

Prevention of Hematomas and Seromas

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ABSTRACT

Hematoma and seroma formation in surgical wounds has negative effects on wound healing and subsequent morbidity to patients. This is of particular pertinence in cosmetic procedures in which the patient has chosen to undergo surgery electively. Over the past several decades there has been considerable interest in the use of ancillary techniques to assist in closing wounds and achieving hemostasis to prevent hematoma and seroma formation. These techniques include application of tissue sealants or platelet gels, application of quilting sutures, and the use of sclerotherapy to obliterate chronic seromatous cavities. The experience with these techniques in a multitude of surgical specialties is positive and additionally supported in animal models. However, the experience within the plastic surgery literature is mixed. This suggests minimal benefit of ancillary procedures over basic principles of surgical hemostasis and the use of postoperative closed suction drains. Presented here is a summary of the evidence reported using these techniques. Despite the questionable efficacy of these techniques, further appropriated investigations should be performed before eliminating these potentially beneficial adjuncts.

KEYWORDS: Hematoma, seroma, fibrin glue, platelet gel

Over the past several decades there has been considerable interest in the use of adjuvant techniques in assisting surgeons' ability to close wounds and achieve hemostasis to prevent hematoma and seroma formation. These techniques include application of tissue sealants or platelet gels, application of quilting sutures, and the use of sclerotherapy to obliterate chronic seromatous cavities. Use of these therapies potentially reduces the incidence of hematoma and seroma, allows reduction of surgical time, and lessens the necessity for drains. The hypothetical advantage with these adjuncts is an overall decrease in operative complications and increased quality of care for patients.

Among the concerns of plastic surgeons are the negative effect on wound healing and tension on flaps secondary to fluid accumulation. In addition, in the setting of aesthetic surgery, such complications confer an overall negative prognosis that significantly alters

patients' safety and limits the ability to improve cosmesis. Therefore, topical sealants have a specific role as a prophylactic intraoperative strategy to prevent postoperative morbidity.

Postoperative fluid collections represent sequelae of events that ultimately contribute to negative soft tissue healing events. Formation of a hematoma or seroma has been reported in between 10 and 45% of patients undergoing abdominoplasty procedures^{1,2} and 8 to 13% of rhytidectomy procedures.^{3,44} The etiology is multifactorial, involving inadequate hemostasis, lymphatic disruption, shearing between tissue surfaces, creation of surgical dead space, and systemic coagulopathy. Mediators of inflammation have also been implicated in the formation of seroma in the presence of surgical dead space. The normal migration of macrophages and polymorphonuclear leukocytes and release of histamines and prostaglandins cause vasodilation and production of

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interstitial fluid.³ This results in the accumulation of serous fluid in the potential cavity.

The complications of these fluid accumulations present significant morbidity for patients involving further therapeutic interventions. Say and Donegan⁴ and Hayes and Bryan⁵ have documented a negative correlation between seroma formation, wound infection, and alteration of normal wound healing. Increased skin flap necrosis resulting from tension on the vascularly compromised overlying skin flaps also plagues the outcomes associated with hematomas and seromas.⁶ Hematomas resulting from sustained capillary bed bleeding from the raw surface of surgical wounds also contribute to the morbidity associated with procedures requiring large amounts of soft tissue dissection. These potential effects of fluid accumulation pose certain safety concerns for patients. Complications, as such, may require therapeutic use of antibiotics for the treatment of wound infections, prolonged use of suction drains, and operative or minimally invasive intervention for evacuation or blood transfusion. All the mentioned negative outcomes place the patients at unfavorable risks and place a strain on the health care system causing more lengthy hospital stays and additional costs.

Prevention of the formation of hematomas and seromas begins preoperatively with the assessment for potential coagulopathy and cessation of antiplatelet

drugs and anticoagulants. Intraoperatively, attention to surgical hemostasis and placement of drains serve to reduce risks. In the postoperative period, rapid evaluation and evacuation of postoperative fluid collection assist in eliminating further complications. Tissue sealants or platelet gel and quilting sutures potentially provide an additional intraoperative modality for prevention of fluid accumulation. The mechanism is their ability to act as a hemostatic agent tissue sealant and improve wound healing.⁷⁻⁹ There are numerous unblinded studies and anecdotal reports documenting the benefits of these modalities. These data, however, have been equally contradicted in follow-up studies. Unfortunately, this has created a situation in which the true efficacy of these promising adjunctive modalities remains to be known.

