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*Case Control Study*

Use of a saline-coupled bipolar sealer open liver resection for hepatic malignancy: Medical resource use and costs

Nichols CI *et al.* Bipolar Sealer forliver resection

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**Author contributions:** Nichols CI and Vose JG designed the research; Nichols CI performed data analyses; Nichols CI and Vose JG analyzed the data; and Nichols CI and Vose JG wrote the paper and revisions.

**Institutional review board statement:** Given this study used de-identified patient data, it was not subject to Institutional Review Board (IRB) approval. The study dataset and full study tables are available from the corresponding author.

**Informed consent statement:** All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

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Abstract

***AIM***

To evaluated outcomes associated with use of a saline coupled bipolar sealer during open partial liver resection.

***METHODS***

This retrospective analysis utilized the United States Premier insurance claims database (2010 - 2014). Patients were selected with codes for liver malignancy and partial hepatectomy or lobectomy. Cases were defined by use the saline-coupled bipolar sealer; controls had no use. A Propensity Score algorithm was used to match one case to five controls. A deviation-based cost modeling (DBCM) approach provided an estimate of cost-effectiveness.

***RESULTS***

One hundred and forty-four cases and 720 controls were available for analysis. Patients in the Case cohort received fewer transfusions *vs* controls (18.1% *vs* 29.4%, *P* = 0.007). In DBCM, more patients in the case cohort experienced “on-course” hospitalizations (53.5% *vs* 41.9%, *P* = 0.009). The cost calculation showed an average savings in total hospitalization costs of $1027 for cases *vs* controls. In multivariate analysis, cases had lower odds of receiving a transfusion (OR = 0.44, 95%CI: 0.27 – 0.71, *P* = 0.0008).

***CONCLUSION***

Use of a saline-coupled bipolar sealer was associated with a greater proportion of patients with an “on course” hospitalization.

# Key words: Liver resection; hepatocellular carcinoma; costs

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**Core tip:** This is an interesting paper and well written. The current results will be great helpful to the surgical fields when evaluating the benefits and costs of alternative blood-management technologies during liver resection.

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INTRODUCTION

Liver resection remains the only curative treatment for primary and metastatic liver malignancy. However, despite advances in surgical technique over the past two decades, blood transfusions are still required in a proportion of patients undergoing liver resection (3.3%-59%), varying by the extent of the procedure and device combinations used[1–5]. Predictors of transfusion include factors related to the operative procedure (resection technique, extent of resection, tumor size, need for other major resections during the same hospitalization) as well as patient-specific characteristics (pre-operative hemoglobin and albumin levels, pre-operative biliary drainage, and diagnosis of a primary liver tumor, coronary artery disease, or cirrhosis)[6–9].

The most serious complication associated with transfusion, beyond simple transfusion-related reactions or immunomodulatory effects, is the increased risk of tumor recurrence[6,8–10]. In a meta-analysis of 22 studies evaluating the impact of perioperative allogenic blood transfusion on long term outcomes following hepatocellular carcinoma (HCC) resection, authors found the risk of tumor recurrence was significantly higher among patients with a transfusion at one (OR = 1.70, 95%CI: 1.38-1.10), three (OR = 1.22, 95%CI: 1.08-1.38), and five years (OR = 1.16, 95%CI: 1.08-1.24) post-resection compared with patients with no transfusion. This finding was confirmed in a Cochrane meta-analysis evaluating the risk of cancer recurrence following surgery for colorectal cancer among patients with versus without receipt of a transfusion.[11] These studies suggest that transfusion may result in immunosuppression in the early postoperative period, which could allow for the progression of residual carcinoma and influence survival[12].

Prior research has demonstrated the effects of surgical technique, peri-operative blood management protocols, and use of surgical technologies on the risk of transfusion[1–5]. Peri-operatively, studies have examined autologous blood donation, intravenous iron therapy, and strict transfusion protocols. Intraoperatively, other studies have examined the effects of clamping the hepatic artery and portal vein (*i.e.,* Pringle’s Maneuver), topical hemostatic agents, and use of technologies such as the Cavitron Ultrasonic Surgical Aspirator (CUSA), saline-coupled bipolar sealer (SCBS), argon beam coagulation (ABC), harmonic scalpel, bipolar scissors, vessel sealers, cell saver systems, and hydrodissector[13]. The majority of these studies examined clinical outcomes alone, with few examining the total cost of the procedure or incremental costs associated with complications. Two prior high-quality cost studies applied a novel methodology, deviation-based cost modeling (DBCM), however the primary comparison was of open versus laparoscopic approach rather than specific surgical technologies utilized during the procedure[14,15].

Given that few studies to date summarize total direct hospitalization costs by choice of surgical technology during hepatic resection, we sought to examine the resource use and costs by technology choice. Specifically, in the present study we evaluated the clinical and economic outcomes associated with the SCBS during open partial liver resections, using real-world data from a nationally representative US claims database.

**MATERIALS AND METHODS**

## *Data source and patient population*

This retrospective database analysis reviewed recent healthcare insurance claims data from the Premier Perspective database (Premier Inc., Charlotte, NC). Data were analyzed over the period 01/2010 to 06/2014. The database includes information on patient demographics, diagnosis and procedure codes, and cost information for over 2,000 hospitals and 300 million patient encounters. This database is limited to the inpatient period, with no ability to track patients longitudinally in follow-up. The Premier database allows for tracking of total hospitalization cost information on a per-patient basis. However, the inherent tradeoff of working with retrospective claims data is the reliance on ICD-9 diagnosis and procedure codes to identify liver resections – with the codes providing no information on the specific number of segments, lobes, or tissue volume resected. Given this study used de-identified patient data, it was not subject to Institutional Review Board (IRB) approval. The study dataset and full study tables are available from the corresponding author.

