Langenbecks Arch Surg (2015) 400:247–252
DOI 10.1007/s00423-014-1270-y

ORIGINAL ARTICLE

A comparison of the outcome using Ligasure™ small jaw and clamp-and-tie technique in thyroidectomy: a randomized single center study

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Received: 7 April 2014 / Accepted: 28 December 2014 / Published online: 13 January 2015

Abstract
Purpose Hypoparathyroidism and paralysis of the recurrent laryngeal nerve (RLN) still remain the most frequent specific complications of thyroid surgery. This study evaluates the effects of employment of a recently introduced device (LigaSure™ Small Jaw, LSJ), compared to the traditional clamp-and-tie (CT) technique, on the short- and long-term outcome of the patients who underwent thyroidectomy.
Methods This prospective, randomized study included 190 patients enrolled from October 2011 to July 2013. The numbers of patients in the LSJ group and the CT group were both 95. We studied the following: operative times, intraoperative and postoperative blood losses, intact parathormone (iPTH) and calcium serum levels, and the incidence of RLN paralysis.
Results The two cohorts were homogeneous for age, sex, surgical indication, BMI, ASA score, and estimated thyroid volume. Operation time has been 73.90±23.35 min in group CT and 60.20±22.36 min in group LSJ (p=0.002). Intraoperative blood losses have been 47±18 ml in group CT and 38±14 in group LSJ (p=0.002), while postoperative blood losses have been 45±21 ml in group CT and 40±20 in group LSJ (p=0.105). The mean calcium blood level in group CT has been 8.12, 7.79, and 7.92 mg/dl in the first, second, and third postoperative days, respectively, as well as 8.26, 7.97, and 8.22 mg/dl for group LSJ (p>0.05). Basal and post-thyroidectomy iPTH levels have been 46.49 and 23.64 pg/ml in group CT (Δ=49.15 %), as well as 51.06 and 27.73 (Δ=45.69 %) in group LSJ (p>0.05). Permanent RLN paralysis was 1.05 % in LSJ group and 0 % in CT group.
Conclusion The employment of LSJ reduces in a statistically significant way both operative times and intraoperative blood losses. No significant differences were found as far as postoperative RLN paralysis and hypoparathyroidism.

Keywords Thyroidectomy · LigaSure Small Jaw · Clamp-and-tie technique · iPTH · RLN paralysis

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Introduction

At the end of the nineteenth century, Theodor Kocher developed and standardized a surgical technique of precise tying of peduncle vessels and meticulous thyroid gland dissection. This innovation, along with the progress of antisepsis and asepsis, allowed, just in the years he received the Nobel Prize for Medicine, to reduce below 1 % both morbidity and mortality related to thyroid surgery [1]. Since then, there were no substantial improvements in thyroid surgery. In the last two decades, there has been an introduction of new surgical techniques such as the minimally invasive video-assisted approach, the intraoperative recurrent laryngeal nerve (RLN) monitoring and new hemostatic devices [2].

LigaSure™ Small Jaw (LSJ), according to its producer, Covidien [3], provides a combination of pressure and energy to create vessel fusion, of which permanently seals vessels up to 7 mm in diameter. TissueFect™ sensing technology monitors changes in tissue impedance 3.333 times a second and adjusts energy output accordingly to deliver the appropriate amount of energy for the desired tissue effect. LigaSure™ tissue fusion, like LigaSure™ vessel sealing, uses the body's own collagen and elastin to create a permanent fusion zone. Therefore, hemostasis is not related to thrombus formation in

the proximal vessel, and the effect is limited to the target tissue or vessel without charring and with a limited (less than 2 mm) thermal diffusion to adjacent structures [4]. The absence of clips and sutures reduces the infectious risk and fibrosis [5].

The thyroid, due to its vascularization and to the delicacy of adjacent anatomical structures, is an ideal field of application for LSJ. The latter has, in comparison with the previous LigaSure™ Precise (LSP), an incorporated tissue divider [6]. Since September 2011, we have used this device to seal, cut, blunt dissect, and atraumatically grasp, thus minimizing the exchange of surgical instruments if compared to traditional "clamp-and-tie" technique or the previous LSP.

Presently, there are few guidelines for the employment of hemostatic devices in thyroid surgery [7]. The aim of this study has been to verify the results of LSJ in thyroid surgery, in comparison with conventional surgical techniques, on patients' outcome. We have analyzed safety and efficacy of this device in terms of hemostasis, reduction of operative time, and effects on intact parathormone (iPTH) blood level and RLN paralysis.