TISSUE SEALANTS AS ADJUNCTS TO HEMOSTASIS

Tissue sealants are available in a variety of forms including fibrin glue, topical thrombin, and platelet gels. The interest in these products as hemostatic agents comes from their ability to mimic the last step in the coagulation cascade, particularly the conversion of fibrinogen to fibrin through the activity of calcium and thrombin, leading to clot formation and stabilization (Fig. 1).

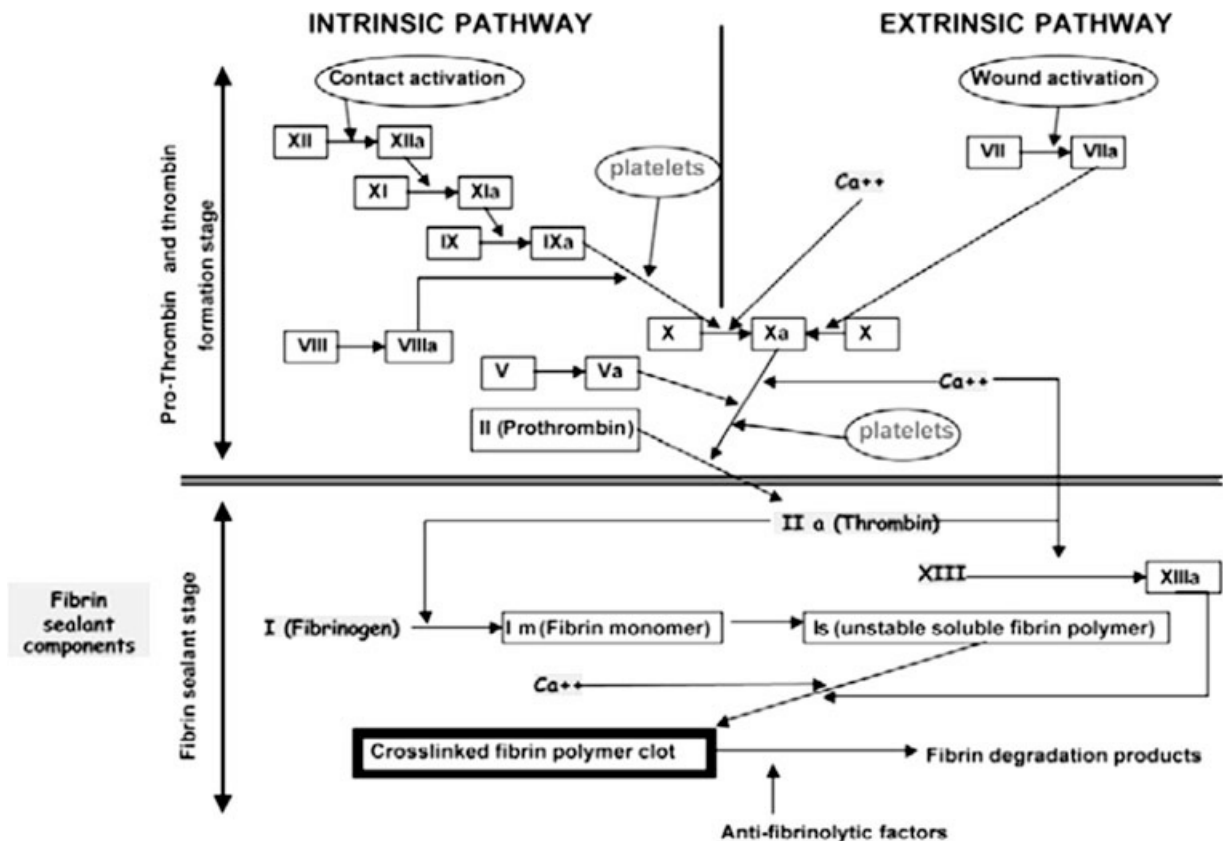


Figure 1 Schematic depicting the locations of action of fibrin sealant and platelet concentrates.¹⁰

