# Tisseel and Its Effects on Wound Drainage Post-Thyroidectomy: Prospective, Randomized, Blinded, Controlled Study

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**Abstract**

*Objective:* This randomized, blinded, controlled study examines the effects of fibrin sealant (Tisseel, Laboratoire de production Baxter AG, Vienna, Austria) on wound drainage following thyroidectomy.

*Methods:* Fifty-six consecutive patients were enrolled in the study. Patients were randomized into Tisseel and non-Tisseel treatment groups. Wound drain output was tallied in 8-hour increments by observers blinded to the treatment groups.

*Results:* Fifty-six patients completed the study. Significant decreases in wound drainage were found in the first 8 hours in the Tisseel group. Eight hours postoperatively, wound output in the Tisseel group was reduced by 44% compared with the non-Tisseel group. A significant decrease in the total drainage over the 64-hour time period of 43% was noted between the treatment and control groups. Post-thyroidectomy wound drainage was reduced and trended to earlier drain removal. No significant changes in the length of hospital stay were noted, nor were postoperative complications encountered in either treatment group.

*Conclusions:* Fibrin sealants offer a unique opportunity to safely decrease post-thyroidectomy wound drainage. This investigation furthers the evidence that fibrin sealants could safely enable the implementation of drain-free thyroidectomies.

**Sommaire**

*Objectif:* Cette étude contrôlée, à allocation aléatoire et à l'aveuge examine les effets d'un scellant de fibrine (Tisseel, Laboratoire de production Baxter AG, vienna, Austria) sur le drainage des plaies de thyroidectomie.

*Méthode:* Nous avons enrôlé 56 patients dans cette étude. Les patients ont été randomisés en deux groupes soit un avec, l'autre sans l'utilisation de Tisseel. Le drainage a été mesuré aux 8 heures par des observateurs ne connaissant pas le groupe des patients.

*Résultats:* Cinquante-six patients ont complété l'étude. Nous avons noté une diminution significative de 44% du drainage des 8 premières heures dans le groupe traité avec Tisseel. Pour les 64 premières heures la diminution a été de 43%, elle aussi statistiquement significative. Cette réduction du drainage est associée à une tendance vers un retrait plus précoce des drains. Par contre nous n'avons pas noté de diminution dans le séjour hospitalier et nous n'avons noté aucune complication postopératoire.

*Conclusion:* Le scellant de fibrine offre une opportunité unique de diminuer le drainage post-thyroidectomie. Cette investigation supporte le concept que la colle de fibrine pourrait permettre la thyroiudectomie sans drain.

**Key words:** fibrin glue, thyroidectomy, Tisseel, wound drainage

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Fibrin glues, such as Tisseel, (Laboratoire de production Baxter AG, Vienna, Austria), augment natural healing by mimicking the final stages of the coagulation cascade. This, in essence, forms a stable matrix allowing cells involved in inflammation and wound healing to aggregate in the wound bed.[1] Research has shown that with the addition of fibrin glue, wound healing is enhanced, wound tensile strength is increased, and less edema and fewer ecchymoses are observed.[2–7] Fibrin glues are both biocompatible and biodegradable[8] and

are shown to be completely absorbed within 3 to 7 days following application.[9] A potential disadvantage of using fibrin glues is the theoretical risk of viral transmission from pooled blood donor products. To eliminate the risk of viral transmission, commercial fibrin products undergo stringent donor screening and sterilization.[10–12] In fact, fibrin glues have been commercially available in Europe for over 20 years, with no documented transmission of infection.

Debate over the feasibility and safety of drain-free thyroidectomies has been ongoing for years. Owing to both the serious and occasionally life-threatening risk of postoperative complications, namely, hematomas, seromas, and infection, and despite evidence that not all thyroidectomies require prophylactic drainage,[13,14] many surgeons are reluctant to abandon the use of drains to minimize these risks. As such, studies continue to examine feasible adjuncts to minimize the risk of postoperative complications. Matthews and Briant performed a retrospective analysis of 30 patients undergoing a variety of thyroid surgeries, including parathyroidectomy in the absence of thyroid surgery.[15] In this study, the treatment group received intraoperative pressure followed by fibrin glue and placement of an extra drain. They concluded that the use of fibrin glue decreased postoperative wound drainage and shortened hospital stay.[15] In a retrospective study, Lachachi and colleagues also concluded that fibrin glue was a useful adjunct to thyroidectomy.[16] To date, no prospective, randomized, controlled, blinded study has examined the effects of fibrin glues on post-thyroidectomy wound drainage. This investigation was undertaken to prospectively compare patients undergoing total or hemithyroidectomies in either a control group (non-Tisseel) or a Tisseel-treated group.

