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Restrictive Blood Transfusion Protocol in Liver Resections Patients Reduces Blood Transfusions with No Increase in Patient Morbidity

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Abstract

Background—Management of anemia in surgical oncology patients remains one of the key quality components in overall care and cost. Continued reports demonstrate the effects of hospital transfusion, which has been demonstrated to lead to a longer length of stay, more complications, and possibly worse overall oncologic outcomes. The hypothesis for this study was that a dedicated restrictive transfusion protocol in patients undergoing hepatectomy would lead to less overall blood transfusion with no increase in overall morbidity.

Methods—A cohort study was performed using our prospective database from 1/2000 to 6/2013. September of 2011 served as the separation point for the date of operation criteria because this marked the implementation of more restrictive blood transfusion guidelines.

Results—a total of 186 patients undergoing liver resection were reviewed. The restrictive blood transfusion guidelines reduced the percentage of patients that received blood from 31.0% before 09/01/2011 to 23.3% after this date (p=0.03). The liver procedure that was most consistently associated with higher levels of transfusion was a right lobectomy (16%). Prior surgery and endoscopic stent were the two preoperative interventions associated with receiving blood. Patients who received blood before and after the restrictive period had similar predictive factors: Major hepatectomies, higher intra-operative blood loss, lower pre-operative hemoglobin, older age, prior systemic chemotherapy, and lower pre-operative nutritional parameters (all P<0.05). Patients who received blood did not have worse overall progression free survival or overall survival.

Conclusion—A restrictive blood transfusion protocol reduces the incidence of blood transfusions and the number of packed red blood cells transfused. Patients who require blood have similar pre-operative and intra-operative factors that cannot be mitigated in oncology patients. Restrictive use of blood transfusions can reduce cost and does adversely effects patients undergoing liver resection.

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Keywords

Hepatectomy; liver resection; blood transfusion; complications

Introduction

Surgical oncology patients are at a high risk for presenting with related anemia pre-operatively, and the perioperative management of their anemia is strongly related to patients' overall morbidity and mortality.(1), (2), (3) Specifically within the field of surgical oncology, procedures involving the liver are generally considered to be more complicated and carry a greater risk of bleeding that requires intervention.(4), (5), (6) Several studies have shown that managing anemia in these patients with allogeneic blood transfusions can negatively impact the patients' recovery even in the absence of procedural errors.(7), (8), (9), (10) While the cause has not been determined definitively, a physiological response known as “transfusion-related immunomodulation” or “TRIM” has been proposed as the possible mechanism.(11)

The published literature makes a strong case that blood transfusions should be avoided whenever possible due to documented adverse effects. However, blood transfusions are inevitably required in some cases to reach an oxygen-carrying capacity in the patient that is adequate for tissue perfusion.(12) The challenge then becomes identifying which patients will be negatively impacted by receiving a transfusion and which patients will the transfusion benefit. Based on the theoretical relationship between blood transfusions and patient outcomes, we hypothesized that a dedicated restrictive blood transfusion protocol would reduce the overall number of transfusions without increasing patient morbidity.

Methods

After obtaining IRB approval, this prospective evaluation study of a restrictive blood transfusion protocol was conducted between January 2009 and June 2013. Written informed consent was obtained from all study participants. All of the patients used in this study underwent a surgical operation for the treatment of cancer of the liver. Patient data was divided according to two criteria, date of operation and administration of a blood transfusion. September of 2011 served as the separation point for the date of operation criteria because this marked the implementation of more restrictive blood transfusion guidelines. Results from the data collected in each group were compared to determine if the transfusion protocol affected the overall frequency of blood transfusions, the value of the indicators for needing a transfusion, or the patients' outcomes.

Blood Transfusion Usage Guidelines

The purpose was to provide guidance for usage of blood components in a manner which optimizes patient care while judiciously utilizing limited resources. To provide the basis for prospective evaluation of blood transfusion practices.

