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Prophylactic Use of Fresh Frozen Plasma in Patients Undergoing Liver Resection: Does it Make any Sense?

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Abstract

Background: The use of fresh frozen plasma in liver resection has recently been questioned due to the lack of supportive evidence. The aim of the study was to evaluate the clinical impact of a transfusion protocol implemented in our Institution based on the avoidance of prophylactic use of plasma.

Methods: 172 adult undergone liver resection were analyzed retrospectively: 104 (study group) underwent surgery between 1/1/2012 and 06/30/2013 and 68 during 2009 (historic group). Prior to the implementation of this protocol in 2009, the prophylactic administration of plasma was a practice in cirrhotic and non-cirrhotic patients when major liver resection was performed.

Results: Clinical characteristics, indication and type of resection were similar in both groups. The median of blood loss during surgery was similar. The new protocol induced a significant decrease in the intraoperative use of plasma and red blood cells: none of patients in the study group received plasma whereas 50% of patients in the historic group received a mean of 1000 ml of plasma and the rate of red blood cells transfusion went from 18% to 6% of patients. The overall in-hospital major complication rate was similar. In the historic group the rate of re-intervention was significantly higher (9 vs. 3%, p=0.01) the median in-hospital stay (10 vs. 7, p<0.05). There were no differences in the postoperative residual liver function.

Conclusion: In liver resections, the avoidance of routine administration of FFP was not associated to an increase of neither perioperative bleeding nor postoperative complications nor worse liver function.

Keywords: Blood coagulation disorders; Blood-blood coagulation disorders; Therapy-hemostasis-liver diseases; Blood-hepatectomy-transfusion

Introduction

Liver resection surgery has been traditionally associated with significant blood loss requiring blood products transfusion [1]. The complex anatomy of this organ, the pre-existing hemostatic changes associated to chronic liver disease in some patients, and the transient liver dysfunction caused by surgical intervention in the others, have been evoked as causative factors for transfusion in this type of surgery. Because of developments in both surgical and anesthetic techniques, the median blood loss associated with the procedure has fallen dramatically although there are still a significant number of patients who receive substantial amounts of blood products perioperatively.

In the perioperative period of hepatic resection, due to the temporary inability or impairment of the liver remnant to synthesize clotting factors, routine laboratory tests such as the prothrombin time and the platelet count are frequently abnormal and point to a hypocoagulable state. During decades, the traditional concept that patients with liver dysfunction have a hemostasis-related bleeding tendency has promoted the transfusion of fresh frozen plasma (FFP) as a common practice to prophylactically correct hemostatic abnormalities during liver surgery even in patients without previous coagulation defects [2-4]. However, this policy is not really evidence-based and it has been recently called into question. In fact, there is scarce literature that provides evidence for favorable effects of the administration of FFP before invasive procedures on patient outcomes [5,6]. The literature is even scarcer regarding the role of FFP in liver resection; both for patients with pre-existing impaired liver function as well as for patients with normal hepatic function underwent liver resections.

In the past decade, with more sophisticated laboratory tests and laboratory experiments it has been shown that patients with liver disease may be in hemostatic balance as a result of concomitant changes in both pro- and antihemostatic pathways. This observation has been key in the implementation of a different approach toward transfusion of blood products mainly in the setting of liver transplantation where some centers have reported that it is possible to perform liver transplantation surgery without any requirement for blood transfusion [7].

In the Hospital Clinic of Barcelona, liver resection surgeries have been performed for more than 20 years. The prophylactic administration of FFP was a standard practice into the anesthetic protocol until 2009 to supplement clotting factors and maintain colloid osmotic balance through the administration of albumin. Based on the recent advances in hemostatic disorders in liver disease, and the lack of evidence for routine use of FFP and its potential adverse effects, currently we avoid prophylactic use of FFP and, the correction of hematic losses and of coagulation associated disorders are performed carefully, based on dynamic and real-time testing [8,9].

