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Minimally invasive video-assisted thyroidectomy: reflections after more than 2400 cases performed

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Abstract
Background The minimally invasive video-assisted approach was developed for primary hyperparathyroidism in 1997 and the year after for thyroid disease. Since then, the technique has been adopted worldwide, and indications moved from the initial benign disease to low-risk and intermediate-risk carcinoma, demonstrating a level of oncologic radicality comparable to the conventional open approach when inclusion criteria are strictly respected.
Methods Between 1998 and 2014, 2412 minimally invasive video-assisted thyroidectomies (MIVAT) were performed in our department. The indication for surgery in 825 patients (34.3 %) was a malignant tumor, in particular, a papillary carcinoma in 800 patients. Among them, 528 patients operated on between 2000 and 2009 had a mean complete follow-up of 7.5 (standard deviation, 2.3) years.
Results A total thyroidectomy was performed in 1788 patients (74.1 %) and a hemithyroidectomy in 564 (23.4 %). Also performed was central compartment lymphadenectomy in 31 patients (1.3 %) and parathyroidectomy for the presence of a solitary parathyroid adenoma in 29 (1.2 %). Mean duration of the procedure was 41 (standard deviation, 14) minutes. After a mean follow-up of 7. 5 years, 528 patients who underwent MIVAT for low-risk or intermediate-risk papillary carcinoma presented a cure rate of 85 % (undetectable thyroglobulin), comparable with the 80 % rate reported in patients who had undergone open thyroidectomy during the same period.
Conclusions After a long experience and a considerable number of procedures performed in a single center, MIVAT is confirmed as a safe operation, with a complication rate comparable with open thyroidectomy. MIVAT offers a cure rate for the treatment of low-risk and intermediate-risk malignancies that is comparable with an open procedure when inclusion criteria are strictly respected.

Keywords Thyroid carcinoma · Minimally invasive video-assisted thyroidectomy (MIVAT) · Thyroidectomy

After the first videoscopic procedure [1] in the neck was proposed in 1996 to operate on primary hyperparathyroidism (PHP), other approaches were soon conceived, partly to avoid long insufflations in the neck [2] and partly to find other viable accesses for operations on the thyroid gland. These operations suggested not only a cervical access, such as minimally invasive video-assisted thyroidectomy (MIVAT) [3], but also extracervical accesses such as the axillary [4], the breast [5], and others [6].

The thyroid endoscopic operation that has probably become more widespread, not only in Europe but also in the USA [7], has been the MIVAT, although some limited modifications from the original description have been necessary to adapt it to different backgrounds [8]. Despite the preference by most AA to restrict MIVAT to benign diseases [9], the indications were soon expanded [10], particularly when the first reports appeared [11, 12] showing that the completeness of the procedure could also guarantee a radical oncologic resection.

After more than 2400 cases performed in our department by using this procedure during a 16-year period, we undertook a complete review of the entire series, together with an extensive examination of the corresponding literature, to evaluate the results and limits of this technique.

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Patients and methods

MIVAT has been our technique for minimally invasive access to thyroid diseases since the late 1990s [3], and despite the recent introduction of robot-assisted trans-axillary thyroidectomy (RATT) in our practice, MIVAT remains our most performed minimally invasive operation in the neck. We consistently perform MIVAT through a 1.5-cm incision, 2 cm above the sternal notch in the central neck, using a 30°, large 5-mm endoscope. The technique, characterized by external retraction without any insufflation of the neck, has already been widely described [13].

Our experience with MIVAT is represented by 2412 cases between 1998 and 2014 comprising 351 men (14.5 %) and 2061 women (85.5 %), with a mean age of 40.3 [standard deviation (SD), 12.3] years. They represent approximately 15 % of the entire series of 36,122 thyroidectomies performed in the same period in our unit. According to the preoperative ultrasound workup, the mean thyroid volume was 15 (SD, 6.25) mL and the mean diameter of the predominant nodule was 22.6 (SD, 11) mm (Table 1). Among the inclusion criteria for patients undergoing this procedure are that the diameter of nodules must not exceed 3.5 cm, with a maximum total thyroid volume of 20 mL. A significant degree of echographically evident thyroiditis and the presence of enlarged lymph nodes suggestive of malignancy constitute an absolute contraindication for this surgery.