Red Blood Cells—Hemodynamically stable patients were transfused at a hemoglobin trigger of 7g/dL, with a goal hemoglobin of 7-9g/dL. Level one evidence has shown such a "restrictive policy" is as effective as a more liberal strategy (transfusion for Hgb<10) in the critically ill. An exception to this policy is patients with evidence of myocardial ischemia(13). Epoetin or darbepoetin was recommended for patients with chemotherapy associated anemia at a Hgb concentration that is approaching or has fallen below 10 g/dL. The target for therapy should be a hemoglobin level of 12 g/dL. Erythropoesis stimulating agents (ESAs) were discontinued if there was no evidence of response after 6-8 weeks. These agents were not recommended in patients with active malignancy who are not receiving chemotherapy or radiation therapy based on the FDA black box warning: "Use of ESAs increased the risk of death when administered to a target Hb of 12 g/dL in patients with active malignant disease receiving neither chemotherapy nor radiation therapy. ESAs are not indicated in this population"(14). Iron levels were monitored in patients on ESA therapy with replacement indicated in the setting of iron insufficiency.

Plasma—Plasma transfusion was indicated in the presence of coagulopathic bleeding or in the presence of an INR greater than 2.0(15). FFP transfusion was indicated for urgent warfarin reversal(15) FFP administration was indicated in anticipation of an invasive procedure with significant risk of bleeding and an INR > 1.5. If time allowed, vitamin K should was used for reversal of warfarin in order to reduce FFP transfusion requirements(15).

Platelets—Platelet count <50,000 in surgical patients in the presence of excessive bleeding was an indication for platelet transfusion(15), as well as in anticipation of an invasive procedure with significant risk for bleeding(16). Platelet transfusion was not indicated in surgical patients with normal platelet function and a platelet count of > 100,000(15). Platelet transfusion was indicated in patients with a platelet count <10,000(16). Platelet transfusion was considered in the presence of massive transfusion when timely assessment of platelet count is not feasible.

Cryoprecipitate—Cryoprecipitate was administered in the setting of uremic bleeding or in patients with fibrinogen concentration <100mg/dL and coagulopathic bleeding. Transfusion of cryoprecipitate was otherwise rarely indicated if the fibrinogen concentration is greater than 150 mg/dL(15).

Surgical Technique—All hepatic resections were completed using a thermal energy tissue sealing and cutting device in combination with vascular staplers for parenchymal transection. Extrahepatic vascular control was used on a selective basis. Total vascular inflow occlusion via the pringle maneuver was not used in any patient. Both our Open and Laparoscopic surgical and anesthetic techniques have been described previously(17-20). The surgical technique has been published previously and in short the abdomen is explored laparoscopically and the liver is mobilized and surveyed using laparoscopic ultrasound. The line of transection is identified and marked with electrocautery. The liver parenchyma is transected using a combination of hemostatic assist devices, clips, and vascular staplers. Patients, inflow and outflow is controlled either through an extra-hepatic vascular dissection

or intraparenchymally during parenchymal transection depending on the location of the tumor.

The technique for anesthetic management during hepatectomy has been previously reported(19). In principle, a high stroke volume variation (goal >14) was achieved while maintaining a urine output of 25mL/h and a systolic blood pressure > 90 mmHg during parenchymal transection(21).

Adverse events-complications were recorded using an established validated 5 point complication scale(22, 23).

Statistical Analysis—Statistical analysis was performed using IBM SPSS Statistics (Version 21.0, Armonk, NY). Patient demographics such as age, gender, race, BMI, and comorbidities were recorded for all patients. Details of surgical resection including type of hepatectomy, estimated blood loss, operative time, parenchyma transection time, pringle time were recorded for all patients. Postoperative outcomes such as complications, length of stay, and readmission were recorded for all patients. Continuous, ordinal, and nominal variables were compared using the student t-test, Mann-Whitney U test, and chi-square test respectively. Correlation between CVP and SVV were evaluated using the Pearson coefficient. A value of $p < 0.05$ was considered statistically significant for all calculations. A Power analysis was initially performed that in order to achieve a correlation of 0.8 or greater 35 patients would be the minimum based on a 2 for SVV monitoring in relation to CVP.