## Materials and Methods

### Subjects

Fifty-six consecutive patients between October 2002 and March 2004 undergoing hemithyroidectomy and total thyroidectomy by two surgeons at the University of Alberta Hospital were enrolled. Patients with anterior neck dissection in conjunction with thyroid surgery remained in the study group, but patients with lateral neck dissection were excluded. Patients with lateral neck dissections have increased surgical fields, and it was felt that postoperative drainage would be elevated and not be comparable to the study group. Participating patients consented to enrolment and were older than 18 years of age. Block randomization was chosen to divide patients into Tisseel and non-Tisseel groups as there were multiple surgical centers involved and the number of individuals within the treatment and control groups would remain relatively even. To eliminate any confounding factors, both groups received a single drain and no pressure was applied intraoperatively to either group. The end points of the study included total wound drainage, duration of drain placement, length of hospital stay, and any complications. In compliance with Health Ethics Research Board guidelines, approval was sought and obtained prior to enrolment of patients in the study.

### Surgical Protocol

At the time of surgery, each patient was randomly assigned to either a Tisseel or a non-Tisseel group, recorded in a central location and not noted in the patient's operative record. As such, the nursing staff and patients were blinded to treatment. All surgeries followed a standard approach and procedure. Once hemostasis was achieved, patients either received 2 mL of Tisseel (thrombin 500 IU/mL) applied by Duploject (Laboratoire de production Baxter AG, Vienna, Austria) to the wound bed (Tisseel group) or no treatment (non-Tisseel group). Wound closure continued in a standard fashion for both groups, and each patient received a fully perforated 7 mm Jackson-Pratt drain. Prior to the patient's anesthetic being discontinued, any intraoperative drainage was removed from the suction drain system so that there was no drainage at anesthetic end time (T = 0).

Drainage was measured every 8 hours following anesthetic end time, and drains were removed when the volume was less than 10 mL. Patients were discharged following drain removal if no other medical conditions compelled their continued hospitalization. Follow-up with their surgeon occurred 3 to 4 weeks postoperatively, at which time, the blind was broken. Had any complications been encountered, the blind would have been broken earlier.

### Statistical Analysis

Measurements are expressed as mean ± standard error of the mean. A Student's paired *t*-test examined differences between the Tisseel and non-Tisseel treatment groups on the total amount of wound drainage postoperatively. All other assessments of Tisseel and non-Tisseel groups were performed with a one-way analysis of variance and Tukey comparison, and $p$ values less than .05 were considered significant.

## Results

The addition of Tisseel to the incision during thyroidectomy surgeries caused a reduction in wound drainage. Fifty-six patients, 26 treated with Tisseel and 30 controls, were enrolled in the study; the mean age was 49 and 50 years, respectively. Of these 56 patients, 31 underwent hemithyroidectomy, whereas 25 received

total thyroidectomies (Table 1). All patients enrolled completed the study, and no hematomas, seromas, infection, or recurrent laryngeal nerve injuries occurred in either group. There were no allergic reactions to the Tisseel noted within the treatment group.

Figure 1 demonstrates a significant decrease in Tisseel-treated patients' wound drainage (30.9 ± 2.8 mL) within the first 8 hours following surgery compared with controls (55.1 ± 5.5 mL; $p < .001$). Wound drainage reduction was observed in both hemithyroidectomy and total thyroidectomy treatment groups (Figure 2). Patients who underwent hemithyroidectomy in the Tisseel group had modest drainage (27.1 ± 2.5 mL), whereas hemithyroidectomy patients in the non-Tisseel group produced a significantly larger amount of fluid (53.4 ± 7.5 mL; $p < .001$). Similarly, less drainage (24.5 ± 4.6 mL) was collected from Tisseel patients during a total thyroidectomy, whereas those who did not receive Tisseel had increased drainage (54.3 ± 4.5 mL; $p < .001$). Tisseel treatment also resulted in a decrease in the total drainage from surgical sites. Figure 3 highlights this reduction by displaying both individual data points and the means of all patients within the treatment groups. Patients who received Tisseel had a moderate amount of drainage (69.4 ± 5.3 mL) from the surgical site, whereas patients in the control group had significantly more (121.1 ± 22.1 mL; $p < .001$). Although not statistically significant, there was an improvement at 40, 48, and 56 hours postoperatively in Tisseel-treated groups in relation to earlier drain removal (Figure 4). At these time points, drains remained in only 23.1%, 3.8%, and 0% of Tisseel patients, whereas in the non-Tisseel group, drains were present in 46.7%, 23.3%, and 13.3% of the patients, respectively.

