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Patterns of Topical Hemostatic Material Use and Major Bleeding in Hepatectomy

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Research Article

Keywords: Hemostatics, Hepatectomy, Perioperative bleeding, Healthcare cost

Posted Date: July 28th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10108692/v1

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Additional Declarations: Competing interest reported. SN, HY, and HK are affiliated with the Department of Health Quality Assessment at the University of Tokyo, a social collaboration department supported by the National Clinical Database, Johnson & Johnson K.K., Nipro Corporation, and Intuitive Surgical Sàrl. SN and HK have received research grants from Pfizer Japan Inc. for work unrelated to this study. KM, AM, YH, YK, and JI are employees of Johnson & Johnson K.K. Medical Company. HY has received speaker fees from Chugai Pharmaceutical Co., Ltd. GW has received speaker fees and consultation fees from Johnson & Johnson K.K. HK reports receiving consultation fees from EPS Corporation, speaker fees from Beyer Japan and Novartis Japan, and a research grant from Amgen KK for work unrelated to this study.

Abstract

Background

Evidence regarding real-world utilization patterns of topical hemostatic materials and their association with major bleeding remains limited. We aimed to characterize utilization patterns of topical hemostatic materials among patients undergoing hepatectomy, to describe the incidence of bleeding complications, and to examine the association between major bleeding and postoperative healthcare resource utilization and costs.

Methods

This study used hospital-based data, including claims and discharge summaries, from Japan between 2020 and 2023. Patients who received topical hemostatic materials and underwent hepatectomy, including both open and laparoscopic approaches, were identified. Descriptive analyses were conducted to assess the prevalence of primary hemostatic agents, flowable microfibrillar collagen, fibrin sealants, and sheet-type biological tissue adhesives/sealants, and the incidence of major bleeding. Postoperative length of stay, postoperative intensive care unit (ICU) stay, and postoperative hospitalization costs were summarized according to major bleeding status using medians and interquartile ranges (IQRs).

Results

A total of 3,328 open and 620 laparoscopic hepatectomy cases were identified. In open hepatectomy, the combination of primary hemostatics and sheet-type biological tissue adhesives/sealants was most frequently used (39.1%). In laparoscopic hepatectomy, primary hemostatics alone was the most frequently observed pattern (35.3%). Major bleeding occurred across all topical hemostatic material utilization patterns and was generally more frequent in open (35.2%–46.1%) than laparoscopic hepatectomy (15.5%–35.4%). Major bleeding was associated with longer operative time, prolonged postoperative length of stay and ICU stay, and higher postoperative hospitalization costs. Among patients with and without major bleeding, respectively, in open hepatectomy, median (IQR) postoperative length of stay was 15 (11–23) versus 12 (9–16) days, ICU stay 2 (1–4) versus 1 (1–2) days, and postoperative hospitalization costs 643.6 (445.0–1,138.7) versus 460.0 (358.0–653.5) thousand Japanese yen. In laparoscopic hepatectomy, the corresponding values were length of stay 10 (7–15) versus 8 (6–11) days, ICU stay 1 (1–2) versus 1 (1–1) day, and costs 574.6 (401.6–1,036.5) versus 395.5 (313.3–503.1) thousand Japanese yen.

Conclusions

Patterns of topical hemostatic material use varied by operative approach, and major bleeding was consistently associated with increased postoperative healthcare resource utilization and costs.

BACKGROUND

Perioperative bleeding during hepatectomy remains the primary concern in the intraoperative or postoperative period, although advances have been made in managing intraoperative bleeding. Hepatectomy carries a major risk of major bleeding, both during surgery and afterward, compared to non-hepatectomy groups [1]. Perioperative massive bleeding is linked to increased morbidity, mortality, and higher hospital costs [2–6]. While current practices have reduced major bleeding[7] and improved long-term survival [8,9], controlling intraoperative bleeding during hepatectomy remains challenging, and excessive blood loss can adversely affect surgical outcomes[10]. Various topical hemostatic agents

and sealants (topical hemostatic materials) have been developed and widely used to control surgical bleeding[11–13]. To date, several types of topical hemostatic materials are available, including primary hemostatic agents, flowable collagen-based materials, fibrin sealants, and sheet-type biological tissue adhesives. Despite their usage, some patients still experience major bleeding [13]. Additionally, with the increasing use of laparoscopic hepatectomy, the technical environment for controlling bleeding has changed, possibly affecting the selection and application of topical hemostatic materials. However, there is limited evidence regarding current usage patterns of these products, their relationship with postoperative complications, and their association with healthcare resource utilization and costs. Therefore, this study aims to characterize contemporary real-world utilization patterns of topical hemostatic materials in open and laparoscopic hepatectomy and to describe perioperative major bleeding and associated postoperative healthcare resource utilization and costs.