Fibrin sealants are freeze-dried homologous plasma preparations. They are supplied as two separate components: a fibrinogen/fibronectin/factor XII concentrate dissolved in an antifibrinolytic solution with a thrombin and calcium. Traditionally, the origin of these components is either pooled human plasma or bovine tissue. The variable compositions of commercially available sealants are demonstrated in Table 1. Addition of platelets further augments the hemostatic process by providing a frame for fibrin polymerization. Fibrin clot formation generated by the use of these products is independent of the patient's coagulation pathway. Their hemostatic efficacy has been supported by variable experimental and clinical evidence.^{11,12}

The properties of fibrin glue and platelet gels have been extensively studied. Fibrin glues have been shown to act as tissue sealants that provide strong tissue bonds independent of suturing. Several studies have confirmed a positive correlation in tissue strength related to wound fibrinogen concentration.⁸⁻¹⁵ Incisions treated with fibrin sealant displayed increased tensile strength in experiments by Jorgensen et al,¹⁵ Piechotta and Flemming,¹³ and Sierra.¹⁴ Fibrin sealants provide supplemental local fibrinogen adhesive that augments the shear strength and eliminates the dead space of surgically created wounds.

Fibrin glue and platelet concentrates augment wound healing, which has been demonstrated in the oral, orthopedic, and plastic surgery literature. Fibrin acts as a scaffold for cell migration, and thrombin and activated factor XIIIa are mitogenic for fibroblast and catalyze cross-linking of collagen and many cell adhesion molecules such as fibronectin.¹⁰ The beneficial wound healing properties of platelet-rich plasma (PRP) are attributed to stimulation of the release of growth factors including platelet-derived growth factor, vascular endothelial growth factor, and transforming growth factor β (TGF β).¹⁶ Clinically, fibrin glue provided less edema and ecchymosis after 200 rhytidectomies performed by Marchac and Sandor.¹⁷ Others have demonstrated osteogenic and osteoinductive properties of platelet concentrates and fibrin glue to augment healing of nonvascularized bone grafts and periodontal defects.^{18,19} Their supportive role in healing of skin grafts and chronic wounds is also well established.^{20,21}

Several animal models have demonstrated the hemostatic effect and a decrease in seroma formation with the use of tissue sealants. Fibrin sealants decreased the amount of ecchymosis and hematoma formation in dogs when applied to arteriotomies after removal of femoral artery catheters.²² In this study, Ismail et al showed that when fibrin sealant was applied to contralateral control groins, there was a significant reduction in bleeding-associated complications ($p = 0.008$). This hemostatic advantage was also found in heparinized dogs ($p = 0.016$). Jackson et al supported these findings using

a porcine model (Fig. 2).²³ In a randomized, blinded, placebo-controlled study, blood loss was significantly less when 4-mm femoral arteriotomies were treated with fibrin sealant dressing compared with a control dressing (4.9 versus 82.5 mL; $p < 0.0005$). Kulber et al reported a reduction in seroma formation and flap necrosis in rats treated with human-derived tissue sealant after harvest of the latissimus dorsi muscle.⁶ The potential benefit of fibrin sealant was additionally displayed when used as a therapeutic modality after seroma was diagnosed (group III; Table 2). These results mimic data reported by Lindsey³ and Hardara²⁴ and their coworkers, who found reduction of seroma after mastectomies performed in mice treated with fibrin glue. Similarly, Eroglu et al found that intraoperative fibrin glue application in a guinea-pig mastectomy model also decreased postoperative seroma formation with statistical significance.^{25,45}

