; SMD, standardised mean difference; TSH, thyroid-stimulating hormone; VAS, visual analogue scale)

Study details	Key efficacy findings	Key safety findings	Comments
		hypoparathyroidism were reported in either group. **Mean intraoperative blood loss (4 studies):** • MIVAT=33.7 ml • Conventional thyroidectomy=36.1 ml SMD=-0.170, 95% CI -0.392 to 0.054 (no heterogeneity Q=4.287, p=0.232) Wound infection: MIVAT: 0.6%, CT: 1.7%	

Abbreviations used: CI, confidence interval; CT, conventional thyroidectomy; IP, interventional procedures; MIVAT, minimally invasive video-assisted thyroidectomy; ns, not significant; OR, odds ratio; POSAS, Patient and Observer Assessment scale; PSAQ, Patient scar assessment questionnaire; RATT, robot-assisted transaxillary thyroidectomy; RCT, randomised controlled trial; SMD, standardised mean difference; TSH, thyroid-stimulating hormone; VAS, visual analogue scale)

Study details	Key efficacy findings	Key safety findings	Comments
Docimo G (2012)[2] **Non-randomised comparative study** Italy Recruitment period: 2007–11 Study population: patients with benign or malignant thyroid disease (80% multinodular goitre, 11% carcinoma) **n=982 (179 MIVAT versus 592 minimally invasive thyroidectomy versus 211 conventional thyroidectomy)** Age: mean 45 years Sex: 78% female Patient selection criteria: benign or malignant thyroid disease. Patients with thyroid nodule <35mm and/or thyroid volume ≤30ml were treated by MIVAT. Patients with thyroid nodule between 35 mm and 50 mm and/or thyroid volume between 30 ml and 80 ml were treated by minimally invasive thyroidectomy. Conventional thyroidectomy was used for patients with thyroid volume>80ml and/or thyroid nodule >50mm, recurrences, high-risk carcinoma, or suspected positive lymph nodes. Technique: All patients were treated by total thyroidectomy. The MIVAT procedure was done using a Harmonic Ace scalpel (Ethicon Endosurgery). **Follow-up: not reported**	Number of patients analysed**: 982 (179 versus 592 versus 211)** **Mean operative time (minutes):** • MIVAT=69.4±19 • Minimally invasive thyroidectomy=54.1±12 • Conventional thyroidectomy=46.3±14, p<0.05 **Mean skin incision length (cm):** • MIVAT=1.5±0.5 • Minimally invasive thyroidectomy=3.4±0.2 • Conventional thyroidectomy=8.2±1, p=not reported **Patient satisfaction with cosmetic result 1–6 months after operation (VAS 0–10, where 10 represents the most excellent cosmetic result):** • MIVAT=7±1.5 • Minimally invasive thyroidectomy=8±2 • Conventional thyroidectomy=5±1.3, p<0.05 (MIVAT and minimally invasive thyroidectomy versus conventional thyroidectomy) **Postoperative pain at 8 hours (measured on a VAS from 0 to 10):** • MIVAT=2.6±2.1 • Minimally invasive thyroidectomy=2.6±1.9 • Conventional thyroidectomy=2.9±2.2, p=not significant **Postoperative pain at 36 hours (measured on a VAS from 0 to 10):** • MIVAT=1.1±1.3 • Minimally invasive thyroidectomy=1.0±1.2 Conventional thyroidectomy=1.9±1.9, p<0.05	**All complications:** • MIVAT=9.5% (17/179) • Minimally invasive thyroidectomy=9.3% (55/592) • Conventional thyroidectomy=11.4% (26/211), p=not significant **Transitory hypocalcaemia**: • MIVAT=7.8% (14/179) • Minimally invasive thyroidectomy=7.9% (47/592) • Conventional thyroidectomy=8.5% (18/211), p=not significant **Definitive hypocalcaemia (6 months+)**: • MIVAT=0.6% (1/179) • Minimally invasive thyroidectomy=0.7% (4/592) • Conventional thyroidectomy=1.0% (2/211), p=not significant **Postoperative bleeding needing reintervention:** • MIVAT=0% (0/179) • Minimally invasive thyroidectomy=0.2% (1/592) • Conventional thyroidectomy=0.5% (1/211), p=not significant **Transient recurrent laryngeal nerve palsy:** • MIVAT=0.6% (1/179) • Minimally invasive thyroidectomy=0.3% (2/592) • Conventional thyroidectomy=1.0% (2/211), p=not significant **Definitive recurrent laryngeal**	**Study design issues**: • Consecutive patients. • The treatment was chosen according to thyroid size and disease characteristics (described in patient selection criteria) **Study population issues**: • The 3 groups were similar with regard to age and sex.

Abbreviations used: CI, confidence interval; CT, conventional thyroidectomy; IP, interventional procedures; MIVAT, minimally invasive video-assisted thyroidectomy; ns, not significant; OR, odds ratio; POSAS, Patient and Observer Assessment scale; PSAQ, Patient scar assessment questionnaire; RATT, robot-assisted transaxillary thyroidectomy; RCT, randomised controlled trial; SMD, standardised mean difference; TSH, thyroid-stimulating hormone; VAS, visual analogue scale)

Study details	Key efficacy findings	Key safety findings	Comments
Conflict of interest/source of funding: not reported		**nerve palsy:** • MIVAT=0.6% (1/179) • Minimally invasive thyroidectomy=0.2% (1/592) • Conventional thyroidectomy=0.5% (1/211), p=not significant	

Abbreviations used: CI, confidence interval; CT, conventional thyroidectomy; IP, interventional procedures; MIVAT, minimally invasive video-assisted thyroidectomy; ns, not significant; OR, odds ratio; POSAS, Patient and Observer Assessment scale; PSAQ, Patient scar assessment questionnaire; RATT, robot-assisted transaxillary thyroidectomy; RCT, randomised controlled trial; SMD, standardised mean difference; TSH, thyroid-stimulating hormone; VAS, visual analogue scale)

Study details	Key efficacy findings	Key safety findings	Comments
Del Rio P (2014)[3] **Non-randomised comparative study** Italy Recruitment period: 2005–10 Study population: patients with follicular lesions, papillary carcinoma, Plummer's adenoma, Basedow' disease or goitre. **n=1573 (300 MIVAT versus 1273 conventional thyroidectomy)** Age: not reported Sex: not reported Patient selection criteria: inclusion criteria - nodule <3.5 cm in diameter; thyroid volume <30ml; goitre, hyperfunctioning thyroid, follicular lesion and low risk carcinoma. Absolute contraindications included previous neck surgery, short neck in obese patient, laterocervical nodes metastases and clinical thyroiditis. Relative contraindications included previous neck radiotherapy, nodes at VI level Technique: All patients were treated by total thyroidectomy. The MIVAT procedure was done using an Ultracision CS 14 (Ethicon Endosurgery) and/or Single Use Automatic Clip Applier S-90 (Autosuture). **Follow-up: 12 months** Conflict of interest/source of funding: not reported	Number of patients analysed: **1573 (300 versus 1273)** **The mean operative time** MIVAT (2005-09)=58.6 minutes MIVAT (2009-10)=46.9 minutes (p<0.05) **Postoperative pain (at 1 hour, measured on a VAS from 0 to 10):** **2005-09** • MIVAT=2.54±1.15 • Conventional thyroidectomy=2.56±1.19, p=not significant **2009-10** • MIVAT=2.89±1.39 • Conventional thyroidectomy=2.93±1.46, p=not significant **Postoperative pain (24 hours):** **2005-09** • MIVAT=1.04±0.83 • Conventional thyroidectomy=1.13±0.92, p<0.001 **2009-10** • MIVAT=2.05±1.08 • Conventional thyroidectomy=2.23±1.06, p<0.001	**Clinical hypocalcaemia**: 2005 - 09 • MIVAT=7.58% • Conventional thyroidectomy=12.4% p=not significant **2009-10** • MIVAT=8.1% • Conventional thyroidectomy=13.9% p=not significant **Symptomatic hypocalcaemia (time period not stated)**: • MIVAT=8.1% • Conventional thyroidectomy=13.9%, p=not significant **Transitory nerve palsy:** **2005-09** • MIVAT (2005-09)=2.84% • MIVAT (2009-10)=1.12% (1/89) • Conventional thyroidectomy (2009-09)=2.84% (9/469) (p=not significant for MIVAT versus CT 2009-10) 1 case of reintervention for postoperative bleeding in the CT group.	**This study was identified during the update literature search at the time of consultation. It has replaced Del Rio 2010 (this study now appears in appendix A)** **Study design issues**: • Results are split into 2 separate time periods: 2005-09 and 2009-10. The MIVAT cases in t he later time period were with new inclusion criteria that excluded short neck in obese patients and clinical thyroiditis. • Patients treated by MIVAT were matched with patients treated by total open thyroidectomy by the same surgeons. **Study population issues**: • The baseline characteristics of the 2 groups are not reported in the paper.

Abbreviations used: CI, confidence interval; CT, conventional thyroidectomy; IP, interventional procedures; MIVAT, minimally invasive video-assisted thyroidectomy; ns, not significant; OR, odds ratio; POSAS, Patient and Observer Assessment scale; PSAQ, Patient scar assessment questionnaire; RATT, robot-assisted transaxillary thyroidectomy; RCT, randomised controlled trial; SMD, standardised mean difference; TSH, thyroid-stimulating hormone; VAS, visual analogue scale)

Study details	Key efficacy findings	Key safety findings	Comments
Miccoli P (2009)[4] **Non-randomised comparative study** Italy Recruitment period: 1999–2005 Study population: patients with papillary thyroid cancer **n=234 (184 MIVAT versus 50 conventional thyroidectomy)** Age: mean 39 years (range 8–77) Sex: 83% (194/234) female Patient selection criteria: papillary thyroid cancer not exceeding 30mm on its largest axis, determined by ultrasound; thyroid volume <30ml as measured by ultrasound; absence of enlarged lymph nodes both in the central and lateral neck compartment; absence of thyroiditis in biochemical and echographic examination. Technique: During the MIVAT procedure, haemostasis was achieved with a harmonic scalpel and titanium clips. For conventional thyroidectomy, haemostasis was obtained by tying or titanium clips. **Follow-up: mean 3.6 years (range 1–8, median 5 years)** Conflict of interest/source of funding: none	Number of patients analysed: **221 (171 versus 50)** 13 patients in the MIVAT group were excluded from the analysis because MIVAT was converted to conventional thyroidectomy (due to unexpected findings of oesophageal infiltration [9 patients], and difficult dissection for unexpected thyroiditis [4 patients]). At the time of thyroid remnant ablation, no differences in serum Tg, TSH levels, or radioactive iodine neck uptake were observed between the 2 groups. The cumulative dose of radioactive iodine to definitively cure the papillary thyroid cancer was the same between the groups. **There were no thyroid cancer-related deaths in either group.** **There were no recurrences in either group.** **Disease status at follow-up** MIVAT: 86.6% (148/171) disease-free; 13.4% (23/171) persistent disease Conventional thyroidectomy: 76.0% (38/50) disease-free; 24.0% (12/50) persistent disease p value: ns for both (Patients were considered 'disease free' when whole body scan, serum Tg after endogenous or exogenous TSH stimulation, and circulating Tg antibodies were all negative. Patients with any one of these factors positive and without a disease-free period of at least 12 months were defined as having 'persistent disease'.)	**Complications** **Hypoparathyroidism:** • MIVAT=3.5% (6/170) • Conventional thyroidectomy=6.1% (3/49), p=0.4 **Vocal cord palsy:** • MIVAT=2.9% (5/170) • Conventional thyroidectomy=2.0% (1/49), p=0.7 NB: it is not clear from the paper how many of these were permanent. The paper states that there was a similar rate of permanent hypoparathyroidism and/or nerve cord palsy in both groups (p=0.46). There was no postoperative bleeding in either group.	There may be some patient overlap with Miccoli et al, 2009. **Follow-up issues**: • Postoperative complications were not assessed in 2 patients (1 from each group). **Study design issues**: • Patients chose their treatment group. • Recurrent laryngeal nerve injury was considered permanent if persistent at 6 months. All patients with vocal cord palsy at 3 months were sent to a voice therapist. **Study population issues**: • The 2 groups were similar with regard to age, mean follow-up, tumour size, lymph node metastases, and De Groot's class. • Of the 221 patients analysed, 89% were considered to have 'low risk' papillary thyroid cancer and 11% were considered to have 'intermediate risk' papillary thyroid cancer. **Other issues**: After total thyroidectomy, all patients were treated with radioactive iodine to ablate postsurgical thyroid remnants. All patients received hormone

Abbreviations used: CI, confidence interval; CT, conventional thyroidectomy; IP, interventional procedures; MIVAT, minimally invasive video-assisted thyroidectomy; ns, not significant; OR, odds ratio; POSAS, Patient and Observer Assessment scale; PSAQ, Patient scar assessment questionnaire; RATT, robot-assisted transaxillary thyroidectomy; RCT, randomised controlled trial; SMD, standardised mean difference; TSH, thyroid-stimulating hormone; VAS, visual analogue scale)

Study details	Key efficacy findings	Key safety findings	Comments
			therapy with levothyroxine at a TSH-suppressive dosage until clinical remission of the disease. They were then shifted to substitutive therapy.

Abbreviations used: CI, confidence interval; CT, conventional thyroidectomy; IP, interventional procedures; MIVAT, minimally invasive video-assisted thyroidectomy; ns, not significant; OR, odds ratio; POSAS, Patient and Observer Assessment scale; PSAQ, Patient scar assessment questionnaire; RATT, robot-assisted transaxillary thyroidectomy; RCT, randomised controlled trial; SMD, standardised mean difference; TSH, thyroid-stimulating hormone; VAS, visual analogue scale)

Study details	Key efficacy findings	Key safety findings	Comments
Gao W (2013)[5] **Non-randomised comparative study** China Recruitment period: 2005–7 Study population: patients with papillary thyroid microcarcinoma **n=68** (35 MIVAT versus 33 conventional thyroidectomy) Age range: 16–65 years Sex: 78% (53/68) female Patient selection criteria: exclusion criteria included thyroid volume >25ml as measured by ultrasonography; evidence of lateral neck lymph node metastasis by needle biopsy; evidence of thyroiditis in biochemical and echographic examinations; history of previous neck surgery or head and neck irradiation; evidence of distant metastases by ultrasonography and CT; abnormal vocal cord movement assessed by preoperative laryngoscopy. Technique: all patients underwent total thyroidectomy and central compartment lymph node dissection. **Follow-up: mean 5 years** Conflict of interest/source of funding: none	Number of patients analysed: **68 (35 versus 33)** There were no conversions to open surgery. **Mean satisfaction score** (3 months after the procedure, measured on a 10-point VAS with 10 representing the best possible outcome): • MIVAT=9.4±0.6 • Conventional thyroidectomy=5.2±0.8, p<0.01 No patient from either group experienced a thyroid cancer-related death or recurrence during the follow-up period. There were no differences between the groups with regard to the degree of surgical completeness (no residual thyroid tissue or central neck lymph nodes on postoperative ultrasonography; serum Tg levels 3 months after surgery and the rate of ^{131}I uptake in the thyroid bed were similar in the 2 groups). **Mean operative time (minutes):** • MIVAT=113.8±14.1 (97.2 in the last 5 patients to be treated) • Conventional thyroidectomy=96.8±6.7 **Length of hospital stay:** • MIVAT=3 days • Conventional thyroidectomy=4 days **Mean postoperative pain score** (24 hours after the procedure, measured on a 10-point VAS with 10 representing the worst possible outcome): • MIVAT=2.4±0.7 • Conventional thyroidectomy=3.2±0.8, p<0.01 **Mean postoperative severity of voice and swallowing alterations score** (24 hours after the procedure, measured on a 10-point VAS with 10 representing the worst possible outcome): • MIVAT=1.5±0.6	There were no patients who developed permanent recurrent laryngeal nerve paralysis, permanent hypoparathyroidism, wound infections or postoperative bleeding in either group. **Temporary recurrent laryngeal nerve dysfunction:** • MIVAT=2.9% (1/35) • Conventional thyroidectomy=0% (0/33), p=0.33 **Temporary hypoparathyroidism:** • MIVAT=8.6% (3/35) • Conventional thyroidectomy=30.3% (10/33), p=0.02 **Mean postoperative severity of voice and swallowing alterations score** (24 hours after the procedure, measured on a 10-point VAS with 10 representing the worst possible outcome): • MIVAT=1.5±0.6 • Conventional thyroidectomy=3.0±0.8, p<0.01	**Study design issues**: • Single centre, retrospective analysis. **Study population issues**: • Baseline data were similar between the groups with regard to age, sex, tumour size, multifocality, lymph node metastases, extrathyroidal invasion, and tumour stage. **Other issues**: • All patients underwent postoperative thyrotropin-stimulating hormone-suppressive therapy with levothyroxine sodium. All patients underwent serum Tg measurement 3 months after surgery and were then treated with 30 or 100 mCi ^{131}I to ablate the postsurgical thyroid remnant.