Patients age 18 and older with records included International Classification of Diseases (ICD-9-CM) or Current Procedural Technology (CPT) procedure codes for liver resection during a hospitalization episode (50.22 – partial hepatectomy or 50.3 x – lobectomy), accompanied by a diagnosis code for primary malignant neoplasm of the liver (155.0x) or metastatic neoplasm of the liver (197.7 x), were selected. Those with benign neoplasms (211.5 x) were excluded to reduce the potential confounding effects of different liver pathology and bleeding risk. Total liver resection and transplant procedures were excluded. Operations using ablation procedures or laparoscopic approaches (as identified by ICD-9-CM codes and key terms in Premier Chargemaster records) were excluded due to the high cost of these procedures and to better isolate the effects of SCBS use. Open SCBS device use was identified by the hospital Chargemaster file; laparoscopic SCBS models were excluded.

## The “case” cohort was defined as any hospitalization episode meeting all inclusion criteria listed above, where the SCBS was used. The “control” cohort was defined as cases in which the SCBS was not used. Similar to prior cost analyses,[16] patients in the top one percent of total hospitalization cost within each cohort were excluded from analysis in order to reduce the effects of extreme outliers (> $87,262 among Cases and > $153,428 among Controls). Figure 1 provides a summary of patient selection.

## *Study measures*

## Study measures included patient demographic, clinical, hospital, and surgeon characteristics, transfusion procedures and other complications during index hospitalization, hospital length of stay (LOS) and costs. Comorbidity status was evaluated with diagnoses recorded during the one year prior to admission (baseline period) through the index hospitalization episode. The Charlson Comorbidity Index (CCI) score, a composite measure of physical health status commonly used in studies of medical claims and chronic disease[17,18] was calculated for each patient. For this study, malignancy, metastatic solid tumor, and mild or moderate liver disease were excluded from the CCI calculation as these were present for most patients.

## *Propensity score matching*

## In order to address selection bias and ensure demographic and hospitalization characteristics were similar across the case and control cohorts, a propensity-score matching algorithm was applied. Each case was matched to five controls based on age group, gender, race, region, primary payor, procedure type, indicating diagnosis, other comorbid liver-related conditions, CCI, surgeon specialty, and the proportion of surgeons with history of at least one liver procedure performed in the prior year. These matching covariates were chosen both based on significant differences observed in unmatched cohorts (*P* values < 0.05), and on the basis of clinical and demographic factors that may have impacted surgeon choice of technology use. Matching was applied using the nearest neighbor approach, with a caliper width of 0.10 of the standard deviation of the logit of the propensity score.

## *Hospital resource use and deviation-based cost modeling*

## Transfusion procedures were identified by ICD-9 (V58.2, 99.00-99.04) or CPT codes (36430, P9010, P9011) or presence of the term “blood transfusion” in the hospital Chargemaster file. Topical hemostat use was identified by any mention of “hemostat” or “sealant” in the Chargemaster file under the “Medical Surgical Supplies” category.

A deviation-based cost modeling (DBCM) approach was employed to account for variation in resource use associated with different hospital LOS categories and severity of complications[14,15,19]. Vanounou *et al*[15,19] originally developed this approach in analyses evaluating the economic impact of pancreaticoduodenectomy procedures and a comparison of laparoscopic versus open liver resection. This methodology measures the frequency and severity of deviations from an “expected” postoperative course and calculates the economic consequences of hospitalizations that do not follow expected outcomes. The benefits of this approach are the incorporation of complications, LOS, and costs into one measure, providing a single outcomes-based metric that provides more information than simply clinical or cost data alone[14,15]. Data on LOS and complications were combined to create four deviation classes: on-course, minor, moderate, and severe. Definitions for each class are listed in Table 1. Once deviation groups were defined, a weighted average mean cost (WAMC) was calculated by multiplying the percentage of patients in each category by the mean cost of that category.

## *Data analyses*

## Analyses were performed using the Instant Health Data Suite (Boston Health Economics, Inc., Boston, MA) and SAS software (Version 9.2, SAS Institute, Cary, NC). All costs were inflation-adjusted to 2014 USD using the medical care component of the Consumer Price Index. Statistical significance testing was performed with the Chi-square (*χ*2) test for categorical variables (or Fisher's Exact with cell frequencies < 10) and Wilcoxon-Mann-Whitney test for non-normal continuous variables. Predictors of topical hemostat use and transfusion, controlling for demographic and clinical characteristics, provider specialty and experience, and study cohort, were evaluated using logistic regression analysis.

# RESULTS

## *Demographic and clinical characteristics*

Between January 2010 and June 2014, 152 cases and 2,993 unmatched controls were available for analysis after applying all sample selection criteria, with procedures performed at 284 hospitals nationally. Following application of the propensity score algorithm 144 cases and 720 controls were available for matched analyses (Table 2). Post-match, differences between cohorts were removed, with all clinical characteristics statistically similar.

