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Effectiveness of an advanced hemostatic pad combined with harmonic scalpel in thyroid surgery. A prospective study

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ABSTRACT

Introduction: Hemostasis during thyroidectomy is essential; however the most efficient and cost-effective way to achieve this is unclear. The aim of this study was to evaluate the outcome of total thyroidectomy (TT) performed with the combination of harmonic scalpel (HS) and an advanced hemostatic pad (Hemopatch).

Methods: Patient undergone TT were divided into two groups: HS + hemopatch and HS + traditional hemostasis groups. The primary endpoint was 24-h drain output and blood-loss requiring reintervention. Secondary endpoints included surgery duration, postsurgical complications and hypocalcemia rates.

Results: Between September 2014 and March 2015, 60 patients were enrolled (30 to Hs + Hemopatch, 30 to Hs and standard hemostasis); 71.4% female; mean age 48.5 years. The 24-h drain output was lower in the HS + hemopatch group compared with standard TT. HS and hemopatch also had a shorter mean surgery time ($p < 0.0001$) vs standard TT.

Conclusion: combination of hemopatch plus HS is effective and safe for TT with a complementary hemostatic approach.

1. Introduction

Total thyroidectomy (TT) is the preferred option for the management of benign multinodular goiter and the standard treatment for cancer [1–4]. An accurate dissection and hemostasis is essential in order to provide a clear surgical field during TT, minimize the risk of structural damage, prevent post-surgical hemorrhage and avoid the need for surgical drains; however, the safest, most efficient and cost-effective way to achieve these goals is still under debate. Besides the traditional surgical hemostatic techniques, different hemostatic approaches which further minimize the risk of bleeding and complications during thyroidectomy have become available. These include ultrasonic coagulation [5–15], bipolar coagulation and modern topical hemostatic agents [16–18].

2. Methods

2.1. Study design

This single-center, prospective study investigated the hemostasis efficacy and safety of Advanced Hemostatic Pad. The bovine collagen patch coated with a protein reactive pentaerythritol polyethylene glycol ether tera-succinimidyl glutarate (NHSPEG) is Hemopatch (Baxter AG, Vienna, Austria) (PCC).

When in contact with tissue, NHS-PEG forms covalent bonds between the collagen pad and tissue proteins, which seals the tissue and induces hemostasis in open and laparoscopic procedures.

Two groups were assessed: patients receiving Hemopatch, and

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patients receiving traditional hemostatic procedures alone (gauze, ligature, electrocauterization) during TT. The study was conducted in accordance with the Declaration of Helsinki and according to local and regional ethical standards. Written informed consent was obtained from all patients.

2.2. Patients

Patients were included if they were 18–70 years of age and were planning to undergo total thyroidectomy due to thyroid disease. Patients were excluded from the study if they had diabetes, chronic renal disease or other metabolic diseases, had received previous neck irradiation or surgery, had cervico-mediastinal goiters, required lymphadenectomy, had a planned video assisted thyroidectomy (minimally invasive) or one lobe pathology where only hemi-thyroidectomy was planned, had known coagulopathy, had active or past history of malignant systemic disease, were pregnant or lactating females, were known to abuse drug or alcohol, or were receiving chronic cortisone or platelet inhibitors.

2.3. Treatments and surgical technique

Total thyroidectomy was performed using institutional guidelines by experienced surgeons. A 4–6 cm Kocher incision was made at the lower neck crease two fingers above the suprasternal notch with a scalpel. Traditional hemostatic procedure was performed as follows: after division of the platysma, the cervical linea alba is opened without division of the strap muscles. The thyroid lobe is dissected progressively from the strap muscles. Thyroid vessels were ligated and divided, rotating the thyroid lobe medially before dividing vessels in the ligament of Berry, supervising and saving the recurrent laryngeal nerve, and the thyroid lobe is removed. The procedure was repeated for the contra lateral lobe. After a check for hemostasis, a drain is placed in the thyroid bed. The cervical linea alba and platysma are sutured with absorbable sutures, and the skin is closed by an intracutaneous running suture. Surgical hemostasis is used if additional hemostasis was deemed necessary and Hemopatch was used for bleeding not responding to in particular in the Gruber and Sappey ligaments, avoiding electrocautery injuries to recurrent nerves.