One of the main indications was papillary carcinoma, but another significant indication was the indeterminate or Thy3 nodule. In particular, 825 patients (34.3 %) were operated on for a malignant tumor, which was papillary carcinoma in 800 patients (Fig. 1). All papillary carcinomas in the present series were preoperatively staged as low-risk or intermediate-risk tumors [12].

Table 1 Patients' variables

Variables	*n*/ %
Patients	2412
Male	351/14.5 %
Females	2061/85.5 %
Mean age	40,30 years (DS 12.3)
Mean age M	40,28 years (DS 12.3)
Mean age F	40,32 years (DS 12.3)
Mean thyroid volume	15 mL (DS 6.25)
Mean nodule diameter	22.6 mm
Surgical procedures	
Total thyroidectomy	1788/74.1 %
Hemithyroidectomy	564/23.4 %
Tx + central compartment	31/1.3 %
Tx + parathyroidectomy	29/1.2 %

Fewer cases were represented by medullary carcinomas and by prophylactic thyroidectomy in carriers of the *RET* gene mutation (15 patients). In only three patients was the procedure performed for a thyroglossal duct carcinoma. MIVAT was performed in 971 patients (40.2 %) for the presence of an indeterminate lesion. The indications in the remaining 594 patients were toxic goiter in 156 (6.4 %) and multinodular goiter in 438 (18.2 %; Table 1). A completion thyroidectomy was the indication in 22 patients (0.9 %).

All patients underwent a direct laryngoscopy before and after surgery. Definitive hypoparathyroidism was defined when the 6-month postoperative concentrations of parathyroid hormone and serum calcemia were <13 and 8.0 mg/dL, respectively.

The ultrasensitive method for measuring thyroglobulin serum levels is used. The first measurement is currently performed 6 months after surgery. If radioactivated iodine ablation is not performed, the measurement will be repeated 18 and 36 months after surgery in the presence of constant values of thyroglobulin. The measurement in a patient who undergoes radioactivated iodine ablation is performed 6–8 months after its administration (12–14 months after surgery). In the presence of undetectable serum thyroglobulin levels, the measurement will be performed 18–24 months after the last measurement. If thyroglobulin is detectable, the procedure will be repeated 12 months after the last measurement, and a test is also performed under stimulation.

Indications for postoperative radioiodine ablation for differentiated thyroid carcinoma in our center at the time of the treatment were as follows:

- Single focus of carcinoma larger than 1 cm
- Multifocal disease
- Locally advanced disease
- Presence of lymph nodes metastases
- Presence of distant metastases

Results

A total thyroidectomy was performed in 1788 patients (74.1 %) and a hemithyroidectomy in 564 (23.4 %). A central compartment lymphadenectomy was performed in 31 patients (1.3 %) with a preoperative diagnosis of neoplasm, and 29 patients also underwent a parathyroidectomy for the presence of a solitary parathyroid adenoma (1.2 %) during a total thyroidectomy. A PHP had been diagnosed in 20 patients before surgery, and the adenoma was not known preoperatively in 9 patients. Mean duration of the procedure was 41 (SD, 14) minutes (Table 1).

A conversion to standard open thyroidectomy (SOT) was necessary in 41 patients (1.7 %), mainly because of