**Table 1** Characteristics of Patients Undergoing Thyroid Surgery

| | *Tisseel* | | | *Non-Tisseel* | | |
|---|---|---|---|---|---|---|
| *Patient* | *Age* | *Sex* | *Surgery** | *Age* | *Sex* | *Surgery** |
| 1 | 64 | F | Hemi | 56 | F | Total |
| 2 | 63 | F | Hemi | 66 | F | Hemi |
| 3 | 27 | F | Hemi | 61 | F | Total |
| 4 | 39 | F | Hemi | 53 | M | Total |
| 5 | 54 | F | Hemi | 49 | M | Hemi |
| 6 | 34 | F | Total | 42 | F | Hemi |
| 7 | 60 | F | Total | 52 | F | Total |
| 8 | 29 | F | Hemi | 31 | F | Hemi |
| 9 | 53 | F | Total | 59 | F | Total |
| 10 | 61 | F | Hemi | 62 | M | Total |
| 11 | 32 | F | Hemi | 59 | F | Total |
| 12 | 49 | F | Hemi | 61 | M | Total |
| 13 | 50 | F | Total | 28 | F | Total |
| 14 | 56 | F | Hemi | 42 | F | Hemi |
| 15 | 53 | F | Hemi | 61 | M | Hemi |
| 16 | 40 | M | Total | 58 | M | Hemi |
| 17 | 73 | M | Hemi | 50 | F | Total |
| 18 | 39 | F | Hemi | 64 | F | Hemi |
| 19 | 71 | F | Total | 58 | F | Hemi |
| 20 | 51 | F | Hemi | 62 | F | Total |
| 21 | 50 | M | Hemi | 39 | M | Hemi |
| 22 | 54 | F | Total | 59 | M | Hemi |
| 23 | 38 | F | Total | 49 | F | Hemi |
| 24 | 47 | M | Total | 35 | F | Total |
| 25 | 30 | F | Hemi | 47 | M | Hemi |
| 26 | 56 | F | Hemi | 26 | F | Total |
| 27 | — | — | — | 54 | M | Total |
| 28 | — | — | — | 42 | M | Total |
| 29 | — | — | — | 41 | F | Hemi |
| 30 | — | — | — | 31 | F | Total |

*Hemi = hemithyroidectomy; Total = total thyroidectomy.

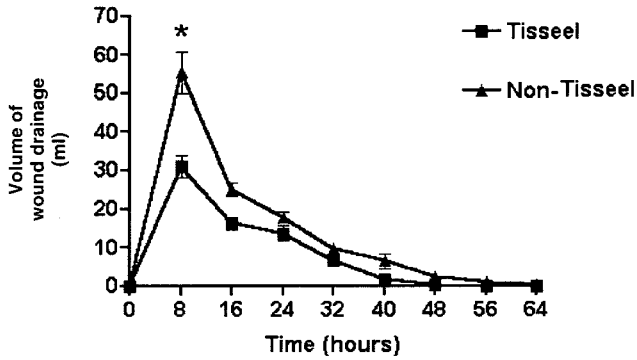


**Figure 1** Mean fluid volume collected from post-thyroidectomy wounds in both treatment groups. Tisseel group, $n$ = 26; non-Tisseel group, $n$ = 30. Data are presented as the mean ± standard error of the mean of values for each treatment group. *Significant difference between Tisseel and non-Tisseel treatment ($p < .001$).

## Discussion

Fibrin glues, such as Tisseel, can potentially reduce drainage from postoperative wounds. Using Tisseel's

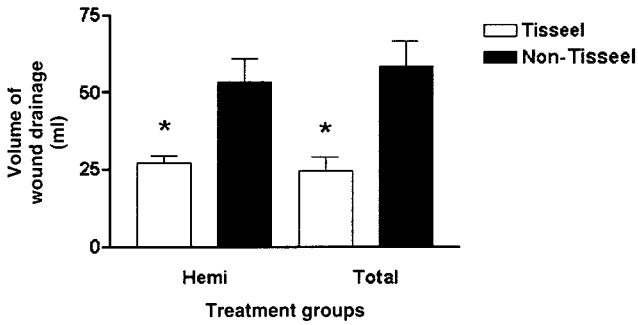


**Figure 2** Hemithyroidectomy and total thyroidectomy drainage in first 8 hours postoperatively in the Tisseel and non-Tisseel groups. Hemithyroidectomy surgical group: Tisseel treatment, $n$ = 17; non-Tisseel treatment, $n$ = 14. Total thyroidectomy surgical group: Tisseel treatment, $n$ = 9; non-Tisseel treatment, $n$ = 16. Data are presented as the mean ± standard error of the mean of values for each treatment group. *Significant difference between Tisseel and non-Tisseel treatment ($p < .001$).