## *Inpatient complications*

In matched analysis, patients in the Case cohort had lower incidence of transfusions versus the control cohort, with an absolute risk reduction of 11.3% and relative risk reduction of 38.7% (18.1% *vs* 29.4%, *P* = 0.007). Additionally, patients in the Case cohort had fewer cases of acute kidney failure occurring during the same hospitalization episode (3.5% *vs* 8.8%, *P* = 0.048). All other inpatient complications were statistically similar across cohorts, including infection, UTI, acute respiratory failure, pneumonia, DVT, hemorrhage or hematoma, wound disruption, and bile leak. One patient (0.694%) in the Case cohort had evidence of bile leak *vs* eight patients in the Control cohort (1.11%), however this difference was not significant (*P* = 1.00). No patients in the case cohort experienced acute liver failure, PE, or transfusion-related complications, while 1.8%, 1.0%, and 0.6% of control patients developed these complications during the inpatient visit (all *P* > 0.05).

Overall, 25.0% of the case cohort showed evidence of topical hemostat use during the liver resection procedure, while 17.2% of the control cohort showed evidence of topical hemostat use (*P* = 0.038). Among patients with topical hemostat use, the incidence of transfusions was lower in the case cohort, however the difference was not statistically significant (25.0% *vs* 37.9%, *P* = 0.108), Figure 2. When a topical hemostat was not used, the case cohort had lower incidence of transfusion compared to the control cohort (15.7% *vs* 27.7%, *P* = 0.009).

## *DBCM analysis*

Length of stay was shorter in the case cohort, however the difference was not statistically significant (7.38 *vs* 8.18, *P* = 0.210; Table 3); the median LOS was six days for each cohort. A greater proportion of patients in the case cohort had an on-course hospitalization vs. the control (53.5% *vs* 41.9%, *P* = 0.013; Table 4). The proportion in other deviation classes was statistically similar across cohorts. Mean total hospitalization costs were greater among those with an on-course hospitalization in the case cohort *vs* controls ($18,000 *vs* $16,813, *P* = 0.031); costs in other deviation classes were not statistically different. Overall, accounting for the distribution of patients in each deviation class and mean cost by deviation class, the WAMC for the case cohort was $25503 *vs* $26530 for controls. This represents an average savings of $1027 in the total hospitalization cost per patient when the SCBS was used.

## *Predictors of topical hemostat use and incidence of transfusion*

In logistic regression analysis of predictors of topical hemostat use, patients residing in the South were at greater odds of topical hemostat use compared to those in the Northeast, while patients with the surgery performed by a surgical oncologist were at lower odds of hemostat use compared to general surgeons (Table 5). Patients in the case cohort were at higher odds of topical hemostat use *vs* controls (OR = 2.56, 95%CI: 1.70-3.86, *P* < 0.001).

In a regression evaluating predictors of a transfusion during the hospitalization (Table 5), patients aged 75 or older (*vs* ages 18 to 44), Black race (versus Caucasian), and patients residing in the South (*vs* Northeast), and patients operated on by an other surgical specialist (*vs* general surgeons) were at higher odds of receiving a transfusion. Patients undergoing a lobectomy (versus partial hepatectomy) were at higher odds, as were patients whose diagnosis was a primary malignancy (versus metastatic). Controlling for topical hemostat use, patients in the case cohort were at lower odds of transfusion versus controls (OR = 0.44, 95%CI: 0.27 – 0.71, *P* = 0.0008)

# DISCUSSION

This retrospective database analysis evaluated the use of the SCBS in open partial liver resection for hepatic malignancy. After matching, patients treated with the SCBS had a lower incidence of transfusions (18.1% *vs* 29.4%, *P* = 0.007). Controlling for topical hemostat use, the reduction of transfusion incidence in univariate analysis was confirmed in multivariate analysis, with SCBS use associated with a lower odds of transfusion versus no use (OR = 0.44, 95%CI: 0.27 – 0.71). Overall, DBCM analyses indicated an average cost savings of $1027 among cases when accounting for the proportion within each “hospital deviation” class, with significantly more patients in the SCBS cohort with an “on course” hospitalization (defined as no complications and a LOS less than the median). We believe this study, despite the lack of clinical detail on number of lobes resected, provides information on “real-world” practice outside of a controlled prospective study or randomized controlled trial.

This study adds to a growing body of research evaluating the safety and efficacy of SCBS in liver resections. Authors at the University of Pittsburgh Starzl Transplant Institute performed a single-arm study evaluating the safety of the SCBS (formerly of “TissueLink Medical”) in 170 open liver resection procedures performed between 2001 and 2004[20]. Overall, 3.5% of patients were transfused and 2.4% developed a postoperative bile leak. There were no cases of postoperative hemorrhage, hepatic failure, liver abscess, or reoperation. The authors concluded the SCBS was effective in achieving intraoperative hemostasis in hepatic resection. The observed transfusion rate is much lower than in our present study, however this is likely due to comparing outcomes from a single high-volume hospital versus our present study, which includes data from 284 hospitals.

In a prospective single-arm study in Italy, the incidence of early surgical complications (including bleeding, biliary leakage, and abscess development) following 12 partial hepatectomies with the SCBS was evaluated[21]. Mean blood loss was 20 mL (range 5 to 80 mL), with no transfusions and a mean LOS of six days[21]. This LOS is similar to the 7.4 d observed in the case cohort of our study.