In all patients a suction surgical drain was placed for the first 24 h, as part of this study, in order to better objectivize and quantify blood loss, although some centers did not longer consider drainage useful after thyroidectomy.

All patients received the same postoperative protocol. Surgical drain was removed after 24 h; a neck ultrasonographic evaluation was performed 48 h after surgery to verify the presence of seroma or blood collections. All patients in the study were discharged on postoperative day 3 (72 h after surgery) for better evaluation of the postoperative course. The postoperative follow-up care included indirect laryngoscopy to check vocal cord mobility. An indirect laryngoscopy was performed on postoperative day 2 to assess transitional or permanent paralysis of laryngeal nerve; in case of incidence of dysphonic voice, laryngoscopy was also reconsidered after 1 week and 3 months.

The serum calcium level also was measured for all patients at 6, 12, 24, 48 h. In case of symptomatic hypocalcemia, intravenous calcium was administered; in asymptomatic hypocalcemic patient, oral calcium was given.

2.4. Study endpoints

The primary endpoint was the drain output (ml) after 24 h and the presence of a significant blood loss (if patient needed to return to OR). Secondary endpoints included presence of seroma, the duration of surgery, post-surgical complications and postsurgical serum calcium level.

2.5. Statistical analysis

Qualitative and quantitative descriptive analyses were performed for all the variables collected. Qualitative variables were analyzed using frequencies and percentages. Quantitative variables were studied through the mean, standard deviation (SD), median and interquartile (IQR) range (25 percentile e 75 percentile).

Parametric (analysis of variance [ANOVA]) and nonparametric tests (Wilcoxon) were used for comparisons of numerical variables. For the primary endpoint a Bonferroni adjustment was performed to account for multiplicity. Fisher's exact test was used for comparison of categorical variables. In all statistical hypotheses, the significance level was set at a ¼ 0.05. All analyses were performed with the SPSS software version 17.0.

3. Results

3.1. Baseline characteristics and patient disposition

Between September 2014 and March 2015, 60 patients were enrolled (30 to Hemopatch, 30 to standard hemostasis). Of the 60 patients, 70% were female and the mean age was 42.3years.There were no meaningful differences between the two treatment groups with respect to demographic or baseline characteristics (Table 1). However, the type of thyroid disease in each group varied slightly between the treatment groups.

3.2. Surgical outcome

Surgery was uneventful in the majority of patients. Three patients standard TT had surgical complications, with one patient having dysfonia with a saturated O_2 of 98%.Compared with Hemopatch group, fewer patients who received standard hemostasis during surgery had a dry surgical field at the end of surgery and before placement of the drain according to the surgeon (100% vs 85.6%, $p < 0.001$). No other meaningful differences between the two treatment groups with respect to surgery were reported.

3.3. Efficacy outcomes

The mean of 24-h drain output was 50.1 ± 21.4 mL in Hemopatch group vs 90.3 ± 24.2 mL in standard TTgroup (95% CI _ 63.5, _32.3; $p < 0.0001$) (Table 2).

Incidence of post-operative seroma was higher in standard hemostasis group.

There was a statistically difference in the length of surgery: patients in the Hemopatch group had a shorter mean surgery time, compared with standard hemostasis ($p < 0.0001$) (Table 2). Only

Table 1
Baseline characteristic/demographics and surgical parameters.

Characteristic/Demographics	Hemopatch TT (N = 30)	Standard TT (N = 30)
Mean age, years	50.2 ± 11.7	49.5 ± 12.1
Range	22.1–70.5	22.8–68.8
Gender N (%)		
Male	8 (26.6)	10 (30.3)
Female	22 (73.4)	20 (69.7)
Thyroid disease, N (%)		
Goiter	26 (80.6)	24 (80)
Hyperthyroid goiter	2 (9.7)	3 (10)
Carcinoma	2 (9.7)	3 (10)

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Table 2
Secondary endpoints.