Material and methods

From October 2011 to July 2013, we enrolled 190 patients scheduled for total thyroidectomy. Inclusion criteria were all the total thyroidectomies performed for benign disease, 18 years and older.

Exclusion criteria included the following: previous thyroid surgery, preoperative cytological diagnosis of thyroid cancer, associated parathyroid diseases, or abnormalities of vocal cords motility evaluated by preoperative routine laryngoscopy. The approval of the Departmental Ethical Board was requested and obtained.

Primary endpoints were the functional outcomes, hypoparathyroidism and RLN paralysis. Secondary endpoints considered the following intraoperative outcomes: operative time, blood loss, and postoperative outcomes such as drain output or neck fluid collection.

A preoperative thyroid volume valuation was obtained using ultrasound gland measures according to the ellipsoid formula (height × width × depth × 0.529 and both lobe volumes are added) [8].

Preoperative serum calcium, corrected, if required, according to albumin levels, has always been within normal ranges, as well as measurement of iPTH level performed on peripheral blood samples before induction of anesthesia and therefore administration of propofol, a drug which could modify its level [9].

Written informed consent was obtained, and patients have been randomized into two groups: 95 patients underwent total extra capsular thyroidectomy with traditional clamp-and-tie technique (CT group), while in 95 patients, vascular pedicle were sealed by LSJ (LSJ group) and no sutures were performed. Bipolar forceps were used in both techniques with the same application. No clips were used.

Just before the thyroidectomy, a software randomized patients into one of the two groups. All patients were operated on by two surgeons (F.M.F. e G.P.); both of them had performed more than 1000 thyroidectomies and had previous experience with LSP. Duration of surgery was calculated from cutaneous incision to skin closure.

Intraoperative blood losses have been calculated by the increased weight of the gauzes used (giving to whole blood a specific weight of 1.050 g/cc), adding the amount of blood within aspirator. All thyroidectomies were performed under general anesthesia and orotracheal intubation on patients with a hyperextended neck and slight anti-Trendelenburg position.

We performed a transverse cervicotomy 2–3 cm above the jugulum; after an incision of platysma and of linea alba colli, strap muscles were divaricated. The RLN was searched and identified in each procedure, and the division branches of superior and inferior thyroid vessels were cut close to the thyroid capsule. A careful exploration was performed to preserve as many parathyroids as possible, avoiding an excessive dissection, searching for one or two missing parathyroids. Ten minutes after thyroidectomy, iPTH was measured again, and if there was a difference (Δ) of >75 %, the parathyroids were evaluated. If one was devascularized, it was replanted, after fragmentation, in a pouch within the sternocleidomastoid muscle. The same procedure was performed in case of a parathyroid gland accidentally removed. The replantation time was not considered within the operative time. We subsequently anatomically closed the surgical wound after positioning a Redon drain in the surgical wound; the removed thyroid gland was sent for definitive histological examination and searched for parathyroids.

iPTH measurement has always been performed by immunological PTH-STAT (short turnaround time) Elecsys, which gives results in 9 min. The range of this test is 15–65 pg/ml. Postoperative hematic losses have been evaluated considering the content of the drain during the first postoperative day (1POD).

Vocal function has been evaluated immediately after surgery and on 1POD. All patients underwent an ear nose throat specialist visit and a laryngoscopy to evaluate the motility of the true vocal cords on 2POD.

The morning after surgery, the iPTH level was measured once again; furthermore, patients have been monitored at 24, 48, and 72 h to detect postoperative hypocalcemia defined as a corrected level of total serum calcium ≤7.6 mg/dl (1.9 mmol/l) at 72 postoperative hours.

Incidence and severity of hypocalcemia, as well as the related signs and symptoms, if present, were registered on the appropriate form. Patients with hypocalcemia at discharge

(CA3POD) received a prescription for calcium 1000 mg and calcitriol 0.25 mcg three times per day.

Hypocalcemia was considered permanent when requiring calcium supplements 6 months after thyroidectomy; RLN paralysis was considered permanent if lasting more than 6 months after surgery. The outcome assessor was blinded until the completion of the study.

All variables underwent bilateral Z test on means for independent samples for two groups, as usual for these sample sizes that allow to apply central limit theorem. The objective is to accept alternative hypothesis with significance values $\alpha = 0.05$ and power=90 % (evaluated with respect to null basic parameter values given by previous estimates of CT similar groups) when the difference of interesting means is at least higher than 5 %. Analysis was performed by using the SPSS software package version 21 (SPSS Inc., Chicago, IL).