METHODS

Study Design and Data Source

This descriptive observational study used data from Medical Data Vision's EBM Provider® database in Japan between 2020 and 2023. The database contains data on inpatients and outpatients from approximately 32% of acute care hospitals registered under the Diagnosis Procedure Combination (DPC) system in Japan (ref: JSPE DB survey). Information on disease diagnoses, medical procedures, and drug dispensing is recorded in the database. In addition, detailed clinical and diagnostic information, including emergency status, height, weight, and cancer stage, is documented in a standardized discharge summary form. The study was registered with the ethics committee of the University of Tokyo (ethics review number: 2025428NIe) and was conducted in accordance with institutional ethical guidelines.

Study Population

We included patients with topical hemostatic material use and aged ≥20 years, who underwent open or laparoscopic hepatectomy and had elective admission within the same hospitalization episode as the surgery. Hepatectomy procedures were identified using administrative procedure codes, as listed in Supplementary Table 1. Patients who had undergone other surgeries concomitantly were excluded, except for cholecystectomy. The study population was stratified into two groups according to operative approach, open hepatectomy and laparoscopic hepatectomy, and all analyses were performed separately for each group.

Topical hemostatic material use

Topical hemostatic material use during surgery was identified using Japanese reimbursement codes for hemostatic drugs and materials. For hemostatic materials, detailed information on individual agents was obtained from claims data. The products were then categorized into the following groups: (1) primary hemostatics, including gelatin, gelatin film, gelatin sponge hemostatic materials, oxidized cellulose, microfibrillar collagen, and starch-based absorbable local hemostatic materials; (2) flowable microfibrillar collagen; (3) fibrin sealants, including fibrinogen with factor XIII preparations; and (4) sheet-type biological tissue adhesives/sealants, including fibrinogen-containing agents. These categories were defined based on clinically meaningful differences, including product form and typical intraoperative applications, such as the initial control of active bleeding. The list of topical hemostatic materials is provided in Supplemental Table 2.

Patient and hospital characteristics

We assessed patients' comorbid conditions at admission using disease category codes for the main diagnosis, subdiagnosis, primary diagnosis leading to hospitalization, and comorbid diagnoses present at admission. The list of baseline comorbidities is shown in Supplemental Table 3. Information on body mass index (BMI), smoking status including pack-years, TNM classification based on the UICC clinical classification, and cancer stage was extracted from the standardized discharge summary form. Hospital characteristics were assessed using data on hospital scale defined by the number of beds and designation as a government-designated cancer care hospital.

Perioperative major bleeding-related measures

We described the incidence of major bleeding, defined as a composite of intra- and postoperative blood transfusion of at least 2 units (400 ml), identified from red blood cell concentrate dispensing records (Supplemental Table 4) or diagnosis codes indicating bleeding complications occurring after admission. Autologous blood transfusion was not included in the assessment of major bleeding. Because detailed intraoperative blood loss data were unavailable, transfusion records or diagnoses were used as proxies for major bleeding. The list of transfusion procedures and diagnostic codes used to define bleeding complications is provided in Supplemental Table 5.

Healthcare resource utilization measures and costs

We assessed the following healthcare resource utilization measures and costs: allogeneic transfusion (≥400 mL), including intraoperative and postoperative transfusion; operating room time, defined as the total duration of anesthesia in the operating room; postoperative length of stay, defined as the number of days from the day after surgery to the discharge date; postoperative hospitalization costs, defined as medical costs incurred from the day after surgery to the discharge date; postoperative intensive care unit (ICU) stay, defined as the number of days from the day after surgery to the discharge date; and postoperative surgery, defined as re-exploratory laparotomy (Supplemental Table 6) performed on or after postoperative day one.

Statistical Analyses

We calculated the prevalence of topical hemostatic material utilization patterns for open and laparoscopic hepatectomy in each study population. To compare patient characteristics, we tabulated patient characteristics and hospital characteristics. We described the incidence of major bleeding across patterns of topical hemostatic materials use. To characterize the relationship between perioperative major bleeding and postoperative measures, data were summarized by operative approach (open or laparoscopic hepatectomy). No adjustment was performed because the study was descriptive in nature and not intended to estimate causal effects. Missing values were reported as a separate category, and no imputation was performed. All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

Prevalence of patterns of topical hemostatic material use

Among patients who used at least one topical hemostatic material on the day of surgery, 3,328 underwent open hepatectomy and 620 underwent laparoscopic hepatectomy. Across operative approaches, primary hemostatics were commonly used in both open (72.3%) and laparoscopic hepatectomy (73.9%). Use of sheet-type biological tissue

adhesives/sealants varied by surgical approach, with higher utilization in open hepatectomy (66.7%) than in laparoscopic hepatectomy (43.2%). Fibrin sealants were used in a similar proportion of cases in open (18.5%) and laparoscopic hepatectomy (20.0%), while flowable microfibrillar collagen accounted for a smaller proportion of use in both approaches (3.2% in open and 6.6% in laparoscopic hepatectomy) (Table 1).