In common practice, the hemostatic properties of tissue sealants have been exploited in a multitude of clinical scenarios. Interest in tissues sealants is most prevalent in cardiovascular surgery. These agents have been utilized to prevent local bleeding along suture holes, staple lines, anastomoses, fistulas, and raw surfaces.²⁵ In a review of their experience, Matthew et al reported a 94% success rate in reducing blood loss associated with 689 thoracic and cardiac procedures.²⁶ Similar success was achieved in a prospective, randomized study to investigate the potential of fibrin tissue adhesive to reduce blood loss after total knee arthroplasty. The mean postoperative blood loss in the fibrin tissue adhesive group was 360 mL compared with 878 mL in the control group (518 mL mean difference; $p < 0.0001$).²⁷ Fibrin sealants have supplemented numerous urologic, gynecologic, ophthalmologic, and neurosurgical procedures.²⁸ The hemostatic effect of fibrin sealants additionally reduces perioperative bleeding complications in patients with congenital or acquired coagulopathies. Fibrin sealant has been used to stop bleeding from dental extraction in patients undergoing anticoagulation.²⁹ Martinowitz et al have demonstrated this hemostatic property in patients with hemophilia and von Willebrand's disease after major and minor surgical procedures.^{30,31} Generally, the use of these products as surgical adjunctive therapy has been accepted and is well established in current clinical practice.

Fibrin glue and PRP have been shown to decrease perioperative blood loss and the need for postoperative transfusion when used as a tissue sealant in several clinical trials. Carless et al³² reported a retrospective meta-analysis of the results of 15 studies involving more than 830 patients. Fibrin sealant reduced the rate of allogenic blood transfusion by 54% (95% confidence interval [CI] = 0.32 to 0.68) in 388 patients and reduced the average blood loss by 134 mL (95% CI = 51 to 217) in studies involving 442 patients. Similar results were

Table 1 Components of Available Commercial Fibrin Sealants

	Autocolle*	Beriplast [†]	BoilHeal [‡]	SmartPreP [§]	Tisseel [¶]	Tissuocol ^γ	Quixil**	VIGuard F.S. ^{††}
Fibrinogen (mg/mL)	50–65 autologous	65–115	80	50–60 autologous	70–100	70–100	60–100	50–95
Fibronectin (mg/mL)	4–10 autologous	—	—	4–10 autologous	2–9	2–9	—	—
Factor XIII (μg/mL)	25–30 autologous	40–80	75	20–40 autologous	10–50	10–50	0	3–5
Thrombin (IU/mL)	300–600 autologous	400–600 homologous	250 homologous	500–1000 Bovine	400–600 bovine	8 homologous	1000 homologous	200 homologous
Growth factors ^{‡‡}	Present	Absent	Absent	Present	Absent	Absent	Absent	Absent

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[†]Aventis Behring, Marburg, Germany.

[‡]Kaketsuken Biopharmaceutical, Japan.

[§]Harvest Autologous Hemobiologics, Norwell, MA.

[¶]Baxter Immuno AG, Vienna, Austria.

^γCentre de Transfusion Sanguine, Tours, France.

**Omnix-Biopharmaceutical, Japan.

^{††}Vitex V.I. Technologies, Watertown, MA.

^{‡‡}Platelet-derived growth factor, transforming growth factor β.