Lastly, two studies have examined the combined use of the SCBS and CUSA. In the largest study of SCBS use in liver resection to date, authors at four hepatopancreaticobiliary units in Europe evaluated the safety and efficacy of combined use of SCBS plus CUSA during 114 minor and 199 major hepatectomies. Authors reported a transfusion rate of 10.5% and two postoperative deaths (0.6%), concluding the combined method is associated with decreased blood loss[9]. A similar Japanese study also evaluated the combined use of CUSA and SCBS (*n* = 55) *vs* CUSA with traditional bipolar electrosurgery (*n* = 54)[22]. The SCBS and CUSA cohort demonstrated significantly lower total blood loss (677mL *vs* 1076 mL, *P* = 0.0486), shorter transection time (81 min *vs* 115 min, *P* = 0.0025) and fewer ties required (13.1 *vs* 22.8, *P* < 0.001) *vs* the traditional electrosurgery and CUSA cohort[22]. While the combined use of SCBS and CUSA is evaluated in these studies, other device combinations or techniques may provide equivalent outcomes at lower cost. This is an area for future research.

Although it was observed in the present study that a greater proportion of the case cohort had concurrent use of topical hemostats during the procedure (25.0% *vs* 17.2%, *P* = 0.038), it appears hemostat use was reserved for the most severe cases. We infer this due to the incidence of transfusion being greater in both univariate and multivariate analyses among those with topical hemostat use versus no use, regardless of SCBS. However, there is likely an unmeasured confounder that is not readily observed in insurance claims data that may have influenced surgeon selection of both the SCBS and a hemostat. Nonetheless, incidence of transfusion remained numerically lower in the case cohort versus controls both when topical hemostats were used during the procedure and when they were not.

Limitations of this study center on the lack of detailed clinical detail in the insurance claims dataset used for analysis, which included only diagnosis and procedure codes, and items listed in the hospital Chargemaster. Therefore, we could not evaluate the number of liver segments resected, the relative complexity of the procedure, pre- and post-operative hemoglobin levels, the Hg level triggering a transfusion, or number of units of blood transfused. Also, as noted, specific line-item costs for blood were not available for approximately two-thirds of patients. However, blood costs were captured in the next level roll-up of cost reporting under OR costs. During patient selection we did not attempt to query the Chargemaster file to evaluate concurrent devices used with the SCBS, as the only comparison in this study was at the highest level of use versus no use. Given the array of device choices during hepatic resection, and the variance of names listed in the Chargemaster file, we did not attempt to compare concurrent device use. Future studies may address the question of device synergy in influencing clinical outcomes (*e.g.,* SCBS plus CUSA). Finally, while we observed a reduction in the incidence of transfusion associated with use of SCBS in the present study, the SCBS is not designed to provide hemostasis in the event of bleeding from large vessels – thus additional technology or techniques to control bleeding that cannot be accounted for may have been present.

This retrospective database analysis demonstrated that use of the SCBS in open partial liver resection for hepatic malignancy is associated with reduction in the need for transfusion, and is cost-effective in a deviation-based cost modeling analysis. This technology provides an alternative solution for bleeding control in partial liver resection compared to traditional methods.

# ACKNOWLEDGEMENTS

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**COMMENTS**

***Background***

Despite advances in surgical technique over the past two decades, blood transfusions are still required in a proportion of patients undergoing liver resection, varying by the extent of the procedure and device combinations used. Predictors of transfusion include factors related to the operative procedure as well as patient-specific characteristics.

***Research frontiers***

Prior research has demonstrated the effects of surgical technique, peri-operative blood management protocols, and use of surgical technologies on the risk of transfusion. The majority of these studies examined clinical outcomes alone, with few examining the total cost of the procedure or incremental costs associated with complications. Two prior cost studies applied a novel methodology, deviation-based cost modeling (DBCM), however the primary comparison was of open versus laparoscopic approach rather than specific surgical technologies utilized during the procedure.

***Innovations and breakthroughs***

This retrospective database analysis evaluated the use of a saline-coupled bipolar sealer (SCBS) in open partial liver resection for hepatic malignancy. After matching, patients treated with the SCBS had a lower incidence of transfusions (18.1% *vs* 29.4%, *P* = 0.007). Controlling for topical hemostat use, the reduction of transfusion incidence was confirmed in multivariate analysis, with SCBS use associated with a lower odds of transfusion (OR = 0.44, 95%CI: 0.27 – 0.71). Overall, DBCM cost analyses indicated an average cost savings of $1027 among cases when accounting for the proportion falling into each “hospital deviation” class, with significantly more patients in the SCBS cohort with an “on course” hospitalization (defined as no complications and a length of stay less than the median).

***Applications***

This analysis demonstrated that use of the SCBS in open partial liver resection for hepatic malignancy is associated with reduction in the need for transfusion, and is cost-effective in a deviation-based cost modeling analysis. This technology provides an alternative solution for bleeding control in partial liver resection compared to traditional electrosurgical methods.

***Terminology***

A DBCM approach was employed in this study. This methodology measures the frequency and severity of deviations from an “expected” postoperative course and calculates the economic consequences of hospitalizations that do not follow expected outcomes. The benefits of this approach are the incorporation of complications, length of stay, and costs into one measure, providing a single outcomes-based metric that provides more information than simply clinical or cost data alone.

***Peer-review***

This is an interesting paper and well written. The current results will be great helpful to the surgical fields when evaluating the benefits and costs of alternative blood-management technologies during liver resection.