In contrast to the frequency of individual topical hemostatic materials, the distribution of combination use in open hepatectomy showed that the most common pattern was the combination of primary hemostatics and sheet-type biological tissue adhesives/sealants (39.1%), followed by use of sheet-type biological tissue adhesives/sealants alone (21.8%) and primary hemostatics alone (18.2%) (Table 1). The complete distribution of topical hemostatic material use patterns is illustrated in Figure 1.

Among patients undergoing laparoscopic hepatectomy, the most frequent pattern was primary hemostatics alone (35.3%), followed by the combination of primary hemostatics and sheet-type biological tissue adhesives/sealants (22.3%) and sheet-type biological tissue adhesives/sealants alone (17.6%). Compared with open hepatectomy, laparoscopic procedures more often involved single-product use of primary hemostatics, whereas combinations of multiple product types were less common (Table 1 and Figure 1).

Patient Characteristics

Overall, patient characteristics were generally comparable across the major topical hemostatic material use groups (Tables 2 and 3). Compared with patients who received the combination of primary hemostatics and sheet-type biological tissue adhesives/sealants, overall patient characteristics were generally similar among those who received primary hemostatics alone or sheet-type biological tissue adhesives/sealants alone. For laparoscopic hepatectomy, baseline patient and hospital characteristics were also largely similar across patterns of topical hemostatic material use, with no marked differences observed in demographic or clinical variables. However, a higher proportion of cases using the combination of primary hemostatics and sheet-type biological tissue adhesives/sealants was observed at larger hospitals (≥500 beds) in laparoscopic hepatectomy (Supplemental Table 7).

Perioperative major bleeding events

The incidence of major bleeding varied across the patterns of topical hemostatic material use for both open and laparoscopic hepatectomy (Table 4). For open hepatectomy, major bleeding occurred in 46.1% of patients who received a combination of primary hemostatics and sheet-type biological tissue adhesives/sealants, 37.6% of patients who received sheet-type biological tissue adhesives/sealants alone, and 35.2% of patients who received primary hemostatics alone.

For laparoscopic hepatectomy, major bleeding occurred in 34.1% of patients who received a combination of primary hemostatics and sheet-type biological tissue adhesives/sealants, 25.7% of patients who received sheet-type biological tissue adhesives/sealants alone, and 15.5% of patients who received primary hemostatics alone. Across operative approaches, the incidence of major bleeding was generally higher in open hepatectomy than in laparoscopic hepatectomy, regardless of the patterns of topical hemostatic material use.

Healthcare resource utilization and costs according to bleeding status

Postoperative healthcare resource utilization and costs stratified by bleeding status are summarized in Table 5. Across both open and laparoscopic hepatectomy, patients who experienced major bleeding consistently required greater postoperative resources than those without major bleeding.

Among patients with major bleeding, intraoperative and postoperative allogeneic transfusion ≥400 mL was more frequently observed in open hepatectomy (80.0%) than in laparoscopic hepatectomy (56.5%). Operating room time was longer among patients with major bleeding, with median (IQR) durations of 469 (384–561) minutes compared with 400 (325–475) minutes among those without major bleeding in open hepatectomy. A similar pattern was observed in laparoscopic hepatectomy, with longer operating room times among patients with major bleeding than among those without major bleeding. Postoperative length of stay was also prolonged in patients with major bleeding. In open hepatectomy, median (IQR) length of stay was 15 (11–23) days in patients with major bleeding and 12 (9–16) days in those without major bleeding, whereas laparoscopic hepatectomy demonstrated the same directional difference. Postoperative ICU stay was longer among patients with major bleeding for both operative approaches. In open hepatectomy, median (IQR) ICU stay was 2 (1–4) days compared with 1 (1–2) day among patients without major bleeding, with comparable differences observed in laparoscopic hepatectomy.

Postoperative hospitalization costs were likewise higher among patients with major bleeding for both operative approaches. For open hepatectomy, median (IQR) costs were 643.6 (445.0–1138.7) thousand Japanese yen among patients with major bleeding and 460.0 (358.0–653.5) thousand Japanese yen among those without major bleeding. A similar pattern was observed for laparoscopic hepatectomy, with median (IQR) costs of 574.6 (401.6–1036.5) thousand Japanese yen in patients with major bleeding and 395.5 (313.3–503.1) thousand Japanese yen in those without major bleeding. Reoperation after postoperative day 1 was infrequent in both open and laparoscopic hepatectomy (Table 5).