A literature review was also performed via PubMed to determine the available information reported from previous studies on the effects of blood transfusions. The criteria for the initial search included the presence of the words “blood” and “transfusion” in the title or abstract and “surgery” within the text of the article, publication within the last five years, humans as the species of interest, written in English, and published in a core clinical journal. This search yielded 286 results which were further narrowed to 53 results when “cancer” was included as a criteria included in the text of the article. Of the 53 results, articles were either selected or eliminated based upon their relevance to the perioperative effects of blood transfusions on patient outcomes. This discretionary elimination process produced four articles that were used as the foundation for this study.(24), (25), (26), (27) All other sources used in this study were drawn from references contained within the four previously mentioned articles.

Results

A total of 186 patients underwent liver resection in this time period, 87 patients that did not receive a blood transfusion between 09/01/2009-09/01/2011 and 39 patients that had received a blood transfusion in the same time period. From 09/01/2011-05/23/2013, there were 46 patients included in this study that did not receive a blood transfusion and 14 that did.

The group of patients from 09/01/2009-09/01/2011 that did not receive a blood transfusion will be considered “Pre-Transfusion Protocol No Blood”. Patients in the same time interval that did receive a transfusion will be referred to as “Pre-Transfusion Protocol Blood”. For

the period of time between 09/01/2011-05/23/2013, patients that did not receive a transfusion constitute “Post-Transfusion Protocol No Blood” and those that had a transfusion, “Post-Transfusion Protocol Blood”.

Table #1 includes data regarding the baseline characteristics of the patients. The median patient age in the four groups ranged from 58.4 years old in Pre-Transfusion Protocol No Blood to 64.1 years old in Post-Transfusion Protocol No Blood with Pre-Transfusion Protocol Blood and Post-Transfusion Protocol Blood being 62.7 and 62.6 years, respectively. The median BMI of the patients was lowest in Pre-Transfusion Protocol Blood (26.6) and highest in Post-Transfusion Protocol Blood (29.2). The median BMI in the No Blood groups was 28.1 before the transfusion protocol and 29.0 after the transfusion protocol. The percentage of patients with cardiac and pulmonary comorbidities was 38.5% and 12.8% for Pre-Transfusion Protocol Blood, versus the Pre-Transfusion Protocol No Blood percentages of 12.6% and 5.7%. The association between cardiac and pulmonary comorbidities was significant when comparing all patients that received blood with all that did not (p=0.015; p=0.028) and between the Blood and No Blood groups before the transfusion protocol (p=0.004; p=0.016). Chemotherapy treatment with 5FU was significantly different between Post-Transfusion Protocol Blood and Post-Transfusion Protocol No Blood (p=0.003) and also Post-Transfusion Protocol Blood compared to Pre-Transfusion Protocol Blood (p=0.042). A higher percentage of patients in the No Blood group before the transfusion protocol received treatment with Oxaliplatin than the Blood group, but the difference was not significant (p=0.071). After the transfusion protocol, treatment with Oxaliplatin was significantly associated with patients that received blood (p=0.012), and the relationship was also significant when comparing all patients that received blood with all that did not (p=0.006). Platelet and creatinine levels did not prove to be an indicator of receiving blood, but hemoglobin was significantly different between all patients that received blood and all that did not and also between Pre-Transfusion Protocol No Blood and Pre-Transfusion Protocol Blood (p=0.003; p=0.026).

Table #2 consists of data related to the patients' operations. The restrictive blood transfusion guidelines reduced the percentage of patients that received blood transfusions from 31.0% before 09/01/2011 to 23.3% after this date. The liver procedure that was most consistently associated with higher levels of transfusion was a “right lobectomy.” The association was significantly different between Pre-Transfusion Protocol Blood and Pre-Transfusion Protocol No Blood (p=0.029). Eleven and five tenths percent of patients in Pre-Transfusion Protocol Blood underwent a right lobectomy compared to only 2.3% of the patients in Pre-Transfusion Protocol No Blood. Post-Transfusion Protocol Blood had the highest percentage of patients that had a right lobectomy at 50%, while only 39.1% of patients in Post-Transfusion Protocol No Blood had the same procedure. However, this difference was not significant (p=0.543). The median number of units transfused was 2.0 in Pre-Transfusion Protocol Blood and 4.0 in Post-Transfusion Protocol Blood. The average total blood loss was higher in the two groups of patients that received transfusions, 696.3mL in Pre-Transfusion Protocol Blood and 636.4mL in Post-Transfusion Protocol Blood. Pre- and Post-Transfusion Protocol No Blood had an average of 271.4mL and 270.5mL of total blood loss, respectively. The differences in total blood loss were significant when comparing Pre- and Post-Transfusion Protocol Blood with Pre- and Post-Transfusion Protocol No Blood

