



Predisposing factors for seroma formation in patients undergoing thyroidectomy: Cross-sectional study



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ABSTRACT

Introduction: Seroma is defined as collection of fluid within the surgical site during postoperative period that causes several complications. Recognition of predisposing risk factors can lead to avoid seroma formation after thyroidectomy.

Materials and methods: A cross-sectional study was carried out during a 3-year period and 678 patients were enrolled the study. We recorded demographic data, past medical history and the type of thyroidectomy were for all patients. We measured total and ionized serum calcium and albumin level in all patients before surgery and a day after it. All patients underwent total or subtotal thyroidectomy and if needed central neck dissection was performed subsequently. Patients underwent serial aspiration if they had seroma formation.

Results: The overall post-thyroidectomy seroma incidence was 2.2%. There was no statistically significant correlation while evaluating gender, age and body mass index with post-operative seroma formation. However, seroma formation was significantly higher in patients underwent total thyroidectomy ($P = 0.041$). The results of postoperative laboratory tests showed a significant lower level of ionized calcium in patients with seroma formation ($P < 0.0001$). Logistic regression showed statistically significant value for variables including age, BMI and decreased ionized calcium level, in developing of seroma. **Conclusion:** We showed that Seroma formation was lower during thyroidectomy via electrical vessel sealing system in comparison with previous studies. In our study, older age, greater body mass index and decreased ionized calcium level were predictors of seroma formation.

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1. Introduction

Recent development in thyroid neoplasms diagnosis has led to increase in number of thyroidectomies [1,2]. Although, it has been a minimally invasive and safe procedure since the late nineteenth century, some serious complications associated with parathyroid and thyroid surgeries result in patients dissatisfaction and prolonged hospitalization [3,4]. According to previous studies, main complications of thyroid surgeries includes recurrent laryngeal nerve injury, hypocalcemia, surgery site infection, hematoma and

seroma formation [5,6].

Seroma is defined as collection of fluid within the surgical site during postoperative period. Seroma formation is one of the common complications of surgeries such as, breast, laparoscopic inguinal hernia repair, and axillary lymphadenectomy [7,8]. The reported incidence for seroma subsequent to conventional thyroid surgery varies from 1.3% to 7%. Cosmetic problems, regional swelling, flap necrosis, and risk of surgical site infection are the most common complications, due to seroma formation among thyroidectomy patients, that lead to prolonged hospital stay and higher admission costs [9,10].

The overall etiology and pathophysiology of the seroma is not completely understood [11]. To prevent development of seroma, some surgeons benefit neck drainage after thyroidectomy. However, its overall efficacy is still unknown, considering studies that

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suggested the drains to be used only in critical cases or when the dead space is very large, [4,12].

Considering several complications of the seroma and lack of the appropriate prevention for this undesirable issue, recognizing risk factors may lead to avoid it in thyroidectomy patients. In addition, it has been hypothesized that serum calcium level may play a role in seroma formation through affecting coagulation process [11]. In current study, we aimed to study the predisposing factors on post-operative seroma incidence in patients underwent thyroidectomy by electrical sealing tools.

2. Materials and methods

2.1. Study population

In order to evaluate predictive factors of seroma formation in patients undergo thyroidectomy, an observational cross-sectional study was carried out in thoracic surgery wards of Imam Reza and Taleghani hospitals, Tabriz, Iran. The study protocol was approved by ethics committee of Tabriz University of Medical Sciences, and our report designed in line with the PROCESS criteria [13]. We studied 738 consecutive patients between March 2013 to March 2016, who underwent thyroid surgery including total thyroidectomy (with or without neck dissection), near total thyroidectomy, subtotal thyroidectomy.

Patients with history of coagulopathies or anti-coagulant drugs consumption (who had impaired results of prothrombin time (PT), partial thromboplastin time (PTT) and international normalized ratio (INR) test), hypocalcaemia (total calcium < 8.5 mg/dL or ionized calcium < 1.9 mmol/dL) and calcium supplement consumption, were excluded. In addition, patients who suffered complications such as surgical site infection, recurrent laryngeal nerve palsy and hematoma, did not enroll in the study. Of 738 patients, 60 patients excluded and 678 patients enrolled the study. All patients provided written informed consent to participate in the study. Demographic data including age, sex, body mass index (BMI) were collected prospectively from hospital records for all patients during admission, as well as clinical characteristics such as past diseases history, drug history, thyroid examination, surgical procedure and perioperative course. We measured serum total and ionized calcium level and albumin level in all patients one day prior to the surgery and first postoperative day. Demographic features (including age, sex), body weight, body height, history of hypertension, thyroidectomy type, serum calcium level and serum albumin level were evaluated for further correlation with seroma formation.