Results

All the 190 patients enrolled met the inclusion criteria, and no patient refusal or dropout was registered.

The two cohorts were homogeneous for age, sex (16 males in each group), surgical indication, body mass index (BMI), American Society of Anesthesiologists (ASA) score, and estimated gland volume. Tables 1 and 2 show baseline data. The quantitative variables have been compared using normal Z test, categorical variables (ASA, indication) using χ^2 test, and BMI using ODDS ratio. The p values show that the two groups are not significantly different.

Mean age was 49.27 years (±10.99 SD) for group CT and 48.42 (±10.81 SD) for group LSJ, with 16 males in group CT (8.4 %) and 16 in group LSJ.

Most thyroidectomies (154 cases out of 190, 81 %) were performed for multinodular goiter, followed by Hashimoto thyroiditis (17/190, 8.9 %) and Basedow disease (8/190, 4.2 %); a follicular proliferation was present in 11 cases (11/190, 5.8 %).

Table 1 Baseline comparison of the two groups (n=190). Analysis of quantitative variables

	Age (years)		Gland volume (ml)	
	CT	LSJ	CT	LSJ
Min	28	25	7.03	6.87
Max	75	80	17.38	17.70
Mean	49.27	48.42	12.49	12.58
Median	45	48	12.40	12.49
SD	10.99	10.81	2.46	2.57
p value	0.44		0.72	

Table 2 Baseline comparison of the two groups (n=190). Analysis of categorical variables

BMI			ASA class			Indication		
	CT	LSJ		CT	LSJ		CT	LSJ
≤24.9 kg/m^2	38	34	I	16	17	Multinodular goiter	73	81
≥25 kg/m^2	57	61	II	40	37	Basedow	3	5
ODDS ratio	1.196		III	35	37	Follicular	7	4
Test statistics	0.596		IV	4	4	Hashimoto	12	5
p value	>0.5		p value	>0.3		p value	>0.2	

Table 3 shows description of the variables in the groups. Table 4 shows the results of variables: time of surgery, intraoperative blood losses, and postoperative blood losses. Duration of thyroidectomy has been 73.90±23.35 min in group CT and 60.20±22.36 min in group LSJ (p=0.002).

Intraoperative blood losses have been 47.44±18.14 ml in group CT and 37.90±14.36 in group LSJ (p=0.002), while postoperative blood losses (Redon drainage) have been 45.37±21.37 ml in group CT and 39.80±20.50 in group LSJ (p=0.105).

Both experimental and control groups were made up of 95 patients. LSJ means have generally been superior than group CT, but there is a statistical significance ($p \leq 0.05$) only for operative time and intraoperative blood losses.

Figure 1 shows comparisons between means of three measurements (first, second, and third postoperative days) of serum calcium: CA1POD, CA2POD, and CA3POD. In this case, a bilateral test for CA1POD has been performed to verify the equivalence of the value in the populations. There was no statistically significant difference between observed values ($p > 0.05$), although the means of the CT group were lower in every measurement.

Seventeen group CT patients (17.9 %) showed hypocalcemia (<7.6 mg/dl) versus 12 group LSJ patients (12.6 %) (p=0.42). Figure 2 shows the means for variables iPTH basal, iPTH, and post-iPTH1POD, without any statistical significance ($p > 0.05$).

Parathyroid auto-transplantation was performed in nine group CT patients (9.4 %) and in ten group LSJ patients (10.5 %): Postoperative calcium levels were below normal respectively in six and seven patients. Overall, only two patients (one of group CT and one of group LSJ) needed calcium supplements at 6 months follow-up.

In six patients (three from group CT and three from group LSJ), there was an alteration of vocal function with decrease of the vocal tone. In five out of six cases, postoperative indirect laryngoscopy on 2POD did not show hypomobility of vocal cord, and this symptom has been treated by systemic as well as by nebulizer cortisone therapy with complete "restitutio ad integrum". In one case, 1.05 % (group LSJ),