(p=0.000), Pre-Transfusion Protocol Blood with Pre-Transfusion Protocol No Blood (p=0.000), and Post-Transfusion Protocol Blood with Post-Transfusion Protocol No-Blood (p=0.040). The values for total blood loss in Table 2 represent the medians for each group. Average operative time was higher in the two groups receiving blood transfusions with the average operation taking 167.5 minutes in Pre-Transfusion Protocol Blood, 194.7 minutes in Post-Transfusion Protocol Blood, 129.2 minutes in Pre-Transfusion Protocol No Blood, and 127.9 minutes in Post-Transfusion Protocol No Blood. Average operative time was significant in the same comparisons as total blood loss with p-values of 0.001, 0.000, and 0.009 in each. Prior surgery and endoscopic stent were the two preoperative interventions most associated with also receiving a blood transfusion, but endoscopic stent was the only category that reached significance in comparing Pre-Transfusion Protocol Blood with Pre-Transfusion Protocol No Blood (p=0.029). The percentage of patients in Pre-Transfusion Protocol Blood with a prior surgery and endoscopic stent were 14.7% and 11.8%, respectively, which was compared to only 9.9% of patients in Pre-Transfusion Protocol No Blood with a prior surgery and 2.8% with an endoscopic stent. These values for Post-Transfusion Protocol Blood were 30% and 20% which was higher than the non-transfused patients in Post-Transfusion Protocol No Blood where only 15.4% had a prior surgery and 7.7% had an endoscopic stent. Although the median value for number of tumors was the same for each group (1.0), there was some variability in the average number of tumors which was significant in comparing Post-Transfusion Protocol Blood with Pre-Transfusion Protocol Blood (p=0.003). The median size of the largest tumor was 6.0cm for both groups that received blood, but there was a significant difference with a p-value of 0.001. The size of the largest tumor was also significantly different in Pre-Transfusion Protocol Blood and Pre-Transfusion Protocol No Blood.

Table #3 represents the data collected on the outcomes of the patients in the cohort. The data suggest that there is an association between blood transfusion and the risk of a complication which was significant in all patients that received blood versus no blood (p=0.000), patients that received blood versus no blood before and after the restrictive protocol (p=0.012 and p=0.001), and also transfused patients after the protocol versus patients transfused before the protocol (p=0.024). Overall, Post-Transfusion Protocol No Blood and Post-Transfusion Protocol Blood had a general risk of complication of 61.8% and 80%, respectively, while their non-transfused counterparts only had complications in 35.1% of patients in Pre-Transfusion Protocol No Blood and 4.5% in Post-Transfusion Protocol No Blood. Intraoperative complications of hemorrhage and hypotensive episode were more likely in the two transfused groups with 2.6% of patients in Pre-Transfusion Protocol Blood experiencing a hemorrhage and hypotensive episode and 7.1% of patients in Post-Transfusion Protocol Blood with the same complications. Only 1.1% of patients in Pre-Transfusion Protocol No Blood had a hemorrhage, and none of the patients had a hypotensive episode. Similarly, none of the patients in Post-Transfusion Protocol No Blood had a hemorrhage and 2.2% had a hypotensive episode. Infection was only seen in the transfused groups where it afflicted 2.6% of patients in Pre-Transfusion Protocol Blood and 7.1% in Post-Transfusion Protocol Blood. The average length of stay was only 5.5 days for Pre-Transfusion Protocol No Blood and 6.0 days for Post-Transfusion Protocol No Blood but increased to 11.2 days in Pre-Transfusion Protocol Blood and 11.4 days in Post-Transfusion Protocol Blood. The median