DISCUSSION

In this descriptive observational study of patients who received topical hemostatic materials during open and laparoscopic hepatectomy, approximately 80% of patients undergoing open hepatectomy and 75% of those undergoing laparoscopic hepatectomy used a combination of primary hemostatics and sheet-type biological tissue adhesives/sealants, or one of these materials alone. The incidence of major bleeding varied across patterns of topical hemostatic material use. Major bleeding during or after hepatectomy was associated with longer operative time, prolonged postoperative length of stay and ICU stay, and higher postoperative hospitalization costs.

Bleeding risk during hepatectomy may be influenced by patient-related factors, including the severity of underlying liver disease and associated conditions such as portal hypertension or renal dysfunction[14,15], as well as tumor-related factors such as greater tumor size[16]. Another important technical determinant of bleeding during hepatectomy is the need to dissect and control major hepatic veins during parenchymal transection, as bleeding due to hepatic vein injury can contribute substantially to intraoperative bleeding[17,18]. In the present study, patient characteristics were generally similar across the patterns of topical hemostatic material use among patients who received topical hemostatic materials during surgery, although detailed technical factors could not be directly assessed. In clinical practice, the selection of topical hemostatic materials is also influenced by their physical properties and suitability for different intraoperative situations.

In open hepatectomy, sheet-type biological tissue adhesives/sealants were more frequently used than in laparoscopic hepatectomy when applicable, as their flat transection surfaces allow for structural stability with secure apposition, whereas primary hemostatic agents are often used as an initial option for bleeding control. Meanwhile, in laparoscopic hepatectomy, patterns of topical hemostatic material use differed modestly from those observed in open hepatectomy. These differences likely reflect technical considerations related to instrument handling in a minimally invasive setting[19]. Certain topical hemostatic materials may be less amenable to manipulation through trocar ports, whereas

others are more easily deployed, leading to preferential use in laparoscopic procedures. Taken together, these findings suggest that patterns of topical hemostatic material use are primarily shaped by intraoperative technical factors rather than by baseline patient characteristics.

The incidence of major bleeding varied across topical hemostatic material categories, with the highest incidence observed among patients receiving a combination of primary hemostatics and sheet-type biological tissue adhesives/sealants in both open and laparoscopic hepatectomy. Previous studies have reported that the incidence of perioperative major bleeding after hepatectomy ranges from 14% to 49%[2,20–22], indicating substantial variability across studies, likely reflecting differences in study populations, definitions of bleeding, and perioperative practices. The overall prevalence of perioperative major bleeding observed in our study was comparable to that reported previously. Although the temporal sequence between bleeding events and topical hemostatic material use could not be assessed, our results provide descriptive data on contemporary bleeding incidence stratified by operative approach, including open and laparoscopic hepatectomy. These findings highlight the importance of interpreting bleeding incidence across hemostatics categories in light of intraoperative conditions and surgical complexity.

In this study of patients undergoing open hepatectomy, perioperative major bleeding was associated with a substantial increase in postoperative healthcare resource utilization and costs. Patients with major bleeding experienced longer operating room times, prolonged hospital stays, higher postoperative hospitalization costs, and longer ICU stays compared with those without major bleeding. Although this study was descriptive in nature and does not allow causal inference, these findings highlight the considerable healthcare burden associated with perioperative bleeding in hepatectomy. Taken together, our results emphasize the importance of effective intraoperative bleeding management and careful surgical planning to mitigate postoperative morbidity and healthcare resource use.

In addition to the limitations discussed above, several other limitations should be acknowledged. First, the coding accuracy, including bleeding complications, was not validated, leading to misclassification of the bleeding measurement. In general, the DPC system collected the most relevant diagnoses occurring after admission (up to 4) related to the procedure or hospitalization for reimbursement purposes. Therefore, the diagnosis of bleeding complications has high specificity but low sensitivity. Second, information on the individual surgeon's preferences could not be obtained, which may influence both topical hemostatic material selection and bleeding management. Finally, the generalizability of the finding is limited to non-DPC institutions or other healthcare systems.

In conclusion, across operative approaches, nearly 80% of patients undergoing hepatectomy received either a combination of primary hemostatics and sheet-type biological tissue adhesives/sealants or either material alone. Patterns of topical hemostatic material use varied according to operative approach, and major bleeding was observed across all product categories. Major bleeding was consistently associated with greater postoperative healthcare resource utilization and costs, underscoring the importance of understanding real-world use of topical hemostatic materials when considering intraoperative conditions and surgical decision-making.

Declarations

Ethics approval and consent to participate

This study was registered with the ethics committee of the University of Tokyo (ethics review number: 2025428NIe) and was conducted in accordance with institutional ethical guidelines.