Table 3 Description of variables in the two groups

	Time (min)	Ca 1POD (mg/dl)	Ca 2POD (mg/dl)	Ca 3POD (mg/dl)	PTH basal (pg/dl)	PTH post (pg/dl)	PTH 1POD (pg/dl)	Intraop. blood loss (ml)	Redon (ml)
Group CT									
Min	40	6.8	6.2	6.4	11.2	4	2.3	22	10
Max	100	10.9	9.8	9.6	79.7	84.5	69.9	102	120
Mean	73.90	8.12	7.79	7.92	46.49	23.64	22.30	47.44	45.37
Median	70	8.4	8.1	8	42.5	17.5	23.65	42	50
SE	1.4	0.07	0.09	0.09	1.97	1.81	1.61	1.87	2.11
95 % CI	(70.84, 76.32)	(8.11, 8.39)	(7.7, 8.07)	(7.81, 8.17)	(44.18, 51.89)	(20.16, 27.25)	(19.26, 25.63)	(43.57, 50.8)	(38.29, 46.65)
Group LSJ									
Min	35	7.1	6.2	6.4	17.6	5.4	2.3	10	10
Max	130	10.9	9.8	9.8	130	73.1	67	86	100
Mean	60.20	8.26	7.97	8.22	51.06	27.73	22.26	37.90	39.80
Median	60	8.2	7.9	8.3	41.05	19.1	23.75	34	50
SE	1.41	0.06	0.08	0.09	2.49	2.00	1.78	1.55	2.04
95 % CI	(58.07, 63.62)	(8.06, 8.32)	(7.71, 8.04)	(7.94, 8.330)	(45, 54.75)	(21.36, 29.22)	(19.45, 26.42)	(34.2, 40.28)	(38.42, 46.42)

there was a hypomobility of the vocal cords, with lowered vocal tone at 6 months follow-up. We did not observe postoperative major bleedings, infections, seromas, or hematomas. There were no parathyroids in each postoperative specimen.

Discussion

Thyroid is a surgical field where precision and thoroughness are highly important. The anatomical knowledge, as in every surgical procedure, should always be associated with the more appropriate instruments. A comparison of an old, albeit effective, surgical technique with a new and advanced device, yet not fully investigated, is not trivial.

According to the observed results, by using LSJ, there was a significant reduction of postoperative time: 13.7 min (18.64 %), which optimized the utilization of the operative room. According to literature, there is a reduction of operative time of 6.4–32.4 min in LigaSure™ thyroidectomy [10, 11], which may counterbalance the price of the disposable device [12–15].

There was a 20.1 % (p=0.002) reduction of the intraoperative blood loss; according to many papers, LigaSure™ also reduces the length of surgical incision, the postoperative pain, and the duration of hospital stay without raising the complication rate [13–15].

We did not observe statistically significant differences between the sutureless and conventional techniques as far as calcium and iPTH levels; however, group LSJ showed CA1POD, CA2POD, and CA3POD progressively higher (+1.72, +2.31, and +3.79 %) if compared with group CT (Fig. 1).

Postoperative hypocalcemia, although always reported by the literature as the most frequent complication, varies in definition among studies. Dionigi et al. [16] defined it temporary if the patient was symptomatic or serum calcium <2.2 mmol/l for at most 12 months and permanent if it lasted over 12 months. Pons et al. [17] defined the hypocalcemia temporary when the ionized calcium was <1.8 mmol/l for at most 1 month after surgery, permanent if over 1 month. Regardless this important inhomogeneity, a recent meta-analysis by Edafe et al. [18] reported a median incidence of transient and permanent hypocalcaemia after total thyroidectomy being 27 (19–38) and 1 (0–3)%, respectively. In our series, the total incidence was 15.6 % (29 patients out of 190), with no statistical significant difference in the two compared groups.

We evaluated the effects on RLN not only by the vocal assessment but also by indirect laringoscopy on 2POD. A study reported that symptomatic vocal assessment is not a sufficient evaluation ,and 2POD is the most proper timing to assess a possible nerve injury [16]. The results of our experience did not show any difference regarding short-term vocal evaluation using the two surgical techniques, therefore confirming literature data. The clamp-and-tie technique may have a lower incidence of permanent RLN paralysis according to the results of a recent network meta-analysis [7], although

Table 4 Bilateral normal mean tests of variables: time of surgery and intraoperative and postoperative blood loss

	Time		Intraoperative blood loss		Redon	
	Z value	p value	Z value	p value	Z value	p value
Difference of means	2.91	0.002	2.8	0.002	1.26	0.105