**REFERENCES**

1 **Guo JY**, Li DW, Liao R, Huang P, Kong XB, Wang JM, Wang HL, Luo SQ, Yan X, Du CY. Outcomes of simple saline-coupled bipolar electrocautery for hepatic resection. *World J Gastroenterol* 2014; **20**: 8638-8645 [PMID: 25024620 DOI: 10.3748/wjg.v20.i26.8638]

2 **Ikeda M**, Hasegawa K, Sano K, Imamura H, Beck Y, Sugawara Y, Kokudo N, Makuuchi M. The vessel sealing system (LigaSure) in hepatic resection: a randomized controlled trial. *Ann Surg* 2009; **250**: 199-203 [PMID: 19638927 DOI: 10.1097/SLA.0b013e3181a334f9]

3 **Nanashima A**, Abo T, Arai J, Takagi K, Matsumoto H, Takeshita H, Tsuchiya T, Nagayasu T. Usefulness of vessel-sealing devices combined with crush clamping method for hepatectomy: a retrospective cohort study. *Int J Surg* 2013; **11**: 891-897 [PMID: 23954369 DOI: 10.1016/j.ijsu.2013.07.012]

4 **Saiura A**, Yamamoto J, Koga R, Sakamoto Y, Kokudo N, Seki M, Yamaguchi T, Yamaguchi T, Muto T, Makuuchi M. Usefulness of LigaSure for liver resection: analysis by randomized clinical trial. *Am J Surg* 2006; **192**: 41-45 [PMID: 16769273 DOI: 10.1016/j.amjsurg.2006.01.025]

5 **Xia F**, Wang S, Ma K, Feng X, Su Y, Dong J. The use of saline-linked radiofrequency dissecting sealer for liver transection in patients with cirrhosis. *J Surg Res* 2008; **149**: 110-114 [PMID: 18541264 DOI: 10.1016/j.jss.2008.01.002]

6 **Cockbain AJ**, Masudi T, Lodge JP, Toogood GJ, Prasad KR. Predictors of blood transfusion requirement in elective liver resection. *HPB (Oxford)* 2010; **12**: 50-55 [PMID: 20495645 DOI: 10.1111/j.1477-2574.2009.00126.x]

7 **Lucas DJ**, Schexneider KI, Weiss M, Wolfgang CL, Frank SM, Hirose K, Ahuja N, Makary M, Cameron JL, Pawlik TM. Trends and risk factors for transfusion in hepatopancreatobiliary surgery. *J Gastrointest Surg* 2014; **18**: 719-728 [PMID: 24323432 DOI: 10.1007/s11605-013-2417-9]

8 **Pulitanò C**, Arru M, Bellio L, Rossini S, Ferla G, Aldrighetti L. A risk score for predicting perioperative blood transfusion in liver surgery. *Br J Surg* 2007; **94**: 860-865 [PMID: 17380562 DOI: 10.1002/bjs.5731]

9 **Sima CS**, Jarnagin WR, Fong Y, Elkin E, Fischer M, Wuest D, D'Angelica M, DeMatteo RP, Blumgart LH, Gönen M. Predicting the risk of perioperative transfusion for patients undergoing elective hepatectomy. *Ann Surg* 2009; **250**: 914-921 [PMID: 19953711]

10 **Liu L,** Wang Z, Jiang S, Shao B, Liu J, Zhang S, Zhou Y, Zhou Y, Zhang Y. Perioperative allogenenic blood transfusion is associated with worse clinical outcomes for hepatocellular carcinoma: a meta-analysis. PLoS One 2013; 8: e64261 [DOI: 10.1371/journal.pone.0064261]

11 **Amato A**, Pescatori M. Perioperative blood transfusions for the recurrence of colorectal cancer. *Cochrane Database Syst Rev* 2006;**(1):** CD005033 [PMID: 16437512 DOI: 10.1002/14651858.CD005033.pub2]

12 **Sugita S**, Sasaki A, Iwaki K, Uchida H, Kai S, Shibata K, Ohta M, Kitano S. Prognosis and postoperative lymphocyte count in patients with hepatocellular carcinoma who received intraoperative allogenic blood transfusion: a retrospective study. *Eur J Surg Oncol* 2008; **34**: 339-345 [PMID: 17400417 DOI: 10.1016/j.ejso.2007.02.010]

13 **Felekouras E,** Petrou A, Neofytou K, Giakoustidis A, Bagenal J, Cananzi F, Pikoulis E, Mudan S. Combined ultrasonic aspiration and saline-linked radiofrequency precoagulation: a step toward bloodless liver resection without the need of liver inflow occlusion: analysis of 313 consecutive patients. *World J Surg Oncol* 2014; **12**: 357 [DOI: 10.1186/1477-7819-12-357]

14 **Cannon RM**, Scoggins CR, Callender GG, Quillo A, McMasters KM, Martin RC. Financial comparison of laparoscopic versus open hepatic resection using deviation-based cost modeling. *Ann Surg Oncol* 2013; **20**: 2887-2892 [PMID: 23636514 DOI: 10.1245/s10434-013-2993-7]

15 **Vanounou T,** Steel JL, Nguyen KT, Tsung A, Marsh JW, Geller DA, Gamblin TC. Comparing the clinical and economic impact of laparoscopic versus open liver resection. *Ann Surg Oncol* 2010; **17**: 998-1009 [PMID: 20033324 DOI: 10.1245/s10434-009-0839-0]

16 **Crawshaw BP**, Chien HL, Augestad KM, Delaney CP. Effect of laparoscopic surgery on health care utilization and costs in patients who undergo colectomy. *JAMA Surg* 2015; **150**: 410-415 [PMID: 25806476 DOI: 10.1001/jamasurg.2014.3171]