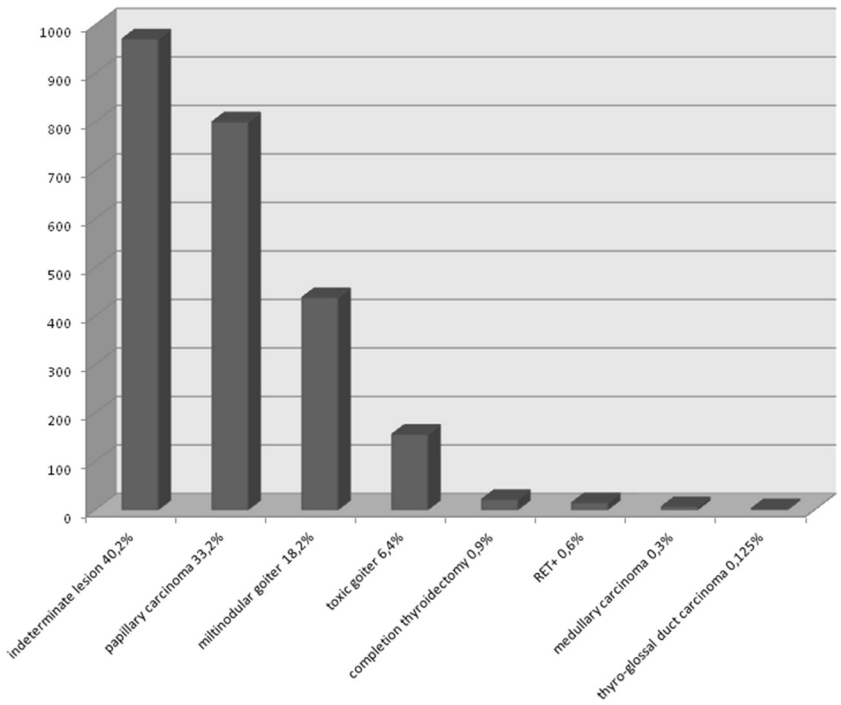

Fig. 1 Preoperative diagnosis

bleeding from the upper pedicle in two patients, unexpected posterior tracheal invasion in 18, involvement of lymph nodes not evident at echography in five, esophageal infiltration in five, infiltration of strap muscles in four, and finally, because of the presence of serious thyroiditis that had escaped the ultrasonographic evaluation in seven patients (Table 2). Three patients (0.12 %) required a reoperation because of a postoperative hematoma. The mean hospital length of stay after surgery was 1.5 days.

Complications included transient hypoparathyroidism (Table 2) in 5 % of the patients, whereas only 0.4 % experienced a definitive hypoparathyroidism. Definitive unilateral recurrent nerve palsy occurred in 30 patients (1.2 %), and wound sepsis occurred in three patients.

The final histologic assessment confirmed the presence of a papillary carcinoma in all patients who had undergone surgery with this diagnosis. Of the 971 patients whose indication for surgery was an indeterminate nodule, 167 were found to have a papillary carcinoma at the final histologic assessment. In more detail, 155 of the 822 follicular nodules showed a papillary carcinoma, mainly in its follicular variant, and 12 of 135 oxyphilic nodules showed a papillary carcinoma (none were a Hurtle cell carcinoma; Fig. 2). An incidental carcinoma was found in three of the 438 patients operated on for multinodular goiter (422 patients with only multinodular goiter and 16 with also a PHP).

A completion thyroidectomy was necessary in only 22 of 564 patients because a total thyroidectomy had been performed in most of the patients, mainly because a nodule was present in the contralateral lobe.

Table 2 Conversions, operative time and complications

Conversions	41/1.7 %
Mean operative time	41 min (DS 14)
Mean hospital stay	1.5 day
Complications	
Transient hypoparathyroidism	120/5 %
Definitive hypoparathyroidism	10/0.4 %
Unilateral recurrent nerve palsy	30/1.2 %
Wound sepsis	3/0.12 %
Hematoma	3/0.12 %

Follow-up

MIVAT was performed in 825 patients for a differentiated thyroid cancer. Because the recruitment of patients with carcinomas was very limited in the early phase of our experience, we started our oncologic database from the year 2000. From that point to 2009, 598 patients underwent a total thyroidectomy for a papillary carcinoma. The database did not have an evaluation for 70 patients, and they were considered as lost at follow-up; consequently, a full follow-up was possible in 528 patients only. Mean follow-up was 7.5 (SD, 2.3) years. Thyroglobulin was undetectable in 450 patients (85.2 %) but was detectable in 78 patients (14.8 %), with a mean value of 0.47 (SD, 0.62) ng/mL (Table 3).

Radioactive iodine treatment was administered to 490 patients (92.8 %); of these, 420 (79.5 %) received a single