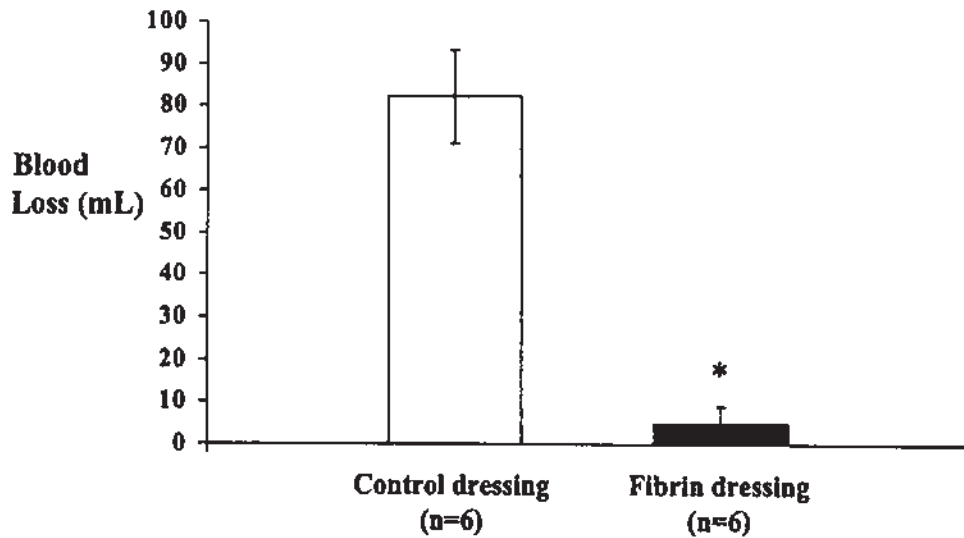


Figure 2 Mean blood loss is reduced after application of fibrin sealant to experimental arteriotomies. * $p=0.005$.²³

obtained in a retrospective review of 19 trials with a total of 1452 patients treated with platelet-rich plasmapheresis.³³ The relative risk reduction for patients treated with PRP was 29% with an average absolute risk reduction of 19% (95% CI=0.09 to 0.29). Despite the encouraging results of these reviews, they lack statistical strength because of their heterogeneity, small sample size, and unrandomized and unblinded nature.

In addition to indiscernible significance of these data, the efficacy of tissue sealants in clinical trials with patients has been mixed. Jain et al performed a randomized clinical trial investigating the use of drains and fibrin sealant following mastectomy.³⁴ They found a significant reduction in length of stay and postoperative pain scores in the cohort that did not have any post-mastectomy drains. In addition, fibrin sealant in the no-drain cohort was associated with a statistically significant reduction in the incidence and total volume of seroma. Along the same lines, Moore et al showed in another randomized prospective trial involving modified radical mastectomy patients that fibrin sealant decreased drain output and facilitated earlier drain removal.³⁵

On the other hand, the work of Dinsmore and colleagues resulted in opposite findings.³⁶ These inves-

tigators found that fibrin glue actually increased drain output after modified radical mastectomy. This increased the time to drain removal. Three years later, investigators from Turkey also studied modified radical mastectomy patients and found that fibrin application had no significant benefit on axillary lymphatic drainage, drain removal time, or seroma formation.³⁷

The experience reported in the plastic surgery literature is also varied. As mentioned previously, Marchac and Sandor in 1994 reported decreased edema and hematoma formation in 200 rhytidectomy patients.¹⁷ However, in 2005 with more experience, Marchac and Greensmith reported contradictory findings.³⁸ In a prospective randomized fashion, patients were used as their own controls. Fibrin glue was used as an adjunct to 30 rhytidectomy patients on one side and the other side was the control. There was essentially no difference in hematoma, ecchymosis, and edema formation.

With regard to rhytidectomy procedures, the majority of the plastic surgery literature on preventing hematomas has focused on this category. Jones and Grover³⁹ reported an extensive review of 910 patients in which various modes of hematoma prevention were tested. In this series, the effect of dressings, drains, fibrin

Table 2 Seroma Formation and Skin Flap Necrosis after Latissimus Dorsi Harvest in an Experimental Model; Fibrin Sealant Applied after Seroma Evacuated⁶

Group	n	No. of Seromas	Average Total Fluid (mL)	Multiple Aspirations (%)	Flap Necrosis (%)
I (control)	20	18	21*	60	80 [†]
II (fibrin)	20	4	6*	5	10 [†]
III (seroma/fibrin)	20	10	28	50	40 [†]

*Student's *t* test, $p < 0.05$.

[†]Chi-squared, $p < 0.001$.

glue, and tumescence on hematoma rate was investigated retrospectively. No difference in hematoma rate was observed with the use of dressings ($p > 0.5$), drains ($p > 0.4$), fibrin glue ($p > 0.6$), or tumescence ($p > 0.5$). In a separate part of their study, the specific effect of withdrawing adrenaline from the tumescence solution was compared in a group of 461 face lifts. Tumescence without adrenaline significantly reduced the incidence of hematoma requiring surgical evacuation ($p < 0.0001$). The authors hypothesized that adrenaline causes reactive vasodilation of vessels that were not identified at surgery because of the vasoconstrictive effect of the drug. The investigation therefore suggests a negative benefit of ancillary procedures and highlights the importance of stringent adherence to surgical technique.