17 **Charlson ME**, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; **40**: 373-383 [PMID: 3558716]

18 **Deyo RA**, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol* 1992; **45**: 613-619 [PMID: 1607900]

19 **Vanounou T**, Pratt W, Fischer JE, Vollmer CM, Callery MP. Deviation-based cost modeling: a novel model to evaluate the clinical and economic impact of clinical pathways. *J Am Coll Surg* 2007; **204**: 570-579 [PMID: 17382215 DOI: 10.1016/j.jamcollsurg.2007.01.025]

20 **Geller DA**, Tsung A, Maheshwari V, Rutstein LA, Fung JJ, Marsh JW. Hepatic resection in 170 patients using saline-cooled radiofrequency coagulation. *HPB* (Oxford) 2005; **7**: 208-213 [PMID: 18333192 DOI: 10.1080/13651820510028945]

21 **Currò G**, Lazzara S, Barbera A, Cogliandolo A, Dattola A, De Marco ML, De Leo E, Rampulla V, Lazzara C, Navarra G. The Aquamantys® system as alternative for parenchymal division and hemostasis in liver resection for hepatocellular carcinoma: a preliminary study. *Eur Rev Med Pharmacol Sci* 2014; **18**: 2-5 [PMID: 25535183]

22 **Kaibori M**, Matsui K, Ishizaki M, Sakaguchi T, Matsushima H, Matsui Y, Kwon AH. A prospective randomized controlled trial of hemostasis with a bipolar sealer during hepatic transection for liver resection. *Surgery* 2013; **154**: 1046-1052 [PMID: 24075274 DOI: 10.1016/j.surg.2013.04.053]

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**Specialty type:** Gastroenterology and hepatology

**Country of origin:** United States

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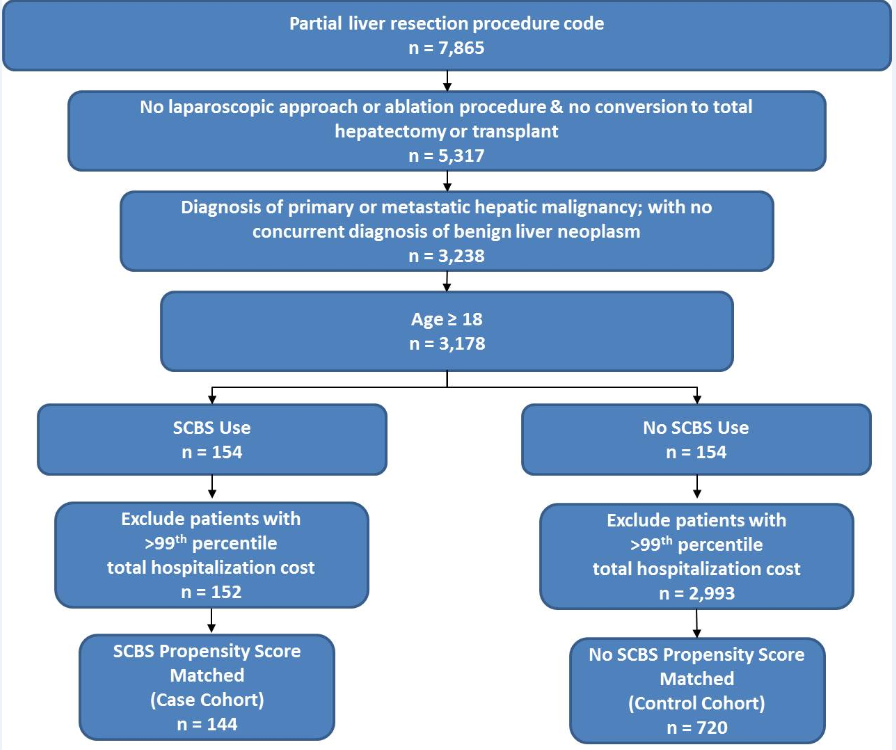
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Grade B (Very good): 0

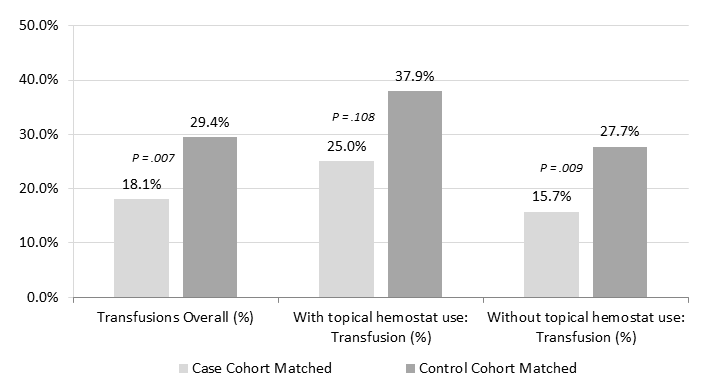
Grade C (Good): C, C

Grade D (Fair): 0

Grade E (Poor): 0



**Figure 1 Patient selection.**



**Figure 2 Transfusions and topical hemostat use.**

## Table 1 Definition of deviation mix for deviation-based cost modeling

|  |  |  |
| --- | --- | --- |
| Deviation | LOS | Complication Group1 |
| On Course | ≤ 50th percentile | No complication |
|  |  |  |
| Minor Deviation | LOS > 50th percentile | No complication |
|  | ≤ 50th | Minor complication, no moderate or major |
|  |  |  |
| Moderate Deviation | LOS > 50th percentile | Minor complication, no moderate or major |
|  | Any LOS | Moderate no major |
|  |  |  |
| Major Deviation | Any LOS | Major |

1Minor complication: Transfusion, UTI, hemorrhage/hematoma, wound disruption, or transfusion complications; Moderate complication: DVT, PE, pneumonia, infection, or bile leak; Major Complication: Acute respiratory failure, acute kidney injury, or acute liver failure. LOS: Length of stay.

