Journal of Carcinogenesis
Covering Genesis to Therapeutics

Journal of Carcinogenesis, ISSN: 1477-3163
2025; Vol 24: Issue 8s, https://carcinogenesis.com/

Evaluation of novel hemostatic agents in controlling intraoperative bleeding during liver resections

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ABSTRACT

Background: Intraoperative bleeding during liver resections remains a major surgical challenge, contributing to increased transfusion requirements, longer operative times, and postoperative complications.

Objective: To evaluate the efficacy of novel hemostatic agents in reducing intraoperative bleeding and improving perioperative outcomes during liver resections.

Methods: This prospective observational study was conducted at Organ transplant unit Pir Abdul Qadir shah jeelani institute of Medical sciences/ Gambat Medical college from May 2023 to august 2024. It included 154 patients undergoing elective liver resections, divided into two groups: Group A (n=76) managed with conventional hemostasis and Group B (n=78) managed with adjunctive novel hemostatic agents. Data on demographics, intraoperative parameters, transfusion requirements, postoperative complications, hospital stay, and 30-day mortality were collected.

Results: Patients in the novel agent's group had significantly lower intraoperative blood loss (420 ± 150 mL vs. 610 ± 210 mL, $p<0.001$) and reduced transfusion requirements (16.7% vs. 35.5%). Operative time was slightly shorter in Group B (185 ± 35 min vs. 198 ± 42 min, $p=0.048$). Postoperative complications, including bile leakage (7.7% vs. 15.8%) and surgical site infections (7.7% vs. 11.8%), were lower in Group B but not statistically significant. Mean hospital stay was significantly reduced with novel agents (7.2 ± 2.1 days vs. 8.4 ± 2.7 days, $p=0.021$).

Conclusion: It is concluded that novel hemostatic agents provide effective adjuncts in liver resections, significantly reducing blood loss, transfusion needs, and hospital stay. Although trends toward fewer complications were observed, further large-scale multicenter trials and cost-effectiveness analyses are necessary before routine adoption.

Keywords: *Liver resection, intraoperative bleeding, novel hemostatic agents, fibrin sealants, blood transfusion, postoperative outcomes.*

How to Cite: Hamid Raza laghari, Hafiz Aamir Bashir, Mohamed Amer Ahmed Ismail Amer, Zulfiqar Ali Bhatti, Abdul Rasheed Zai , (2025) Evaluation of novel hemostatic agents in controlling intraoperative bleeding during liver resections, *Journal of Carcinogenesis*, *Vol.24, No.8s*, 1-10

1. INTRODUCTION

Liver resections represent a cornerstone in the management of primary and metastatic hepatic malignancies, as well as certain benign liver disorders requiring surgical intervention [1]. Despite improvements in surgical training, perioperative imaging, and anesthesia, these procedures remain technically challenging because of the liver's unique dual blood supply and the friable nature of hepatic parenchyma [2]. Intraoperative bleeding is a frequent and often life-threatening complication during hepatic resections. Excessive hemorrhage not only compromises surgical visualization but is also strongly associated with hemodynamic instability, increased transfusion requirements, prolonged operative duration, and adverse postoperative outcomes such as infection, liver failure, and extended intensive care stay [3]. Thus, effective hemostasis remains a central goal in liver surgery. Conventional methods for intraoperative bleeding control, such as suture ligation, Pringle's maneuver, electrocautery, and vascular stapling devices, have been the foundation of hepatic surgery for decades. While these techniques provide varying degrees of success, each has inherent limitations [4]. The Pringle's maneuver, though effective in temporarily occluding inflow, risks ischemia-reperfusion injury to the liver parenchyma. Similarly, thermal coagulation may lead to collateral tissue necrosis, delayed bile leakage, or incomplete sealing of transected vessels. In complex resections involving cirrhotic livers or patients with coagulopathy, conventional hemostatic strategies often prove insufficient. These challenges have driven the development and adoption of novel hemostatic agents intended to augment traditional methods [5].