length of stay was 8.0 days for both transfused groups and 5.0 for both groups that did not receive blood. The difference in length of stay was significantly longer in Pre-Transfusion Protocol Blood versus Post-Transfusion Protocol Blood (p=0.009). New recurrence was not directly associated with receiving a blood transfusion as the recurrence was greater in the non-transfused group (Pre-Transfusion Protocol No Blood = 23.0%; Pre-Transfusion Protocol Blood = 12.8%) before 09/01/2011 and in the transfused group (Post-Transfusion Protocol Blood = 21.4%; Post-Transfusion Protocol No Blood = 9.3%) after 09/01/2011. The median Karnofsky score was 100 for Pre-Transfusion Protocol No Blood, Post-Transfusion Protocol No Blood, and Post-Transfusion Protocol No Blood and 90 for Pre-Transfusion Protocol Blood. Upon the last follow-up, Pre- and Post-Transfusion Protocol No Blood reported higher percentages of patients with no evidence of disease (48.3%; 60.5%) and patients alive with disease (42.5%; 34.9%) than in the two groups that had received a transfusion. There was a statistical significance to the percentage of patients that died of other causes in Pre-Transfusion Protocol Blood versus Pre-Transfusion Protocol No Blood (p=0.002) and also in the Blood versus No Blood groups (p=0.011).

Discussion

The aim of this study was to examine the impact that a restrictive blood transfusion protocol has on frequency of transfusions and also on overall outcomes in patients undergoing liver procedures. The data collected and analyzed in this study suggests that the restrictive protocol served its purpose of limiting the amount of blood transfusions performed in the perioperative time period. This is shown by looking at the percentages of patients that received a transfusion before and after the protocol. Although the results were not statistically significant, there was a reduction from 31% to 23% of patients receiving a transfusion after the protocol was put in place. Other factors that were predictors of receiving blood are also important discussion points to determine the necessity for transfusion. Complication rates, infection, number of units transfused, patients receiving a right lobectomy, and intraoperative time were all increased in the group of patients receiving blood after the protocol date which appears to indicate that these patients had a greater need for transfusion than their counterparts before the restrictive protocol.

The data also suggests that the implementation of the protocol did not negatively affect patient outcomes as neither the Karnofsky score nor the patient's status upon final follow-up significantly changed. In fact, there was an increase in the percentage of patients with no evidence of disease in both the blood and no blood groups after the protocol. The average length of stay significantly decreased in Post-Transfusion Protocol Blood compared to Pre-Transfusion Protocol Blood.

In 2012, Froman et al(28) performed a study to examine the impact of a “3-part transfusion reduction initiative”, abbreviated TRI, on transfusions and patient complications. Their study included a total of 368 patients undergoing elective resection for colorectal cancer with 272 pre-TRI and 96 post-TRI. The results showed a decrease in transfusion rates and hemoglobin levels in the post-TRI group compared to the pre-TRI group. There was no difference in complications or 30-day mortality rates between the two groups. They concluded that the TRI was successful as it reduced the number of transfusions without affecting observed

complications. These results supported the findings in our study and provide more strength to the claim that restrictive transfusion protocols are effective in limiting transfusions without negatively impacting patient outcomes.

The results of our study with respect to the impact of blood transfusion on patient morbidity and mortality coincide with several other studies having similar purposes. Jagoditsch et al(29) performed a study in which 597 patients undergoing rectal cancer surgery were followed to determine if there was an association between the type or number of blood units and the short-term and long-term outcomes for the patients. They concluded that increased numbers of blood units were associated with postoperative mortality. While our study did not explore the differences in type of blood units, the number of units transfused was an important variable to compare the impact of a restrictive blood transfusion protocol. Miki et al(10) sought to determine the role of blood transfusion in long-term survival and disease recurrence. Their findings indicate that blood transfusion with intense surgical stress can induce a systemic overproduction of interleukin-6, which may have an effect on disease recurrence and long-term survival.

