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Minimally Invasive Video-Assisted Thyroidectomy: Analysis of Complications From a Systematic Review

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Abstract

Background. Nowadays, minimally invasive video-assisted thyroidectomy (MIVAT) is considered a safe and effective option. However, its complication rate has not been specifically discussed yet. The aim of this systematic review was enrolling a large number of studies to estimate early and late complications (transient and definitive, uni- and bilateral laryngeal nerve palsy; transient and definitive hypocalcemia; cervical hematoma; hypertrophic or keloid scar) of MIVAT compared with conventional technique. *Methods*. The review was performed according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) criteria in PubMed and Embase. Search terms were "minimally invasive," "video-assisted," and "thyroidectomy." We enrolled randomized clinical trials, nonrandomized trials, and noncontrolled trials. *Results*. Thirty-two articles were considered suitable. Complication rate of MIVAT was quite similar to conventional technique: only one randomized trial found a significant difference concerning overall skin complication, and a single trial highlighted hypocalcemia significantly increased in MIVAT, concerning serologic value only. No difference concerning symptomatic nor definitive hypocalcemia was found. *Conclusions*. We can confirm that MIVAT is a safe technique. It should be adopted in mean-high-volume surgery centers for thyroidectomy, if a strict compliance with indication was applied.

Keywords

review, transient complications, definitive complications, minimally invasive video-assisted thyroidectomy, MIVAT, conventional thyroidectomy

Introduction

Since Bellantone et al[1] and Miccoli et al[2] in 1999 described the feasibility of adapting video-assisted parathyroidectomy technique[3] to thyroid surgery for small follicular nodules, minimally invasive video-assisted thyroidectomy (MIVAT) was adopted all over the world because of its reproducibility and its likeness to conventional thyroidectomy (CT), which allowed experienced surgeons to take typical advantages of endoscopic procedures in terms of reduced scar size and postoperative course without relevant changes in surgical technique.[4,5] Initially, this technique was indicated for surgical treatment of benign nodule smaller than 3.5 cm or differentiated low-risk carcinomas up to 2 cm, in a gland with total volume lesser than 25 mL and in absence of thyroiditis or lymph nodes involvement.[6] Nowadays, preoperatively estimated thyroid volume represents the only selection parameter in benign pathology. Instead, in suspected or proven malignancy, only accurate clinical staging can determine its indication to a minimally invasive procedure. The main change in MIVAT technique was the introduction of energy-based surgical instruments that allowed an easier conduct and a decrease in procedure length.[7-10] Nowadays, MIVAT seems to be an appreciable choice to perform thyroidectomies in the presence of small glands satisfying standard requirements because it offers similar advantages over conventional techniques.[10-12] In the past 20 years, several overviews and systematic reviews discussed different aspects of MIVAT.[13-17] Three meta-analysis studies concerning

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overall results of MIVAT have been published.[18-20] All of them included a relatively small number of articles; moreover, the latest study was published 3 years ago and the item of complication rate has not been specifically discussed yet. We performed this systematic review with the aim of maximizing the number of studies enrolled and estimating early and late complications (transient and definitive, uni- and bilateral laryngeal nerve palsy; transient and definitive hypocalcemia; cervical hematoma; hypertrophic or keloid scar) of MIVAT compared with conventional technique.

Methods

The present study was carried out in agreement with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement,[21] by following a predefined protocol. We preferred to perform a systematic review rather than a meta-analysis because we aimed to implement as widely as possible data concerning complications of MIVAT including largest number of studies existing in literature that were heterogeneous in design terms (randomized/nonrandomized, controlled/noncontrolled, etc). No institutional ethical board statement was needed.

Search Strategy

A systematic comprehensive search of full texts was undertaken of PubMed (MEDLINE) and Embase databases from January 2000 to June 2018 for published peer-reviewed trials concerning results of MIVAT, compared with CT in case of controlled trials. Search terms were "minimally invasive," "video-assisted," and "thyroidectomy." In articles found in PubMed, we used related citations function for searching additional relevant studies. Moreover, any publication of referral researchers in minimally invasive thyroid and parathyroid surgery field were checked. This search strategy was designed and conducted according to a collective decision of all authors of the present article. It was led by 2 authors, mutually blinded regarding the search process. The articles included were written in English or Italian language.