2.2. Procedure

All patients underwent surgery and operations were performed by an experienced surgeon (S.Z.R.H, general and thoracic surgeon) with more than 10 years' of experience in thyroid surgery, using LigaSure™ Small Jaw (LSJ) Instrument. Thyroid surgery was performed using a 3–4 cm collar incision immediately 1 cm below cricothyroid cartilage. Platysma muscle was cut and subsequently superior and inferior subplatysmal flaps were raised up to the superior border of thyroid cartilage and sternal notch, respectively. In order to provide enough exposure of thyroid gland, especially in large goiters, strap muscles were divided by monopolar cutter in midline. Then, superior thyroid pedicle was individually divided and ligated. Subsequently, recurrent laryngeal nerve (RLN) were identified as well as parathyroid glands in each side and preserved if possible. Subsequently, inferior thyroid pedicle was ligated using LSJ. Inadvertently removed parathyroid glands or glands with disrupted blood flow were immediately auto transplanted in

ipsilateral sternocleidomastoid (SCM) muscle. Hemovac drain implantation was up to surgeon's decision and placed into the thyroid bed deep to the strap muscles to provide neck drainage and fixation was performed by 0–1 silk sutures. Patients' drains were removed if drainage was < 50 cc in a 48-hour period.

Post-operative physical examination was performed by the surgeon, at the end of the first and third weeks, as well as the end of the second month postoperative. In case of clinical suspicion for fluid accumulation in surgical site, patients underwent neck ultrasonographic study. Subsequently, percutaneous aspiration was done using a 5 cc syringe with 21-gauge pinhead, and aspirated fluid amount measured and recorded. All patients with seroma underwent serial aspiration until resolution.

2.3. Statistical analysis

All data were analyzed using SPSS version 22. Software (SPSS Inc., Chicago, IL). In order to express quantitative values, we used mean \pm SD. Variables analysis performed using student t-test and X [2] test for paired data analysis and results with $p < 0.05$ were considered as statistically significant. A linear regression was run to determine the effect of age, gender, smoking, hypertension, surgery type, drain implementation and serum calcium on post operative seroma formation.

2.4. Ethics

To participate in study, all patients asked to provide their informed consent. This study was approved by the Institutional Review Board (IRB) of the Research Chancellor of the Tabriz University of Medical Sciences, Tabriz, Iran.

3. Results

In current study, 678 patients undergone subtotal and total thyroidectomy, enrolled. Of 678 patients, 560 (82.5%) were female and 118 (17.5%) were male with mean age of 43.39 ± 3.52 . One hundred-and-four patients (15.3%) had positive history for hypertension disease and had received anti-hypertensive drugs. Patients' demographic data including body height and weight, body mass index (BMI) and surgical procedures are summarized in Table 1. Drain implemented in 183 patients (26.9%), who were suspicious to develop hematoma, considering thyroid bed-side after resection. Of 183 patients, 147 patients (80.3%) had undergone total thyroidectomy with subsequent neck dissection and 36 patients (19.7%) underwent total thyroidectomy without neck dissection.

Post-thyroidectomy seroma developed in 15 patients (2.2%). Of these, seroma formation detected in 10 (66.7%) patients during first post-operative week, and in 5 patients (33.3%) during second post-operative week. All patients were undergone total thyroidectomy, however, neck dissection was performed only in 8 patients (53.3%). Seroma location was above suprasternal notch in all patient, however, extended up to level of the superior thyroid notch of thyroid cartilage in 2 patients. The suffered area minimum and maximum calculated 6 cm [2] and 15 cm [2], respectively. Seroma aspiration performed as instructed in all suffering patients, and the frequency of aspiration was varying between 1 and 5 attempts. Seroma resolved in most of the patients in less than three aspiration attempts. Aspirated volume and number of attempts to recover patients seroma are listed in Table 2. During follow-up, none of the patients developed post-operative complications such as incision leak due to seroma, cosmetic problems and surgery site infections (SSI).

Comparing seroma incidence with regard to patients' gender, age and BMI correlation with post-operative seroma formation in

Table 1
Patients demographic data and peri-operative findings and their regression for seroma formation.