The negative impact of blood transfusion has been demonstrated in several studies.(7), (9), (10), (12) In 2013, Cannon et al(30) specifically showed that transfusion with packed red blood cells was associated with postoperative complications in patients undergoing hepatectomy. However, some patients still require a transfusion as a lifesaving measure. For these patients, alternatives to whole blood transfusion may fulfill the same needs as a traditional transfusion without exposing them to the potential hazards. One alternative to allogeneic whole blood transfusion that has been studied is autologous blood donation, where the patient donates their own blood prior to the operation and then receives their own blood if a transfusion becomes necessary.(31) Leukocyte-depleted red blood cells have also been examined to determine if they provide a benefit over conventional whole blood. Skanberg et al(32) investigated this relationship and determined that transfusion with leukocyte-depleted red blood cells improved the postoperative outcomes in patients. Aside from alternatives to transfusion with packed red blood cells, conservation of the patient's own blood during surgery may reduce the need for transfusion and thus prevent the associated complications.(33), (34), (35)

The use of blood conservation techniques for every patient becomes too economically inefficient and would outweigh the potential benefits. Establishing adequate predictors for blood loss based on risk profiles can balance the economic burden of conservation strategies with the benefits of avoiding transfusion and make blood conservation techniques a plausible option.(3), (36) Since patients undergoing hepatic resections are at increased risk for intraoperative blood loss, blood conservation methods are especially beneficial for patients that would otherwise require lesser amounts of transfused products.(37)

The impact and strength of the results of this study are limited by the sample size of patients following the implementation of the restrictive protocol. In the years to come, it will be important to repeat this study because as the number of patients in this cohort increases, the actual impact of the restrictive transfusion protocol will become clearer. Variables that were correlated but not statistically significant may become significant with a larger cohort, and

other factors contradicting the hypothesis of this study may be skewed by the relatively small group of patients following the restrictive protocol.

In conclusion, our study has demonstrated that the restrictive blood transfusion protocol was effective in reducing the rates of transfusion without increasing patient morbidity. In moving forward, one area that deserves further investigation is the creation of a common standard for transfusion. Studies have shown that there is variability in the frequency of transfusions at different institutions.(38), (39) Although the final decision is left in the hands of the operating medical staff, a common standard for transfusion, evaluated for its safety and effectiveness, could potentially reduce unnecessary transfusions and provide continuity between institutions that ensures the highest standard of patient care.

Acknowledgments

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Table #1

Baseline Patient Characteristics Before and After Protocol

	9/2009-9/2011 No Transfusion (n=87)	9/2009-9/2011 Received Transfusion (n=39)	After 9/2011 No Transfusion (n=46)	After 9/2011 Received Transfusion (n=14)	P-Values
Age	58.4	62.7	64.1	62.6	
BMI	28.1	26.6	29.0	29.2	
Gender					
Male	47.1% (41)	46.2% (18)	52.2% (24)	64.3% (9)	
Female	52.9% (46)	53.8% (21)	47.8% (22)	35.7% (5)	
Race/Ethnicity					
White (non-Hispanic)	89.3% (78)	86.5% (34)	93.3% (43)	85.7% (12)	
Black	9.5% (8)	13.5% (5)	6.7% (3)	14.3% (2)	
Other	1.2% (1)	0.0%	0.0%	0.0%	
Past Medical History					
Cardiac Comorbidity	12.6% (11)	38.5% (39)	34.8% (16)	7.1% (1)	0.015 *,0.004 ‡, 0.080 $^{\delta}$
Pulmonary	5.7% (5)	12.8% (5)	19.6% (9)	7.1% (1)	0.028 *,0.016 ‡
Comorbidity	5.7% (5)	15.4% (6)	10.9% (5)	28.6% (4)	0.077 †
Diabetes	6.9% (6)	7.7% (3)	8.7% (4)	7.1% (1)	
Alcohol	26.4% (23)	41.0% (16)	37.0% (17)	14.3% (2)	
Tobacco	1.1% (1)	2.6% (1)	10.9% (5)	0.0%	0.026 *, 0.047 ‡
Hepatic Pancreatitis	0.0%	0.0%	0.0%	0.0%	
Past Surgical History					
TAH	13.8% (12)	17.9% (7)	6.5% (3)	7.1% (1)	
Cholecystectomy	14.9% (13)	15.4% (6)	17.4% (8)	14.3% (2)	
Colon	11.5% (10)	15.4% (6)	19.6% (9)	14.3% (2)	
Appendectomy	5.7% (5)	2.6% (1)	6.5% (3)	7.1% (1)	
Orthopedic	6.9% (10)	23.1% (9)	15.2% (7)	14.3% (2)	
Diagnosis					
Metastatic	47.1% (41)	46.2% (18)	50.0% (23)	50.0% (7)	