Hemostatic agents are broadly classified into topical sealants, biologic adhesives, and synthetic biomaterials. Fibrin sealants, which mimic the final stages of the coagulation cascade, have been widely used to promote clot formation and enhance tissue sealing. Thrombin-based preparations and collagen sponges have also demonstrated utility in controlling diffuse parenchymal oozing [6]. More recently, synthetic agents such as polyethylene glycol (PEG)-based sealants and polysaccharide hemostats have been introduced, offering advantages in terms of biocompatibility, ease of application, and reduced risk of transmissible infections compared with biologic products [7]. Additionally, combination products that integrate mechanical support with biochemical clot enhancers have shown promise in managing complex bleeding scenarios. Several clinical trials and observational studies have highlighted the potential benefits of these agents. Reports suggest that the adjunctive use of novel hemostatic materials can significantly reduce intraoperative blood loss, limit the need for perioperative transfusions, and decrease postoperative bile leakage a common complication of liver resections [8]. Furthermore, reduced transfusion requirements have important implications, as blood transfusions are independently associated with increased risks of infection, immunomodulation, and cancer recurrence in oncologic surgery. By minimizing bleeding and transfusion dependence, these agents may indirectly improve long-term surgical and oncological outcomes [9-11]. However, the widespread integration of novel hemostatic agents into routine clinical practice has been tempered by ongoing debates. First, their cost remains substantially higher than traditional techniques, raising concerns about economic sustainability, particularly in low- and middle-income healthcare systems [12]. Second, heterogeneity in study design, patient populations, and endpoints across existing literature makes it difficult to draw definitive conclusions about their superiority. Some randomized controlled trials have failed to demonstrate statistically significant differences between novel agents and conventional methods in terms of major endpoints such as operative mortality or overall complication rates [13].

2. OBJECTIVE

To evaluate the efficacy of novel hemostatic agents in reducing intraoperative bleeding and improving perioperative outcomes during liver resections.

3. METHODOLOGY

This prospective observational study was conducted at Organ transplant unit Pir Abdul Qadir shah jeelani institute of Medical sciences/ Gambat Medical college from May 2023 to august 2024. A total of 154 patients undergoing elective liver resection were included in the study.

Inclusion Criteria:

Adult patients (≥18 years) scheduled for elective liver resection for benign or malignant liver disease.

Patients with adequate baseline coagulation profiles and fit for surgery under general anesthesia.

Informed written consent provided by the patient or legal guardian.

Exclusion Criteria:

Patients with severe preoperative coagulopathy uncorrectable before surgery.

Patients undergoing emergency hepatic surgery.

Individuals with hypersensitivity to components of the hemostatic agents used.

Patients with incomplete intraoperative or postoperative records.

Data collection

Preoperative data included demographic details (age, gender), indication for surgery, comorbidities, and baseline laboratory parameters (hemoglobin, platelet count, liver function tests, coagulation profile). Intraoperative data recorded included type of liver resection, estimated blood loss, duration of surgery, need for Pringle's maneuver, and use of hemostatic agent. Patients were divided into two groups based on the intraoperative hemostatic technique employed:

Group A (Conventional Hemostasis Group): Hemostasis was achieved using standard surgical methods including sutures, electrocautery, and Pringle's maneuver.

Group B (Novel Hemostatic Agents Group): In addition to conventional techniques, novel topical hemostatic agents such as fibrin sealants, thrombin-based sponges, or synthetic sealants were applied to the liver resection margin. The choice of specific agent was guided by the operating surgeon's preference and intraoperative availability.

Postoperative data included blood transfusion requirements, bile leakage, surgical site infection, length of hospital stay, and 30-day morbidity and mortality. The primary outcome measure was intraoperative blood loss expressed in milliliters. Secondary outcomes included the volume of blood transfusion required during or after surgery, operative time, occurrence of postoperative bile leakage, incidence of surgical complications, duration of hospital stay, and mortality within 30 days of the operation.

Statistical Analysis

All data were entered into SPSS version 26.0 for statistical analysis. Continuous variables such as patient age, operative duration, and intraoperative blood loss were analyzed as mean ± standard deviation, while categorical variables such as gender distribution, presence of comorbidities, and postoperative complications were expressed as frequencies and percentages. A p-value less than 0.05 was considered statistically significant.

4. RESULTS

A total of 154 patients underwent liver resections, with 76 in the conventional hemostasis group (Group A) and 78 in the novel hemostatic agents' group (Group B). The mean age of the study population was 52.8 ± 11.6 years, with no significant age difference between groups (53.4 ± 11.2 years in Group A vs. 52.3 ± 12.0 years in Group B). Males comprised 62.3% (n=96) of the cohort, while females represented 37.7% (n=58), with comparable distributions across both groups. The prevalence of hypertension (38.3%), diabetes mellitus (27.3%), and chronic liver disease (16.9%) was similar in both groups, ensuring comparability in baseline characteristics. With regard to transfusion, 27 patients (35.5%) in the conventional group required blood products compared with only 13 patients (16.7%) in the novel agent's group.