There are numerous reports regarding the use of adjunctive procedures in body contouring. The efficacy of the use of fibrin glue in this population of patients has yet to be elucidated. A subset of surgeons believe in the ability of quilting sutures to obliterate the large cavities, such as those created by abdominoplasty. The theory is that quilting the cavity with suspension sutures will improve tissue adherence and augment lymphatic reorganization in order to prevent seroma formation and improve hemostasis. Although this theory has been anecdotally exploited in many practices, there have been no organized studies to support its use. To the contrary, McCarthy et al⁴⁰ evaluated 71 patients undergoing transverse rectus abdominis musculocutaneous (TRAM) breast reconstruction whose donor sites were comparatively closed with and without quilting sutures. The drain output per day decreased with quilting sutures; however, the time to drain removal was not significantly different between the two groups. In addition, in this series there was no significant decrease in the incidence of seroma formation with the use of abdominal quilting sutures.

Postoperatively, chronic seroma formation poses equal threats with regard to negative wound healing and patients' safety. Kulber et al⁶ exploited the characteristics of fibrin glue in a therapeutic model (Table 2). After diagnosis of persistent seroma, application of fibrin glue into the seroma cavity after aspiration prevented subsequent recurrence in a rat model. Butler studied the effect of percutaneous administration of fibrin sealant on the management refractory postoperative donor site seromas.⁴¹ In a series of four patients, seromas were first completely aspirated. Then, utilizing a double-lumen catheter, 20 mL of fibrin sealant was instilled into the donor site seroma cavity. Interestingly, after a single percutaneous treatment of fibrin sealant, there was 100% resolution of the refractory seromas in all four cases. Long-term follow-up of over 70 weeks confirmed these lasting results. Although the data for fibrin glue are varying regarding preventing recurrent hematoma and seroma formation, its use in the management of refractory seromas is promising.

Sclerotherapy, which has been advocated in many specialties to promote tissue adherence, has also been postulated to decrease the recurrence of seroma in soft tissue defects. Although theoretically promising, the current reports have not shown support. Rice et al⁴² performed a prospective, randomized, double-blinded trial to evaluate the effect of intraoperatively administered topical tetracycline on the occurrence of postoperative seroma formation in mastectomy wounds. Thirty-two patients were compared with controls. There were no significant differences in total volume of closed suction drainage or duration of drain usage. Surprisingly, seroma was greater in the tetracycline group than the control group (53% versus 22%, $p = 0.01$). Similarly, McCarthy et al⁴³ obtained equal results in a group of mastectomy patients that experienced prolonged seroma formation. This study was terminated because of the significant pain experience in the sclerotherapy group without any beneficial effect on seroma treatment. Their benefits in preventing seroma formation in soft tissue defects has yet to be proved.

CONCLUSION

Postoperative hematoma and seroma formation poses significant challenges to the healing wound and potential serious morbidity to patients. The use of adjunctive procedures in plastic surgery to prevent these complications is of extreme interest. With respect to fibrin glue or PRP (topical tissue sealants), there has been valuable theoretical evidence in research animals to support their use. The clinical evidence, however, is equivocal. There have been few large-scale prospective randomized clinical trials that have correctly evaluated their efficacy. Because of the associated expense of these agents, the negative data support their futility. However, the positive effects seen among the majority of surgical specialties cannot be ignored. There may also be a role for fibrin glue products in preventing persistent seromas. Before eliminating these agents from the plastic surgeon's armamentarium, appropriate investigation must be performed.

With the increase in postbariatric body contouring procedures, there have been extensive efforts to prevent hematoma and seroma formation. The quilting sutures and sclerosing agents may not be advantageous in this quest. Again, with reputable studies with tissue sealants, there may be proven efficacy with the use of these agents among this subset of plastic surgery patients. These investigations have yet to be done. Ultimately, based on the data presented here, ancillary procedures to prevent postoperative hematoma and seroma formation have been of questionable benefit in plastic surgery. This suggests minimal benefits of these techniques over basic principles of surgical hemostasis and the use of postoperative closed suction drains.

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