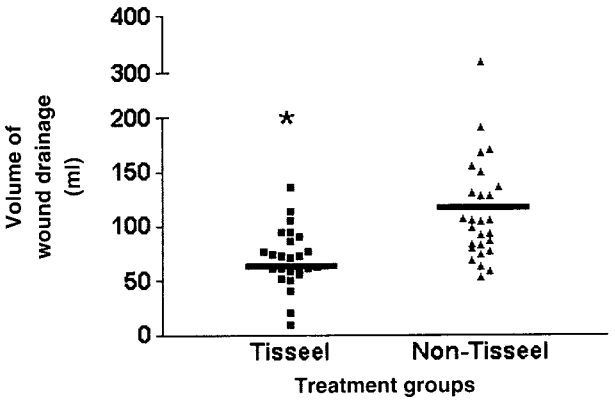


**Figure 3** Drainage of all postoperative wounds over 64 hours in Tisseel and non-Tisseel groups. Tisseel group, $n$ = 26; non-Tisseel group, $n$ = 30. Data are presented as data points corresponding to individual patients and a bar that represents the mean. *Significant difference between Tisseel and non-Tisseel treatment ($p < .001$).

ability to form a coagulum and enhance hemostasis, the surgeon has another therapeutic adjunct to potentially eliminate serious complications, such as hematomas, seromas, and infection. This investigation determined the effectiveness of Tisseel to reduce post-thyroidectomy wound drainage. Importantly, this is a prospective, randomized, blinded, controlled study. A significant decrease in drainage during the first 8-hour postoperative period of nearly 50% was observed in the Tisseel-treated group. Notably, this decrease was independent of the type of surgery performed. Both total and hemithyroidectomies had a significant and marked reduction in wound drainage. The trend of decreased drainage appeared to continue for the duration in which the drain was in situ. A significant decrease was also noted in the total wound drainage over 64 hours, with Tisseel-treated patients again having 43% less drainage than the control group. Although it appears that there was a reduction in drainage, the trend to earlier drain removal was not statistically significant; thus, there was no clear reduction in either the duration of drain placement or hospital stay. The relatively limited number of patients involved in the study may be responsible for the lack of statistical significance between the two groups. Increasing the number of patients could improve the possibility of identifying subtle differences, such as a reduction in hospitalization. A more noteworthy role in the length of hospital stay observed in this study is the unlikelihood of patient discharge in the middle of the night, when wound drainage has tapered enough to qualify for drain removal. Another important observation was that Tisseel application did not show an increase in patient morbidity. This finding is critical in the use of human blood products because such products must be free of pathogens, with a limited side-effect profile to attain wide clinical application.

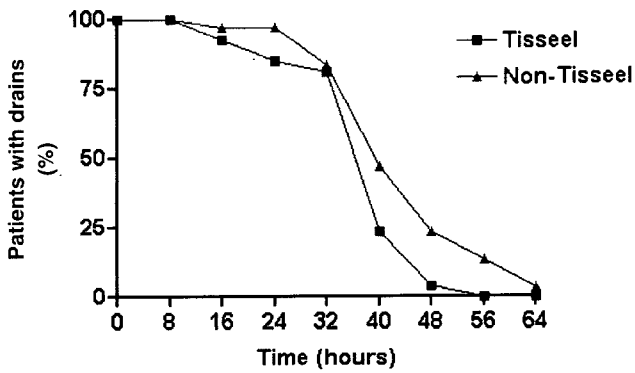


**Figure 4** Patients with drains in place over time in both treatment groups. Tisseel group, $n$ = 26; non-Tisseel group, $n$ = 30. Data are presented as the mean ± standard error of the mean of values for each treatment group.

## Conclusion

The addition of Tisseel decreases wound drainage. Current data suggest that Tisseel would be a safe and effective adjunct in drain-free thyroidectomies. We are currently designing a prospective, randomized, controlled trial comparing thyroidectomy and Tisseel with and without postoperative drain placement.

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