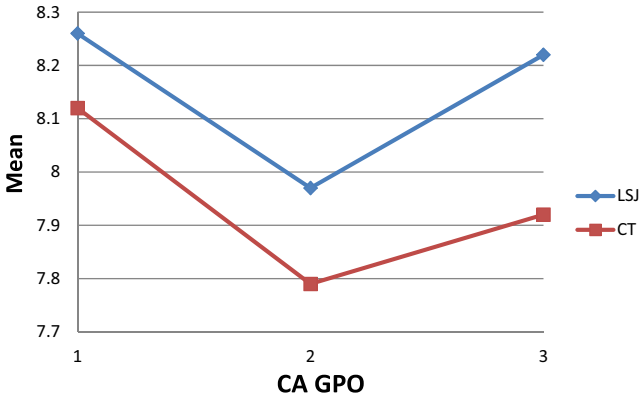

Fig. 1 Mean values of CA POD in the two groups

in our experience, the incidence on our population did not allow to draw conclusions.

Some other vessel closing techniques have been released on the market, including harmonic scalpel and clips, and their outcomes compared to CT have been investigated [19–21]. To our knowledge, this is the first randomized study comparing results of CT technique and LSJ applied to total thyroidectomy, as other authors performed only thyroid lobectomy [22], or their paper was a retrospective historical control study [23]. The major limitation of all these studies is that the operating surgeon could not be blinded to the result of randomization, although this bias is impossible to remove.

Despite the fact that the present study was not designed for a cost analysis, it was able to shed some light on the subject. The use of a technological device is undoubtedly more expensive than resorbable sutures or clips. Nevertheless, some studies investigating different devices showed no difference in cost compared with traditional hemostasis methodologies [24]. Moreover, taking into account charges for operating room times and the estimated saving in operative time, hemostasis devices use may be cost-effective [11, 12]. In addition, those devices might be effectively and safely shared by many patients, contributing to enhanced cost-effectiveness, as previously reported [25].

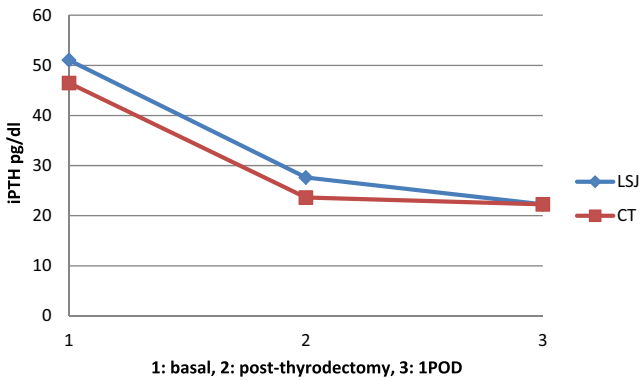

Fig. 2 Mean values of iPTH in the two groups

Conclusion

In conclusion, we did not find statistical significance as far as the rate of RLN paralysis and postoperative hypothyroidism. The usage of an electrothermal bipolar tissue sealing device such as LSJ reduces operative time and intraoperative blood losses in a statistically very significant way. Further studies, multicenter randomized controlled trials, are required to define the technical "gold standard" for thyroid surgery.

Acknowledgments The authors would like to thank Carla Rossi for contributing the statistical analysis.

Funding No funding or sponsoring was received for this study.

Conflicts of interest None.

Authors' contributions Study conception and design were by F.M. Frattaroli and S. Coiro. S. Coiro, F. De Lucia, E. Manna, and J.M. Frattaroli were responsible for acquisition of data. Analysis and interpretation of data were done by F. Fabi, F.M. Frattaroli, and S. Coiro. F.M. Frattaroli and S. Coiro drafted the manuscript. Critical revision of the manuscript was done by G. Pappalardo, F.M. Frattaroli, and S. Coiro.