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We decided to conduct this retrospective study to demonstrate that the new protocol based on avoiding prophylactic administration of FFP is not associated with an increase in the perioperative hemorrhage during liver resection surgery.

Patients and Methods

With the approval of the Hospital Clinic ethics committee, the medical history records 172 adult patients who had undergone elective liver resection were analyzed retrospectively. Patients undergoing other surgeries besides the hepatectomy, living liver donors and those in whom the surgery was not finally performed were not considered eligible. All data from the perioperative course were prospectively documented. In 2010, a new protocol based on avoiding prophylactic transfusion to correct coagulation disorder was implemented. Because the completion of the protocol was really consistent from 2012, two study periods were defined and compared: 104 consecutive patients (study group) underwent liver resection between 1/1/2012 and 06/30/2013 and 68 consecutive patients performed from 1/1/2009 to 31/12/2009 (historic group).

Surgical procedure

Four hepato-biliary surgeons performed all the procedures during the study period, with two surgeons participating in each procedure. Parenchyma transection was done using crushing clamp technique or ultrasonic dissector under intermittent pedicle clamping. Hemostasis was achieved with bipolar coagulation; small vascular or biliary pedicles were clipped or ligated. Following the Barcelona-Clínic Liver Cancer Group significant portal hypertension (>10 mmHg) was considered as a contra-indication to liver resection.

Anesthetic protocol

Six anesthesiologists were involved with the liver surgery during the study period. Monitoring was standardized in all patients (invasive arterial pressure and central venous pressure) as was the anesthesic technique (Fentanil, Propofol, Cisatracurium and Desflurane). Peridural technique was systematically performed if open surgery was planned when ratio prothrombin time and platelets count were less than 1,4 and over 60×10^9 pl/L, respectively. Coagulation was not monitored intraoperatively unless uncontrollable bleeding. Patients were maintained with a CVP <5 mmHg and a mean arterial pressure > 70 mmHg by minimizing fluid administration and use of norepinephrine during all study period. Furosemide was given when urine output was less than 0.5 ml/Kg/h. The triggering hemoglobin level for red blood cell (RBC) transfusion was 7 g/L. Cell saver, prophylactic antifibrynolitic drugs and factor VII were not used in any case.

	Historic Controls n=68	Study Group n=104	*p-value*
Age (yr-old)	62 (56-74)	63 (52-69)	0.36
Sex (M/F)	47/21	71/33	1
BMI (kg/m^2)	25 (21-28)	26 (23-29)	0.16
ASA Score I II III IV	 3 (4%) 44 (65%) 20 (29%) 1 (2%)	 12 (12%) 72 (69%) 19 (18%) 1 (1%)	0.18
Presence of cirrhosis n (%)	18 (26)	20 (19)	0.26
Previous abdominal surgery n (%)	43 (63)	69 (66)	0.74
Indication to hepatic resection Primary liver tumor Liver metastases Other benign tumor	 30 (44%) 28 (40%) 10 (16%)	 37 (36%) 56 (53%) 11 (11%)	0.37
Hemoglobin (mg/dL)	13 (11.8-14)	13 (12-14.4)	0.25
Ratio Prothrombin Time	1.07 (1.01-1.12)	1.03 (0.96-1.10)	0.01
Platelets (x10^9/L)	183 (150-286)	201 (148-260)	0.86

Definition of Abbreviations: BMI=Body Mass Index; ASA = American Society of Anesthesiologists; *p*=statistical significance comparing both groups. Data expressed as median (25-75%)

Table 1: Comparison of preoperative clinical and demographic characteristics between historic controls (2009) and study group (January 2012-June 2013).

Before 2010 (historic group), FFP (1000 ml) was systematically administered once liver resection was completed to every cirrhotic patient, and to those non-cirrhotic patients only when major liver resection was performed, even in absence of bleeding. In case of uncontrollable bleeding, plasma, platelets of fibrinogen were given based on routine coagulation test. After 2010 (study group), surgical and anesthetic techniques were identical but for the systematic avoidance of prophylactic FFP transfusion.