	9/2009-9/2011 No Transfusion (n=87)	9/2009-9/2011 Received Transfusion (n=39)	After 9/2011 No Transfusion (n=46)	After 9/2011 Received Transfusion (n=14)	P-Values
Colorectal	13.8% (12)	12.8% (5)	8.7% (4)	21.4% (3)	
Metastatic to Liver	11.5% (10)	20.5% (8)	13.0% (6)	7.1% (1)	
Hepatocellular	9.2% (8)	12.8% (5)	8.7% (4)	0.0%	
Cancer	10.3% (9)	0.0%	6.5% (3)	7.1% (1)	0.056‡
Cholangio	5.7% (5)	2.6% (1)	10.9% (5)	14.3% (2)	
Carcinoma	1.1% (1)	2.6% (1)	2.2% (1)	0.0%	
Gallbladder Cancer	1.1% (1)	2.6% (1)	0.0%	0.0%	
Benign Liver/Billiary					
Periampullary					
Tumors					
Other					
Chemotherapy Treatment					
5FU	33.3% (29)	23.1% (9)	15.0% (7)	57.1% (8)	0.003†,0.042δ
CPT11	0.0%	0.0%	0.0%	14.3% (2)	0.080*,0.051†,0.0 66δ
Oxalopoatin	31.0% (7)	20.5% (8)	15.0% (7)	50.0% (7)	0.006*,0.071‡,0.0 12†0.046δ
Other	33.3% (29)	23.1% (9)	25.0% (12)	50.0% (7)	0.090δ
Blood Values					
Platelets	208.5	221.5	209.0	198.0	
Hemoglobin	13.2	12.5	13.5	11.4	0.003*, 0.026‡
Creatinine	0.9	0.9	0.9	0.7	

*all patients that received blood compared to all patients that did not receive blood

†patients after the protocol that received blood compared to patients after the protocol that did not receive blood

‡patients before the protocol that received blood compared to patients before the protocol that did not receive blood

δpatients before the protocol that received blood compared to patients after the protocol that received blood

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Table #2

Operative Data Before and After Protocol

	9/2009-9/2011 No Transfusion (n=87)	9/2009-9/2011 Received Transfusion (n=39)	After 9/2011 No Transfusion (n=46)	After 9/2011 Received Transfusion (n=14)	P-Values
Liver Procedure	Lap 75% Open 25%	Lap 51% Open 49%	Lap 82% Open 18%	Lap 62% Open 38%	
Atypical Resection	1.1% (1)	0.0%	0.0%	0.0%	
Central Liver Resection	3.4% (3)	2.3% (1)	2.2% (1)	0.0%	
L. Lateral Segmentectomy	21.8% (19)	4.6% (2)	19.6% (9)	14.3% (2)	
L. Lobectomy	16.1% (14)	2.3% (1)	2.2% (1)	7.1% (1)	
L. Trisegmentectomy	26.4% (23)	5.7% (3)	2.2% (1)	0.0%	
R. Lobectomy	2.3% (2)	11.5% (5)	39.1% (18)	50.0% (7)	0.029‡
R. Posterior Sectorectomy	16.1% (14)	4.6% (2)	0.0%	0.0%	
R. Trisegmentectomy	12.6% (11)	11.5% (5)	19.6% (9)	14.3% (2)	
Segmentectomy	16.1% (14)	4.6% (2)	15.2% (7)	14.3% (2)	
Number of Units	N/A	2.0	N/A	4.0	
Transfused					
Total Blood Loss	200.0	600.0	200.0	400.0	0.000 *,0.000‡, 0.040 †
Operative Time	129.2	167.5	127.9	194.7	0.001 *,0.000‡, 0.009 †
Preoperative Intervention					
None	78.9% (69)	67.6% (26)	74.4% (34)	40.0% (6)	
Prior Surgery	9.9% (9)	14.7% (6)	15.4% (7)	30.0% (4)	
Embolization	8.5% (7)	0.0%	2.6% (1)	10.0% (1)	
Endoscopic Stent	2.8% (2)	11.8% (5)	7.7% (4)	20.0% (2)	0.029‡
Portal Vein Embolization	0.0%	5.9% (2)	0.0%	0.0%	
Preoperative Intent					
Cure	84.4% (73)	93.1% (36)	84.4% (39)	100% (14)	
Palliation	15.6% (14)	6.9% (3)	15.6% (7)	0.0%	
Number of Tumors	1.0	1.0	1.0	1.0	0.003δ
Size of Largest Tumor	3.5	6.0	3.1	6.0	0.007‡,0.001δ