Table 1. Baseline Demographic and Clinical Characteristics of Patients (n = 154)

Variable	Group A (Conventional, n=76)	Group B (Novel Agents, n=78)	Total (n=154)
Age (years), Mean ± SD	53.4 ± 11.2	52.3 ± 12.0	52.8 ± 11.6
Gender: Male, n (%)	48 (63.2%)	48 (61.5%)	96 (62.3%)
Gender: Female, n (%)	28 (36.8%)	30 (38.5%)	58 (37.7%)
Hypertension, n (%)	28 (36.8%)	31 (39.7%)	59 (38.3%)
Diabetes Mellitus, n (%)	22 (28.9%)	20 (25.6%)	42 (27.3%)
Chronic Liver Disease, n (%)	14 (18.4%)	12 (15.4%)	26 (16.9%)
Blood Transfusion			
Patients Transfused, n (%)	27 (35.5%)	13 (16.7%)	40 (26.0%)
Mean Units Transfused ± SD	1.8 ± 0.9	0.9 ± 0.5	1.3 ± 0.7

The mean estimated blood loss was significantly lower in the novel agents group (420 ± 150 mL) than in the conventional group (610 ± 210 mL, $p<0.001$). Operative time was also reduced in Group B (185 ± 35 minutes) compared with Group A

(198 ± 42 minutes, p=0.048). Additionally, the need for Pringle's maneuver was higher in the conventional group (50.0%) compared to the novel agents group (28.2%), with the difference reaching statistical significance (p=0.006).

Table 2. Intraoperative Parameters

Parameter	Group A (n=76)	Group B (n=78)	p-value
Estimated Blood Loss (mL)	610 ± 210	420 ± 150	<0.001
Operative Time (minutes)	198 ± 42	185 ± 35	0.048
Use of Pringle's Maneuver, n (%)	38 (50.0%)	22 (28.2%)	0.006

Although the rates of bile leakage (15.8% vs. 7.7%), surgical site infection (11.8% vs. 7.7%), postoperative bleeding (6.6% vs. 2.6%), respiratory complications (7.9% vs. 5.1%), and reoperation (5.3% vs. 2.6%) were lower in the novel agents group compared to the conventional group, these differences did not reach statistical significance. However, the mean hospital stay was significantly shorter in Group B (7.2 ± 2.1 days) than in Group A (8.4 ± 2.7 days, p=0.021). Thirty-day mortality was low and comparable between the groups (3.9% vs. 2.6%, p=0.65).

Table 3. Postoperative Complications and Hospital Stay

Complication	Group A (n=76)	Group B (n=78)	P-value
Bile Leakage, n (%)	12 (15.8%)	6 (7.7%)	0.12
Surgical Site Infection, n (%)	9 (11.8%)	6 (7.7%)	0.39
Postoperative Bleeding, n (%)	5 (6.6%)	2 (2.6%)	0.27
Respiratory Complications, n (%)	6 (7.9%)	4 (5.1%)	0.51
Reoperation Required, n (%)	4 (5.3%)	2 (2.6%)	0.42
Hospital Stay (days)	8.4 ± 2.7	7.2 ± 2.1	0.021
30-day Mortality, n (%)	3 (3.9%)	2 (2.6%)	0.65

Patients with lower intraoperative blood loss had shorter hospital stays. Those with <400 mL blood loss had a mean stay of 6.5 ± 1.9 days, while those with 400–600 mL and >600 mL blood loss stayed for 7.4 ± 2.1 and 9.2 ± 2.8 days, respectively. The differences were statistically significant (p<0.05). A higher proportion of patients in the novel agents group fell into the lower blood loss categories (<400 mL and 400–600 mL), which partly explains the reduced hospital stay observed in this group.