Consent for publication

Not applicable

Availability of data and materials

The data used in this study were obtained from Medical Data Vision Co., Ltd. under a data use agreement. Because the data are commercially licensed and subject to contractual restrictions, they are not publicly available and cannot be shared by the authors.

Competing interests

SN, HY, and HK are affiliated with the Department of Health Quality Assessment at the University of Tokyo, a social collaboration department supported by the National Clinical Database, Johnson & Johnson K.K., Nipro Corporation, and Intuitive Surgical Sàrl. SN and HK have received research grants from Pfizer Japan Inc. for work unrelated to this study. KM, AM, YH, YK, and JI are employees of Johnson & Johnson K.K. Medical Company. HY has received speaker fees from Chugai Pharmaceutical Co., Ltd. GW has received speaker fees and consultation fees from Johnson & Johnson K.K. HK reports receiving consultation fees from EPS Corporation, speaker fees from Beyer Japan and Novartis Japan, and a research grant from Amgen KK for work unrelated to this study.

Funding

This study was funded by the collaborative research fund of the University of Tokyo, supported by Johnson & Johnson K.K. Medical Company.

Authors' Contributions

SN contributed to formal analysis, investigation, methodology, software, visualization, and writing of the original draft. KM contributed to conceptualization, investigation, methodology, project administration, resources, validation, and critical review and editing of the manuscript. AM contributed to conceptualization, investigation, methodology, validation, and critical review and editing of the manuscript. YH contributed to conceptualization, investigation, methodology, resources, data curation, formal analysis, software, validation, and critical review and editing of the manuscript. JI contributed to conceptualization, investigation, methodology, validation, and critical review and editing of the manuscript. HY contributed to funding acquisition, validation, and critical review and editing of the manuscript. GW contributed to critical review and editing of the manuscript from a surgical perspective. HK contributed to conceptualization, funding acquisition, investigation, methodology, validation, supervision, and critical review and editing of the manuscript. All authors read and approved the final manuscript.

Acknowledgements

Not applicable

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Tables

Table 1. Patterns of topical hemostatic material use in open and laparoscopic hepatectomy

	Open (n=3328)	Laparoscopic (n=620)
Individual materials		
Primary hemostatics, n(%)	2405 (72.3)	458 (73.9)
Flowable microfibrillar collagen, n(%)	105 (3.2)	41 (6.6)
Fibrin sealants, n(%)	616 (18.5)	124 (20.0)
Sheet-type biological tissue adhesives/sealants, n(%)	2221 (66.7)	268 (43.2)
Combination patterns of materials		
- PR, n(%)	605 (18.2)	219 (35.3)
- SH, n(%)	724 (21.8)	109 (17.6)
- PR+SH, n(%)	1301 (39.1)	138 (22.3)
- Other combinations, n(%)	698 (21.0)	154 (24.8)

Abbreviations: PR, primary hemostatic agents; SH, sheet-type biological tissue adhesives.

Table 2. Patient characteristics among 3328 patients who underwent open hepatectomy

	Combination			
Characteristics	PR+SH (n=1301)	PR (n=605)	SH (n=724)	Other combinations (n=698)
Age, years, median	72.0 (64.0,77.0)	71.0 (65.0,77.0)	72.0 (66.0,78.0)	71.0 (64.0,77.0)
Age ≥75 years, n(%)	470 (36.1)	213 (35.2)	277 (38.3)	240 (34.4)
Sex, women, n(%)	396 (30.4)	179 (29.6)	252 (34.8)	210 (30.1)
BMI (kg/m2)				
- <18, n(%)	66 (5.1)	42 (6.9)	45 (6.2)	38 (5.4)
- 18-<25, n(%)	840 (64.6)	395 (65.3)	464 (64.1)	466 (66.8)
- ≥25, n(%)	394 (30.3)	159 (26.3)	214 (29.6)	193 (27.7)
- Missing, n(%)	1 (0.1)	9 (1.5)	1 (0.1)	1 (0.1)
Smoking, pack-year ≥30, n(%)	371 (28.5)	176 (29.1)	194 (26.8)	182 (26.1)
Hypertension, n(%)	440 (33.8)	181 (29.9)	238 (32.9)	274 (39.3)
Hyperlipidemia, n(%)	117 (9.0)	44 (7.3)	57 (7.9)	59 (8.5)
Coronary heart disease, n(%)	11 (0.9)	5 (0.8)	7 (1.0)	12 (1.7)
Angina, n(%)	53 (4.1)	19 (3.1)	34 (4.7)	32 (4.6)
Heart failure, n(%)	41 (3.2)	24 (4.0)	26 (3.6)	27 (3.9)
Atrial fibrillation, n(%)	35 (2.7)	25 (4.1)	24 (3.3)	15 (2.2)
Peripheral arterial disease, n(%)	8 (0.6)	2 (0.3)	1 (0.1)	3 (0.4)
Chronic kidney disease, n(%)	44 (3.4)	11 (1.8)	11 (1.5)	20 (2.9)
Cirrhosis, n(%)	41 (3.2)	18 (3.0)	28 (3.9)	29 (4.2)
Other Liver disease, n(%)	74 (5.7)	33 (5.5)	52 (7.2)	52 (7.5)
Diabetes mellitus, n(%)	468 (36.0)	193 (31.9)	219 (30.3)	190 (27.2)
Anemia, n(%)	111 (8.5)	21 (3.5)	50 (6.9)	25 (3.6)
Thrombocytopenia, n(%)	7 (0.5)	2 (0.3)	6 (0.8)	3 (0.4)
Rheumatoid arthritis, n(%)	5 (0.4)	4 (0.7)	2 (0.3)	4 (0.6)
Deep vein thrombosis, n(%)	29 (2.2)	5 (0.8)	9 (1.2)	14 (2.0)
Charlson comorbidity index, mean	4.4 (2.9)	4.1 (2.8)	4.5 (2.9)	4.1 (2.9)
T category				
- T0 Tis, n(%)	3 (0.2)	2 (0.3)	5 (0.7)	3 (0.4)
- T1, n(%)	152 (11.7)	77 (12.7)	88 (12.2)	69 (9.9)
- T2, n(%)	271 (20.8)	133 (22.0)	147 (20.3)	176 (25.2)
- T3, n(%)	243 (18.7)	104 (17.2)	124 (17.1)	127 (18.2)