Outcome	Hemopatch TT (N = 30)	Standard TT (N = 30)
Drain output over 24 h, ML		
Mean ± SD	50.1 ± 21.4	90.3 ± 24.2*
Length of surgery, min.		
Mean ± SD	52.8 ± 16.2	80.1 ± 21.2*
Hospital stay, days		
mean ± SD	2.5 ± 0.56	2.68 ± 0.58

*p < 0.001.
SD: Standard deviation.

two patient in standard hemostasis group developed temporary laryngeal nerve paralysis; however, this condition resolved at the 3-month follow-up visit. No significant differences in the rates of hypocalcaemia (serum calcium <8.0 mg/dL) were observed between treatment groups (p = 0.37). Laboratory hypocalcaemia was reported in 18.6% and 21.7% of patients in the Hemopatch group and standard hemostasis groups, respectively. Similar results for the rate of symptomatic hypocalcaemia was also observed (p = 0.52).

4. Discussion

To our knowledge this is the first study to investigate the hemostasis efficacy and safety of Hemopatch in patients undergoing TT. This study showed that the use of Hemopatch can reduce drain output compared with the standard TT, avoiding post-operative seroma incidence.

Another study [19] shows that using a combination of Floseal plus the HS is effective and safe for TT. Mean surgery time can be reduced as well as 24-h post-surgical drain output and seroma formation, without any increased risk of post-surgical complications. In our study the latter model of HS, the Harmonic Focus, was used. It has been shown that this device can reduce mean operative time in a prospective randomized study that compared outcomes using two models of HS: the Harmonic Focus (n = 45) and the older Harmonic Ace (n = 45) in patients undergoing thyroid surgery [20]. We found similar data regarding operative time, showing a reduction in the duration of surgery, allowing a shorter anesthesia and a possibility to save time for other surgery in a single center. All of the surgeons who performed TT in this study were considered experts, with over 100 previous thyroidectomies conducted. The effect of a surgeons previous experience had been investigated in a retrospective analysis which considered the effect of the 'learning curve' in the use of the HS, by comparing outcomes after total thyroidectomy in the 12 months prior to adoption of the HS (2003; n = 77) and in a period of12 months, 2 years after the HS was adopted (2006; n = 106). Results showed that, once past the learning curve, the HS significantly reduces operative time and postoperative hypocalcaemia, and is as safe as conventional surgery with regard to voice change and bleeding. These individual studies showing benefits with the HS are further supported by three meta-analyses [21,22].

Cost-effectiveness of the HS over traditional methods has also been demonstrated in an analysis of data from a randomized controlled trial of 198 patients undergoing surgery with the ultrasound scalpel (n = 96) or traditional surgical methods (n 0102) using a hospital, third party payer and societal perspectives [23]. The HS provided a shorter mean operation time (p < 0.001) and greater improvements in quality of life (p = 0.002) versus traditional methods and cost effectiveness was demonstrated from a hospital perspective (saving euro 119/patient) and a societal perspective (lower medical and non-medical resource consumption during the 3 months post discharge follow-up period), calculated as an overall saving of V325.36/patient [24].

Haemorrhage after thyroid surgery is rare, but if it occurs it is a life-threatening condition necessitating emergency surgery. Swirta [25] in a retrospective analysis in a group of 8931 consecutive patients report 40 (0.45%) patients with haemorrhage and emergency surgery. Bleeding occurred within first 24 h following surgery in 38 (95%) patients; risk factors were identified: male sex, older age > 70 years, hyperthyroidism, smoking and thyroid operation undertaken by resident in training in general surgery.

Godbale [26] in a cohort study in 5490 patients report 4.2% hemorrhage frequency, and identified independent risk factors for hemorrhage age, male gender, malignant histology and extent of surgery. Median time for onset of postoperative hemorrhage was 3 h (range 0–105).