Abbreviations used: CI, confidence interval; CT, conventional thyroidectomy; IP, interventional procedures; MIVAT, minimally invasive video-assisted thyroidectomy; ns, not significant; OR, odds ratio; POSAS, Patient and Observer Assessment scale; PSAQ, Patient scar assessment questionnaire; RATT, robot-assisted transaxillary thyroidectomy; RCT, randomised controlled trial; SMD, standardised mean difference; TSH, thyroid-stimulating hormone; VAS, visual analogue scale)			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
	Conventional thyroidectomy=3.0±0.8, p<0.01		

Abbreviations used: CI, confidence interval; CT, conventional thyroidectomy; IP, interventional procedures; MIVAT, minimally invasive video-assisted thyroidectomy; ns, not significant; OR, odds ratio; POSAS, Patient and Observer Assessment scale; PSAQ, Patient scar assessment questionnaire; RATT, robot-assisted transaxillary thyroidectomy; RCT, randomised controlled trial; SMD, standardised mean difference; TSH, thyroid-stimulating hormone; VAS, visual analogue scale)

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>De Napoli L (2013)[6]

Non-randomised comparative study

Italy
Recruitment period: 2007–12

Study population: paediatric patients with thyroid disease

n=99 (34 MIVAT [24 indeterminate thyroid nodule, 12 cytologically confirmed papillary thyroid cancer, 4 Graves’ disease, 6 RET gene mutation] versus 65 conventional thyroidectomy [12 indeterminate thyroid nodule, 19 cytologically confirmed papillary thyroid cancer, 25 Graves’ disease, 6 multinodular goitre, 1 thyroglossal duct carcinoma, 2 suspected medullary thyroid cancer)

Age: median 16 years (range 6–18)
Sex: 84% (83/99) female

Patient selection criteria: age <19 years; nodule not exceeding 40mm; ultrasound estimated thyroid volume <30ml; absence of echographic evidence of enlarged suspicious lymph nodes both in the central and lateral neck compartment; no evidence of thyroiditis.

Technique: all patients underwent total thyroidectomy.

Follow-up: mean 20 months (range 7–36)

Conflict of interest/source of funding: none</td>
<td>Number of patients analysed: 99 (34 versus 65)

There were no conversions to conventional thyroidectomy.

Mean operative time (minutes):
• MIVAT=40±6.6
• Conventional thyroidectomy=49.3±12.9
p=0.0007

Postoperative hospital stay
<table>
<tr><th>Length of hospital stay</th><th>MIVAT n=34</th><th>Conventional thyroidectomy n=65</th></tr>
<tr><td>1 day</td><td>53% (n=18)</td><td>24.6% (n=16)</td></tr>
<tr><td>2 days</td><td>35.2% (n=12)</td><td>61.5% (n=40)</td></tr>
<tr><td>3 days</td><td>11.8% (n=4)</td><td>12.3% (n=8)</td></tr>
<tr><td>4 days</td><td>0</td><td>1.6% (n=1)</td></tr>
</table>
p=0.034 between the 2 groups</td>
<td>Transient hypoparathyroidism (resolved within 6 months):
• MIVAT=35.3% (12/34)
• Conventional thyroidectomy=35.4% (23/65), p=not significant

Permanent hypoparathyroidism (needing therapy with calcitriol and calcium carbonate):
• MIVAT=5.9% (2/34)
• Conventional thyroidectomy=6.1% (4/65), p=not significant

Transient postoperative unilateral vocal cord palsy (assessed by direct laryngoscopy):
• MIVAT=5.9% (2/34)
• Conventional thyroidectomy=6.1% (4/65), p=0.95

There were no cases of permanent vocal cord paralysis.

Postoperative bleeding needing reoperation:
• MIVAT=0% (0/34)
• Conventional thyroidectomy=1.5% (1/65), p=0.46</td>
<td>Study design issues:
• Patients’ parents chose either MIVAT or conventional thyroidectomy.

Study population issues:
• There were no statistically significant differences between the groups with regard to age, sex, and nodule size.

Other issues:
• All patients with vocal cord palsy at 3 months were sent to a voice therapist.
• There are some discrepancies between the table and the text of the paper with regard to the rate of complications reported: the figures have been taken from the main text.</td>
</tr>
</table>

Abbreviations used: CI, confidence interval; CT, conventional thyroidectomy; IP, interventional procedures; MIVAT, minimally invasive video-assisted thyroidectomy; ns, not significant; OR, odds ratio; POSAS, Patient and Observer Assessment scale; PSAQ, Patient scar assessment questionnaire; RATT, robot-assisted transaxillary thyroidectomy; RCT, randomised controlled trial; SMD, standardised mean difference; TSH, thyroid-stimulating hormone; VAS, visual analogue scale)

Study details	Key efficacy findings	Key safety findings	Comments
Miccoli P (2006)[7] **Case series** Italy Recruitment period: 1998 onwards Study population: patients with benign or malignant thyroid disease (30% papillary carcinoma, 27% follicular adenoma, 25% multinodular goitre, 8% Hurthle cell adenoma, 4% Graves' disease, 3% toxic adenoma, 3% other) **n=833** Age: not reported; Sex: 86% (715/833) female Patient selection criteria: inclusion criteria included thyroid nodules <30mm and thyroid gland volume <25ml; Graves' disease gland smaller than 20ml in volume; no history of thyroiditis; no previous neck surgery or irradiation; follicular tumour or 'low risk' papillary carcinoma; RET gene mutation carriers with normal pentagastrin-stimulated calcitonin levels. Technique: lobectomy was done in 323 (39%) patients and total thyroidectomy in 510 (61%) patients. In 15 patients with familial medullary carcinoma (gene RET mutation carriers), total thyroidectomy and central compartment lymphadenectomy was done. Haemostasis was achieved using a harmonic scalpel (Harmonic, Johnson and Johnson, USA), without clips or ligatures. **Follow-up: not reported**	Number of patients analysed: **833** Conversion to conventional thyroidectomy=1.9% (16/833) (in 2 patients, completion thyroidectomy was done after the frozen section was found to be positive for papillary carcinoma, in 2 patients the conversion was needed because of intraoperative bleeding, in 9 patients it was due to unexpected oesophageal infiltration, and in 2 patients it was due to difficult dissection caused by misdiagnosed thyroiditis). In 13 patients where definitive diagnosis of carcinoma was made after video-assisted lobectomy, a completion total thyroidectomy was done through the same access and using the same procedure on the opposite side. All 15 carriers of RET gene mutation who underwent total thyroidectomy and central compartment lymphadenectomy, had undetectable serum levels of calcitonin 6 months after surgery with a mean follow-up of 15 months (range 6–42).	**Operative complications** • Transient monolateral recurrent nerve palsy=0.9% (8/833) • Definitive monolateral recurrent nerve palsy=0.8% (7/833) • Bilateral transient recurrent nerve palsy=0.1% (1/833) • Hypoparathyroidism=3.9% (20/510 total thyroidectomies) • Permanent hypocalcaemia needing substitutive therapy=0.4% (2/510 total thyroidectomies) • Postoperative bleeding needing reoperation=0.1% (1/833) • Wound sepsis=0.2% (2/833)	There may be some patient overlap with Miccoli et al, 2009. **Study population issues**: • The authors note that cancer was originally excluded as an indication but they now include 'low risk' papillary carcinoma.

Abbreviations used: CI, confidence interval; CT, conventional thyroidectomy; IP, interventional procedures; MIVAT, minimally invasive video-assisted thyroidectomy; ns, not significant; OR, odds ratio; POSAS, Patient and Observer Assessment scale; PSAQ, Patient scar assessment questionnaire; RATT, robot-assisted transaxillary thyroidectomy; RCT, randomised controlled trial; SMD, standardised mean difference; TSH, thyroid-stimulating hormone; VAS, visual analogue scale)			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Conflict of interest/source of funding: not reported			

Abbreviations used: CI, confidence interval; CT, conventional thyroidectomy; IP, interventional procedures; MIVAT, minimally invasive video-assisted thyroidectomy; ns, not significant; OR, odds ratio; POSAS, Patient and Observer Assessment scale; PSAQ, Patient scar assessment questionnaire; RATT, robot-assisted transaxillary thyroidectomy; RCT, randomised controlled trial; SMD, standardised mean difference; TSH, thyroid-stimulating hormone; VAS, visual analogue scale)

Study details	Key efficacy findings	Key safety findings	Comments
Fan Y (2010)[8] **Case series** China Recruitment period: 2005 – 8 Study population: patients with benign or malignant (low-risk differentiated carcinoma) thyroid disease (33% benign multinodular goitre, 55% follicular adenoma, 6% carcinoma, 2% Hashimoto's thyroiditis, 2% subacute thyroiditis, 2% diffuse hyperplasia, 1% other) **n=300** Age: mean 55 years (range 23–71) Sex: 88% (264/300) female Patient selection criteria: thyroid nodule with a maximum diameter of 35mm, ultrasound-estimated volume <30ml. Absolute contraindications were medullary or previous thyroid surgery, undifferentiated carcinoma, lymph node metastases, previous neck irradiation. Relative contraindications were thyroiditis, thyroid nodule largest diameter <6.0cm. Technique: general anaesthesia was used for 295 patients and regional block anaesthesia in 5. The procedure was performed with an ultrasonic scalpel (Ethicon Endo-Surgery Inc., USA). Of the 300 procedures, 182 (61%) were unilateral lobectomy and 118 were bilateral thyroidectomy. **Follow-up: mean 12 months (range 6–36)**	Number of patients analysed: **300** Conversion to open thyroidectomy in patients with benign thyroid nodules=0.7% (2/300) (the nodules proved to be too large in 1 patient and there was massive haemorrhage in the other) Conversion to open thyroidectomy with a 4cm-long incision was needed for selective lymphadenopathy in 18 patients (6.0%) after frozen sections revealed differentiated thyroid carcinoma. No evidence of recurrence was found at follow-up. 'Most patients' considered the cosmetic outcome excellent, and 5 patients considered it acceptable because of mild skin burns. Mean operative time=35 minutes (range 20–70) for unilateral lobectomy and 58 minutes (range 35–90) for bilateral thyroidectomy. Mean postoperative stay=2.5 days (range 1–5) Postoperative pain was described as 'minimal' in all patients.	**Operative complications** • Transient unilateral recurrent nerve palsy=2.3% (7/300) • Permanent unilateral recurrent nerve palsy=1.7% (5/300) • Superior laryngeal nerve injury=1.7% (5/300) • Transient hypoparathyroidism=3.0% (9/300) • Mild skin burn from the ultrasonic scalpel=1.7% (5/300) There were no wound infections, postoperative bleeding that needed reoperation, permanent hypoparathyroidism, or bilateral recurrent laryngeal nerve palsy.	**Follow-up issues**: • No losses to follow-up were described. **Study design issues**: • Single centre. • Cosmetic results were evaluated by all the patients using both a numerical and verbal response scale. The verbal response scale had 4 options: 1(poor), 2 (acceptable), 3 (good), and 4 (excellent). Patients were asked to grade the cosmetic appearance of their wound and complaints about the neck region 1 month after surgery. **Other issues**: The authors note that a lot of conventional thyroidectomy experience and endoscopy and ultrasonic scalpel skills are needed by surgeons to perform MIVAT

Abbreviations used: CI, confidence interval; CT, conventional thyroidectomy; IP, interventional procedures; MIVAT, minimally invasive video-assisted thyroidectomy; ns, not significant; OR, odds ratio; POSAS, Patient and Observer Assessment scale; PSAQ, Patient scar assessment questionnaire; RATT, robot-assisted transaxillary thyroidectomy; RCT, randomised controlled trial; SMD, standardised mean difference; TSH, thyroid-stimulating hormone; VAS, visual analogue scale)			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Conflict of interest/source of funding: none			

Abbreviations used: CI, confidence interval; CT, conventional thyroidectomy; IP, interventional procedures; MIVAT, minimally invasive video-assisted thyroidectomy; ns, not significant; OR, odds ratio; POSAS, Patient and Observer Assessment scale; PSAQ, Patient scar assessment questionnaire; RATT, robot-assisted transaxillary thyroidectomy; RCT, randomised controlled trial; SMD, standardised mean difference; TSH, thyroid-stimulating hormone; VAS, visual analogue scale)

Study details	Key efficacy findings	Key safety findings	Comments
Sahm M (2011)[9] **Case series** Germany Recruitment period: 2004–10 Study population: patients with thyroid nodules without any storage at thyroid scintigraphy, thyroid cysts, or benign thyroid adenomas with local complaints **n=116** Age: mean 49 years (range 19–80) Sex: 91% (105/116) female Patient selection criteria: maximum size of thyroid nodules was 35mm and maximum size for lobe of the thyroid gland was 25cm^3 on preoperative thyroid sonography. Exclusion criteria included larger goitre, recurrence after thyroid surgery, or preoperative evidence of a neoplasm. Technique: an ultrasonic scalpel (CS14; Ethicon Endosurgery, Johnson & Johnson, USA) was used for preparation and vessel sealing. Neuromonitoring was done using a needle electrode. There were 14 total thyroidectomies, 22 nearly total thyroidectomies, and 80 lobectomies. **Follow-up: mean 22 months (range 1–64)** Conflict of interest/source of funding: none	Number of patients analysed: **96** ***Cosmetic results*** **Mean observer scar assessment score**=8.1 (range 5–23) (a score of 5 indicates normal skin, the best possible result, and a score of 50 indicates the worst possible result). **Mean patient scar assessment score**=9.7 (range 6–37) (a score of 6 indicates normal skin, the best possible result, and a score of 60 indicates the worst possible result). **Patient satisfaction:** • Very satisfied=76% (73/96) • Satisfied=20.8% (20/96) • Not satisfied=3.1% (3/96) **Mean overall patient satisfaction**=1.3 (range 1–3) (assessed by a patient interview about current complaints with detailed questions at the time of the follow-up examination and about satisfaction with the cosmetic results; the scale used to answer was 1 (very satisfied), 2 (satisfied), 3 (not satisfied), 4 (very dissatisfied	**Complications** • Postoperative haemorrhage needing revision (paratracheal or muscular) =4.3% (5/116) • Early postoperative wound seroma (treated by nonoperative therapy) =4.3% (5/116) • Transient monolateral recurrent nerve palsy=2.6% (3/116) (all 3 patients had a positive sign on intraoperative neuromonitoring) • Definitive monolateral recurrent nerve palsy=1.7% (2/116) • Mild hypoparathyroidism (serum calcium 2.00–2.19mmol/l versus normal serum calcium 2.2–2.5mmol/l) =36.2% (42/116) • Moderate hypoparathyroidism (serum calcium 1.80–1.99)=3.4% (4/116) (all patients were asymptomatic) • Severe symptomatic hypoparathyroidism (serum calcium ≤1.79mmol/l)=1.7% (2/116) 9.3% (9/116) patients reported postoperative wound-healing complications at follow-up (5 prolonged wound swelling, 4 postoperative wound seroma). 10 (8.6%) women had a keloid, 5 of whom reported traction of the scar or a feeling of pressure.	**Follow-up issues**: • Follow-up data were available for 82.8% (96/116) of patients. **Study design issues**: Scar assessment was done using the Patient and observer assessment scale (POSAS), which is a validated tool for complete scar assessment.

Abbreviations used: CI, confidence interval; CT, conventional thyroidectomy; IP, interventional procedures; MIVAT, minimally invasive video-assisted thyroidectomy; ns, not significant; OR, odds ratio; POSAS, Patient and Observer Assessment scale; PSAQ, Patient scar assessment questionnaire; RATT, robot-assisted transaxillary thyroidectomy; RCT, randomised controlled trial; SMD, standardised mean difference; TSH, thyroid-stimulating hormone; VAS, visual analogue scale)

Study details	Key efficacy findings	Key safety findings	Comments
Materazzi (2014)[10] **Randomised trial** Italy Recruitment period: 2012–13 Study population: patients undergoing hemithyroidectomy. **n=62** (30 MIVAT [21 nodular goitres, 9 microfollicular nodules] versus 32 robot-assisted transaxillary thyroidectomy (RATT) [19 nodular goitres, 3 toxic adenomas, 10 microfollicular nodules]) Age: MIVAT mean 37 years (range 21–62), RATT mean 32 years (range 18-73) Sex: MIVAT 96.7% (29/30) female, RATT 96.9% (31/32) female [calculated by IP analyst] Patient selection criteria: benign disease, maximum nodule diameter up to 4cm, and total thyroid volume of less than 30mL. Exclusion criteria included symptoms attributable to the thyroid nodule, malignant disease, intrathoracic goitre, previous neck operation or neck irradiation, need for central or lateral compartment lymphadenectomy, permanent medication for pain and anticoagulation. Technique: MIVAT: a Harmonic scalpel was used for the dissection and haemostasis, as well as titanium clips. Subcuticular stitches and glue were used to close the wound. Drains were never used. There were 16 right	Number of patients analysed: **62 (30 versus 32)** No conversion to open cervicotomy needed. **Mean operative time (minutes):** | | MIVAT n=30 | RATT n=32 | p value | |---|---|---|---| | "Open to close time" (without docking time in RATT group) | 46.50±10.5 | 84.25±48.76 | 0.0001 | | Total operative time (intubation/extubation) | 71.60±13.3 | 121.50±46.8 | 0.0001 | **Mean postoperative stay (days):** | | MIVAT n=30 | RATT n=32 | p value | |---|---|---|---| | Postoperative length of stay | 1.15 (1-3) | 1.85 (1-4_ | 0.0001 | **Cosmetic results** Patient scar assessment questionnaire (PSAQ)* | | MIVAT n=30 | RATT n=32 | p value | |---|---|---|---| | PSAQ A | 13.62±2.94 | 16.93±3.78 | <0.0001 | | PSAQ C | 9.75±3.48 | 8.69±2.14 | 0.162 | | PSAQ SA | 12.03±3.65 | 15.71±4.60 | <0.018 | | PSAQ SC | 6.55±1.92 | 7.24±2.18 | 0.173 | *A appearance, C consciousness, SA satisfaction with appearance, SC satisfaction with symptoms.* *Higher scores indicate poorer outcomes.	**Complications** Transient recurrent laryngeal nerve injury (both patients healed completely in 2 months): • MIVAT= 3.3% (1/30) • RATT= 3.1% (1/32) Subcutaneous haematoma over the major pectoralis fascia • RATT= 3.1% (1/32) There were no long-term complications.	**This study was identified during the updated literature search at the time of consultation.** **Follow-up issues:** none **Study design issues:** • Scar assessment was done 2 months after surgery using the PSAQ, which is designed specifically for the assessment of linear scars. This is composed of 4 subscales: scar appearance, consciousness, satisfaction with scar appearance, and satisfaction with scar symptoms. • Overall satisfaction was assessed 1 month after surgery using the SF-36 2 questionnaire.