Inclusion/Exclusion Criteria and Study Selection Process

All the randomized controlled trials (RCTs) found with our research were included. Due to small number of the RCTs available, which involved a limited number of patients, we also recruited all the clinical controlled trials available in literature. The following inclusion criteria were adopted: studies concerning adult patients with nodular (uni- or multi) thyroid, benign or malignant disease, scheduled for thyroidectomy (uni- or bilateral); Grave's disease; comparison of CT to Miccoli's technique; use of ligations, clips, and energy-based surgical instrument for performing hemostasis. We excluded pediatric patients, neck lymph node dissection and parathyroid procedures performed as primary object of the study, and articles suggesting relevant technical changes to Miccoli's technique. Duplicate records were also excluded; multiple studies involving the same cohort of patients were considered just once. Editorials, expert opinions, and case reports were not considered for this review. We included previous notable reviews only for discussion but not for extracting data for the present review. In a first step of study recruitment, 2 more reviewers evaluated all titles and abstracts of included studies. Then we performed a second phase of screening of full-text articles, concerning qualitative assessment of studies, by 2 more reviewers, separating trials according to research method: prospective, randomized controlled, controlled nonrandomized, and noncontrolled trials.

Data Extraction

Two more investigators (different from those who performed the search) collected the data of included studies in extraction forms provided. If a disagreement between reviewers' judgement appeared, a third reviewer was asked for a supplemental evaluation. The data noted were descriptive, and for systematic review, the following were noted: title of article, year of publication, journal, study design, and sample size. Demographic details, laryngeal nerve palsies (transient and definitive), hypocalcemia (transient and definitive), cervical hematoma, and hypertrophic/keloid scar were noted for this review onto a standardized form.

Results

The search process was performed as shown in Figure 1. A total of 238 articles was found after checking by stated key words. Sixty-eight abstracts were selected for potential eligibility by evaluation of titles. Finally, 32 articles were considered suitable for this systematic review according to aims and scope. Among these trials, 8 were randomized prospective (Table 1),[21-29] 7 were nonrandomized (Table 2),[30-36] and 17 were uncontrolled (Table 3).[37-52] After a descriptive analysis of overall data was performed, a wide range of variability concerning the results can be observed.

Transient vocal fold palsy ranged from 1.3%[34] to 18%.[40] This last datum comes from a case series of only 11 patients. In 3 trials, 2 randomized[22,24] and 1 nonrandomized[32] involving, respectively, 31, 10, and 21 patients, no recurrent laryngeal palsy was found. The large series of