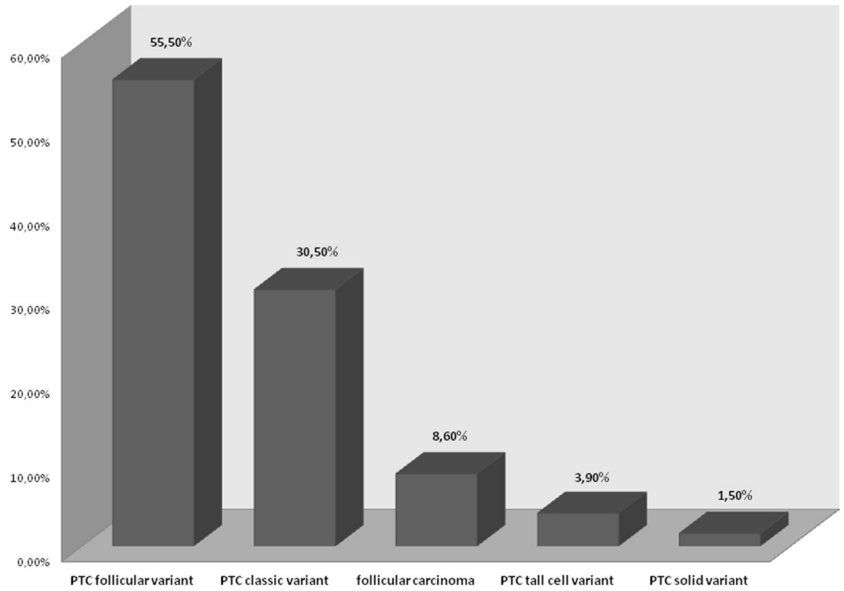

Fig. 2 Histology of indeterminate nodules ultimately found to be malignant

Table 3 Patients' follow-up

Variables	*n*/ %
Patients affected by PTC	528
Mean duration of follow-up	7.5 years (DS2.3)
PTC recurrences	24/4.5 %
Tg undetectable (<0.1)	450/85.2 %
Tg detectable (mean value 0.47 DS 0.62)	78/14.8 %

dose of 31.65 (SD, 12.96) mCi, and multiple administrations were necessary in 70 patients (13.3 %). The mean dose was 159.3 (SD, 56.3) mCi in residual disease and was 265.5 (SD, 97.2) mCi in recurrent disease. Thirty-eight patients did not receive radioactive iodine treatment (Table 4).

Recurrence was documented in 24 patients (4.5 %; Table 3). A redo surgery was performed in 14 patients, and 10 were treated with a repeat administration of radioactive iodine. In the same period (2000–2009), 234 patients with a comparable stage disease underwent a conventional thyroidectomy. The cure rate in this control group was very similar: after an identical follow-up, 80 % of the patients were cured.

The 15 patients harboring a *RET* gene mutation who had undergone a prophylactic thyroidectomy showed undetectable serum levels of calcitonin 6 months after the operation, and this value did not change over the years.

Discussion

Although the technical aspects of the MIVAT operation have remained mostly the same throughout the years, some adaptations seemed necessary in different surgical settings, such as in the USA, where Terris et al. [8] described very few marginal changes. In the most recent reports [14, 15], a trend toward a slight enlargement of the skin incision was noted, leading to 3–3.5-cm wounds, but this was mainly due to the effort of expanding the indications for MIVAT to larger-sized nodules and higher-volume glands [10, 15, 16]. Despite this trend elsewhere, the length of the incision in our series did not vary throughout the years, remaining within 1.5–2 cm according to the original description [13].

The expanded indications, of course, involve not only the size of the lesions but, more consistently, also the nature of these lesions. In fact, in an early phase, all the endoscopic accesses proposed for the thyroid in the cervical area [3] or in an extracervical region [4–6] implied a preoperative diagnosis of benign disease. Only few years later did some studies state that an endoscopic thyroidectomy could reach the same level of completeness as a conventional operation [11]. These studies encouraged many authors to use MIVAT to treat malignant thyroid tumors or at least low-risk or intermediate-risk

Table 4 Radioiodine ablation table

Patients (528)	I131
38/7.2 %	Not performed
420/79.5 %	Single ablation (31.65 mCi DS 12.96)
50/9.5 %	Remnant ablation multiple ablations (159.3 mCi DS 56.3)
20/3.8 %	Recurrence ablation multiple ablations (265.5 mCi DS 97.2)

differentiated carcinomas [12, 17]. In particular, one prospective randomized controlled study conclusively demonstrated that the outcome in lymph node recurrence for these low-risk and intermediate-risk papillary carcinomas was the same after MIVAT as after conventional surgery after an adequate follow-up period [12].