Abbreviations used: CI, confidence interval; CT, conventional thyroidectomy; IP, interventional procedures; MIVAT, minimally invasive video-assisted thyroidectomy; ns, not significant; OR, odds ratio; POSAS, Patient and Observer Assessment scale; PSAQ, Patient scar assessment questionnaire; RATT, robot-assisted transaxillary thyroidectomy; RCT, randomised controlled trial; SMD, standardised mean difference; TSH, thyroid-stimulating hormone; VAS, visual analogue scale)

Study details	Key efficacy findings	Key safety findings	Comments
lobectomies and 14 left lobectomies. RATT: the da Vinci S system and the Maryland dissector (Intuitive Surgical Inc.) were used in all procedures. The Harmonic scalpel was also used for dissection. Drains were used. There were 15 right lobectomies and 17 left lobectomies. **Follow-up: 2 months** Conflict of interest/source of funding: not reported	**Patient overall satisfaction** Short form (SF-36) 36-item health survey questionnaire scores*		

	MIVAT n=30	RATT n=32	p value
SF-36 PF	93.96±10.21	95.34±10.1	0.627
SF-36 RP	77.58±41.37	63.65±47.23	0.222
SF-36 BP	97.55±8.14	80.65±21.42	0.0005
SF-36 GH	78.51±17.71	90.70±12.10	0.0001
SF-36 VT	62.24±24.18	73.52±21.98	0.090
SF-36 SF	74.03±27.34	90.01±23.41	0.006
SF-36 RE	58.62±50.12	78.51±39.07	0.100
SF-36 MH	70.20±19.84	78.45±19.80	0.108

PF physical functioning, RP role physical, BP bodily pain, GH general health, VT vitality, SF social functioning, RE role-emotional, MH mental health.

*Higher scores indicate better quality of life

Table 2b Summary of key efficacy and safety findings on minimally invasive video-assisted parathyroidectomy

Abbreviations used: CP, conventional parathyroidectomy; MIVAP, minimally invasive video-assisted parathyroidectomy; OMIP, open minimally invasive parathyroidectomy; SD, standard deviation; SF, short-form; VAS, visual analogue scale

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Hessman O (2010)[11]

RCT

Sweden and Denmark

Recruitment period: 2003–07

Study population: patients with primary hyperparathyroidism (solitary parathyroid adenoma)

n=143 (68 MIVAP versus 75 OMIP)

Age: mean 63 years
Sex: 80% (115/143) female

Patient selection criteria: biochemically verified primary hyperparathyroidism with an unequivocal localisation on sestamibi scintigraphy of a solitary parathyroid adenoma. Exclusion criteria included negative or equivocal preoperative localisation study, familial hyperparathyroidism, previous neck surgery or neck irradiation, concomitant need for thyroid surgery, pregnancy, and suspected ectopic parathyroid localisation.

Technique: all patients underwent surgery under general anaesthesia with the neck semi-extended. The MIVAP approach used was either the medial gasless technique (n=26) or a lateral approach with gas insufflation (n=42). Intraoperative nerve monitoring was not used. Intraoperative parathyroid hormone monitoring was used in both groups to guide the operation. An extended ipsilateral dissection and contralateral dissection were done when necessary.

Follow-up: 6 months

Conflict of interest/source of funding: none</td>
<td>Number of patients analysed: 143 (68 versus 75)

Conversions to bilateral neck exploration:
• MIVAP=25% (17/68)
• OMIP=17% (13/75), p=0.26
In addition, 18% (12/68) of the MIVAP procedures were converted to focused open procedures. There was a tendency for a higher rate of conversion in the MIVAP group because of difficulties in adenoma localisation (5 MIVAP, 1 OMIP), bleeding (3 MIVAP), and difficult dissection (4 MIVAP).

Mean operative time (minutes):
• MIVAP=84.0
• OMIP=60.2, p=0.001

Cure rate=96.5% (138/143) (2 of the failed operations were MIVAP and 3 were OMIP, p=0.731)

Mean cosmesis score at 6-month follow-up (VAS, 0–100 with 100 as the best possible)
• MIVAP=92
• OMIP=95, p=0.411

Mean scores for neck discomfort at 6-month follow-up (VAS, 0–100 with 100 as the worst neck discomfort)
• MIVAP=4.2
• OMIP=4.4, p=0.649

Mean postoperative pain score (VAS, 0–100 with 0 for no pain and 100 for the worst pain imaginable)
<table>
<tr><th>Follow-up</th><th>MIVAP n=68</th><th>OMIP n=75</th><th>p value</th></tr>
<tr><td>Day 1</td><td>21.8</td><td>16.4</td><td>0.112</td></tr>
<tr><td>Week 1</td><td>7.1</td><td>7.5</td><td>0.845</td></tr>
</table>
</td>
<td>Postoperative complications
The number of complications did not differ between the 2 groups (p=0.799)
The following postoperative complications were reported for the whole cohort:
• Postoperative haematoma=2.8% (4/143) (none needed surgical intervention)
• Postoperative wound infection=0.7% (1/143)
• Postoperative urinary tract infection=0.7% (1/143)
• Deep vein thrombosis=0.7% (1/143) (1 week after surgery, in a patient who had MIVAP converted to bilateral neck exploration because of multigland disease)
Follow-up
Unilateral vocal cord paresis:
• MIVAP=2.9% (2/68) (resolved within 3 months)
• OMIP=1.3% (1/75) (permanent – present at 6 months)</td>
<td>Study design issues:
• Multicentre (3 centres).
• Randomisation was done separately for each centre, in blocks of 5 using sealed envelopes.
• Patients were blinded to their treatment allocation until 6 months after the surgery.
• Primary outcome measures were duration of operation and postoperative pain. Secondary outcome measures were complications, persistent or recurrent disease, conversion rates, and cosmetic result.

Study population issues:
• There were no significant differences in baseline characteristics between the groups.

Other issues:
• The authors note that the participating surgeons may not have reached the plateau of the learning curve.</td>
</tr>
</table>

Abbreviations used: CP, conventional parathyroidectomy; MIVAP, minimally invasive video-assisted parathyroidectomy; OMIP, open minimally invasive parathyroidectomy; SD, standard deviation; SF, short-form; VAS, visual analogue scale

Study details	Key efficacy findings	Key safety findings	Comments
	Week 4 | 1.9 | 3.2 | 0.301		

Abbreviations used: CP, conventional parathyroidectomy; MIVAP, minimally invasive video-assisted parathyroidectomy; OMIP, open minimally invasive parathyroidectomy; SD, standard deviation; SF, short-form; VAS, visual analogue scale

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Barczynski M (2006)[12]

RCT

Poland

Recruitment period: 2002–04

Study population: patients with primary hyperparathyroidism (preoperative diagnosis of solitary parathyroid adenoma)

n=60 (30 MIVAP versus 30 OMIP)

Age: mean 59 versus 62 years; sex: 85% (51/60) female

Patient selection criteria: diagnosis of primary hyperparathyroidism confirmed by biochemical evaluation (increased serum calcium >2.6mmol/l and serum intact parathyroid hormone level >65pg/ml), a single parathyroid gland disease, parathyroid adenoma not exceeding 30mm in the largest diameter, no previous neck surgery, and absence of nodular goitre needing one-step thyroid surgery. Exclusion criteria included a family history of primary hyperparathyroidism, negative or discordant localisation studies, suspicion of multiglandular disease, extracervical ectopy, parathyroid cancer, concomitant goitre >30ml in volume, pregnancy or lactation, age <18 years, high-risk patients American Society of Anesthesiology grade 4, and emergency surgery for hypercalcaemic crisis.

Technique: an intraoperative quick intact parathyroid hormone assay was used. All procedures were extended from a targeted procedure to unilateral neck exploration or bilateral neck exploration as necessary.

Follow-up: 6 months</td>
<td>Number of patients analysed: 60 (30 versus 30)

Further exploration was needed in 2 patients: 1 MIVAP patient had subtotal parathyroidectomy for parathyroid hyperplasis using a video-assisted approach; 1 OMIP patient had conversion to unilateral neck exploration for double adenoma.

Postoperative pain (at 4 hours, VAS)
• MIVAP=24.9±6.0
• OMIP=32.2±4.6, p<0.001
Postoperative pain (at 24 hours, VAS)
• MIVAP=15.5±5.4
• OMIP=20.4±4.7, p<0.001

Postoperative follow-up of cosmetic satisfaction, and quality of life (mean±SD)
<table>
<tr><td></td><td>MIVAP n=30</td><td>OMIP n=30</td><td>p value</td></tr>
<tr><td>Cosmetic satisfaction at 6 months (VAS)</td><td>90.5±10.3</td><td>87.5±5.8</td><td>0.16</td></tr>
<tr><td colspan="4">Quality of life on 7th postoperative day (SF-36)</td></tr>
<tr><td>Physical functioning</td><td>88.4±6.9</td><td>84.6±4.7</td><td>0.02</td></tr>
<tr><td>Bodily pain</td><td>90.3±4.7</td><td>86.5±4.9</td><td>0.003</td></tr>
</table>
Cosmetic satisfaction increased with time in both groups.

All patients were cured, and none had persistent disease at 6 month’s follow-up. Mean serum calcium levels were within the reference range and were not significantly different between the groups at 24, 48, and 72 hours after surgery or at 1 and 6 months follow-up.

Serum intact parathyroid hormone levels at 6 months follow-up (pg/ml):
• MIVAP=46.5±9.4
• OMIP=45.1±7.6, p=0.52</td>
<td>Postoperative symptomatic transient hypocalcaemia:
• MIVAP=3.3% (1/30)
• OMIP=6.7% (2/30)

Postoperative asymptomatic transient hypocalcaemia:
• MIVAP=6.7% (2/30)
• OMIP=3.3% (1/30)

Transient recurrent laryngeal nerve palsy:
• MIVAP=0% (0/30)
• OMIP=3.3% (1/30) (resolved within 1 month)</td>
<td>There may be some patient overlap with Barczynski M, 2007.

Study design issues:
• Patients were randomised using sealed envelopes.
• Both patients and nurses were blinded to treatment allocation (the lower part of the neck was covered with a dressing to conceal the length of the scar for the initial 7 days after surgery).
• Patients were given a standard quality-of-life questionnaire (the Medical Outcomes Trusts Short Form 36 Health Survey) on postoperative day 7.

Study population issues:
• Preoperative clinical and biochemical data were similar between the groups; 4 patients in the MIVAP group and 5 in the OMIP group were considered asymptomatic.</td>
</tr>
</table>

Abbreviations used: CP, conventional parathyroidectomy; MIVAP, minimally invasive video-assisted parathyroidectomy; OMIP, open minimally invasive parathyroidectomy; SD, standard deviation; SF, short-form; VAS, visual analogue scale			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Conflict of interest/source of funding: not reported	Operative time was similar in the 2 groups.		

Abbreviations used: CP, conventional parathyroidectomy; MIVAP, minimally invasive video-assisted parathyroidectomy; OMIP, open minimally invasive parathyroidectomy; SD, standard deviation; SF, short-form; VAS, visual analogue scale

Study details	Key efficacy findings	Key safety findings	Comments
Miccoli P (1999)[13] **RCT** Italy Recruitment period: March–November 1998 Study population: patients with primary hyperparathyroidism **n=38 (20 MIVAP versus 18 CP)** Age: range 22–80 (mean 48 years in MIVAP group, 60 years in CP group) Sex: 63% (24/38) Patient selection criteria: sporadic form of primary hyperparathyroidism, no prior neck surgery, absence of thyroid nodules, and preoperative ultrasonography suggestive for solitary parathyroid adenoma. Technique: MIVAP was done using a 3–4 minute carbon dioxide insufflation before the operative space was maintained with small external retractors. Conventional titanium vascular clips were used. No effort was made to identify the ipsilateral parathyroid gland. In the last 2 patients, a bilateral superficial cervical block with laryngeal mask was used instead of general anaesthesia. **Follow-up: 6 months** Conflict of interest/source of funding: not reported	Number of patients analysed: **38 (20 versus 18)** 2 patients had multiglandular disease that was discovered during surgery and were excluded from the study (1 in each group). **Operative time (minutes):** • MIVAP=57±15 • CP=70±18, p<0.05 **Postoperative pain at 12 hours (VAS 1–10):** • MIVAP=2 • CP=5, p<0.03 **Postoperative pain at 48 hours (VAS 1–10):** • MIVAP=2 • CP=3, p<0.03 **Postoperative inactivity period (days):** • MIVAP=12±5.5 • CP=16±6, p=not reported **Patient satisfaction at 6 months (opinion on aesthetics of the scar, score ranged from 1 [poor] to 10 [excellent]); estimated from graphical presentation:** • MIVAP=7.5 • CP=4.5, p<0.03 **All patients were normocalcaemic 6 months after the procedure.**	**Postoperative fever:** • MIVAP=5.0% (1/20) • CP=22.2% (4/18) **Wound infection:** • MIVAP=0% (0/20) • CP=5.6% (1/18) **Postoperative symptomatic transient hypocalcaemia:** • MIVAP=5.0% (1/20) • CP=16.7% (3/18) **Laryngeal nerve palsy (6 months postoperatively):** • MIVAP=5.0% (1/20) • CP=0% (0/18)	There may be some patient overlap with Miccoli P et al, 2008. **Study design issues**: • Patients were randomised by coin tossing. **Study population issues**: • There were no statistically significant differences between the groups with regard to demographics data and laboratory and ultrasound findings (size and location of the adenoma).

Abbreviations used: CP, conventional parathyroidectomy; MIVAP, minimally invasive video-assisted parathyroidectomy; OMIP, open minimally invasive parathyroidectomy; SD, standard deviation; SF, short-form; VAS, visual analogue scale

Study details	Key efficacy findings	Key safety findings	Comments
Barczynski M (2007)[14] **Non-randomised comparative study** Poland Recruitment period: 2002–07 Study population: patients with primary hyperparathyroidism localised to a single adenoma **n=168 (100 MIVAP versus 68 OMIP)** Age: mean 60 years Sex: 87% (146/168) female Patient selection criteria: biochemically verified primary hyperparathyroidism localised to a single adenoma on preoperative imaging, adenoma size not exceeding 30mm at the largest axis, and absence of any concomitant thyroid pathology that would need surgical treatment. Exclusion criteria included previous neck surgery, history of cervical irradiation, multinodular goitre or suspected thyroid carcinoma, suspected multinodular disease of the parathyroid glands, familial hyperparathyroidism, and suspected MEN syndrome. Technique: Intraoperative parathyroid hormone monitoring was used in both groups. **Follow-up: mean 33 months (range 4–53)** Conflict of interest/source of funding: not reported	Number of patients analysed: **168 (100 versus 68)** **Conversions:** • MIVAP=5% (conversion to video-assisted bilateral neck exploration) • OMIP=5.8% (conversion to open bilateral neck exploration), p=not significant **Number of exposed recurrent laryngeal nerves:** • MIVAP=88% (88/100) • OMIP=66% (45/68), p=0.05 **Postoperative normocalcaemia within 6 months of surgery:** • MIVAP=99% (1 patient was later diagnosed with persistent hyperparathyroidism resulting from another adenoma in the chest cavity) • OMIP=100%, p=not significant **Mean operating time (minutes):** • MIVAP=34.4±13.9 • OMIP=31.5±10.7, p=not significant **Mean postoperative pain at 4 hours (VAS):** • MIVAP=25.8±5.6 • OMIP=38.7±5.6, p<0.001 **Mean postoperative pain at 24 hours (VAS):** • MIVAP=14.1±5.1 • OMIP=19.8±4.4, p<0.001 **Patient's subjective satisfaction with cosmetic result (1 month postoperatively, VAS):** • MIVAP=85.4±12.4 • OMIP=77.4±9.7, p=0.01 **Patient's subjective satisfaction with cosmetic result (6 months postoperatively, VAS):** • MIVAP=90.5±10.3	**Transient recurrent laryngeal nerve palsy:** • MIVAP=1% (1/100) • OMIP=2.9% (2/68), p=not significant **Transient hypocalcaemia:** • MIVAP=10% (10/100) • OMIP=11.8% (8/68), p=not significant	There may be some patient overlap with Barczynski M, 2006. **Follow-up issues**: • No losses to follow-up were described. **Study design issues**: • All the patients were operated on by the same team. **Study population issues**: • There were no statistically significant differences in baseline characteristics (age, sex ratio, total serum calcium, intact parathyroid hormone serum value, alkaline phosphatase, and creatinine) between the 2 groups.

Abbreviations used: CP, conventional parathyroidectomy; MIVAP, minimally invasive video-assisted parathyroidectomy; OMIP, open minimally invasive parathyroidectomy; SD, standard deviation; SF, short-form; VAS, visual analogue scale			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
	• OMIP=87.5±5.8, p=not significant There was 1 case of recurrent hyperparathyroidism diagnosed 36 months after the procedure (study group not stated).		