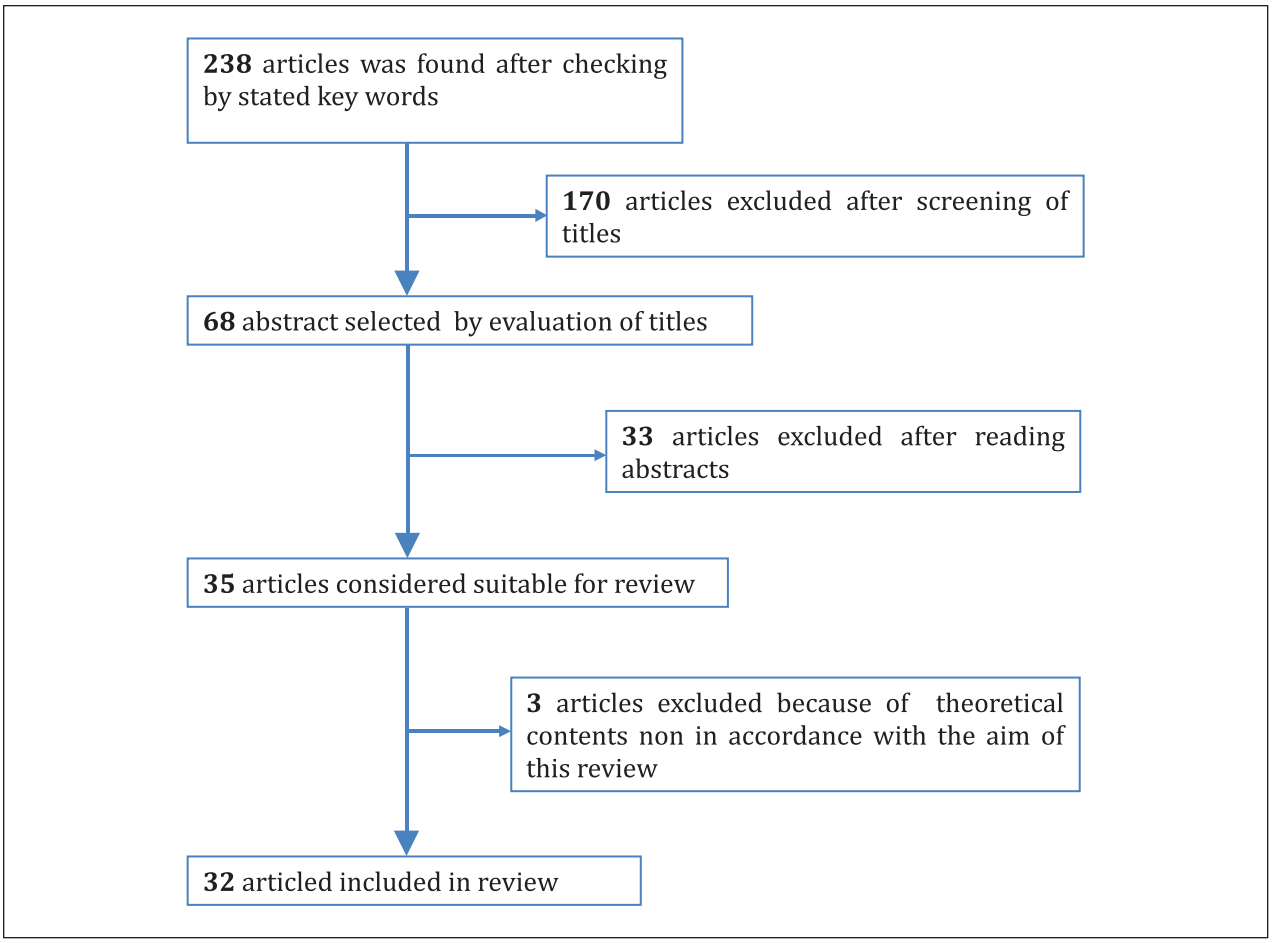

Figure 1. Study selection process.

Table 1. Summary of Complication Rate: Prospective Randomized Controlled Trials.

Author	Year	Indic	NC	TRLNP	DRLNP	TH	DH	Hemor	S	SSI	Keloid	Significance
Miccoli et al[21]	2001	Nod D	25/24	1/2	0/0	1/0	0/0	0/0	0/0	0/0	?	ns
Bellantone et al[22]	2002	Nod D	31/31	0/0	0/0	0/0	0/0	0/0	0/0	0/0	?	None
Chao et al[23]	2004	Nod D	52/59	3/5	0/0	?	?	0/0	?	?	?	ns
Lombardi et al[24]	2005	Nod D	10/10	0/0	0/0	2/2	0/0	0/0	0/0	0/0	?	ns
Hegazy et al[25]	2007	Follic Nod	33/35	1/1	0/0	0/1	0/0	1/0	?	?	?	ns
El-Labban[26]	2009	Nod D	38/38	2/1	1/0	2/2	0/0	0/0	?	2/2	?	ns
Di et al[28]	2011	PTMC cnd	31/37	3/2	0/0	3/1	0/0	0/0	?	0/0	?	ns
Dionigi et al[29]	2011	Nod D	56/56	3/3	0/0	6/7	0/0	0/1	0/2	0/3	1/2	$P < .05$ (total sc)