**Table 2 Patient demographics *n* (%)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Unmatched** | | ***P* value** | **Matched** | | ***P* value** |
| **SCBS** | **No SCBS** | **SCBS** | **No SCBS** |
| *n* | 152 | 2993 |  | 144 | 720 |  |
| Age, mean (SD) | 62 (12.5) | 61.58 (12.1) | 0.683 | 61.49 (12.5) | 62.14 (12.1) | 0.568 |
| Age Group |  |  |  |  |  | 0.960 |
| 18 to 44 | 10 (6.6) | 262 (8.8) | 0.868 | 10 (6.9) | 49 (6.8) |  |
| 45 to 54 | 29 (19.1) | 536 (17.9) |  | 28 (19.4) | 143 (19.9) |  |
| 55 to 64 | 44 (28.9) | 914 (30.5) |  | 44 (30.6) | 198 (27.5) |  |
| 65 to 74 | 46 (30.3) | 862 (28.8) |  | 41 (28.5) | 220 (30.6) |  |
| 75 Plus | 23 (15.1) | 419 (14.0) |  | 21 (14.6) | 110 (15.3) |  |
| Race |  |  | 0.148 |  |  | 0.692 |
| Black | 18 (11.8) | 368 (12.3) |  | 18 (12.5) | 87 (12.1) |  |
| Caucasian | 83 (54.6) | 1788 (59.7) |  | 76 (52.8) | 407 (56.5) |  |
| Hispanic | 0 (0) | 41 (1.4) |  | 0 (0) | 0 (0) |  |
| Other | 51 (33.6) | 796 (26.6) |  | 50 (34.7) | 226 (31.4) |  |
| Region |  |  | < 0.001 |  |  | 0.892 |
| Midwest | 31 (20.4) | 304 (10.2) |  | 26 (18.1%) | 112 (15.6) |  |
| Northeast | 52 (34.2) | 959 (32.0) |  | 49 (34.0) | 260 (36.1) |  |
| South | 41 (27.0) | 1321 (44.1) |  | 41 (28.5) | 206 (28.6) |  |
| West | 28 (18.4) | 409 (13.7) |  | 28 (19.4) | 142 (19.7) |  |
| Female Sex | 71 (46.7) | 1315 (43.9) | 0.556 | 67 (46.5) | 308 (42.8) | 0.461 |
| Payor |  |  | 0.577 |  |  | 0.903 |
| Commercial | 49 (32.2) | 1166 (39.0%) |  | 49 (34.0) | 234 (32.5) |  |
| Medicare | 21 (13.8) | 362 (12.1) |  | 21 (14.6) | 111 (15.4) |  |
| Medicaid | 73 (48.0) | 1302 (43.5) |  | 65 (45.1) | 341 (47.4) |  |
| Other | 9 (5.9) | 163 (5.5) |  | 9 (6.3) | 34 (4.7) |  |

1Excluding primary malignancy, metastatic solid tumor, mild liver disease, moderate or severe liver disease.*P* values were calculated with the χ**2** test (or Fisher's Exact where cell frequencies < 10), *t*-test (or Wilcoxon Mann-Whitney test for skewed distributions). SCBS: Saline-coupled bipolar sealer.

**Table 3 Clinical characteristics *n* (%)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Unmatched** | | ***P* value** | **Matched** | | ***P* value** |
| **SCBS** | **No SCBS** | **SCBS** | **No SCBS** |
| *n* | 152 | 2993 |  | 144 | 720 |  |
| Procedure Type, |  |  |  |  |  |  |
| Partial hepatectomy | 99 (65.1) | 2061 (68.9) | 0.308 | 98 (68.1) | 478 (66.4) | 0.772 |
| Lobectomy | 53 (34.9) | 964 (32.2) | 0.552 | 46 (31.9) | 251 (34.9) | 0.564 |
| Indicating diagnosis |  |  |  |  |  |  |
| Primary hepatobiliary malignancy | 63 (41.5) | 850 (28.4) | 0.001 | 56 (38.9) | 300 (41.7) | 0.599 |
| Metastatic liver neoplasm | 89 (58.6) | 2143 (71.6) | 0.001 | 88 (61.1) | 420 (58.3) | 0.599 |
| Comorbid liver diagnoses |  |  |  |  |  |  |
| Alcoholic cirrhosis | 1 (0.66) | 33 (1.1) | 0.908 | 1 (0.69) | 4 (0.56) | 1.000 |
| Non-alcoholic cirrhosis | 23 (15.1) | 287 (9.6) | 0.036 | 20 (13.9) | 100 (13.9) | 1.000 |
| Hepatitis A | 0 (0) | 6 (0.2) | 1.000 | 0 (0) | 0 (0) | N/A |
| Hepatitis B | 18 (11.8) | 193 (6.4) | 0.015 | 16 (11.1) | 96 (13.3) | 0.556 |
| Hepatitis C | 17 (11.2) | 271 (9.1) | 0.457 | 17 (11.8) | 71 (9.9) | 0.580 |
| Charlson Score Group1 |  |  | 0.518 |  |  | 0.704 |
| 0 | 76 (50) | 1637 (54.7) |  | 74 (51.4) | 370 (51.4) |  |
| 1 | 45 (29.6) | 816 (27.3) |  | 43 (29.9) | 196 (27.2) |  |
| ≥ 2 | 31 (20.4) | 540 (18.0) |  | 27 (18.8) | 154 (21.4) |  |
| Provider specialty |  |  |  |  |  |  |
| Surgical Oncology | 59 (38.8) | 531 (17.7) | < 0.001 | 56 (38.9) | 285 (39.6) | 0.950 |
| General Surgery | 79 (52.0) | 1993 (66.6) | < 0.001 | 74 (51.4) | 369 (51.3) | 1.000 |
| Other | 14 (9.2) | 469 (15.7) | 0.041 | 14 (9.7) | 66 (9.2) | 0.958 |
| Surgeon Experience, ≥ 1 liver procedure in prior year | 125 (82.2) | 1991 (66.6) | < 0.001 | 117 (81.3) | 595 (82.6) | 0.780 |