Abbreviations used: CP, conventional parathyroidectomy; MIVAP, minimally invasive video-assisted parathyroidectomy; OMIP, open minimally invasive parathyroidectomy; SD, standard deviation; SF, short-form; VAS, visual analogue scale

Study details	Key efficacy findings	Key safety findings	Comments
Melck AL (2012)[15] **Non-randomised comparative study** Canada and USA Recruitment period: 2004–09 Study population: patients with sporadic primary hyperparathyroidism with single-focus concordant imaging results **n=220 (125 MIVAP versus 95 OMIP)** Age: mean 57 versus 61 years (p=0.07) Sex: 76% (168/220) female Patient selection criteria: apparent sporadic primary hyperparathyroidism with single-focus concordant imaging results; no concurrent need for thyroid resection; body mass index <40kg/m^2; no clinical suspicion of parathyroid carcinoma. Exclusion criteria included previous neck surgery; planned concurrent thyroid surgery or concurrent additional procedures that prolonged operative time. Technique: general anaesthesia was used for all patients. In both groups, the ipsilateral parathyroid gland was examined when feasible. Intact parathyroid hormone levels were monitored intraoperatively. The finding of 2 large ipsilateral parathyroid glands and/or a persistent elevation in intact parathyroid hormone level prompted conversion to bilateral exploration. **Follow-up: mean 11 months (range 5–68)** Conflict of interest/source of funding: not reported	Number of patients analysed: **220 (125 versus 95)** **MIVAP conversions to OMIP**=14% (17/125) (7 unimaged multiglandular disease, 7 poor anatomic access to cervical structures, 3 concurrent thyroid lobectomy) 71% of conversions occurred in patients with body mass index 25kg/m^2 or greater. **Mean operative time (minutes, excluding MIVAP conversions to OMIP):** • MIVAP=63 (range 39–120) • OMIP=61 (range 31–167), p=0.56 **Mean incision length (cm, excluding MIVAP conversions to OMIP):** • MIVAP=2.3 (range 1.6–3.7) • OMIP=4.7 (range 3.1–7.5), p<0.001 **Persistent or recurrent primary hyperparathyroidism:** • MIVAP=1.7% (2/118) (both patients had a failed initial exploration; 1 patient had a missed fifth supernumerary hyperplastic gland and the other had a second adenoma) • OMIP=0% (0/86)	**Postoperative complications** **Groin haematoma after arterial line placement:** • MIVAP=0.8% (1/125) • OMIP=0% (0/95), p=1.00 **Early reoperation (cervical seroma):** • MIVAP=0% (0/125) • OMIP=1.1% (1/95), p=0.43 **Pulmonary embolus:** • MIVAP=0% (0/125) • OMIP=1.1% (1/95), p=0.43 There were no cases of permanent vocal cord paralysis or permanent hypoparathyroidism.	**Follow-up issues**: • 7% (16/220) of patients were lost to follow-up (7 MIVAP, 9 OMIP). • Four patients died during follow-up (all were in OMIP group): 1 from unknown causes (age 89 years) and 3 from heart disease (ages 70, 83, and 91years). **Study design issues**: • Retrospective analysis of prospectively collected data. • Study group was determined by patient choice. • All procedures were done by 1 endocrine surgeon. **Study population issues**: • Patients in the MIVAP group had a statistically significant lower body mass index than those in the OMIP group (26.8 versus 31.5kg/m^2, p<0.001). Mean preoperative parathyroid hormone level was significantly lower in the MIVAP group (125 versus 165 pg/ml, p=0.008) and mean adenoma weight was significantly lower in the MIVAP group (927 versus 2120mg, p<0.001). **Other issues**: • The authors note that there was a learning curve involved in MIVAP implementation; after approximately 60 cases, the mean operating time became equivalent to OMIP.

Abbreviations used: CP, conventional parathyroidectomy; MIVAP, minimally invasive video-assisted parathyroidectomy; OMIP, open minimally invasive parathyroidectomy; SD, standard deviation; SF, short-form; VAS, visual analogue scale

Study details	Key efficacy findings	Key safety findings	Comments
Del Rio P (2013)[16] **Non-randomised comparative study** Italy Recruitment period: 2003–11 Study population: patients with sporadic primary hyperparathyroidism localised to a single adenoma **n=157 (76 MIVAP versus 81 CP)** Age: mean 60 years Sex: 83% (131/157) female Patient selection criteria: biochemically verified sporadic primary hyperparathyroidism localised to a single adenoma on preoperative imaging. Exclusion criteria for the MIVAP group included a pathological gland >3cm in size, family history of parathyroid disease, previous neck surgery, and clinical suspicion for a parathyroid carcinoma or an inflammatory thyroid condition. Technique: Intraoperative parathyroid hormone monitoring was used in the MIVAP group. Conventional parathyroidectomy included intraoperative frozen section and bilateral neck exploration. **Follow-up: 6 months** Conflict of interest/source of funding: none	Number of patients analysed: **157 (76 versus 81)** **Conversion to CP=5% (4/76)** **Mean operative time (minutes):** • MIVAP=29.0±7.9 • CP=62.4±26.5, p<0.001 **Mean postoperative pain at 24 hours (VAS):** • MIVAP=2.1±0.6 • CP=3.6±0.5, p<0.001 **Mean calcium (mg/dl) at 6 months:** • MIVAP=8.3±0.9 • CP=8.9±0.8, p=0.09 **Relapse at 6 months:** • MIVAP=2.6% (2/76) • CP=3.7% (3/81), p>0.99	**Postoperative dysphonia (video laryngostroboscopy demonstrated unilateral vocal cord paralysis)** • MIVAP=1% (1/76) • CP=1% (1/81), p>0.99 (patients were referred to speech therapy)	**Study design issues**: • Retrospective review of prospectively collected data. • Historical controls - patients in the MIVAP group were enrolled between 2006 and 2011, patients in the conventional surgery group were enrolled between 2003 and 2006. • A 50% drop in intraoperative parathyroid hormone at 10 minutes was used as confirmation of a cure. **Study population issues**: • Parathyroid gland size was significant larger in the CP group (1.8 versus 1.2cm, p<0.05) and preoperative calcium levels were significantly higher in the MIVAP group (11.7 versus 11.1, p=0.018).

Abbreviations used: CP, conventional parathyroidectomy; MIVAP, minimally invasive video-assisted parathyroidectomy; OMIP, open minimally invasive parathyroidectomy; SD, standard deviation; SF, short-form; VAS, visual analogue scale

Study details	Key efficacy findings	Key safety findings	Comments
Alesina PF (2013)[17] **Case series** Germany Recruitment period: 2006–12 Study population: patients with primary hyperparathyroidism and negative or discordant localisation studies **n=107** Age: mean 58 years Sex: 82% (88/107) female Patient selection criteria: patients with primary hyperparathyroidism and preoperative ultrasound and ^{99}Tc-sestamibi scintigraphy were discordant, negative, or showed bilateral disease. Technique: bilateral exploration, general anaesthesia was used for all procedures. Intact parathyroid hormone levels were measured intraoperatively (cure was defined by a drop to normal range or by a decline of >50% from baseline level). Intraoperative frozen section was selectively used. **Follow-up: mean 45 months (range 1–116)** Conflict of interest/source of funding: none	Number of patients analysed: **107** **Conversion to standard parathyroidectomy**=7.5% (8/107) (all were due to lack of visualisation of 1 or more glands) **Overall cure rate with first operation**=95% (102/107) (reoperation in the immediate postoperative period achieved a cure in 4 out of 5 patients) **Mean operative time**=57±37 minutes (range 20–180) Excluding conversions, 4 parathyroid glands were visualised in 89 patients, 3 glands in 5 patients and 2 glands in 5 patients. Multiglandular disease was diagnosed in 23% (25/107) of patients. **Persistent or recurrent disease**=1.9% (2/107) (1 patient was diagnosed with recurrent hyperparathyroidism 3 years after MIVAP; the second patient had hypercalcaemia and elevated intact parathyroid hormone 4 months after MIVAP, a further video-assisted exploration was done and the left upper parathyroid gland was removed, without achieving a cure.)	**Postoperative complications** • Recurrent laryngeal nerve palsy=1.9% (2/107) (confirmed by postoperative dysphonia and laryngoscopy; 1 resolved after 4 months and the other became permanent) • Symptomatic hypocalcaemia=13.1% (14/107) (2 patients needed vitamin D substitution) There were no cases of bleeding or wound infection. **Follow-up** • Permanent recurrent laryngeal nerve palsy=1.0% (1/107)	**Follow-up issues**: • No losses to follow-up were described. **Study design issues**: • Data were collected in a prospectively maintained database. **Study population issues**: • A thyroid lobectomy was done in 15 patients, a total thyroidectomy in 3 and resection of a solitary thyroid nodule in 1 patient.

Abbreviations used: CP, conventional parathyroidectomy; MIVAP, minimally invasive video-assisted parathyroidectomy; OMIP, open minimally invasive parathyroidectomy; SD, standard deviation; SF, short-form; VAS, visual analogue scale

Study details	Key efficacy findings	Key safety findings	Comments
Miccoli P (2008)[18] **Case series** Italy Recruitment period: 1997–07 Study population: patients with primary hyperparathyroidism **n=652** Age: mean 55 years (range 20–87) Sex: 84% (547/652) female Patient selection criteria: adenoma major diameter <4cm, absence of large goitre, clear preoperative localisation. Relative contraindications included previous neck surgery and hyperplasia. Technique: local anaesthesia was used for 45 patients. A lateral approach was used for 11 patients who had previously undergone neck surgery. Quick intraoperative intact parathyroid hormone assay was used to assess completeness of the resection (confirmed by a decrease of more than 50% compared with baseline). Exploration was started on the side in which the adenoma was suspected to be based on preoperative imaging but bilateral exploration could be achieved through the central incision. **Follow-up: not reported** Conflict of interest/source of funding: not reported	Number of patients analysed: **652** Mean size of removed adenoma=1.8cm in its largest diameter. **Persistent hyperparathyroidism**=0.9% (6/652) (In 4 patients, the adenoma was not found at exploration even after conversion; in 2 patients, the persistence was attributable to a false-positive quick intraoperative intact parathyroid hormone assay result – a second MIVAP revealed a second adenoma missed at the first operation.)	**Complications** • Permanent laryngeal nerve palsy=0.6% (4/652) • Postoperative bleeding that needed reoperation=0.2% (1/652) (displaced clip on a middle thyroid vein) • Transient hypocalcaemia=3.2% (21/652)	There may be some patient overlap with Miccoli P et al, 1999. **Follow-up issues**: • Follow up period was not described. **Study design issues**: • Single centre. **Study population issues**: • 35 patients had a concurrent thyroid resection: 25 thyroid lobectomies and 10 total thyroidectomies.

Abbreviations used: CP, conventional parathyroidectomy; MIVAP, minimally invasive video-assisted parathyroidectomy; OMIP, open minimally invasive parathyroidectomy; SD, standard deviation; SF, short-form; VAS, visual analogue scale

Study details	Key efficacy findings	Key safety findings	Comments
Slater B (2005)[19] **Case report** USA Recruitment period: not reported Study population: patient with pneumothorax after MIVAP **n=1** Age: not reported Sex: not reported Patient selection criteria: not reported Technique: MIVAP was done under regional anaesthesia. Procedure started as a right neck exploration, which was extended through a slightly enlarged incision. **Follow-up: not reported** Conflict of interest/source of funding: not reported	**Pneumothorax after MIVAP** An elderly patient with hyperparathyroidism underwent MIVAP under regional anaesthesia. The superior parathyroid gland was removed but the right inferior gland was not clearly identified and the exploration was extended. The incision was slightly enlarged and an intrathyroidal lesion was enucleated: frozen section confirmed it to be an enlarged parathyroid gland weighing 340mg. After the incision was closed, air bubbling in the operative field was noted but the patient was asymptomatic. A chest x-ray revealed a pneumothorax. A chest tube was placed for 24 hours. The patient had a history of emphysema and the pneumothorax was considered to be likely due to a rupture of a bleb.		**Other issues**: • The paper also describes a second patient who had pneumothorax after OMIP.

Efficacy

Thyroidectomy

Recurrence/survival

A non-randomised comparative study of 234 patients with papillary thyroid cancer treated by minimally invasive video-assisted thyroidectomy (MIVAT) or conventional thyroidectomy reported that 87% (148/171) and 76% (38/50) of patients respectively (p=not significant) were disease-free after a mean follow-up of 3.6 years[4]. The remaining patients had persistent disease. There were no recurrences and there were no thyroid cancer related deaths in either group[4]. A non-randomised comparative study of 68 patients with papillary thyroid microcarcinoma treated by MIVAT or conventional thyroidectomy reported that there were no recurrences and no thyroid cancer related deaths during a mean follow-up of 5 years[5]. A case series of 300 patients with benign or malignant thyroid disease reported no recurrences after a mean follow-up of 12 months[8].

Operating time

A systematic review of 9 studies including 581 patients reported that the mean operative time was significantly shorter in the conventional thyroidectomy group (59 minutes compared with 75 minutes in the MIVAT group; 7 studies; standardised mean difference [SMD]: 1.246, 95% confidence intervals [CI]: 0.227 to 2.266 [significant heterogeneity Q=113.88, p<0.0001])[1].

A non-randomised comparative study of 982 patients reported a significantly longer operating time for MIVAT compared with conventional thyroidectomy (69 versus 46 minutes, p<0.05)[2]. A non-randomised comparative study of 99 paediatric patients treated by MIVAT or conventional thyroidectomy reported a significantly shorter operating time in the MIVAT group (40 versus 49 minutes, p=0.0007)[6]. A non-randomised study of 1573 patients reported that the mean operating time for MIVAT decreased from 58.6 minutes in 2005-09 to 46.9 minutes in 2009-10 (p<0.05)[3]. A randomised study of 62 patients reported significantly shorter mean operative times in the MIVAT group compared with robot-assisted transaxillary thyroidectomy (46 and 84 minutes respectively for the 'open to close time,' and 71.6 and 121.5 minutes respectively for the total operative time, p=0.0001)[10].

Conversion to open surgery

The non-randomised comparative study of 234 patients with papillary thyroid cancer reported that 7% (13/194) MIVAT procedures were converted to conventional thyroidectomy[4]. A case series of 833 patients reported that 2% (16/833) of procedures were converted to conventional thyroidectomy[7]. The case series of 300 patients with benign or malignant thyroid disease reported that MIVAT was converted to open thyroidectomy in 1% (2/300) of patients with

benign thyroid nodules[8]. Conversion to open thyroidectomy with a 4cm-long incision was needed for selective lymphadenopathy in 18 patients (6%) after frozen sections revealed differentiated thyroid carcinoma[8].

Postoperative pain

Postoperative pain scores (measured on a 10-point visual analogue scale [VAS], with a higher score indicating more severe pain) were significantly lower at 24 and 48 hours postoperatively in patients treated by MIVAT than those treated by conventional thyroidectomy in the systematic review of 9 studies including 581 patients (outcome reported in 5 studies). VAS at 24 hours: 1.69 versus 3.39 (SMD =-3.101, 95% CI :-4.840 to -1.361; VAS at 48 hours: 1.05 versus 2.45, SMD=-2.571, 95% CI:-4.247 to -0.896, $p<0.0001$)[1].

Postoperative pain scores measured on a 10-point VAS with higher scores representing more severe pain, were significantly lower at 36 hours postoperatively in patients treated by MIVAT than in patients treated by conventional thyroidectomy (1.1 versus 1.9, $p<0.05$) in the non-randomised comparative study of 982 patients[2]. Postoperative pain scores measured on a 10-point VAS with higher scores representing more severe pain, were significantly lower at 24 hours postoperatively in patients treated by MIVAT than in patients treated by conventional thyroidectomy in the non-randomised comparative study of 1573 patients and a non-randomised comparative study of 68 patients (1.04 versus 1.13 in 2005-09 and 2.05 versus 2.23 in 2009-10, $p<0.001$; 2 versus 3, $p<0.01$)[3,5].

Patient satisfaction/cosmesis

The non-randomised comparative study of 982 patients reported significantly higher satisfaction scores (scale 0–10 with higher scores being better) for MIVAT and minimally invasive thyroidectomy compared with conventional thyroidectomy (7, 8, and 5 respectively, $p<0.05$)[2]. A non-randomised comparative study of 68 patients with papillary thyroid microcarcinoma treated by MIVAT or conventional thyroidectomy reported mean satisfaction scores (measured on a 10-point VAS with 10 representing the best possible outcome) of 9.4 and 5.2 respectively ($p<0.01$) at 3 months follow-up[5]. The case series of 300 patients with benign or malignant thyroid disease reported that ‘most’ patients considered the cosmetic outcome to be ‘excellent’; 5 patients, who had mild skin burns, considered it to be ‘acceptable’[8]. A case series of 116 patients reported that 76% (73/96) of patients were very satisfied, 21% (20/96) were satisfied and 3% (3/96) were not satisfied with the cosmetic results of the procedure[9]. The randomised study of 62 patients reported significantly lower appearance and satisfaction with appearance scores on the Patient Scar Assessment Questionnaire (higher scores indicating poorer outcomes) in the MIVAT group compared with robot-assisted transaxillary thyroidectomy (appearance score: 14 versus 17, $p<0.0001$; satisfaction with appearance score: 12 versus 16, $p<0.018$). The same study also reported significantly higher scores for the SF-36 domain of bodily pain (98

versus 81, p<0.0005) but lower scores for the SF-36 domains of social functioning (74 versus 90, p<0.006) and general health (79 versus 91, p<0.0001) in the MIVAT group (higher scores indicating less disability)[10].