	Combination			
Characteristics	PR+SH (n=1301)	PR (n=605)	SH (n=724)	Other combinations (n=698)
- T4, n(%)	74 (5.7)	48 (7.9)	51 (7.0)	63 (9.0)
- Unknown, n(%)	558 (42.9)	241 (39.8)	309 (42.7)	260 (37.3)
N category				
- N0, n(%)	622 (47.8)	294 (48.6)	326 (45.0)	354 (50.7)
- N1, n(%)	90 (6.9)	39 (6.5)	52 (7.2)	50 (7.2)
- N2+, n(%)	28 (2.2)	17 (2.8)	26 (3.6)	17 (2.4)
- Unknown, n(%)	561 (43.1)	255 (42.2)	320 (44.2)	277 (39.7)
M category				
- M0, n(%)	633 (48.7)	311 (51.4)	338 (46.7)	354 (50.7)
- M1, n(%)	128 (9.8)	54 (8.9)	82 (11.3)	82 (11.8)
- Unknown, n(%)	540 (41.5)	240 (39.7)	304 (42.0)	262 (37.5)
Cancer stage ≥III, n(%)	372 (28.6)	169 (27.9)	207 (28.6)	214 (30.7)

Values are means(SD) or medians(Q25, Q75) for continuous variables; percentages or ns or both for categorical variables.

Values of polytomous variables may not sum to 100% due to rounding.
Abbreviations: PR, primary hemostatic agents; SH, sheet-type biological tissue adhesives.
Table 3. Patient characteristics among 620 patients who underwent laparoscopic hepatectomy