Abbreviations: Indic, indication for thyroidectomy; NC, number of cases (minimally invasive video-assisted thyroidectomy [MIVAT]/control group); TRLNP, transient recurrent laryngeal nerve paralysis; DRLNP, definitive recurrent laryngeal nerve palsy; TH, transient hypocalcemia; DH, definitive hypocalcemia; hemor, hemorrhage; S, seroma; SSI, surgical site infection; Nod D, nodular disease; ns, not significant; Follic Nod, follicular nodules; PTMC, papillary thyroid microcarcinoma; cnd, (ipsilteral) central neck dissection; total sc, total scar complications.

Miccoli et al[50] only reported definitive recurrent laryngeal nerve palsy (RLNP), which was low (1.2%). The overall incidence of this complication ranged from 0, as reported in several articles, to 3.6%.[44] The survey method for transient and definitive RLNP is not homogeneous: in most articles, a postoperative optical fiber laryngoscopy was not described. Del Rio et al[51] in a series of 497 patients reported a transient hypocalcemia incidence of over 32%, in most cases only serologic. In fact, only this trial found a statistically significant difference concerning this complication

Table 2. Summary of Complication Rate: Nonrandomized Controlled Trials.

Author	Year	Indic	NC	TRLNP	DRLNP	TH	DH	Hemor	S	SSI	Keloid	Significance
Ujiki et al[30]	2006	Follic Neo	22/26	1/1 (?)	0/0	?	0/0	0/0	0/0	0/0	?	ns
Dobrinja et al[31]	2009	NodD PTC	68/69	2/3	?	3/5	0/0	2/2	?	?	?	ns[a]
Wu et al[32]	2010	PTC	21/23	0/0	0/0	1/0	0/0	0/0	?	?	?	ns
Del Rio et al[33]	2010	Nod D	211/587	6/7	0/0	73/327	?	0/0	0/2	?	?	$P < .001$[b]
Alesina et al[34]	2011	GD	157/340	2/11	0/0	14/23	0/0	5/8	?	0/0	?	ns
Scerrino et al[35]	2013	Various	125/99	3/2	0/0	8/6	0/0	0/2	7/5	?	?	ns
Fik et al[36]	2014	Various	60/71	1/0	1/0	15/22	0/0	2/0	1/0	2/0	?	ns

Abbreviations: Indic, indication for thyroidectomy; NC, number of cases (minimally invasive video-assisted thyroidectomy [MIVAT]/control group); TRLNP, transient recurrent laryngeal nerve paralysis; DRLNP, definitive recurrent laryngeal nerve palsy; TH, transient hypocalcemia; DH, definitive hypocalcemia; hemor, hemorrhage; S, seroma; SSI, surgical site infection; Follic Neo, follicular neoplasms; ns, not significant; Nod D, nodular disease; PTC, papillary thyroid carcinoma; GD, Grave's disease.
[a]Some patients of this study underwent thyroidectomy *plus* central lymph node dissection in both (MIVAT/conventional) groups.
[b]The difference in hypocalcemia was significant *only* concerning serologic value. No difference concerning symptoms was found.

Table 3. Summary of Complication Rate: Uncontrolled Trials.