	9/2009-9/2011 No Transfusion (n=87)	9/2009-9/2011 Received Transfusion (n=39)	After 9/2011 No Transfusion (n=46)	After 9/2011 Received Transfusion (n=14)	P-Values
Defined Tumor Margin	13.0% (11)	10.8% (4)	9.5% (4)	25.0% (4)	
CVP Total	2.0	3.0	3.0	1.5	

*all patients that received blood compared to all patients that did not receive blood

†patients after the protocol that received blood compared to patients after the protocol that did not receive blood

‡patients before the protocol that received blood compared to patients before the protocol that did not receive blood

δpatients before the protocol that received blood compared to patients after the protocol that received blood

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Table #3

Outcome Data Before and After Protocol

	9/2009-9/2011 No Transfusion (n=87)	9/2009-9/2011 Received Transfusion (n=39)	After 9/2011 No Transfusion (n=46)	After 9/2011 Received Transfusion (n=14)	P-Values
Complication	35.1% (31)	61.8% (24)	4.5% (2)	80% (11)	0.000 *,0.012 ‡, 0.001 †,0.024 δ
Intraoperative Surgical Complication					
None	98.9% (86)	94.9% (37)	97.8% (45)	85.7% (12)	
Hemorrhage	1.1% (1)	2.6% (1)	0.0%	7.1% (1)	
Hypotensive Episode	0.0%	2.6% (1)	2.2% (1)	7.1% (1)	
Grade of Complication					
Oral Antibiotics	24.1% (7)	4.2% (1)	20.0% (1)	0.0%	
IV Antibiotics	55.2% (16)	33.3% (8)	20.0% (1)	20.0% (1)	
Return to ICU Percutaneous Drainage Operative Correction	20.7% (6)	58.3% (14)	40.0% (2)	60.0% (3)	
Organ Diversion	0.0%	0.0%	0.0%	0.0%	
Death	0.0%	4.2% (1)	20.0% (1)	20.0% (1)	
Infection	0.0%	2.6% (1)	0.0%	7.1% (1)	
Length of Stay	5.0	8.0	5.0	8.0	0.009 δ
New Recurrence	23.0% (20)	12.8% (5)	9.3% (4)	21.4% (3)	
Site of Recurrence					
Liver	56.5% (26)	69.2% (9)	25.0% (2)	50.0% (1)	
Lung	19.6% (9)	0.0%	12.5% (1)	0.0%	
Bone	6.5% (3)	0.0%	12.5% (1)	0.0%	
Lymph Nodes	6.5% (3)	7.7% (1)	0.0%	50.0% (1)	
Other	10.9% (5)	23.1% (3)	50.0% (4)	0.0%	
Karnofsky Score	100	90	100	100	
Status					
No Evidence of Disease	48.3% (42)	41.0% (16)	60.5% (26)	57.1% (8)	
Alive with Disease	42.5% (37)	38.5% (15)	34.9% (15)	28.6% (4)	
Died of Disease	8.0% (7)	7.7% (3)	2.3% (1)	0.0%	

	9/2009-9/2011 No Transfusion (n=87)	9/2009-9/2011 Received Transfusion (n=39)	After 9/2011 No Transfusion (n=46)	After 9/2011 Received Transfusion (n=14)	P-Values
Died of Other Cause	1.1% (1)	12.8% (5)	2.3% (1)	14.3% (2)	0.002 *,0.01 1≠,

*all patients that received blood compared to all patients that did not receive blood

†patients after the protocol that received blood compared to patients after the protocol that did not receive blood

≠patients before the protocol that received blood compared to patients before the protocol that did not receive blood

δpatients before the protocol that received blood compared to patients after the protocol that received blood