Alterations to voice and swallowing

Mean postoperative severity of voice and swallowing alterations score (24 hours after the procedure, measured on a 10-point VAS, with 10 representing the worst possible outcome) were significantly lower for patients treated by MIVAT than for patients treated by conventional thyroidectomy (1.5 versus 3, p<0.01) in the non-randomised comparative study of 68 patients[5].

Parathyroidectomy

Cure rate

The RCT of 143 patients treated by MIVAP or open minimally invasive parathyroidectomy (OMIP) reported cure rates of 97% (66/68) and 96% (72/75) respectively (p=0.731)[11]. An RCT of 60 patients treated by MIVAP or OMIP reported that all patients were cured at 6 months follow-up[12]. The RCT of 38 patients treated by MIVAP or conventional parathyroidectomy reported that all patients were normocalcaemic at 6 months follow-up[13]. The non-randomised comparative study of 168 patients treated by MIVAP or OMIP reported postoperative normocalcaemia within 6 months of surgery in 99% (99/100) and 100% (68/68) of patients respectively (p=not significant)[14]. The non-randomised comparative study of 220 patients treated by MIVAP or open minimally invasive parathyroidectomy reported persistent primary hyperparathyroidism in 2% (2/118) of patients in the MIVAP group and no patients in the OMIP[15]. The non-randomised comparative study of 157 patients treated by MIVAP or conventional parathyroidectomy reported recurrence rates of 3% and 4% respectively at 6 months p=not significant)[16]. The case series of 107 patients reported a cure rate of 95% (102/107) with the first operation; reoperation in the immediate postoperative period achieved a cure in a further 4 out of 5 patients[17]. In the same study, 2% (2/107) of patients had persistent or recurrent disease diagnosed at 4 months and 3 years after MIVAP respectively. A case series of 652 patients reported persistent hyperparathyroidism in 1% (6/652) of patients[18].

Conversion

An RCT of 143 patients treated by MIVAP or OMIP reported that 25% (17/68) and 17% (13/75) of procedures respectively were converted to bilateral neck exploration. In addition, 18% (12/68) of the MIVAP procedures were converted to focused open procedures[11]. A non-randomised comparative study of 220 patients treated by MIVAP or OMIP reported that 14% (17/125) of MIVAP procedures were converted to OMIP[15]. A non-randomised comparative study of 157 patients treated by MIVAP or conventional parathyroidectomy reported that 5% (4/76) of

MIVAP procedures were converted to conventional parathyroidectomy[16]. A case series of 107 patients reported conversion in 8% (8/107) of patients[17].

Operating time

The RCT of 143 patients treated by MIVAP or open minimally invasive parathyroidectomy reported a significantly longer operating time for MIVAP (84 versus 60 minutes, p=0.001)[11]. An RCT of 38 patients treated by MIVAP or conventional parathyroidectomy reported a significantly shorter operating time for MIVAP (57 versus 70 minutes, p<0.05)[13]. A non-randomised comparative study of 168 patients treated by MIVAP or open minimally invasive parathyroidectomy reported similar mean operating times in the 2 groups (34 versus 32 minutes, p=not significant)[14]. The non-randomised comparative study of 220 patients treated by MIVAP or open minimally invasive parathyroidectomy reported mean operating times of 63 and 61 minutes respectively, p=0.56[15]. The non-randomised comparative study of 157 patients treated by MIVAP or conventional parathyroidectomy reported that the mean operating time was significantly shorter in the MIVAP group (29 versus 62 minutes, p<0.001)[16].

Postoperative pain

Postoperative pain scores measured on a 100-point VAS with higher scores representing more severe pain, were similar in patients treated by either MIVAP or open minimally-invasive parathyroidectomy in an RCT of 143 patients[11] but they were significantly lower at 24 hours postoperatively in patients treated by MIVAP than in patients treated by open minimally-invasive parathyroidectomy (15.5 versus 20.4, p<0.001 and 14.1 versus 19.8, p<0.001) in an RCT of 60 patients and a non-randomised comparative study of 168 patients[12,14]. Postoperative pain scores measured on a 10-point VAS with higher scores representing more severe pain, were significantly lower in patients treated by MIVAP than in patients treated by conventional parathyroidectomy (2 versus 3 at 48 hours postoperatively, p<0.03) in an RCT of 38 patients[13] and in a non-randomised comparative study of 157 patients (2.1 versus 3.6 at 24 hours postoperatively, p<0.001)[16].

Patient satisfaction/cosmesis

The RCT of 143 patients treated by MIVAP or open minimally invasive parathyroidectomy reported similar cosmesis scores (VAS, 0 to 100 with 100 as the best possible) in the 2 groups at 6-month follow-up (92 versus 95, p=0.411)[11]. The RCT of 60 patients treated by MIVAP or open minimally invasive parathyroidectomy reported similar scores for cosmetic satisfaction at 6 months (90.5 versus 87.5, p=0.16)[12]. The RCT of 38 patients treated by MIVAP or conventional parathyroidectomy reported a significantly higher patient satisfaction score (measured on a scale from 1 [poor] to 10 [excellent]) at 6 months follow-up in the MIVAP group (7.7 versus 4.5, p<0.03)[13]. The non-randomised comparative study of 168 patients treated by MIVAP or open minimally invasive

parathyroidectomy reported a significantly higher score for patient satisfaction with the cosmetic result at 1 month postoperatively in the MIVAP group (85.4 versus 77.4, p=0.01) but the difference in scores was no longer statistically significant after 6 months (90.5 versus 87.5, p=not significant)[14].

Safety

Thyroidectomy

Total complication rate

Total morbidity rates of 10% (29/282) and 14% (42/292) were reported for MIVAT and conventional thyroidectomy respectively (odds ratio: 0.65, 95% CI 0.387 to 1.091) in a systematic review of 9 studies including 581 patients (outcome reported in 7 studies)[1]. Overall postoperative morbidity rates (not further defined) of 10% (17/179), 9% (55/592) and 11% (26/211) were reported for MIVAT, minimally invasive thyroidectomy and conventional thyroidectomy respectively (p=not significant) in a non-randomised comparative study of 982 patients[2].

Skin burn

Skin burn was reported in 2% (5/300) of patients in a case series of 300 patients[,8].

Postoperative bleeding

Postoperative bleeding needing reoperation was reported in less than1% (1/833) and 4% (5/116) of patients in the case series of 116 and 833 patients respectively[7,9].

Wound sepsis

Wound sepsis was reported in <1% (2/833) of patients in the case series of 833 patients[7].

Recurrent laryngeal nerve palsy

Transient inferior laryngeal nerve palsy was reported in 4.8% and 4.4% of patients treated by MIVAT and conventional thyroidectomy respectively (OR:1.086, 95% CI 0.496 to 2.375) in the systematic review of 9 studies including 581 patients (outcome reported in 6 studies)[1]. Permanent inferior laryngeal nerve palsy was reported in 1 patient treated by MIVAT and no patients treated by conventional thyroidectomy in the systematic review of 9 studies including 581 patients (outcome reported in 6 studies)[1]. Transitory nerve palsy was reported in 2.84% and 1.12% of MIVAT patients between 2005 and 2009 and 2009 and 2010 respectively. The same condition was reported in 2.84% of the conventional thyroidectomy patients between 2009 and 2010 (p=not significant for comparison with MIVAT for the same time period)[3]. Transient nerve palsy was reported in 6%

(2/34 and 4/65) of patients treated by either MIVAT or conventional thyroidectomy in a non-randomised comparative study of 99 patients[6]. Transient monolateral recurrent nerve palsy was reported in 1% (8/833), 2% (7/300) and 3% (3/116) of patients respectively in the case series of 833, 300 and 116 patients: definitive monolateral recurrent laryngeal nerve palsy was reported in 1% (7/833), 2% (5/300) and 2% (2/116) of patients respectively[7,8,9]. Bilateral transient recurrent nerve palsy was reported in 1 patient in the case series of 833 patients[7]. Transient recurrent laryngeal nerve injury was reported in 3.3% (1/30) and 3.1% (1/32) of patients treated by either MIVAT or robot-assisted transaxillary thyroidectomy (p not significant) in a randomised study of 62 patients[10].

Superior laryngeal nerve injury

Paralysis of the external branch of the superior laryngeal nerve was reported in no patients treated by MIVAT and 6 patients treated by conventional thyroidectomy in the systematic review of 9 studies including 581 patients (it is unclear how many studies reported this outcome)[1]. Superior laryngeal nerve injury was reported in 2% (5/300) of patients in the case series of 300 patients[8].

Hypoparathyroidism

Transient hypoparathyroidism was reported in 9% (3/35) and 30% (10/33) of patients treated by MIVAT or conventional thyroidectomy respectively (p=0.02) in the non-randomised comparative study of 68 patients[5]. Transient hypoparathyroidism was reported in 35% (12/34 and 23/65) of patients treated by either MIVAT or conventional thyroidectomy respectively in the non-randomised comparative study of 99 patients[6]. Permanent hypoparathyroidism was reported in 6% (2/34 and 4/65) of patients in both groups. Hypoparathyroidism was reported in 4% (20/510 total thyroidectomies) and 3% (9/300) of patients in the case series of 833 and 300 patients[7,8]. Severe symptomatic hypoparathyroidism was reported in 2% (2/116) of patients in a case series of 116 patients[9].

Hypocalcaemia

Transient postoperative hypocalcaemia was reported in 4% (12/289 and 11/292) of patients treated by either MIVAT or conventional thyroidectomy respectively in the systematic review of 9 studies including 581 patients (outcome reported in 5 studies)[1]. Clinical hypocalcaemia was reported in 8% and 12% of MIVAT and conventional thyroidectomy patients respectively between 2005 and 2009 (p not significant). Clinical hypocalcaemia was reported in 8% and 14% of MIVAT and conventional thyroidectomy patients respectively between 2009 and 2010 (= not significant)[3]. Permanent hypocalcaemia needing substitutive therapy was reported in <1% (2/510 total thyroidectomies) of patients in the case series of 833 patients[7].

Parathyroidectomy

Postoperative bleeding

Postoperative bleeding that needed reoperation was reported in 1 patient in a case series of 652 patients (caused by a displaced clip on a middle thyroid vein)[18].

Pneumothorax

Pneumothorax needing a chest tube for 24 hours was described in 1 patient after MIVAP in a case report: the patient had a history of emphysema and the pneumothorax was considered to be likely due to a rupture of a bleb[19].

Vocal cord paresis/recurrent laryngeal nerve palsy

Unilateral vocal cord paresis was reported in 3% (2/68) of patients treated by MIVAP and 1% (1/75) of patients treated by open minimally-invasive parathyroidectomy in the RCT of 143 patients[11]. This resolved within 3 months in the 2 patients treated by MIVAP but was still present at 6 months postoperatively in the patient treated by open minimally-invasive parathyroidectomy. Laryngeal nerve palsy at 6 months postoperatively was reported in 1 patient treated by MIVAP in the RCT of 38 patients[13]. Transient recurrent laryngeal nerve palsy was reported in 1% (1/100) and 3% (2/68) of patients treated by MIVAP or open minimally-invasive parathyroidectomy respectively in the non-randomised comparative study of 168 patients (p=not significant)[14]. Unilateral vocal cord paresis was reported in 1 patient treated by MIVAP and 1 patient treated by conventional parathyroidectomy in the non-randomised comparative study of 157 patients (both patients were referred for speech therapy)[16]. Transient recurrent laryngeal nerve palsy was reported in 1 patient in a case series of 107 patients (resolved after 4 months)[17]. Permanent recurrent laryngeal nerve palsy was reported in 1% (1/107) and <1% (4/652) in 2 case series of 107 and 652 patients respectively[17,18].

Hypocalcaemia

Symptomatic transient hypocalcaemia after the procedure was reported in 3% (1/30) and 5% (1/20) of patients treated by MIVAP, 7% (2/30) of patients treated by open minimally-invasive parathyroidectomy, and 17% (3/18) of patients treated by conventional thyroidectomy in 2 RCTs of 60 and 38 patients respectively[12,13]. Symptomatic hypocalcaemia was reported in 13% (14/107) of patients in the case series of 107 patients (2 patients needed vitamin D substitution)[17].

Validity and generalisability of the studies

MIVAT

- Patient populations were heterogeneous: 2 studies only included patients with papillary thyroid cancer[4,5], 5 studies included patients with benign or malignant

thyroid disease (1 of which included only paediatric patients)[2,3,6,7,8], and 2 studies excluded patients who were diagnosed preoperatively with thyroid malignancy[9,10].
- The extent of dissection varied within and between studies: some patients were treated by thyroid lobectomy and some by total thyroidectomy.
- A non-randomised study and case series were reported from the same centre and there is likely to be some patient overlap between the 2 studies[4,7].

MIVAP

- Two RCTs state that the patients were blinded to their treatment allocation[11,12].
- One case series only included patients with negative or discordant results on preoperative imaging[17]. Two studies specified that such patients were excluded[11,12]. Most studies only included patients with sporadic primary hyperparathyroidism that could be localised preoperatively to a solitary adenoma. Most studies reported that a gasless central approach was used but 2 studies reported that a lateral approach was used for a proportion of the patients treated by MIVAP[11,18].
- The extent of exploration varied within and between studies.
- Although most studies did report 'conversion' rates, it was not always clear what procedure the MIVAP had been converted to. In 2 studies, the procedure was converted to a bilateral neck exploration[11,14], in 1 study it was converted to open minimally invasive parathyroidectomy[15] and in another study it was converted to conventional parathyroidectomy[16].
- An RCT and non-randomised comparative study were reported from the same centre and there is likely to be some patient overlap between the 2 studies[12,14].
- An RCT and case series were reported from the same centre and there is likely to be some patient overlap between the 2 studies[13,18].

Existing assessments of this procedure

The Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S) published a systematic review on minimally invasive parathyroidectomy in 1999[20]. It states:

'**Recommendation to the Royal Australasian College of Surgeons**

The Royal Australasian College of Surgeons has endorsed the ASERNIP-S recommendation that minimally invasive techniques for primary hyperparathyroidism be classified as level '2' procedures, that is, 'the safety and efficacy of the procedures cannot be determined at the present time due to an incomplete and poor quality evidence-base'. However, this review does not examine any cost-benefits. A further recommendation was that the procedures should only be undertaken in the setting of a controlled study with ongoing monitoring under the supervision of the Section of Endocrine Surgery of the

Royal Australasian College of Surgeons. There are numerous types of minimally invasive parathyroidectomy procedures and as yet no firmly established technique has been accepted as the 'gold' standard. Therefore, ongoing monitoring and further studies need to be performed and reported to ensure that minimally invasive parathyroidectomy reaches the high degree of satisfaction noted with a standard open bilateral neck exploration for hyperparathyroidism.'

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Intraoperative nerve monitoring during thyroid surgery. NICE interventional procedure guidance 255 (2008). Available from www.nice.org.uk/guidance/IPG255
- Thoracoscopic excision of mediastinal parathyroid tumours. NICE interventional procedure guidance 247 (2007). Available from www.nice.org.uk/guidance/IPG247

Technology appraisals

- Cinacalcet for the treatment of secondary hyperparathyroidism in patients with end-stage renal disease on maintenance dialysis therapy. NICE technology appraisal guidance 117 (2007). Available from www.nice.org.uk/guidance/TA117

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their specialist society or royal college. The advice received is their individual opinion and does not represent the view of the society.

Mr S Balasubramanian, Professor D Kim, Mr M Stechman (British Association of Endocrine and Thyroid Surgeons)

- One adviser performs the procedure regularly; the other 2 Specialist Advisers have never performed the procedure.
- Two advisers described the procedure as definitely novel and of uncertain safety and efficacy and the other considered it to be a minor variation on an existing procedure which is unlikely to alter that procedure's safety and efficacy. One adviser noted that there are multiple international reports and case series on this procedure but no randomised clinical trials. In the UK at least, this is a novel procedure and the benefits/safety are not clear at present.