1Excluding primary malignancy, metastatic solid tumor, mild liver disease, moderate or severe liver disease. *P* values were calculated with the χ**2** test (or Fisher's Exact where cell frequencies < 10), *t*-test (or Wilcoxon Mann-Whitney test for skewed distributions). SCBS: Saline-coupled bipolar sealer.

**Table 4 LOS, Deviation Mix and weighted average mean cost (Propensity-Matched Cohorts)**

| **Characteristic** | **SCBS** | **No SCBS** | ***P* value** |
| --- | --- | --- | --- |
| Length of Stay (LOS), d |  |  |  |
| mean (SD) | 7.38 (5.18) | 8.18 (7.27) | 0.210 |
| 25th percentile | 4 | 4 |  |
| Median | 6 | 6 |  |
| 75th percentile | 8 | 8 |  |
| Deviation Mix, *n* (%) |  |  |  |
| On Course | 77 (53.5) | 302 (41.9) | 0.013 |
| Minor deviation | 30 (20.8) | 187 (26.0) | 0.208 |
| Moderate deviation | 28 (19.4) | 150 (20.8) | 0.821 |
| Major deviation | 9 (6.3) | 81 (11.3) | 0.074 |
| mean (SD) total hospital cost |  |  |  |
| On Course | 3219 (2781) | 3312 (3092) | 0.405 |
| Minor deviation | 5340 (4013) | 4303 (3828) | 0.156 |
| Moderate deviation | 5968 (4526) | 5728 (5297) | 0.500 |
| Major deviation | 5140 (2928) | 6006 (6251) | 0.824 |
| WAMC Total Hospitalization Cost | $ 25503 | $ 26530 |  |
| WAMC Difference | $ 1027 |  |  |

*P* values were calculated with the Wilcoxon Mann-Whitney test for LOS and total hospitalization cost; and the χ**2** test for hospital deviation mix classes. SCBS: Saline-coupled bipolar sealer; WAMC: Weighted average mean cost.

**Table 5 Logistic regressions of predictors of topical hemostat use and transfusion**

|  | **Predictors of Topical Hemostat Use** | | | **Predictors of Transfusion** | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Parameter** | **Odds Ratio** | **95%CI** | ***P* value** | **Odds Ratio** | **95%CI** | ***P* value** |
| Age Group (*vs* 18 to 44) |  |  |  |  |  |  |
| 75 Plus | 1.03 | 0.5 - 2.12 | 0.421 | **4.55** | 1.95 - 10.59 | < 0.0001 |
| Race (*vs* Caucasian) |  |  |  |  |  |  |
| Black | 1.21 | 0.75 - 1.97 | 0.275 | 1.97 | 1.21 - 3.19 | 0.017 |
| US Geographic Region (*vs* Northeast) |  |  |  |  |  |  |
| South | 3.67 | 2.38 - 5.65 | 0.0004 | 1.87 | 1.19 - 2.96 | 0.001 |
| Partial hepatectomy (*vs* lobectomy) | 1.25 | 0.91 - 1.73 | 0.175 | 1.62 | 1.16 - 2.27 | 0.005 |
| Primary malignancy (*vs* metastatic) | 0.80 | 0.53 - 1.2 | 0.281 | 1.54 | 1 - 2.38 | 0.050 |
| Provider specialty (*vs* general surgery) |  |  |  |  |  |  |
| Surgical Oncology | 0.30 | 0.2 - 0.46 | < 0.0001 | 0.65 | 0.42 - 1.01 | 0.005 |
| Other Specialty | 0.68 | 0.4 - 1.16 | 0.402 | 1.48 | 0.85 - 2.57 | 0.023 |
| Case cohort (*vs* matched controls) | 2.56 | 1.7 - 3.86 | < 0.0001 | 0.44 | 0.27 - 0.71 | 0.0008 |
| Topical Hemostat Use | N/A | N/A | N/A | 1.87 | 1.33 - 2.64 | 0.0004 |

Only covariates that were significant in at least on model (*P* < 0.05) are listed here. Full model covariates included: age group, sex, race, geographic region, resection type, malignancy type, diagnosis of non-alcoholic cirrhosis, Hepatitis B, or Hepatitis C, provider specialty, study cohort, and topical hemostat use.