	Combination			
Characteristics	PR+SH (n=138)	PR (n=219)	SH (n=109)	Other combinations (n=154)
Age, years, median	72.0 (64.0,79.0)	70.0 (63.0,77.0)	73.0 (65.0,79.0)	71.0 (63.0,78.0)
Age ≥75 years, n(%)	53 (38.4)	78 (35.6)	52 (47.7)	52 (33.8)
Sex, women, n(%)	36 (26.1)	73 (33.3)	37 (33.9)	55 (35.7)
BMI (kg/m2)				
- <18, n(%)	3 (2.2)	10 (4.6)	6 (5.5)	6 (3.9)
- 18-<25, n(%)	90 (65.2)	149 (68.0)	73 (67.0)	103 (66.9)
- ≥25, n(%)	45 (32.6)	59 (26.9)	30 (27.5)	44 (28.6)
- Missing, n(%)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.7)
Smoking, pack-year ≥30, n(%)	40 (29.0)	50 (22.8)	35 (32.1)	53 (34.4)
Hypertension, n(%)	52 (37.7)	52 (23.7)	37 (33.9)	50 (32.5)
Hyperlipidemia, n(%)	15 (10.9)	12 (5.5)	8 (7.3)	10 (6.5)
Coronary heart disease, n(%)	1 (0.7)	2 (0.9)	3 (2.8)	3 (2.0)
Angina, n(%)	7 (5.1)	15 (6.9)	7 (6.4)	3 (2.0)
Heart failure, n(%)	2 (1.5)	8 (3.7)	5 (4.6)	5 (3.3)
Atrial fibrillation, n(%)	4 (2.9)	9 (4.1)	5 (4.6)	5 (3.3)
Peripheral arterial disease, n(%)	0 (0.0)	1 (0.5)	0 (0.0)	2 (1.3)
Chronic kidney disease, n(%)	2 (1.5)	5 (2.3)	6 (5.5)	6 (3.9)
Cirrhosis, n(%)	4 (2.9)	3 (1.4)	2 (1.8)	9 (5.8)
Other Liver disease, n(%)	6 (4.4)	10 (4.6)	5 (4.6)	13 (8.4)
Diabetes mellitus, n(%)	52 (37.7)	63 (28.8)	42 (38.5)	45 (29.2)
Anemia, n(%)	8 (5.8)	5 (2.3)	7 (6.4)	2 (1.3)
Thrombocytopenia, n(%)	1 (0.7)	1 (0.5)	1 (0.9)	0 (0.0)
Rheumatoid arthritis, n(%)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.3)
Deep vein thrombosis, n(%)	0 (0.0)	7 (3.2)	2 (1.8)	3 (2.0)
Charlson comorbidity index, mean	4.0 (2.8)	4.7 (3.0)	4.3 (2.9)	4.1 (2.9)
T category				
- T1, n(%)	23 (16.7)	20 (9.1)	15 (13.8)	20 (13.0)
- T2, n(%)	38 (27.5)	51 (23.3)	30 (27.5)	42 (27.3)
- T3, n(%)	22 (15.9)	24 (11.0)	19 (17.4)	26 (16.9)
- T4, n(%)	12 (8.7)	13 (5.9)	9 (8.3)	12 (7.8)

	Combination			
Characteristics	PR+SH (n=138)	PR (n=219)	SH (n=109)	Other combinations (n=154)
- Unknown, n(%)	43 (31.2)	111 (50.7)	36 (33.0)	54 (35.1)
N category				
- N0, n(%)	84 (60.9)	86 (39.3)	62 (56.9)	85 (55.2)
- N1, n(%)	6 (4.4)	14 (6.4)	9 (8.3)	6 (3.9)
- N2+, n(%)	6 (4.4)	6 (2.7)	4 (3.7)	7 (4.6)
- Unknown, n(%)	42 (30.4)	113 (51.6)	34 (31.2)	56 (36.4)
M category				
- M0, n(%)	83 (60.1)	92 (42.0)	59 (54.1)	85 (55.2)
- M1, n(%)	12 (8.7)	17 (7.8)	18 (16.5)	17 (11.0)
- Unknown, n(%)	43 (31.2)	110 (50.2)	32 (29.4)	52 (33.8)
Cancer stage ≥III, n(%)	35 (25.4)	40 (18.3)	28 (25.7)	41 (26.6)

Values are means(SD) or medians(Q25, Q75) for continuous variables; percentages or ns or both for categorical variables.

Values of polytomous variables may not sum to 100% due to rounding.

Abbreviations: PR, primary hemostatic agents; SH, sheet-type biological tissue adhesives.

Table 4. Major bleeding according to topical hemostatic material combinations in open and laparoscopic hepatectomy

	Open (n=3,328)		Laparoscopic (n=620)	
Combination	Total, n	Major bleeding, n (%)	Total, n	Major bleeding, n(%)
Primary hemostatics	605	213 (35.2)	219	34 (15.5)
Sheet-type biological tissue adhesives/sealants	724	272 (37.6)	109	28 (25.7)
Primary hemostatics+Sheet-type biological tissue adhesives/sealants	1301	600 (46.1)	138	47 (34.1)
Other combinations	698	257 (36.8)	154	29 (18.8)
Total	**3,328**	**1,342 (40.3)**	**620**	**138 (22.3)**

Table 5. Healthcare resource utilization and costs stratified by major bleeding status and operative approach

	Open hepatectomy		Laparoscopic hepatectomy	
	No major bleeding (n=1986)	Major bleeding (n=1342)	No major bleeding (n=482)	Major bleeding (n=138)
Allogeneic transfusion ≥400 mL, n(%)	-	1075 (80.1)	-	78 (56.5)
Operating room time, minutes	400.0 (325.0,475.0)	469.0 (384.0,561.0)	441.0 (351.0,558.0)	537.5 (446.0,657.0)
Length of stay, days	12.0 (9.0,16.0)	15.0 (11.0,23.0)	9.0 (8.0,12.0)	12.0 (10.0,18.0)
Postoperative hospitalization cost, thousand JPY	460.5 (358.1,653.6)	643.6 (444.9,1139.2)	395.5 (313.3,503.1)	574.6 (401.6,1036.5)
Postoperative ICU stay, days	1.0 (1.0,2.0)	2.0 (1.0,4.0)	1.0 (1.0,2.0)	3.0 (1.0,4.0)
Reoperation, n(%)	1 (0.1)	10 (0.8)	0 (0.0)	2 (1.5)

Abbreviations: ICU, intensive care unit; IQR, interquartile range; JPY, Japanese yen.