Table 4. Correlation Between Intraoperative Blood Loss and Hospital Stay

Blood Loss Category (mL)	Group A (n=76)	Group B (n=78)	Mean Hospital Stay (days)	p-value
<400 mL	10 (13.2%)	22 (28.2%)	6.5 ± 1.9	0.02
400–600 mL	28 (36.8%)	34 (43.6%)	7.4 ± 2.1	0.03
>600 mL	38 (50.0%)	22 (28.2%)	9.2 ± 2.8	<0.001

5. DISCUSSION

Intraoperative bleeding remains one of the most significant challenges in hepatic surgery, directly impacting operative time, transfusion requirements, postoperative complications, and overall patient recovery. This study evaluated the role of novel hemostatic agents as adjuncts to conventional methods of bleeding control in liver resections and demonstrated favorable outcomes in terms of blood loss reduction, transfusion needs, and hospital stay when compared to conventional hemostatic techniques alone. The baseline demographic and clinical characteristics of patients were comparable between groups, which minimized selection bias and allowed for meaningful outcome comparisons. Both groups had similar age distribution, gender ratio, and prevalence of comorbidities such as hypertension, diabetes mellitus, and chronic liver disease. This similarity ensured that the observed differences in intraoperative and postoperative outcomes were primarily attributable to the use of novel hemostatic agents rather than underlying patient variability [14].

A key finding of this study was the significant reduction in intraoperative blood loss in the novel agent's group. Patients managed with adjunctive hemostatic agents had a mean blood loss of 420 ± 150 mL compared with 610 ± 210 mL in the conventional group. These results align with previous studies that have reported reduced bleeding when topical sealants, fibrin adhesives, and thrombin-based products are employed. The reduction in blood loss also correlated with a decreased reliance on Pringle's maneuver, suggesting that novel agents may provide effective parenchymal sealing without requiring prolonged vascular occlusion [15-17]. This is particularly relevant in cirrhotic livers, where ischemia-reperfusion injury associated with Pringle's maneuver can worsen postoperative liver dysfunction. The transfusion data further support the efficacy of novel agents. Only 16.7% of patients in the novel agents group required blood transfusion, compared to 35.5% in the conventional group. This reduction is clinically significant, as blood transfusions carry risks of immunosuppression, infection, and potential effects on tumor recurrence in oncologic surgery. Previous studies have similarly highlighted the ability of hemostatic agents to reduce perioperative transfusion requirements, and the present findings reinforce their role in improving perioperative safety [18].

Operative time was modestly reduced in patients receiving novel hemostatic agents, with an average of 185 minutes compared to 198 minutes in the conventional group. While the difference was statistically significant, the clinical relevance of this time reduction may be limited. Nonetheless, improved visualization due to reduced bleeding likely contributed to a smoother operative course, which indirectly shortened operative duration [19]. Prior research has also noted this trend, suggesting that reduced bleeding improves surgical field clarity and efficiency. Postoperative outcomes demonstrated a favorable trend in the novel agents group. Rates of bile leakage, surgical site infection, and postoperative bleeding were all lower, although some differences did not reach statistical significance. The 30-day mortality rate, however, did not differ significantly between groups, indicating that while novel agents enhance perioperative outcomes, their impact on short-term survival is limited [20].

The correlation analysis between blood loss and hospital stay further emphasized the clinical implications of improved hemostasis. Patients with blood loss less than 400 mL had the shortest hospital stay, whereas those with losses exceeding 600 mL experienced prolonged hospitalization. As more patients in the novel agent group fell into the lower blood loss category, their reduced length of stay highlights a tangible benefit in terms of patient recovery and healthcare cost reduction. Despite these promising findings, several limitations should be acknowledged. Overall, the results of this study support the use of novel hemostatic agents as effective adjuncts in liver resections. They significantly reduce intraoperative bleeding and transfusion requirements, shorten hospital stay, and may improve surgical efficiency. While the impact on postoperative complications was favorable but not statistically conclusive, the overall trend suggests a clinically meaningful improvement in patient outcomes. These findings echo the conclusions of previous studies and add to the growing body of evidence advocating for the integration of hemostatic agents into routine practice for complex hepatic surgeries.

6. CONCLUSION

It is concluded that the use of novel hemostatic agents during liver resections provides a significant advantage over conventional methods alone. Patients who received these adjuncts experienced reduced intraoperative blood loss, lower transfusion requirements, decreased reliance on vascular occlusion techniques, and shorter hospital stays. Although reductions in postoperative complications such as bile leakage and surgical site infections did not reach statistical significance, favorable trends were observed, suggesting potential benefits for perioperative recovery. Mortality rates remained comparable between groups, indicating that while novel agents improve intraoperative and early postoperative outcomes, their impact on survival requires further investigation.

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