		Seroma Formation		Pv	Logistic Regression
		No	Yes		
Age		41.56 ± 2.41	43.60 ± 1.37	0.28	0.03
Sex	Female	550 (81.2%)	10 (14.7%)	0.102	0.07
	Male	113 (16.7%)	5 (7.4%)		
BMI		27.19 ± 5.18	28.14 ± 5.41	0.15	0.02
Smoking	non-present	568 (83.8%)	11 (1.6%)	0.109	0.42
	present	95 (14%)	4 (0.6%)		
Hypertension	non-present	569 (83.9%)	5 (7.4%)	<0.0001	0.13
	present	94 (14%)	10 (14.7%)		
Pathology	Multinodular goiter	302 (44.5%)	6 (0.9%)	0.07	–
	MTC	19 (2.8%)	2 (0.3%)		
	PTC	174 (25.7%)	4 (0.6%)		
	Thyroid adenoma	152 (22.4%)	3 (0.4%)		
	Others	16 (2.4%)	0		
Staging	I	47 (22.4%)	0	0.8	–
	II	129 (61.4%)	4 (1.9%)		
	III	23 (11%)	2 (1%)		
	IV	5 (2.4%)	0		
Thyroidectomy	Sub total	73 (11.7%)	0	0.148	0.71
	Total	199 (32%)	8 (1.3%)		
Drain	with CNP	335 (53.9%)	7 (1.1%)	0.114	0.88
	non-present	486 (71.7%)	9 (1.3%)		
	present	177 (26.1%)	6 (0.9%)		

Table 2
Data on patients' seroma volume and its management.

	Minimum	Maximum	Mean ± SE
Occurrence Day	4	13	7.53 ± 0.75
Seroma Volume (cm ²)	6	15	8.20 ± 0.73
Aspirations Number	1	5	2.66 ± 0.27
Fluid Volume (cc)	15	68	38.52 ± 3.83

patients underwent thyroidectomy, no statistically significant difference observed. Seroma formation was significantly higher in patients suffering hypertension compared to normal group (P < 0.0001). There was a significantly higher seroma formation in patients underwent total thyroidectomy (P = 0.041), however, central neck dissection did not lead to increased incidence of seroma (P = 0.095).

Pre-operative and postoperative laboratory tests including preoperative serum albumin level, total and ionized calcium are shown in Table 3. However, there were no significant difference between patients with seroma formation and control group, in terms of preoperative albumin and serum calcium levels. Whereas, postoperative laboratory tests results showed a significant lower level of ionized calcium in patients with seroma formation (P < 0.0001).

Pre and postoperative total and ionized calcium level compared between patients with and without seroma formation, that showed a significant decrease on the level of ionized calcium in patients who suffered seroma (P = 0.03).

To evaluate predisposing factors on seroma formation in

patients with thyroidectomy, we used linear regression, that showed a statistically significant value for variables including, patients age, BMI and decreased ionized calcium level in developing of seroma in patients underwent conventional thyroidectomy with LigaSure™ Small Jaw device.

4. Discussion

In current study, we aimed to evaluate overall incidence and predisposing factors of seroma formation subsequent to thyroidectomies using electrical vessel sealing system. Although, lower incidence of post-thyroidectomy seroma causes to underestimation of this complication, some life-threatening and cosmetic problems should not be ignored. There are very few studies discussed post-thyroidectomy seroma formation, its incidence and management. Our study had some limitations. First, since previous studies had described hypertension as a predisposing factor for seroma formation, we aimed to discuss this hypothesis, however, further studies are needed to evaluate other chronic diseases effect on seroma formation. Second, it is the first study to evaluate changes in calcium level and its effect on postoperative seroma formation in patients underwent conventional thyroidectomy. Therefore, we were unable to evaluate the role of preoperative hypocalcemia treatment in prevention of seroma incidence. In addition, we suppose there is a association between extended surgical field, parathyroid manipulation and postoperative hypocalcemia during total thyroidectomies, which might cause bias in evaluation of hypocalcemia and seroma formation correlation. Third, neck ultrasonography was done only in patients who were clinically suspicious

Table 3
Preoperative and postoperative laboratory findings and their regression for seroma formation.

		Seroma Formation		Pv	Logistic Regression
		No	Yes		
Serum Albumin		4.54 ± 0.21	4.52 ± 0.15	0.71	0.66
Total Calcium	Preoperative	9.12 ± 1.27	9.01 ± 1.96	0.14	0.14
	Postoperative	8.32 ± 1.35	8.38 ± 1.24		
Ionized Calcium	Preoperative	1.07 ± 0.14	1.06 ± 0.09	0.84	0.84
	Postoperative	1.02 ± 0.13	0.92 ± 0.03		

for development of seroma, which prevented us from evaluating patients who had asymptomatic seroma.