References

1. Giddings AE (1998) The history of thyroidectomy. J R Soc Med 91(Suppl 33):3–6
2. Alesina PF, Rolfs T, Walz MK (2010) Bipolar thermofusion vessel sealing system (TVS) versus conventional vessel ligation(CVL) in thyroid surgery—results of a prospective study. Langenbecks Arch Surg 395:115–119
3. LigaSure™ Small Jaw Open Instrument. http://surgical.covidien.com/products/vessel-sealing/ligasure-small-jaw#features Accessed 15th February 2014
4. Kennedy JS, Shanahan PL, Taylor KD et al (1998) High burst strength feedback controlled bipolar vessel sealing. Surg Endosc 12:876–878
5. Peterson SL, Stranahan PL, Schmaltz D et al (2002) Comparison of healing process following ligation with sutures and bipolar vessel sealing. Surg Technol Int 10:55–60
6. Glover AR, Gundara JS, Lee JC et al (2014) Thermal sealing systems with and without tissue divider for total thyroidectomy. ANZ J Surg 84(5):383–385
7. Garas G, Okabayashi K, Ashrafian H et al (2013) Which hemostatic device in thyroid surgery? A network meta-analysis of surgical technologies. Thyroid 23(9):1138–1149
8. Shabana W, Peeters E, De Maeseneer M (2006) Measuring thyroid gland volume: should we change the correction factor? AJR Am J Roentgenol 186:234–236
9. Sokoll LJ, Drew H, Udelsman R (2000) Intraoperative parathyroid hormone analysis: a study of 200 consecutive cases. Clin Chem 46: 1662–1668
10. Marrazzo A, Casà L, David M et al (2007) Thyroidectomy with LigaSure versus traditional thyroidectomy: our experience. Chir Ital 59(3):361–365
11. Saint Marc O, Cogliandolo A, Piquard A, Famà F, Pidoto RR (2007) LigaSure vs clamp and-tie technique to achieve hemostasis in total thyroidectomy for benign multinodular goiter: a prospective randomized study. Arch Surg 142(2):150–157

12. Kirdak T, Korun N, Ozguc H (2005) Use of Ligasure in thyroidectomy procedures: results of a prospective comparative study. World J Surg 29:771–774
13. Parmeggiani U, Avenia N, De Falco M et al (2005) Major complications in thyroid surgery: utility of bipolar vessel sealing (Ligasure Precise). G Chir 26:387–394
14. Petrakis IE, Kogerakis NE, Lasithiotakis KG, Vrachassotakis N, Chalkiadakis GE (2004) LigaSure versus clamp-and-tie thyroidectomy for benign nodular disease. Head Neck 26:903–909
15. Shen WT, Baumbusch MA, Kebebew E, Duh QY (2005) Use of the electrothermal vessel sealing system versus standard vessel ligation in thyroidectomy. Asian J Surg 28:86–89
16. Dionigi G, Boni L, Rovera F, Rausei S, Castelnuovo P, Dionigi R (2010) Postoperative laryngoscopy in thyroid surgery: proper timing to detect recurrent laryngeal nerve injury. Langenbecks Arch Surg 395(4):327–331
17. Pons Y, Gauthier J, Ukkola-Pons E et al (2009) Comparison of LigaSure vessel sealing system, harmonic scalpel, and conventional hemostasis in total thyroidectomy. Otolaryngol Head Neck Surg 141:496–501
18. Edafe O, Antakia R, Laskar N et al (2014) Systematic review and meta-analysis of predictors of post-thyroidectomy hypocalcaemia. Br J Surg Mar 101(4):307–320
19. Docimo G, Ruggiero R, Gubitosi A et al (2012) Ultrasound scalpel in thyroidectomy. Prospective randomized study. Ann Ital Chir 83(6): 491–496
20. Duan YF, Xue W, Zhu F et al (2013) FOCUS harmonic scalpel compared to conventional hemostasis in open total thyroidectomy—a prospective randomized study. J Otolaryngol Head Neck Surg 42(1):62
21. Diener MK, Seiler CM, von Frankenberg M et al (2012) Vascular clips versus ligatures in thyroid surgery—results of a multicenter randomized controlled trial (CLIVIT Trial). Langenbecks Arch Surg Oct 397(7):1117–1126
22. Hirunwiwatkul P, Tungkavivachagul S (2013) A multicenter, randomized, controlled clinical trial of Ligasure small jaw vessel sealing system versus conventional technique in thyroidectomy. Eur Arch Otorhinolaryngol 270:2109–2114
23. Kuboki A, Nakajama T, Konno W et al (2013) New technique using an energy-based device versus conventional technique in open thyroidectomy. Auris Nasus Larynx 40:558–562
24. Targarona EM, Balague C, Marin J et al (2005) Energy sources for laparoscopic colectomy: a prospective randomized comparison of conventional electrosurgery, bipolar computer-controlled electrosurgery and ultrasonic dissection. Operative outcome and costs analysis. Surg Innov 12(4):339–344
25. Meurisse M, Defechereux T, Maweja S, Degauque C, Vandelaer M, Hamoir E (2000) Evaluation of the Ultracision ultrasonic dissector in thyroid surgery. Prospective randomized study. Ann Chir 125(5): 468–472