- The comparator to this procedure is open minimally invasive parathyroidectomy/thyroidectomy.
- For parathyroidectomy, theoretical adverse events are: failed exploration, conversion to open parathyroidectomy, persistent hypercalcaemia, recurrent laryngeal nerve injury/neuropraxia, tumour rupture, bleeding, neck haematoma, infection, trocar injury to local neuro-vascular structures or trachea/oesophagus. For thyroidectomy, theoretical adverse events are: conversion to open thyroidectomy, transient or permanent hypocalcaemia, recurrent laryngeal nerve division/neuropraxia, external branch of superior laryngeal nerve division/neuropraxia, bleeding, post-operative neck haematoma, infection, trocar injury to local neuro-vascular structures or trachea/oesophagus.
- One Adviser listed temporary laryngeal nerve weakness and mild seroma as anecdotal adverse events.
- Adverse events reported in the literature for parathyroidectomy: failed exploration, conversion to open parathyroidectomy, persistent hypercalcaemia, recurrent laryngeal nerve injury/neuropraxia, tumour rupture, bleeding. For thyroidectomy: conversion to open surgery, incidence of recurrent goitre, oncological outcomes if used for differentiated thyroid cancer.
- Key efficacy outcomes for parathyroidectomy are rate of post-operative normocalcaemia, recurrent laryngeal nerve palsy rate, rate of post-operative hypocalcaemia, rate of serious complications (trocar injury, significant post-operative bleeding), post-operative pain, cosmesis, and patient satisfaction. Key efficacy outcomes for thyroidectomy are rates of post-operative hypocalcaemia, recurrent laryngeal nerve palsy, and rate of serious complications (trocar injury, significant post-operative bleeding), post-operative pain, cosmesis, and patient satisfaction.
- One Adviser noted that there is likely to be a significant learning curve during which the rate of ‘cure’ in parathyroidectomy may not be at an acceptable level (e.g. >95%), and there is a lack of evidence of benefit of these procedures compared with conventional open or ‘minimally invasive’ parathyroidectomy/thyroidectomy.
- One Adviser noted that parathyroidectomy is performed in very few centres in the UK. It needs all patients to have pre-operative localisation scans to determine eligibility. Thyroidectomy increasingly involves the use of a Da Vinci robot, particularly in countries where neck scars are culturally unacceptable (e.g. South Korea).
- One Adviser stated that the procedure should only be offered in key centres of high volume and excellence by surgeons with experience in thyroid surgery.
- One Adviser stated that supervised mentorship is needed, and availability of appropriate endoscopic and microsurgical instruments.
- One Adviser noted that selection of patients suitable for this approach is variable and controversial. This will impact on the generalisability of the results of published studies.
- One Adviser stated that the procedures take longer, are much more invasive that conventional surgery (esp. robotic trans-mammary and trans-axillary

robotic parathyroidectomy/ thyroidectomy). The complication profile is likely to be different to conventional surgery. Cost is also a significant factor, as is provision of training.
- Two Advisers considered the potential impact of this procedure on the NHS to be moderate, in terms of numbers of patients eligible for treatment and use of resources, and the other considered the potential impact to be major.

Patient commentators' opinions

NICE's Public Involvement Programme was unable to gather patient commentary for this procedure.

Issues for consideration by IPAC

- The evidence base for this procedure was very large and included a number of indications.

References

1. Pisanu A, Podda M, Reccia I et al. (2013) Systematic review with meta-analysis of prospective randomized trials comparing minimally invasive video-assisted thyroidectomy (MIVAT) and conventional thyroidectomy (CT). Lagenbecks Arch Surg 398:1057-1068

2. Docimo G, Tolone S, Gili S et al. (2013) Minimally Invasive Thyroidectomy (MIT) Indications and results. Annali Italiani di Chirurgia 84: 617-622

3. Del Rio P, Arcuri MF, Cataldo S et al. (2014) Are we changing our inclusion criteria for minimally invasive thyroidectomy? Ann. Ital. Chir. 85:28-32

4. Miccoli P, Pinchera A, Materazzi G et al. (2009) Surgical treatment of low- and intermediate-risk papillary thyroid cancer with minimally invasive video-assisted thyroidectomy. Journal of Clinical Endocrinology & Metabolism 94: 1618–22

5. Gao W, Liu L, Ye G et al. (2013) Application of minimally invasive video-assisted technique in papillary thyroid microcarcinoma. Surgical Laparoscopy, Endoscopy & Percutaneous Techniques 23: 468–73

6. De Napoli L, Spinelli C, Ambrosini CE et al. (2013) Minimally invasive video-assisted thyroidectomy versus conventional thyroidectomy in pediatric patients. European Journal of Pediatric Surgery DOI http://dx.doi.org/10.1055/s-0033-1351391

7. Miccoli P, Berti P, Frustaci GL et al. (2006) Video-assisted thyroidectomy: indications and results. Langenbecks Archives of Surgery 391: 68–71

8. Fan Y, Guo B, Guo S et al. (2010) Minimally invasive video-assisted thyroidectomy: experience of 300 cases. Surgical Endoscopy 24: 2393–400

9. Sahm M, Schwarz B, Schmidt S et al. (2011) Long-term cosmetic results after minimally invasive video-assisted thyroidectomy. Surgical Endoscopy 25: 3202–8

10. Materazzi G, Fregoli L, Manzini G et al. (2014) Cosmetic result and overall satisfaction after minimally invasive video-assisted thyroidectomy (MIVAT) versus robot-assisted transaxillary thyroidectomy (RATT): a prospective randomized study. World journal of surgery 38(6):1282-8

11. Hessman O, Westerdahl J, Al-Suliman N et al. (2010) Randomized clinical trial comparing open with video-assisted minimally invasive parathyroid surgery for primary hyperparathyroidism. British Journal of Surgery 97: 177–84

12. Barczynski M, Cichon S, Konturek A et al. (2006) Minimally invasive video-assisted parathyroidectomy versus open minimally invasive parathyroidectomy for a solitary parathyroid adenoma: A prospective, randomized, blinded trial. World Journal of Surgery 30: 721–31

13. Miccoli P, Bendinelli C, Berti P et al. (1999) Video-assisted versus conventional parathyroidectomy in primary hyperparathyroidism: a prospective randomized study. Surgery 126: 1117–21

14. Barczynski M, Cichon S, Konturek A et al. (2007) Comparison of two techniques of minimally invasive parathyroidectomy: Video-assisted (MIVAP) and open (OMIP). Polski Przeglad Chirurgiczny 79: 1264–79

15. Melck AL, Armstrong MJ, Yip L et al. (2012) Case-controlled comparison of video-assisted and conventional minimally invasive parathyroidectomy. American Surgeon 78: 125–32

16. Rio PD, Vicente D, Maestroni U et al. (2013) A comparison of minimally invasive video-assisted parathyroidectomy and traditional parathyroidectomy for parathyroid adenoma. Journal of Cancer 4: 458–63

17. Alesina PF, Hinrichs J, Heuer M et al. (2013) Feasibility of video-assisted bilateral neck exploration for patients with primary hyperparathyroidism and failed or discordant localization studies. Langenbecks Archives of Surgery 398: 107–11

18. Miccoli P, Materazzi G, Bonari G et al. (2008) Minimally invasive video-assisted parathyroidectomy. Operative Techniques in Otolaryngology - Head and Neck Surgery 19: 22–5

19. Slater B, Inabnet WB (2005) Pneumothorax: an uncommon complication of minimally invasive parathyroidectomy. Surgical Laparoscopy, Endoscopy & Percutaneous Techniques 15: 38–40

20. Reeve T et al. (1999) Systematic review of Minimally Invasive Parathyroidectomy. ASERNIP-S Report No. 1. Adelaide, South Australia: ASERNIP-S, June 1999.

Appendix A: Additional papers on minimally invasive video-assisted thyroidectomy/parathyroidectomy

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction tables (table 2a and 2b). It is by no means an exhaustive list of potentially relevant studies. Case series with fewer than 50 patients have not been included unless an important safety outcome is reported.

MIVAT

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in tables 2a and 2b
Alesina PF, Rolfs T, Ruhland K et al. (2010) Evaluation of postoperative pain after minimally invasive video-assisted and conventional thyroidectomy: Results of a prospective study. Langenbeck's Archives of Surgery 395: 845–9	Non-randomised comparative study n=169 (75 versus 94)	The length of the skin incision seems not to influence the perception of pain after thyroid surgery.	Included in Liu et al, 2012 systematic review.
Alesina PF, Singaporewalla RM, Eckstein A et al. (2011) Is minimally invasive, video-assisted thyroidectomy feasible in Graves' disease? Surgery 149: 556–60	Non-randomised comparative study n=497 (157 versus 340)	In selected patients with Graves' disease, MIVAT is feasible and can be performed safely with results comparable with open surgery.	Studies with more patients or longer follow-up are included.
Barczynski M, Konturek A, Cichon S (2008) Minimally invasive video-assisted thyroidectomy (MIVAT) with and without use of harmonic scalpel--a randomized study. Langenbecks Archives of Surgery 393: 647–54	RCT n=76 (38 versus 38) Follow-up=6 months	Harmonic scalpel in the MIVAT operations is safe and facilitates dissection, allowing for a significant decrease in operative time. Other benefits, such as lower blood loss, a scar a few millimetres shorter, or a slightly better early cosmetic result, are offered at slightly increased costs.	Study focuses on the use of a harmonic scalpel.
Barczynski M, Konturek A, Stopa M et al. (2012) Minimally invasive video-assisted thyroidectomy: Seven-year experience with 240 cases. Wideochirurgia I Inne Techniki Maloinwazyjne 7: 175–80	Case series n=240 Follow-up=6 months	MIVAT is suitable for surgeons experienced in thyroid and video-assisted surgery. It is feasible for well-selected patients including cases of T1 thyroid cancer, Graves' disease and concomitant parathyroid adenoma	Studies with more patients or longer follow-up are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in tables 2a and 2b
Bellantone R, Lombardi CP, Bossola M et al. (2002) Video-assisted vs conventional thyroid lobectomy: a randomized trial.Archives of Surgery 137: 301–4	RCT n=62 (31 versus 31)	Satisfaction was higher in the MIVAT group (mean 9.2) than the conventional group (mean 5.8) (p<0.001). Postoperative pain in the first and second days after surgery was lower in the MIVAT group (mean 1.8 and 1.2, respectively) than in the conventional group (mean 6.2 and 5.8, respectively) (p<0.001).	Included in Liu et al, 2012 systematic review.
Bellantone R, Lombardi CP, Raffaelli M et al. (2002) Video-assisted thyroidectomy. Asian Journal of Surgery 25: 315–8	Case series n=73	The conversion rate was 5%. Postoperative complications included 2 transient recurrent nerve palsies, 5 transient symptomatic postoperative hypocalcaemias and 1 wound infection. The cosmetic result was considered excellent by most of the patients.	Larger studies are included.
Byrd JK, Nguyen SA, Ketcham A et al. (2010) Minimally invasive video-assisted thyroidectomy versus conventional thyroidectomy: a cost-effective analysis. Otolaryngology - Head & Neck Surgery 143: 789–94	Non-randomised comparative study n=93 (42 versus 51)	Length of stay (days) was significantly shorter for patients undergoing MIVAT hemithyroidectomy (mean difference -0.8; 95% confidence interval [95% CI] -1.08 to -0.52) and not significantly different between groups for total thyroidectomy (mean difference 0.1; 95% CI -0.36 to 0.56).	Cost effectiveness is the main focus of the study.
Chan CP, Yang LH, Chang HC et al. (2003) An easier technique for minimally invasive video-assisted thyroidectomy. International surgery 88: 109-113	Non-randomised comparative study n=60	There was 1 conversion to open thyroidectomy. The use of a modified Army retractor with a mosaic ring made the MIVAT procedure easier and offered similar advantages.	Study compared MIVAT with and without a self-designed retractor.
Chao TC, Lin JD, Chen MF (2004) Video-assisted open thyroid lobectomy through a small incision. Surgical Laparoscopy, Endoscopy & Percutaneous Techniques 14: 15–19	Non-randomised comparative study n=111 (52 versus 59)	Damage to the external branch of the superior laryngeal nerve occurred in 10% of patients following conventional surgery but in no patients following video-assisted lobectomy (p =0.03). Transient recurrent laryngeal nerve palsy occurred in 9% of patients after conventional surgery and in 6% of patients after video-assisted surgery (p =0.7209).	Larger studies are included.
Del Rio P, Arcuri MF, Pisani P et al. (2010) Minimally invasive video-assisted thyroidectomy (MIVAT): What is the real advantage? Langenbeck's Archives of Surgery 395: 323–6	Non-randomised comparative study N=798 (211 MIVAT versus 587 conventional thyroidectomy)	The aesthetic result in the MIVAT group was defined as excellent in 89.6% (189/211) of patients, good in 9.0% (19/211) and sufficient in 1.0% (2/211) of patients. A skin burn was observed in the 2 patients with a 'sufficient' aesthetic result. **Postoperative pain (at 1 hour, measured on a VAS from 0 to 10):** • MIVAT=2.54±1.15	Was included in table 2 for IPAC 1 meeting but has now been replaced by Del Rio 2014 following the updated literature search at consultation phase.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in tables 2a and 2b
		• Conventional thyroidectomy=2.89±1.39, p=0.11 **Postoperative pain (24 hours):** • MIVAT=1.04±0.83 • Conventional thyroidectomy=2.05±1.08, p<0.001 **Postoperative haemorrhage needing emergency reintervention:** • MIVAT=0% (0/211) • Conventional thyroidectomy=0.3% (2/587), p=0.96 **Serological hypocalcaemia (serum calcium <8mg/dl)**: • MIVAT=28.0% (59/211) • Conventional thyroidectomy=43.3% (254/587), p<0.001 **Symptomatic hypocalcaemia**: • MIVAT=7.6% (16/211) • Conventional thyroidectomy=12.4% (73/587), p=0.41 **Transitory monolateral nerve palsy:** • MIVAT=2.8% (6/211) • Conventional thyroidectomy=1.2% (7/587), p=0.19 **Definitive monolateral nerve palsy (at 6 months):** • MIVAT=1.0% (2/211) • Conventional thyroidectomy=0.5% (3/587), p=not reported **Skin burn:** • MIVAT=1.0% (2/211) • Conventional thyroidectomy=0% (0/587), p=not reported 1 patient with type II diabetes in the MIVAT group had a wound infection.	