The general outcome of our patients who have undergone a thyroidectomy for a malignancy (Table 3 and 4) seems to confirm that the choice of performing a MIVAT in these patients was fully justified. Evaluation of thyroglobulin serum levels also shows excellent results, and so does the general dosage of radioactive iodine necessary for completion and for recurrence in this cohort. Furthermore, all of the patients carrying a *RET* gene mutation who have undergone a prophylactic thyroidectomy [18] via the MIVAT approach show undetectable serum levels of calcitonin. It is not surprising then that malignant tumors constitute more than one-third of the patients in the present series.

Despite this, some AA still tend to limit MIVAT only to benign nodules [5, 18, 19]. The reason is probably due to the personal attitude of the single surgeons toward the necessity of performing a central compartment lymphadenectomy together with thyroidectomy also in low-risk malignancies: no doubt in this case the operation is more challenging and time-consuming. Although we and others [17] have demonstrated the feasibility of the VIth level clearance during MIVAT, some degree of reluctance by few surgeons to approach malignancies by video-assisted surgery can be justified.

The low rate of recurrences (4.5 %) does not reflect the general outcome of differentiated thyroid cancer because all of the patients who underwent a MIVAT were low-risk and, to a lesser extent, intermediate-risk patients [32]. Likewise, the low rate of postoperative hypoparathyroidism (Table 2) should not be a surprise, because the patients who underwent MIVAT were the simplest ones, characterized by small size and the absence of lymph node involvement.

The incidence of permanent recurrent nerve palsy (Table 2) does not appear to exceed the overall trend in similar series [32] but still might be considered as being quite elevated in a tertiary referral center. We point out, however, that patients presenting with a malignancy or a lesion suspicious for malignancy comprised a large proportion of this sample. We further speculate that because we extensively use an ultrasound scalpel (see Fig. 3) to coagulate and divide vessels, the heat transmission could be responsible for this rate. More recently we began more liberal use of small clips to divide the tiny vessels crossing the recurrent nerve. Although we do not yet have comparative data, this could help to further reduce the incidence of this complication.

The conversion rate of 1.7 % is basically quite low (Table 2) and is linked mainly, if not uniquely, to an underestimation of the preoperative echography. In particular, even small differentiated carcinomas, when located posteriorly, can involve a tracheal or esophageal infiltration that could escape ultrasonographic detection. Severe thyroiditis can also escape detection because its diagnosis is generally based on a morphologic echographic pattern rather than on serum levels of antibodies, which were not routinely measured in these patients.

In several controlled studies in which MIVAT was compared with SOT or minimally invasive nonendoscopic thyroidectomy, MIVAT is characterized by a longer operative time, although some significant advantages, such as cosmetic effect and postoperative pain, are almost always reported in favor of MIVAT [14, 19–21]. This does not reflect our data (Table 2), except in the very early phase of our experience when a proper learning curve had not yet been accomplished [11]. This might be the case for some of these studies, where, for example, fewer than 70 MIVAT were performed during a 4-year period [14]. The mean operative time for SOT in our unit is 42 (SD, 10) minutes, which does not differ from that of MIVAT (41 min). Moreover, other controlled studies comparing MIVAT with SOT have reached the same conclusions, stating that the difference in operative time is not statistically significant [22–25].

The comparison would probably be more realistic when considering only centers performing high volumes of MIVAT, as witnessed by reports focused on the learning curve [26, 27]. Our own learning curve is depicted in Fig. 3, where some critical points are clearly highlighted. What could be done to achieve adequate skill more quickly, deserves further comment. We strongly recommend two points at the beginning of the experience: first, to strictly respect the inclusion criteria, in particular the difficulty raised by the presence of a possible thyroiditis, and second, to always start with incisions significantly larger than those that could be used after an adequate experience. This simple trick would leave time for the surgeon to become accustomed watching the screen instead of the operative field, and the incision length could be reduced as time goes by.