Our results showed that overall incidence of seroma formation in patients underwent thyroidectomy by LigaSure™ Small Jaw was 2.2%, however, considering previous studies, seroma incidence subsequent to conventional thyroidectomy has been reported to be approximately 5% [14]. Comparing to literature, incidence of seroma in our study was lower which may be due to use of electrical vessel sealing system that prevented surgery area extension. In study by Shan et al. using breast approach endoscopic thyroidectomy (BAET), seroma incidence was reported to be 2.9% [11]. Although, seroma incidence in patients undergoing robotic thyroidectomy has been reported to be 2%, Ban et al. reported a incidence of 1.73% for chest wall seroma in robot assisted thyroidectomies [11,15]. This discrepancy between several studies on incidence of post-thyroidectomy seroma, may be due to different approaches used in studies. It has been demonstrated that conventional thyroidectomy leads to increased incidence of seroma formation compared to endoscopic techniques. However, considering its unique features, LSJ prevents unnecessary manipulation, despite conventional technique [16]. Thus, we suggest that less manipulation and decreased surgery site extension during thyroidectomy using electrical vessel sealing system might play a role in decreased incidence of seroma formation. We hypothesized that seroma formation subsequent to electrical thyroidectomy is similar to endoscopic approaches, nonetheless, however, further studies are needed to evaluate this hypothesis. Although, endoscopic thyroidectomy has some advantages [11,17,18], need for open surgery in complicated operations and increased incidence of seroma subsequent to this technique [11,19] limits endoscopic thyroid surgery to replace conventional method, as gold standard approach.

We assessed predisposing role of demographic, preoperative and intraoperative factors such as age, gender, BMI, serum calcium levels, and thyroidectomy type, on seroma formation. Older age, increased BMI and severely decreased ionized calcium level are independent factors to facilitate seroma formation on surgical site. In a recent study, they reported age, BMI, history of hypertension and area of surgery extension in subcutaneous layer to have etiologic role for formation of seroma subsequent to breast approach robotic thyroidectomy [11].

Joan et al. reported significant correlation between older age and greater BMI with seroma formation in patients underwent breast reconstructive surgery [20]. Nevertheless, Randolph and his colleagues' experience showed increased seroma formation in patients older than 50 or underwent lymph nodal dissection after breast reconstruction surgery [21], in our study, despite older age, central node dissection during total thyroidectomy had no significant role on post-operative seroma incidence. Therefore, we suggested that older age and greater BMI are predisposing factor for seroma formation subsequent to clean surgeries such as herniorrhaphy, breast reconstruction and thyroidectomies.

Since, the role of calcium is well known in safe and rapid homeostasis and wound healing [22,23], changes in calcium levels may alter the noted processes and increase risk of post-operative seroma and hematoma. Therefore, considering our findings, we hypothesized that hypocalcemia and hypoparathyroidism after thyroidectomy may postpone homeostasis on surgery area leading to seroma formation.

Some studies presented that hypertension history may be a predisposing factor for seroma formation [11,24]. In present study, although seroma incidence was significantly higher in patients with hypertension, linear regression showed no correlation between history of hypertension and seroma formation after thyroidectomy.

Considering seroma management, all patients suffering this complication underwent serial percutaneous aspiration, since it was known as the most effective technique for seroma treatment [25,26]. Most of the patients' seroma resolved following to second aspiration. Only one patient underwent five aspiration attempt which the first one was in the 4th day postoperative and the last one was in the 18th day postoperative. All patients with seroma formation were suffering subclinical hypocalcemia after thyroidectomy, therefore, they received calcium supplementation during their hospital admission period and after discharge if needed. During one-year follow up, none of the patients had any additional complications or cosmetic problems related to their seroma formation. In future studies, sensitivity and specificity of predisposing factors demonstrated in present study need to be evaluated, in order to select best thyroidectomy technique in patients to prevent seroma and its subsequent complications. Although, it would not be const benefit, all patients need to be evaluated via neck ultrasonography to describe overall incidence of seroma, even in asymptomatic patients. In addition, further randomized clinical trials might be useful to compare thyroidectomy techniques in terms of postoperative complications especially seroma.

We concluded that postoperative calcium level changes may predispose patients to seroma formation following thyroid surgery. Seroma formation was lower during thyroidectomy via electrical vessel sealing system, compared to previous studies, due to less extension of surgery area. Older age, greater BMI and decreased ionized calcium were factors that predicted seroma formation in our study. In future studies, patients shall be categorized with regard to extension of surgical field, in order to determine hypocalcemia effect on extension and severity of the seroma properly.

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Author contribution

Dr. Ali Ramouz: study design, data collections, writing.
 Dr. Seyed Ziaeddin Rasihashemi: study design, data acquisition, drafting.
 Dr. Faeze Daghigh: Data analysis, data collections.
 Dr. Esmail Faraji: data collections, writing.
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Conflict of interest

None.

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