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in tables 2a and 2b
Del Rio P, Sommaruga L, Pisani P et al. (2009) Minimally invasive video-assisted thyroidectomy in differentiated thyroid cancer: a 1-year follow-up. Surgical Laparoscopy, Endoscopy & Percutaneous Techniques 19: 290–2	Non-randomised comparative study n=68 (36 versus 32) Follow-up=12 months	**Differentiated thyroid carcinoma** Thyroglobulin values after 12 months were similar in the 2 groups (0.648+/-0.2 ng/mL versus 0.705+/-0.2 ng/mL, p=not significant). MIVAT for the right cases is a safe and valid surgical procedure for differentiated thyroid cancer. This technique has a challenging learning curve, and the surgeons must be experts in conventional thyroid surgery.	Studies with more patients or longer follow-up are included.
Del Rio P, Berti M, Sommaruga L et al. (2008) Pain after minimally invasive videoassisted and after minimally invasive open thyroidectomy--results of a prospective outcome study. Langenbecks Archives of Surgery 393: 271–3	Non-randomised comparative study n=113 (52 versus 61) Follow-up=24 hours	**Both methods are safe, but MIVAT gives not only a better cosmetic result but a reduction of postoperative pain especially at 24h.**	Studies with more patients or longer follow-up are included.
Del Rio P, Sommaruga L, Cataldo S et al. (2008) Minimally invasive video-assisted thyroidectomy: The learning curve. European Surgical Research 41: 33–6	Non-randomised comparative study n=100	After 25 cases, we observed that the MIVAT procedure allows for a lower mean operative time and a reduction of complications.	Studies with more patients or longer follow-up are included.
Dionigi G, Boni L, Rovera F et al. (2011) Wound morbidity in mini-invasive thyroidectomy. Surgical Endoscopy and Other Interventional Techniques 25: 62–7	RCT n=112 (56 versus 56)	The rate for wound morbidity was significantly lower in the MIVAT group (n =1) than in the conventional group (n =8) ($p<0.05$). The incidence of surgical site infection was 5% after conventional thyroidectomy and 0% after MIVAT ($p<0.05$).	Included in Liu et al, 2012 systematic review.
Dionigi G, Boni L, Rovera F et al. (2008) The use of electrothermal bipolar vessel sealing system in minimally invasive video-assisted thyroidectomy (MIVAT). Surgical Laparoscopy, Endoscopy and Percutaneous Techniques 18: 493–7	Case series n=63	No cases needed conversion to open surgery and none involved significant intraoperative complications. Postoperative recovery was uneventful in all procedures. All patients were satisfied with the cosmetic results.	Larger studies are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in tables 2a and 2b
Di JZ, Zhang HW, Han X et al. (2011) Minimally invasive video-assisted thyroidectomy for accidental papillary thyroid microcarcinoma: comparison with conventional open thyroidectomy with 5 years follow-up. Chinese Medical Journal 124: 3293–6	Non-randomised comparative study n=68 Follow-up=5 years	**Papillary thyroid microcarcinoma** MIVAT did not differ significantly from conventional thyroidectomy for papillary thyroid microcarcinoma after 5 years follow-up, but it did have better cosmetic results.	Larger studies are included.
Dobrinja C, Trevisan G, Makovac P et al. (2009) Minimally invasive video-assisted thyroidectomy compared with conventional thyroidectomy in a general surgery department. Surgical Endoscopy 23: 2263–7	Non-randomised comparative study n=137 (68 versus 69)	No differences were found in terms of complications, operative time, and radicality of the procedure. Patients who underwent MIVAT experienced significantly less pain, better cosmetic results, and shorter hospital stay than patients who underwent conventional surgery.	Larger studies are included.
Durel J, Kluka E, and Rohan RW. (2011) Minimally invasive video-assisted thyroidectomy for treatment of benign solitary thyroid nodules in pediatric patients. Ochsner Journal.11 (2) (pp 128-131), 2011.Date of Publication: 2011. 128-131.	Case reports n = 2 FU = 3 months	Both patients discharged at 1 day. No complications. Cosmesis: patients and parents satisfied	Larger studies in table 2
El-Labban GM. (2009) Minimally invasive video-assisted thyroidectomy versus conventional thyroidectomy: A single-blinded, randomized controlled clinical trial. Journal of Minimal Access Surgery 5:97-102.	RCT n = 76 (38 MIVAT versus 38 open) FU = 48 hours	Operating time significantly lower for open thyroidectomy. MIVAT group had significantly less pain at 24hrs and 48hrs. MIVAT group associated with less scaring and more satisfactory cosmetic results. 2 patients had temporary recurrent laryngeal nerve paralysis in the MIVAT group and 1 in the open group. 1 patient in the MIVAT group had permanent recurrentlaryngeal nerve paralysis.	Larger studies with longer follow-up in table 2. This study is included in the systematic review by Pisanu (2013) which will be included in Table 2.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in tables 2a and 2b
Gal I, Solymosi T, Szabo Z et al. (2008) Minimally invasive video-assisted thyroidectomy and conventional thyroidectomy: A prospective randomized study. Surgical Endoscopy and Other Interventional Techniques 22: 2445–9	RCT n=30 (15 versus 15)	Although the complications are comparable between the 2 approaches, conventional thyroidectomy involves less operative time. However, MIVAT offers distinct advantages to selected patients in terms of very good to excellent cosmetic results and reduced postoperative distress.	Included in Liu et al, 2012 systematic review.
Glynn RW, Cashman EC, Doody J et al. (2013) Prophylactic total thyroidectomy using the minimally invasive video-assisted approach in children with multiple endocrine neoplasia type 2. Head and Neck 00:000-000.	Case series n = 6 FU = 42.8 months	Mean operative time: 93 minutes 5 patients discharged at 1 day. 1 patient had a postoperative haematoma and was discharged at 2 days. No cases of laryngeal nerve palsy or postoperative hypoparathyroidism. High levels of postoperative cosmesis reported.	Larger studies in table 2
Hegazy MAF, Khater AA, Setit AE et al. (2007) Minimally invasive video-assisted thyroidectomy for small follicular thyroid nodules. World Journal of Surgery 31: 1743–50	RCT n=68 (35 versus 33)	Despite some MIVAT advantages of less postoperative pain and slightly better cosmesis, minimally invasive open thyroidectomy offers an advantage of less operating time with comparable cosmetic results.	Included in Liu et al, 2012 systematic review.
Inukai M, Usui Y (2005) Clinical evaluation of gasless endoscopic thyroid surgery. Surgery Today 35: 199–204	Non-randomised comparative study n=191	Although gasless endoscopic thyroid surgery took significantly longer to perform than conventional open surgery, the postoperative stay was significantly shorter and patients had fewer complaints about their surgical scar	Larger studies are included.
Kim AJ, Liu JC, Ganly I et al. (2011) Minimally invasive video-assisted thyroidectomy 2.0: Expanded indications in a tertiary care cancer center. Head and Neck 33: 1557–60	Case series n=53	17% of patients had temporary vocal cord paralysis, with only 1 case of vocal cord paralysis persisting >6 months (1.9%). Six patients (11%) experienced temporary hypocalcaemia, requiring postoperative calcium supplementation; no patients experienced permanent hypocalcaemia.	Larger studies are included.
Lang BH, Wong KP (2013) A comparison of surgical morbidity and scar appearance between gasless, transaxillary endoscopic thyroidectomy (GTET) and minimally invasive video-assisted thyroidectomy (VAT). Annals of Surgical Oncology	Non-randomised comparative study n=141 Follow-up=6 months	Gasless transaxillary endoscopic thyroidectomy (GTET) was a technically more challenging procedure and was associated with longer hospital stay, longer operating time, more immediate pain, and increased overall recurrent laryngeal nerve injury and morbidity than MIVAT. The 6-month patient and observer scar assessment scores were similar	Larger studies are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in tables 2a and 2b
20: 646–52		between the 2 procedures	
Liu J, Song T, Xu M (2012) Minimally invasive video-assisted versus conventional open thyroidectomy: A systematic review of available data. Surgery Today 42: 848–56	Systematic review (9 studies) N=697 (335 MIVAT versus 362 conventional thyroidectomy) Follow-up: 2 days to 23 months	**Mean postoperative satisfaction scores** (patients graded the cosmetic appearance of their wound on a scale from 0 to 10, with higher scores being better): 5 studies (n=119 versus 118) reported that patients in the MIVAT group were more satisfied with the cosmetic result (weighted difference 2.59, 95% CI 1.52 to 3.65, p<0.00001). **Postoperative pain score** (measured on a 10-point VAS, with higher scores representing more severe pain): 3 studies (n=68 versus 69) reported that at 6 hours postoperatively, patients in the MIVAT group had less pain than those in the conventional group (mean difference -11.52, 95% CI -17.82 to -5.21, p=0.0003). **Total complication rate (7 studies):** • MIVAT=9.7% (28/289) • Conventional thyroidectomy=13.6% (43/316) OR 0.63, 95% CI 0.37 to 1.06, p=0.08 (I^2=0%) **Transient recurrent laryngeal nerve palsy (reported in 6 studies):** • MIVAT=3.9% (11/279) • Conventional thyroidectomy=4.2% (13/306) OR 0.93, 95% CI 0.40 to 2.18, p=0.87 (I^2=0%) **Transient hypoparathyroidism (4 studies):** • MIVAT=2.9% (5/171) • Conventional thyroidectomy=2.1% (4/191) OR 1.30, 95% CI 0.36 to 4.70, p=0.69 (I^2=0%)	Was included in table 2 for IPAC 1 meeting. Now replaced by Pisanu 2013 following the updated literature search at consultation phase.
Lombardi CP, Raffaelli M, Princi P et al. (2006) Video-assisted thyroidectomy: report on the experience of a single center in more than four hundred cases. World Journal of Surgery 30: 794–80	Case series n=459	Indications for MIVAT are still limited (20% of patients who need thyroidectomy). Nonetheless, in selected patients, it seems a valid option for thyroidectomy and it could be considered even preferable to conventional surgery because of its significant advantages, especially in terms of cosmetic result.	Studies with more patients or longer follow-up are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in tables 2a and 2b
Lombardi CP, Raffaelli M, De Crea C et al. (2007) Report on 8 years of experience with video-assisted thyroidectomy for papillary thyroid carcinoma. Surgery 142: 944–51	Case series n=271 Mean follow-up=20 months	**Papillary thyroid carcinoma** The completeness of the operative resection achieved with video-assisted thyroidectomy seems comparable with that reported for conventional surgery. A longer follow-up is necessary to draw definitive conclusions in terms of recurrence and survival rate	Studies with more patients or longer follow-up are included.
Lombardi CP, Raffaelli M, Princi P et al. (2006) Video-assisted thyroidectomy: report of a 7-year experience in Rome. Langenbecks Archives of Surgery 391: 174–7	Case series n=507	The indications for VAT are still limited. Nonetheless, in selected patients, it seems a valid option for thyroidectomy and even preferable to conventional surgery because of its significant advantages, especially in terms of cosmetic result	Studies with more patients or longer follow-up are included.
Lombardi CP, Raffaelli M, D'alatri L et al. (2008) Video-assisted thyroidectomy significantly reduces the risk of early postthyroidectomy voice and swallowing symptoms. World Journal of Surgery 32: 693–700	RCT n=65 Follow-up=3 months	The incidence and the severity of early voice and swallowing postthyroidectomy symptoms are significantly reduced in patients who undergo VAT compared with conventional surgery.	Studies with more patients or longer follow-up are included.
Lombardi CP, Raffaelli M, De Crea C et al. (2010) Video-assisted thyroidectomy for papillary thyroid carcinoma. Journal of Oncology 2010: article ID 148542	Case series n=359 mean follow-up=22 months	**Papillary thyroid carcinoma** Post operative ultrasonography showed no residual thyroid tissue in all the patients. Mean post-operative (131) uptake was 1.7%. One patient developed lateral neck recurrence. No other recurrence was observed	Studies with more patients or longer follow-up are included.
Lombardi CP, Raffaelli M, De Crea C et al. (2012) Video-assisted versus conventional total thyroidectomy and central compartment neck dissection for papillary thyroid carcinoma. World journal of surgery 36: 1225–30	Non-randomised comparative study n=104 Follow-up=40 months	**Papillary thyroid carcinoma** The results of VA-TT and CCD in selected cases of papillary thyroid carcinoma appear to be comparable to those of conventional surgery. A longer follow-up and larger series are necessary to draw definitive conclusions concerning long-term outcomes	Studies with more patients or longer follow-up are included.
Maeda S, Uga T, Hayashida N (2006) Video-assisted subtotal or near-total thyroidectomy for Graves' disease. British Journal of Surgery 93: 61–6	Case series n=63	There were no conversions to open surgery. Three patients (5 per cent) had temporary recurrent laryngeal nerve palsy that recovered spontaneously. Most patients were satisfied with the surgical results, particularly regarding the placement of the surgical scars.	Larger studies are included.
Miccoli P, Berti P, Raffaelli M et al. (2001) Comparison between minimally invasive	RCT n=49 (25 versus 24)	Despite some MIVAT advantages in terms of postoperative pain and cosmesis, conventional thyroidectomy still offers an	Included in Liu et al, 2012 systematic