Promberger [27] in a retrospective analysis about 30,142 patients report 519 postoperative bleeding (1.7%). Risk factors identified were older age, male sex, extent of resection, bilateral procedure and recurrent disease. Postoperative bleeding occurred in 336 (80.6%) patients within the first h after surgery. Nine patients required urgent tracheostomy and three patient died (mortality rate of 0.01% overall and 0.6% among patients who had surgery for postoperative bleeding).

Weiss [28] in a bivariate analysis of the Nationwide Inpatient Sample database about 150.012 patients report 1.25% rate of hematoma after thyroidectomy. Female sex and high-volume hospitals were important for decreased hematoma risk. Black race, age >45 years, infiammatory thyroid disease, partial thyroidectomy, chronic kidney disease and bleeding disorders increased risk of hematoma.

Campbell [29] in a retrospective multicentric case-control study identified 207 patient who developed a hematoma requiring return to the operating room after thyroidectomy. 47% of hematoma patients returned to the OR within 6 h and 79% within 24 h after thyroidectomy. Risk factors were age, male patients, smokers, anticoagulation medications, Grave's disease, a drain placed, higher pressures postoperatively.

Dehal [30,31] in two retrospective analysis of hospital discharge data from the Nationwide Inpatient Sample database about 147.344 thyroid operation performed between 2000 and 2009 report incidence of postoperative neck hematoma of 1.5%.Higher risk were age 65 years and older, male sex, African Americal race, alcohol abuse, Graves disease, substernal thyroidectomy. Postoperative neck hematoma was 2.1, 1,4 and 0.9% among procedures performed by low-volume, intermediate-volume and high-volume surgeons respectively.

Dixon [32] in a retrospective review of 4140 thyroid operations report a cervical hematoma in 18 patients (0.43%). Emergent bedside decompression was required for only two patients and the remaining 16 patients were explored in the operating room utilizing initial local anesthesia in 11 patients.

In our study, incidence of post-operative complications was low in both groups, in particular for vocal cord palsy. Our findings are in agreement with those reported in previous similar studies [33–38]. The lack of post-surgical complications including nerve injuries at the 3 months' follow-up in any groups was expected due to the high level of surgical expertise. However, substituting electric coagulation near Gruber ligament with hemostasis provided by Hemopatch, could lower incidence of accidental recurrent nerve lesions.

There were also no significant differences between treatment groups in the rate of hypocalcaemia. However, the rate was lower in the Hemopatch group versus standard TT (18.6% vs 21.7%, respectively). This little difference can be explained by a diminished parathyroid gland "stupor" from electrical spread using Hemopatch.

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5. Conclusions

This study shows that using a combination of Hemopatch plus the HS is effective and safe for TT. Mean surgery time can be reduced as well as 24-h post-surgical drain output and seroma formation, without any increased risk of post-surgical complications. We believe that Hemopatch plus the HS could provide a complementary hemostatic approach in patients undergoing total thyroidectomy. Further research is required to investigate the cost effectiveness of this combined approach in patients undergoing thyroidectomy compared with convention and other approaches.

Ethical approval

Ethical approval was requested and obtained from the "Azienda Universitaria Seconda Università di Napoli" ethical committee.

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Author contribution

Roberto Ruggiero: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data; also participated substantially in the drafting and editing of the manuscript.

Ludovico Docimo: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data; also participated substantially in the drafting and editing of the manuscript.

Salvatore Tolone: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data; also participated substantially in the drafting and editing of the manuscript.

Maurizio De Palma: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data; also participated substantially in the drafting and editing of the manuscript.

Mario Musella: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data; also participated substantially in the drafting and editing of the manuscript.

Angela Pezzolla: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Adelmo Gubitosi: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Domenico Parmeggiani: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Raffaele Pirozzi: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Simona Gili: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Simona Parisi: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Antonio D'Alesssandro: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Giovanni Docimo: Gave final approval of the manuscript.

Conflicts of interest

All Authors have no conflict of interests.

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