Author	Year	Indic	NC	TRLNP	DRLNP	TH	DH	Hemor	S	SSI	Keloid
Miccoli et al[37]	2001	Nod D	66	1	0	2	0	0	?	?	?
Mourad e al[4]	2001	Nod D	28	1	0	1	0	1	?	?	1
Musella et al[38]	2003	Nod D	20	1	0	2	0	0	?	?	?
Schabram et al[39]	2004	Nod D	196	4	1	11	0	1	?	2	?[b]
Ruggieri et al[40]	2005	Various	11	2	0	0	0	0	?	?	?
Lombardi et al[41]	2006	Various	507	9	0	73	3	1	?	2	?[c]
Terris et al[42]	2008	Various	216	9	0	5	0	0	1	?	?
Snissarenko et al[43]	2009	Various	172	7	0	?	0	0	?	?	?[b]
Samy et al[44]	2010	Various	55	7	2	2	0	0	0	?	?
Fan et al[45]	2010	Various	280	7	5	9	0	0	?	0	?[d]
Pons et al[46]	2013	Various	50	2	0	5	1	2	?	?	?
Barczyński et al[47]	2012	Various	240	8	2	13	?	0	?	2	?
Haitao et al[48]	2014	Various	194	6	1	7	0	0	?	?	?[e]
Miccoli et al[50]	2016	Various	2412	?	30	120	10	3	?	3	?[b,c]
Capponi et al[49]	2015	Nod D	33	3	0	2	0	0	0	?	?[b]
Del Rio et al[51]	2016	Various	497	12	4	160[f]	1	1	?	?	?
Bellotti et al[52]	2018	Various	110	2	1	11[a]	4[a]	0	?	1	?

Abbreviations: Indic, indication for thyroidectomy; NC, number of cases (minimally invasive video-assisted thyroidectomy [MIVAT]/control group); TRLNP, transient recurrent laryngeal nerve paralysis; DRLNP, definitive recurrent laryngeal nerve palsy; TH, transient hypocalcemia; DH, definitive hypocalcemia; Hemor, hemorrhage; S, seroma; SSI, surgical site infection; Nod D, nodular disease.
[a]Some patients of this study underwent thyroidectomy *plus* central lymph node dissection in both (MIVAT/conventional) groups.
[b]Contemporaneous parathyroidectomy in some cases.
[c]Simultaneous central lymph node dissection in some cases.
[d]Two skin burns described.
[e]Eleven skin burns described.
[f]One hundred and twenty-four of them are only serologic.

that was not confirmed taking into consideration symptomatic hypocalcemia. Several trials reported an incidence around 10%. Only 5 noncontrolled trials reported an incidence of definitive hypoparathyroidism ranging from 0.4% to 3.6%.[41,46,50-52]

Altogether, no definitive RLNPs nor hypocalcemias were reported in controlled trials; 46 definitive RLNPs and 19 hypocalcemias were reported in the uncontrolled ones. Hemorrhagic complication is reported only in one patient of one article among the randomized trials,[25] in 3 nonrandomized trials with a total of 9 patients,[31,34,36] and in 6 noncontrolled trials for a total of 9 patients. Then, it could be affirmed that in the trials examined hemorrhage had a maximum incidence of around 3%. Only 4 articles among RCTs and 4 among nonrandomized trials reported the incidence of seroma; 6 among RCTs and 3 among nonrandomized trials reported incidence of surgical site infection; but only one RCT and one noncontrolled trial

reported clearly the incidence of keloid scar. It should be noted that the article of Dionigi and colleagues found a difference that was statistically significant in favor of MIVAT concerning total amount of scar complications (infections *plus* seromas *plus* keloids).[29]