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in tables 2a and 2b
video-assisted thyroidectomy and conventional thyroidectomy: a prospective randomized study.[Erratum appears in Surgery 2002 Feb;131(2):148]. Surgery 130: 1039–43		advantage in terms of operative time and its safety should not differ. Larger series of patients are needed before deciding whether endoscopic thyroidectomy can offer important advantages	review.
Miccoli P, Elisei R, Materazzi G et al. (2002) Minimally invasive video-assisted thyroidectomy for papillary carcinoma: a prospective study of its completeness. Surgery 132: 1070–3	RCT n=33 Follow-up=1 month	**Papillary thyroid carcinoma** The completeness obtained with MIVAT is similar to that obtained with open thyroidectomy, with the great advantage of a minimal neck wound. No conclusions can be drawn in terms of influence of MIVAT on the outcome of the patients with small papillary thyroid carcinoma	Studies with more patients or longer follow-up are included.
Miccoli P, Materazzi G, Baggiani A et al. (2011) Mini-invasive video-assisted surgery of the thyroid and parathyroid glands: A 2011 update. Journal of Endocrinological Investigation 34: 473–80	Review	Advantages of MIVAT: better cosmetic result; better postoperative course; better intraoperative vision. Disadvantages of MIVAT: longer operative time (learning curve); costs; need for technology; limited indications.	No meta-analysis.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in tables 2a and 2b
Miccoli P, Bellantone R, Mourad M et al. (2002) Minimally invasive video-assisted thyroidectomy: multiinstitutional experience. World journal of surgery 26: 972–5	Case series n=336	The complication rate was not different from that of standard thyroidectomy. The learning curve demonstrates a sharp decrease with increasing experience and the introduction of new technologies. The number of patients eligible for this approach remains low but it should be considered a valid option in selected surgical centers, offering some advantages to patients in terms of cosmetic results and postoperative distress.	Studies with more patients or longer follow-up are included.
Minuto MN, Berti P, Miccoli M et al. (2012) Minimally invasive video-assisted thyroidectomy: an analysis of results and a revision of indications. Surgical Endoscopy 26: 818–22	Case series n=1946	Data confirm the validity of the traditional indications for MIVAT: low-risk differentiated thyroid cancer (DTC), cytologically undetermined nodules, and small-volume benign thyroid disease. The indications may be further and safely extended to those patients with associated thyroiditis and those with intermediate-risk DTC.	Paper focuses in indications rather than patient outcomes.
Mourad M, Pugin F, Elias B et al. (2002) Contributions of the video-assisted approach to thyroid and parathyroid surgery. Acta chirurgica Belgica 102: 323–7	Case series n=57 MIVAT, 57 MIVAP	**Thyroidectomy and parathyroidectomy** The video-assisted approach for thyroid and parathyroid surgery is feasible, safe and effective in selected cases. Benefits for the patients should be further assessed in future prospective comparative trials	Larger studies are included.
Musholt TJ, Clerici T, Dralle H (2011) German Association of Endocrine Surgeons practice guidelines for the surgical treatment of benign thyroid disease. Langenbecks Archives of Surgery 396: 639–49	Practice guidelines	The inclusion and exclusion criteria for choosing a minimally invasive procedure versus a conventional procedure and for choosing between different minimally invasive techniques have not yet been clearly defined.	No patient outcomes.
O'Neill JP, Timon C (2011) Prospective assessment of postoperative pain in patients undergoing minimally invasive video-assisted versus minimally invasive open thyroidectomy. World Journal of Endocrine Surgery 3: 11–4	Non-randomised comparative study n=98	MIVAT appears to reduce the pain in patients shortly after the operation and 24 hours postoperative. The reduction is statistically significant. Male patients appear to report less pain compared to their female counter parts.	Larger studies are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in tables 2a and 2b
Perigli G, Cortesini C, Qirici E et al. (2008) Clinical benefits of minimally invasive techniques in thyroid surgery. World Journal of Surgery 32: 45–50	Non-randomised comparative study n=957 (56 versus 214 versus 687)	When compared with conventional treatment, MIVAT and minimally invasive thyroidectomy provided significant benefit in terms of cosmetic results and postoperative pain. Nevertheless, the main limiting factor for minimally invasive thyroid surgery still remains the size of the thyroid	Studies with more patients treated by MIVAT are included.
Ruggieri M, Straniero A, Maiuolo A et al. (2007) The minimally invasive surgical approach in thyroid diseases. Minerva Chirurgica 62: 309–14	Case series n=75	The central neck minimally invasive approach is safe, less painful, better for cosmetic results, with less paresthetic consequences and easily reproducible in surgical practice. A longer incision (up to 35 mm), does not affect negatively the advantages of minimally invasive procedure.	Procedures were done with or without video assistance.
Samy AK, Ridgway D, Orabi A et al. (2010) Minimally invasive, video-assisted thyroidectomy: first experience from the United Kingdom. Annals of the Royal College of Surgeons of England 92: 379–84	Case series n=55 Follow-up=18 months	Conversions=6.3% No haematoma or re-operation. Transient voice change=11% (n=7), permanent unilateral recurrent laryngeal nerve palsy=3% (n=2) and transient hypocalcaemia=3% (n=2). There is a steep learning curve with rapid improvement observed within the first 30 cases.	Larger studies are included.
Sgourakis G, Sotiropoulos GC, Neuhauser M et al. (2008) Comparison between minimally invasive video-assisted thyroidectomy and conventional thyroidectomy: is there any evidence-based information? Thyroid 18: 721–7	Review and meta-analysis (5 RCTs)	MIVAT is a safe procedure that produces outcomes; in view of short-term adverse events, similar to those of open thyroidectomy, it needs a longer operative time to be accomplished and is superior in terms of immediate postoperative pain and cosmetic results	A more recent systematic review is included.
Shan YZ, Zhou LM, Yu ZF et al. (2012) Comparison between transareola singlesite endoscopic thyroidectomy and minimally invasive video-assisted thyroidectomy. Journal of International Medical Research 40: 2213–9	RCT n=48	Postoperative complaints were comparable between the 2 approaches, although MIVAT involved a shorter operation time	Comparison of transareola single site endoscopic thyroidectomy against MIVAT.
Shimizu K, Kitagawa W, Akasu H et al. (2002) Video-assisted endoscopic thyroid and parathyroid surgery using a gasless method of anterior neck skin lifting: a review of 130 cases. Surgery Today 32: 862–8	Case series n=167	There was less bleeding when the Video-assisted neck surgery method ($p < 0.001$) was used than when conventional surgery was performed, and the operating time has been reduced with experience	Larger studies are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in tables 2a and 2b
Schabram J, Vorlander C, Wahl R A (2004) Differentiated operative strategy in minimally invasive, video-assisted thyroid surgery results in 196 patients. World Journal of Surgery 28: 1282–6	Case series n=196	Conversion to open surgery was necessary in 8% of patients (secondary to malignancy demonstrated on frozen section in 3% and to technical difficulties in 5%). Transient and permanent laryngeal nerve palsy occurred in 2% and 0.5% of patients, respectively. Temporary hypoparathyroidism occurred in 6% of patients exclusively after conversion to open total thyroidectomy or in those patients (n =22) with additional primary hyperparathyroidism.	Larger studies are included.
Steward DL and Hensler MS. (2013) Central node dissection: Comparison of standard open to minimally invasive video-assisted approach. Otolaryngology - Head and Neck Surgery (United States).Conference: Annual Meeting of the American Academy of Otolaryngology-Head and Neck Surgery Foundation 2013 Vancouver, BC Canada.Conference Start: 20130929 Conference End: 20131002.Conference Public 57-	Retrospective non-randomised comparative study n = 185 (51 MIVAT versus 134 open) FU = not reported	Nodal yield MIVAT: 5.0 Open: 6.7 (p=0.04) [Although nodal yield was similar in unilateral cases (4.9 versus 5.5, p=0.58)] Recurrence rates: MIVAT: 2.0% Open: 6.0% (p=0.29) Transient recurrent laryngeal nerve injury MIVAT: 4.1% Open: 5.8% (p=0.67) Transient hypoparathyroidism (defined as postenesthesia care unit parathyroid hormone <15 pg/ml) MIVAT: 29.8% Open: 49.3% (p=0.29)	Abstract only Larger studies in table 2
Terris D J, Gourin CG, Chin E (2006) Minimally invasive thyroidectomy: Basic and advanced techniques. Laryngoscope 116: 350–6	Non-randomised comparative study n=45 (14 versus 31)	Two distinct approaches to minimal access thyroid surgery are now available. The choice of approach depends on a number of patient and disease factors.	Larger studies are included.
Ujiki MB, Sturgeon C, Denham D et al. (2006) Minimally invasive video-assisted thyroidectomy for follicular neoplasm: is there an advantage over conventional thyroidectomy? Annals of Surgical Oncology 13: 182–6	Non-randomised comparative study n=48 (22 versus 26)	MIVAT is as safe and effective as conventional thyroidectomy and is associated with similar narcotic analgesic needs, but it can be performed through smaller incisions. Operative times were significantly longer for MIVAT, but when patients with thyroiditis were excluded, operative times were not significantly different	Larger studies are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in tables 2a and 2b
Vaysberg M, Steward DL (2008) Minimally invasive video-assisted thyroidectomy. Laryngoscope 118: 786–9	Case series n=92	MIVAT has rates of hypocalcaemia, vocal cord paresis, and haematoma comparable with those reported for the traditional open approach. Procedure times varied based on extent of thyroidectomy, patient factors, and experience of the operator and were significantly reduced during the study period	Larger studies are included.
Venkat R and Guerrero MA. (2013) Recent advances in the surgical treatment of differentiated thyroid cancer: A comprehensive review. The Scientific World Journal.2013 , 2013.Article Number: 425136.Date of Publication: 2013.	Review	MIVAT is safe and effective in the hands of a trained surgeon and in selected patients has comparative morbidity and better cosmesis compared to conventional open thyroidectomy.	Alternative systematic review with meta-analysis already included in table 2.
Wu C-T, Yang L-H, Kuo S-J (2010) Comparison of video-assisted thyroidectomy and traditional thyroidectomy for the treatment of papillary thyroid carcinoma. Surgical Endoscopy and Other Interventional Techniques 24: 1658–62	Non-randomised comparative study n=44 Follow-up=60 months	**Papillary thyroid carcinoma** Video assisted thyroidectomy is safe and effective for the treatment of small papillary thyroid carcinomas, and has similar oncological effectiveness to traditional thyroidectomy	Larger studies are included.
Yu JJ, Bao SL, Yu SL et al. (2012) Minimally invasive video-assisted thyroidectomy for the early-stage differential thyroid carcinoma. Journal of translational medicine 10: Suppl 1: S13	Non-randomised comparative study n=135 (24 versus 111) Follow-up=3 months	**Differential thyroid carcinoma** Patients who received MIVAT had significantly shorter incisional length (3 cm versus 7 cm, p<0.0001), shorter operative time (109 min versus 139 min, p=0.014) and fewer operative haemorrhage (29.5 ml versus 69.7 ml, p<0.0001) when compared to the conventional treatment.	Larger studies are included.
Zong G, Liu X, Wang F (2009) Minimally invasive video-assisted thyroidectomy for thyroid adenoma. Chinese-German Journal of Clinical Oncology 8: 460–2	Case series n=128	MIVAT for thyroid adenoma is safe and reliable. This procedure offers a shorter incision, less invasion and better cosmetic results as compared with conventional thyroidectomy.	Larger studies are included.
MIVAP			
Berti P, Materazzi G, Picone A et al. (2003) Limits and drawbacks of video-assisted parathyroidectomy. The British journal of surgery 90: 743–7	Case series n=239 Follow-up=12 months	Conversion =8% Complications included recurrent nerve palsy (0.8%), haemorrhage that needed reoperation 6 h after parathyroidectomy in 1 patient and transient hypoparathyroidism (2.5%). Persistent primary hyperparathyroidism =2%	Studies with more patients or longer follow up are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in tables 2a and 2b
De Crea C, Raffaelli M, Traini E et al. (2013) Is there a role for video-assisted parathyroidectomy in regions with high prevalence of goitre? Acta Otorhinolaryngologica Italica 33: 388–92	Case series n=124 patients with concomitant thyroidectomy Mean follow-up=33 months	There were no conversions to conventional surgery. Transient hypocalcaemia=33% (42/124) 1 transient recurrent nerve lesion.	Larger studies are included.
Garimella V, Yeluri S, Alabi A et al. (2012) Minimally invasive video-assisted parathyroidectomy is a safe procedure to treat primary hyperparathyroidism. Surgeon Journal of the Royal Colleges of Surgeons of Edinburgh & Ireland 10 : 202–5	Case series n=56	Conversion to open procedure=14% (failed exploration in 5 patients, inability to retrieve a very large friable adenoma, lipo-adenoma, and very small parathyroid adenoma). Postoperative complications: 1 temporary recurrent laryngeal nerve palsy. All but 5 patients became normo-calcaemic following surgery.	Larger studies are included.
Gracie D, Hussain SS (2012) Use of minimally invasive parathyroidectomy techniques in sporadic primary hyperparathyroidism: systematic review. Journal of Laryngology & Otology 126: 221–7	Systematic review 26 case series, 7 RCTs, 1 non-randomised comparative study	There is level 1b evidence that minimally invasive surgery is comparable to bilateral neck exploration in terms of efficacy and complication rates. This paper recommends that the treatment of choice for solitary adenoma (in most healthcare centres) should be open minimal incision parathyroidectomy, due to advantages in operative duration, learning curve and cost-effectiveness.	No meta-analysis.
Henry JF, Iacobone M, Mirallie E et al. (2001) Indications and results of video-assisted parathyroidectomy by a lateral approach in patients with primary hyperparathyroidism. Surgery 130: 999–1004	Case series n=166 Follow-up=3–33 months	**Lateral approach** Conversion to conventional parathyroidectomy =16%. Morbidity included 2 local haematomas, 1 definitive recurrent nerve palsy, and 4 capsular fractures. All of the 166 patients were normocalcaemic,	Studies with more patients or longer follow up are included.
Henry JF, Raffaelli M, Iacobone M et al. (2001) Video-assisted parathyroidectomy via the lateral approach versus conventional surgery in the treatment of sporadic primary hyperparathyroidism: Results of a case-control study. Surgical Endoscopy 15: 1116–9	Non-randomised comparative study n=136 (68 versus 68) Follow-up=mean 9 months	**Lateral approach** This study suggests that video-assisted parathyroidectomy by the lateral approach has some advantages over conventional parathyroidectomy in terms of postoperative pain and cosmetic results	Studies with more patients or longer follow up are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in tables 2a and 2b
Lombardi CP, Raffaelli M, Traini E et al. (2008) Advantages of a video-assisted approach to parathyroidectomy. ORL; Journal of Oto-Rhino-Laryngology & its Related Specialties 70: 313–8	Case series n=107	VAP seems to have significant advantages in terms of cosmetic results, postoperative pain, recovery, and patient satisfaction. When compared with other minimally invasive techniques, it offers the significant advantages of being more similar to conventional surgery and reproducible in different surgical settings	Larger studies are included.
Lorenz K, Miccoli P, Monchik J et al. (2001) Minimally invasive video-assisted parathyroidectomy: Multiinstitutional study. World Journal of Surgery 25: 704–7	Case series n=123 Follow-up=3–12 months	Conversion =11% (because of failed localization, failure of the iPTH level to fall appropriately, or technical problems). There was no persistent or recurrent HPT .Oral calcium replacement for symptomatic hypocalcaemia postoperatively=6%. Unilateral transient laryngeal nerve palsy=2%.	Larger studies are included.
Lorenz K, Phuong NT, Dralle H (2002) Diversification of minimally invasive parathyroidectomy for primary hyperparathyroidism: minimally invasive video-assisted parathyroidectomy and minimally invasive open videoscopically magnified parathyroidectomy with local anesthesia. World journal of surgery 26: 1066–70	Non-randomised comparative study n=103	A new technique of minimally invasive open parathyroidectomy with the option of videoscopic magnification under local anesthesia (MIPLA) for localizable adenomas is introduced. Preliminary results of diversified procedures demonstrate effects regarding omission of preoperative diagnostics, overall cost reduction, and increasing patient selection for selective parathyroid surgery because of primary hyperparathyroidism	Larger studies are included.
Maweja S, Sebag F, Hubbard J et al. (2004) Immediate and medium-term results of intraoperative parathyroid hormone monitoring during video-assisted parathyroidectomy. Archives of Surgery 139:1301–3	Case series n=200	**Lateral approach** Intraoperative parathyroid hormone monitoring during video-assisted parathyroidectomy by lateral approach is useful in detecting multiple gland disease not suspected by preoperative localization studies. Overall, IOPTH monitoring predicts medium-term normocalcaemia with a success rate of 98.5% in patients with sporadic primary hyperparathyroidism	Larger studies are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in tables 2a and 2b
Miccoli P, Berti P, Conte M et al. (2000) Minimally invasive video-assisted parathyroidectomy: lesson learned from 137 cases. Journal of the American College of Surgeons 191: 613–8	Case series n=137 Follow-up=15 months	Although not all patients with sporadic primary hyperparathyroidism are eligible for MIVAP, this approach can now be proposed in a bigger proportion (67% of patients). After greater experience has been achieved, the results and the operative time are the same as in traditional surgery, with better cosmetic result and a less painful course	Larger studies are included.
Miccoli P, Berti P, Materazzi G et al. (2003) Minimally invasive video assisted parathyroidectomy (MIVAP). European Journal of Surgical Oncology 29: 188–90	Case series n=270	Conversion=8%. One laryngeal nerve palsy was confirmed 6 months after surgery. Postoperative bleeding needing reoperation, n=1 The mean operative time and complication rate demonstrate that this approach can successfully rival the results of traditional surgery for the treatment of primary hyperparathyroidism.	Larger studies are included.
Miccoli P, Berti P, Materazzi G et al. (2004) Results of video-assisted parathyroidectomy: single institution's six-year experience. World journal of surgery 28: 1216–18	Case series n=370 Follow-up=median 35 months	91% of patients were satisfied with the cosmetic result 6 or more months after the procedure. Complications: transient (3%), hypoparathyroidism, definitive palsies of the recurrent nerve (0.8%), and 1 case of postoperative bleeding. After 6 years of experience, MIVAP appears to be as safe and curative as traditional surgery, with better cosmetic results and better postoperative outcome	Studies with more patients or longer follow up are included.
Miccoli P, Barellini L, Monchik JM et al. (2005) Randomized clinical trial comparing regional and general anaesthesia in minimally invasive video-assisted parathyroidectomy. The British journal of surgery 92: 814–8	RCT (regional versus general anaesthesia) n=51	MIVAP performed under regional anaesthesia was associated with a shorter overall operating time and a reduced need for postoperative pain relief	Small RCT comparing regional against general anaesthesia.
Miccoli P, Berti P, Materazzi G et al. (2008) Endoscopic bilateral neck exploration versus quick intraoperative parathormone assay (qPTHa) during endoscopic parathyroidectomy: A prospective randomized trial. Surgical Endoscopy and Other Interventional Techniques 22: 398–400	RCT n=40 (20 versus 20)	Bilateral exploration can be performed endoscopically, avoiding both the time necessary for quick parathormone assay and its cost, with the same effectiveness, but might in few cases lead to the unjustified removal of parathyroid glands slightly enlarged but not necessarily pathologic.	Paper focuses on the use of quick intraoperative parathormone assay

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in tables 2a and 2b
Mourad M, Pugin F, Elias B et al. (2002) Contributions of the video-assisted approach to thyroid and parathyroid surgery. Acta chirurgica Belgica 102: 323–7	Case series n=57 MIVAT, 57 MIVAP	**Thyroidectomy and parathyroidectomy** The video-assisted approach for thyroid and parathyroid surgery is feasible, safe and effective in selected cases. Benefits for the patients should be further assessed in future prospective comparative trials	Larger studies are included.
Ozimek A, Gallwas J, Stocker U et al. (2010) Validity and limits of intraoperative parathyroid hormone monitoring during minimally invasive parathyroidectomy: a 10-year experience. Surgical Endoscopy 24: 3156–60 .	Case series n=235	Intraoperative iPTH monitoring showed 221 true-positive, 1 false-positive, 6 false-negative, and 7 true-negative results. This calculated to a sensitivity of 97% and a specificity of 88%	Paper focuses on the use of intraoperative parathyroid hormone monitoring.
Prades JM, Asanau A,, Timoshenko AP et al. (2011) Endoscopic parathyroidectomy in primary hyperparathyroidism. European Archives of Oto-Rhino-Laryngology 268: 893–7	Case series n=59 Follow-up=3 months	Conversion=18%. There were no cases of permanent hypocalcaemia or recurrent laryngeal nerve palsy. Postoperative review showed that all calcium and parathyroid hormone levels remained normal at 3 months except for 1 patient with a double adenoma.	Larger studies are included.

Appendix B: Related NICE guidance for minimally invasive video-assisted thyroidectomy/parathyroidectomy

Guidance	Recommendations
Interventional procedures	**Intraoperative nerve monitoring during thyroid surgery. NICE interventional procedure guidance 255 (2008)** 1.1 The evidence on intraoperative nerve monitoring (IONM) during thyroid surgery raises no major safety concerns. In terms of efficacy, some surgeons find IONM helpful in performing more complex operations such as reoperative surgery and operations on large thyroid glands. Therefore, it may be used with normal arrangements for consent, audit and clinical governance. **Thoracoscopic excision of mediastinal parathyroid tumours. NICE interventional procedure guidance 247 (2007)** 1.1 There is limited evidence to support the efficacy of thoracoscopic excision of mediastinal parathyroid tumours. The evidence on safety is also very limited in quantity, and in view of potential complications of the procedure it should only be used with special arrangements for clinical governance, consent, audit and research. 1.2 Clinicians wishing to undertake thoracoscopic excision of mediastinal parathyroid tumours should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that patients understand the potential complications of the procedure and provide them with clear written information. In addition, use of the Institute's information for patients ('Understanding NICE guidance') is recommended. • Audit and review clinical outcomes of all patients having thoracoscopic excision of mediastinal parathyroid tumours (see section 3.1). It is recommended that clinicians undertaking this procedure should collaborate in the collection and review of data. 1.3 Patient selection for thoracoscopic excision of mediastinal parathyroid tumours should be carried out in specialist units and in the context of a multidisciplinary team that includes a thoracic surgeon experienced in thoracoscopic techniques. Preoperative imaging should always be undertaken to confirm the location of the mediastinal tumour.

Technology appraisals	**Cinacalcet for the treatment of secondary hyperparathyroidism in patients with end-stage renal disease on maintenance dialysis therapy. NICE technology appraisal guidance 117 (2007).** 1.1 Cinacalcet is not recommended for the routine treatment of secondary hyperparathyroidism in patients with end-stage renal disease on maintenance dialysis therapy. 1.2 Cinacalcet is recommended for the treatment of refractory secondary hyperparathyroidism in patients with end-stage renal disease (including those with calciphylaxis) only in those: • who have 'very uncontrolled' plasma levels of intact parathyroid hormone (defined as greater than 85 pmol/litre [800 pg/ml]) that are refractory to standard therapy, and a normal or high adjusted serum calcium level, and • in whom surgical parathyroidectomy is contraindicated, in that the risks of surgery are considered to outweigh the benefits. 1.3 Response to treatment should be monitored regularly and treatment should be continued only if a reduction in the plasma levels of intact parathyroid hormone of 30% or more is seen within 4 months of treatment, including dose escalation as appropriate.

Appendix C: Literature search for minimally invasive video-assisted thyroidectomy/parathyroidectomy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	30/04/2014	Issue 4 of 12, April 2014
Database of Abstracts of Reviews of Effects – DARE (CRD website)	30/04/2014	Issue 4 of 12, April 2014
HTA database (CRD website)	30/04/2014	Issue 4 of 12, April 2014
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	30/04/2014	Issue 4 of 12, April 2014
MEDLINE (Ovid)	30/04/2014	1946 to April Week 3 2014
MEDLINE In-Process (Ovid)	30/04/2014	April 29, 2014
PubMed	30/04/2014	N/A
EMBASE (Ovid)	30/04/2014	1974 to 2014 Week 17
JournalTOCS	30/04/2014	N/A

Trial sources searched on 26/11/2013:

- National Institute for Health Research Clinical Research Network Coordinating Centre (NIHR CRN CC) Portfolio Database
- Current Controlled Trials *meta*Register of Controlled Trials – *m*RCT
- Clinicaltrials.gov

Websites searched on 26/11/2013:

- National Institute for Health and Clinical Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- French Health Authority (FHA)
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- General internet search

MEDLINE search strategy

The MEDLINE search strategy was adapted for use in the other sources.

1	Thyroidectomy/ and (Endoscopy/ or Endoscopes/)

2	Parathyroidectomy/ and (Endoscopy/ or Endoscopes/)
3	Thyroidectomy/ and Surgical Procedures, Minimally Invasive/
4	Parathyroidectomy/ and Surgical Procedures, Minimally Invasive/
5	Thyroidectomy/ and Video-Assisted Surgery/
6	Parathyroidectomy/ and Video-Assisted Surgery/
7	((endoscop* or minimally invasive or video assist* or video-assist* or VATS) adj4 (Parathyroidect* or thyroidect*)).tw.
8	MIVAT.tw.
9	MIVAP.tw.
10	or/1-9
11	thyroid neoplasms/ or thyroid nodule/
12	parathyroid diseases/ or exp hyperparathyroidism/ or parathyroid neoplasms/
13	Carcinoma, Papillary/
14	hyperthyroidism/ or graves disease/
15	goiter/ or goiter, nodular/
16	((thyroid* or parathyroid* or hyperparathyroid* or Papillary* or Follicular*) adj4 (neoplasm* or cancer* or carcinoma* or adenocarcinom* or tumour* or tumor* or malignan* or metasta* or nodul*)).tw.
17	(graves adj4 diseas*).tw.
18	(goitre or goiter or thyroid swell* or overact* thyroid or parathyroid).tw.
19	or/11-18
20	10 and 19
21	animals/ not humans/
22	20 not 21
23	**limit 22 to english language**