Apart from our first reports [28], where postoperative pain was evaluated and compared with SOT, no data were collected from the entire series. The literature, in fact, seems concordant about a better postoperative outcome of MIVAT versus SOT. Several prospective controlled studies seem to confirm this [21, 22, 24, 28–30]; in some series, the conclusion is also supported by the decreased consumption of opiates and analgesics after MIVAT [14]. Even more convincing are the results of evidence-based analysis and reviews [19, 31–33]. These same reviews are also

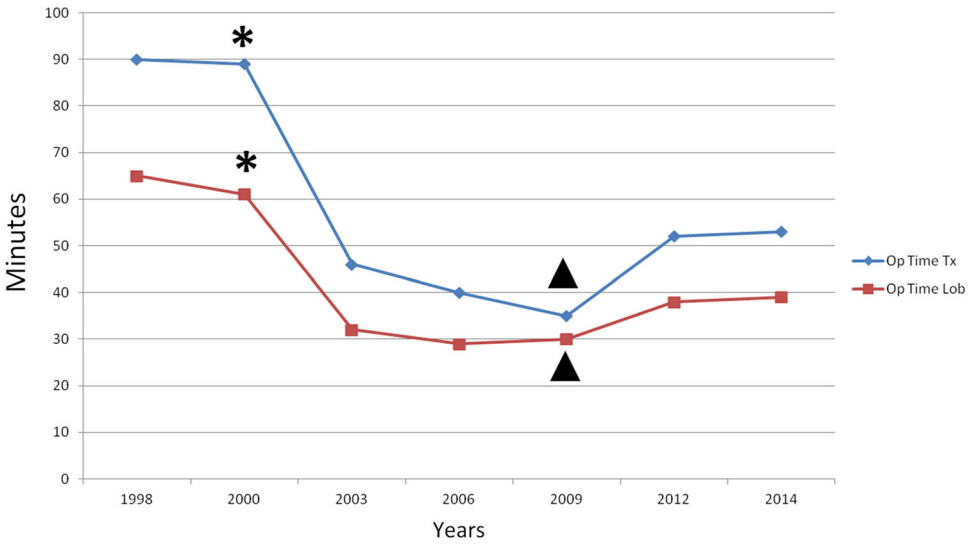

Fig. 3 Learning curve MIVAT. *Asterisk* introduction of harmonic scalpel, *Filled triangle* in 2010 our department moved to a new hospital where operative room sessions were doubled and two new young surgeons, taken from the pool of assistants, started operating

concordant on the better cosmetic result of MIVAT versus SOT [30–34], particularly when expressed as a patient satisfaction score [19]. Even on the long-term (2-year follow-up), the patient and the observer scar assessment score are in favor of MIVAT [35]. Having a consistent experience also with robotic-assisted transaxillary thyroidectomy (RATT), we can assess that RATT seems not to supersede MIVAT in patient satisfaction when two groups of patients undergoing thyroidectomy are compared, and this was demonstrated in a recent controlled study by our group [36].

No doubt the advantage of MIVAT versus RATT is readily evident in cost, especially given that MIVAT always proved not to involve additional costs compared with SOT because most of the instruments are reusable and the energy devices necessary for MIVAT are used in SOT as well [37]. As a further advantage of MIVAT, this approach was recently demonstrated to be safe in patients with a high body mass index [38]. Although we do not have this parameter collected in our database and hence we cannot do a direct comparison, we always assumed that obesity is not a contraindication for this approach because the use of the endoscope also allows optimal visualization in short necks.

Conclusions

After a long experience and a considerable number of procedures performed in a single center, MIVAT is confirmed as a safe operation with a complication rate comparable to SOT. MIVAT can be proposed for the treatment of low-risk or intermediate-risk malignancies and offers significant advantages against classic approaches but needs an adequate learning curve (Fig. 3). This issue characterizes one of the limits of the technique: in fact, the appropriate skills can be achieved quite quickly as long as patient recruitment is adequate, as pointed out by some AA [33].

Another important limit of MIVAT is that, despite the expanded surgical skills by surgeons who have adopted it and the significant technical improvements, this remains an operation still limited to a minority of patients, and the main limit is the size of the nodule and the gland, as we already indicated. This means <20 % of the patients can take advantage of this approach in our experience [32], but the number increases significantly in the USA experience, where approximately 30 % of the patients can undergo MIVAT, according to several reports [7, 10]. This difference could be consistent with the differences of thyroid size existing between endemic and nonendemic goiter regions.

Finally, this operation offers a very good cosmetic outcome, and the scar is barely visible after a limited time. However, the scar lies in the cervical area and can be cosmetically unfavorable if the patient develops a keloid [35]. For this reason, the option of a transaxillary access might be considered in such cases.

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