Discussion

The need of minimally invasive procedures for removing thyroid gland is founded on several reasons, first epidemiologic characteristic of patients recruited for, with a relative but definite prevalence of young women. For this reason, several techniques, aimed to avoid evident neck scar, have been proposed, but critical aspects of each of these procedures (complexity, invasiveness and postoperative discomfort, length of postoperative hospital stay, complications and sequelae, costs) limit their routine diffusion; moreover, there is a partial lack of RCTs, systematic reviews, and meta-analyses comparing each scarless (in the neck) technique of thyroidectomy to conventional procedure.[12] For these reasons, MIVAT still remains a reliable and easily reproducible technique that allows performing, in selected cases, a thyroidectomy through a very small (1.5-2.5 cm) skin incision.[17] Moreover, this minimally invasive procedure follows the course of conventional procedure, and the video assistance is limited to very few steps, such as laryngeal nerves and parathyroid glands and section of upper thyroid pedicle. For this reason, it can be performed by a surgeon skilled in thyroid surgery without special difficulties.[46] Actually, there is a consensus on good outcomes of MIVAT, mainly concerning better cosmetic results and reduced postoperative pain. Aesthetic improvement has been shown in several studies mainly by using specific questionnaires.[21,22,35] The positive effects on pain control, therefore, is a significantly reduced drug administration. This effect is confirmed also in specific pain evaluation biochemical patterns.[53,54] Increase in operative time can be easily solved by ascending learning curve.[54] The literature is almost unanimous in affirming the similarity of MIVAT and CT in terms of complications, although trials published so far[2,22,23,55] are most frequently an overall view of results and complications not specifically discussed. Only a general review concerning MIVAT complications has been published but no systematic reviews or meta-analyses.[56] To date, the advantages in favor of MIVAT have an historical perspective: in the first years, optimization of cosmetic results was the main concern reported in literature.[57] Afterward, the minimal invasiveness was related to the decrease of surgical stress and reduced requirement of analgesic drugs.[53] Another important interest for MIVAT is the reduced incidence of voice and swallowing symptoms, frequently complained after thyroidectomy, especially conventional,[56,58-60] possibly due to image magnification that allows the external branch of superior laryngeal nerve visualization, general reduction in surgical dissection and, therefore, reduced adhesions in the surgical site.[55] With regard to complication rates, none of the articles included in the present review showed a significant incidence of inferior laryngeal nerve palsy, definitive hypoparathyroidism, and hemorrhage. Regarding scar complications, there is an important lack of information, in particular concerning keloid scar that was examined only in one randomized trial and one noncontrolled trial. This matter should be better studied, because a common criticism could be incision stretch for discrepancy between scar length and gland diameter. Anyway, favorable cosmetic results were declared in several published articles.[21,35,37,46] These favorable results are strengthened by conclusions of Dionigi and colleagues, which showed improved results of MIVAT compared with conventional technique by considering overall wound morbidity.[29] It can be explained with the minimal dissection of subplatysmal space needed during MIVAT, which could be a risk factor of seroma arising and, as a consequence, SSI and impairment of cosmetic result.

Our systematic review has some limitations. First, the heterogeneity of trials enrolled and, in particular, the prevalence of noncontrolled trials (n = 17) compared with the randomized (n = 8) and the nonrandomized trials (n = 7). However, we aimed to verify the real foundation of safety of MIVAT with a number of articles as wide as possible in an up-to-date perspective. Since the last meta-analysis appeared in literature concerning MIVAT results dated back to 2015, more trials worthy of systematic evaluation have been published.[20]

Conclusion

The results of this systematic review allow concluding that MIVAT is a safe and reproducible surgical technique. It does not pay a price in terms of increase in complication rate, especially considering permanent ones, such as hypocalcemia and inferior laryngeal palsy. In fact, no controlled trial showed a statistically significant difference in hypocalcemia and nerve injury. Only one article showed a difference in transient hypocalcemia including both clinical and biochemical evaluation. The noncontrolled trials showed results in terms of complications quite similar to that reported for CT. Finally, even scar complications seem to be at least similar, with a possible positive effect toward seroma.

Thus, we can confirm the overall safety of MIVAT and, therefore, we can conclude that this technique, when its indications were strictly applied, guaranteed favorable outcomes; so it should have a wider application in mean-high-volume surgery centers for thyroidectomy.

Author Contributions

Study concept and design: Gregorio Scerrino, Giuseppina Melfa, Giuseppe Salamone, Calogero Porrello, Gaspare Gulotta, Gianfranco Cocorullo
Acquisition of data: Cristina Raspanti, Giulia Rotolo, Leo Licari, Tommaso Fontana, Roberta Tutino
Analysis of data and interpretation: Gregorio Scerrino, Giuseppina Melfa, Leo Licari
Study supervision: Gregorio Scerrino, Leo Licari

Declaration of Conflicting Interests

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