Values are presented as median (Q25, Q75) unless otherwise indicated.

*Allogeneic transfusion included intraoperative and postoperative transfusion.

Figures

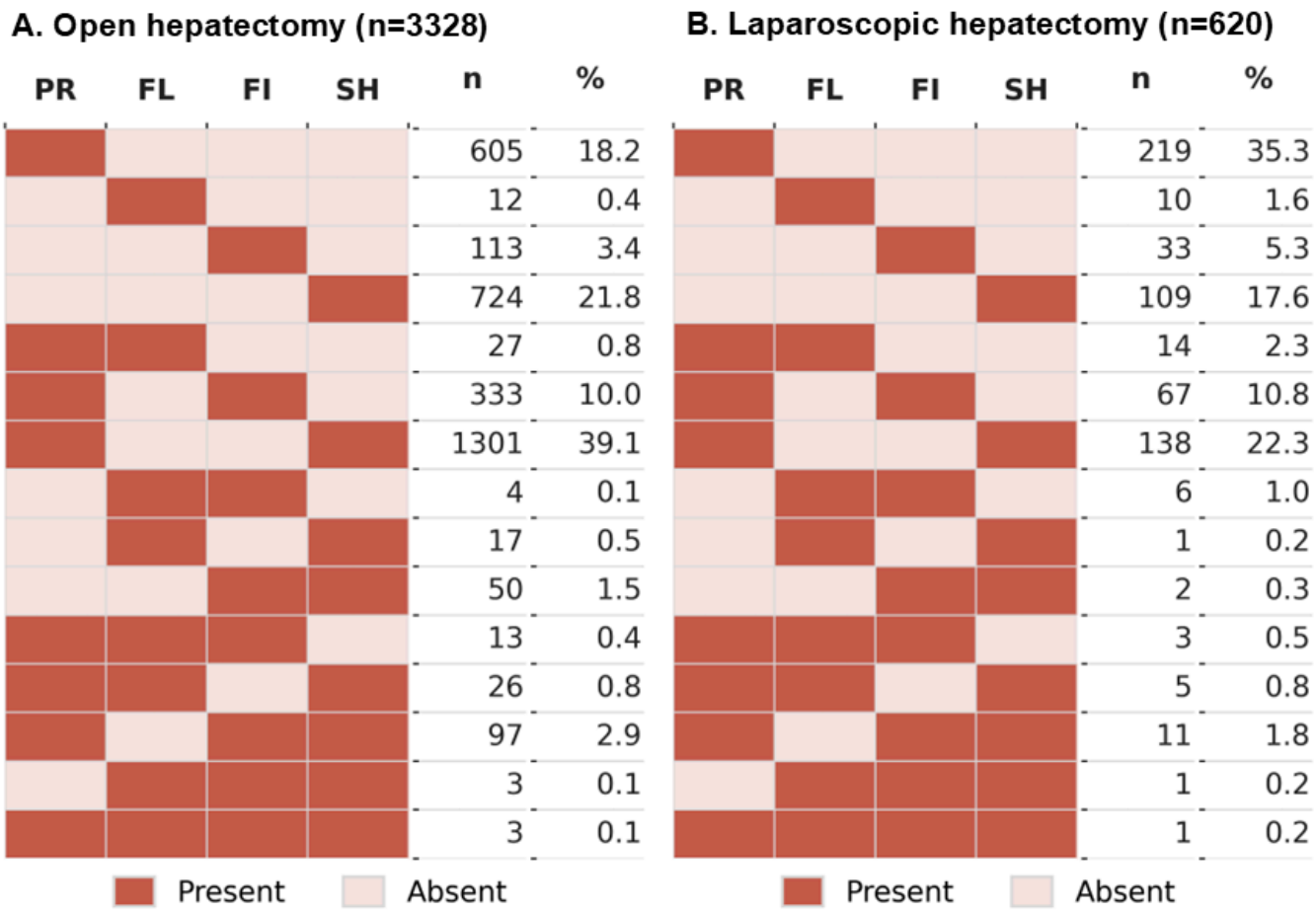


Figure 1

Patterns of topical hemostatic material combinations in open and laparoscopic hepatectomy

A. Open hepatectomy

B. Laparoscopic hepatectomy

Abbreviations: PR, primary hemostatic agents; FL, flowable collagen-based materials; FI, fibrin sealants; SH, sheet-type biological tissue adhesives.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryTable3.xlsx
- 20260622SupplementaryDataPatternsofHemostaticMaterialUse.docx