From the patients' hospital and clinical records the following data were collected: demographic and clinical characteristics, indication to surgery, type and duration of surgery, blood loss and transfusion. The extent of liver resection was defined as major if resection consisted of ≥ 4 Couinaud segments, minor if ≤ 3, and extended liver resection if right or left hepatectomy with more liver segments was performed. Intraoperative blood loss estimated from the volume of blood aspirated into the suction canisters and the weight of laparotomy sponges was prospectively recorded in every medical history. Postoperative transfusion was defined as blood product requirements during the following four postoperative days. Postoperative complications during the in-hospital stay were recorded graded according to the method described by the Clavien-Dindo classification.

The primary endpoint of the study was to evaluate the impact of a new transfusional protocol on the incidence of perioperative blood loss and related complications in the setting of liver resection surgery.

Data analysis

Continuous variables were summarized by means and standard deviations, or medians and interquartile ranges if their distributions were skewed and categorical variables by frequencies and percentages. Statistical analysis was performed with SPSS (Statistical Package for the Social Sciences, Inc., Chicago Ill) version 18. The Mann-Whitney U test and Chi-Squared test were used to assess differences in median and mean, respectively. In all cases, a significant change or difference was defined as a P value of less than 0.05.

Results

Demographics, clinical characteristics and preoperative biochemical data are presented in Table 1. Both groups were similar except for a slightly higher starting ratio prothrombin time in the historic group. Most of patients showed a normal liver function before surgery; only less than one third were cirrhotic. Indication for liver resection included primary malignant liver tumor in 67 patients (39%), liver metastases in 84 patients (49%), and benign tumors in 21 patients (12%). Chronic virus C hepatitis (67%) and alcohol abuse (38%) were the most common etiology of chronic liver disease. The magnitude of the liver resections was similar in both groups (Table 2). Approximately half of patients underwent minor resections whereas the remaining ones underwent major (31%) or extended resection (13%). Laparoscopic approach, in case of minor resections, was more frequently used in the study group (15% vs. 30%, p=0.02).

The median of blood loss during surgery was similar in both groups (200 ml). Intraoperatively, there was a significant decrease in the use

	Historic Controls n=68	Study Group n=104	*p-value*
Type of surgical resection, n (%) Minor Major Extended	 37 (54) 9 (13) 21 (31)	 58 (56) 13 (13) 33 (32)	 0.66
Surgical time, min (range)	192 (150-240)	195 (155-240)	0.66
Laparoscopic approach, n (%)	10 (15)	31 (30)	0.02
Peridural, n (%)	33 (48)	56 (54)	0.39
Blood loss, ml (range)	200 (110-500)	200 (100-350)	0.16
Blood component transfusion			
Intraoperative			
Patients receiving RBC, n (%)	12 (18)	6 (6)	0.02
RBC#, U	2 (2-3.7)	2 (1-2)	0.01
Patients receiving FFP, n (%)	34 (50)	0	<0.01
FFP#, mL	1000 (1000-1000)	0	<0.01
Patients receiving platelets, n (%)	0	0	1
Postoperative			
Patients receiving RBC, n (%)	10 (15)	8 (8)	0.20
RBC#, U	2 (2-3)	2 (2-4)	0.15
Patients receiving FFP, n (%)	3 (4)	2 (2)	0.38
FFP#, mL	500 (500- 1000)	1000 (1000-1000)	0.34
Patients receiving platelets, n (%)	1(1.5)	0	0.39

Definition of Abbreviations: *p* value= statistical significance comparing both groups; # data only from transfused patients. RBC: red blood cells. FFP: Fresh Frozen Plasma. Data expressed as median (25-75%)

Table 2: Comparison of perioperative data between historic controls (2009) and study group (January 2012-June 2013).

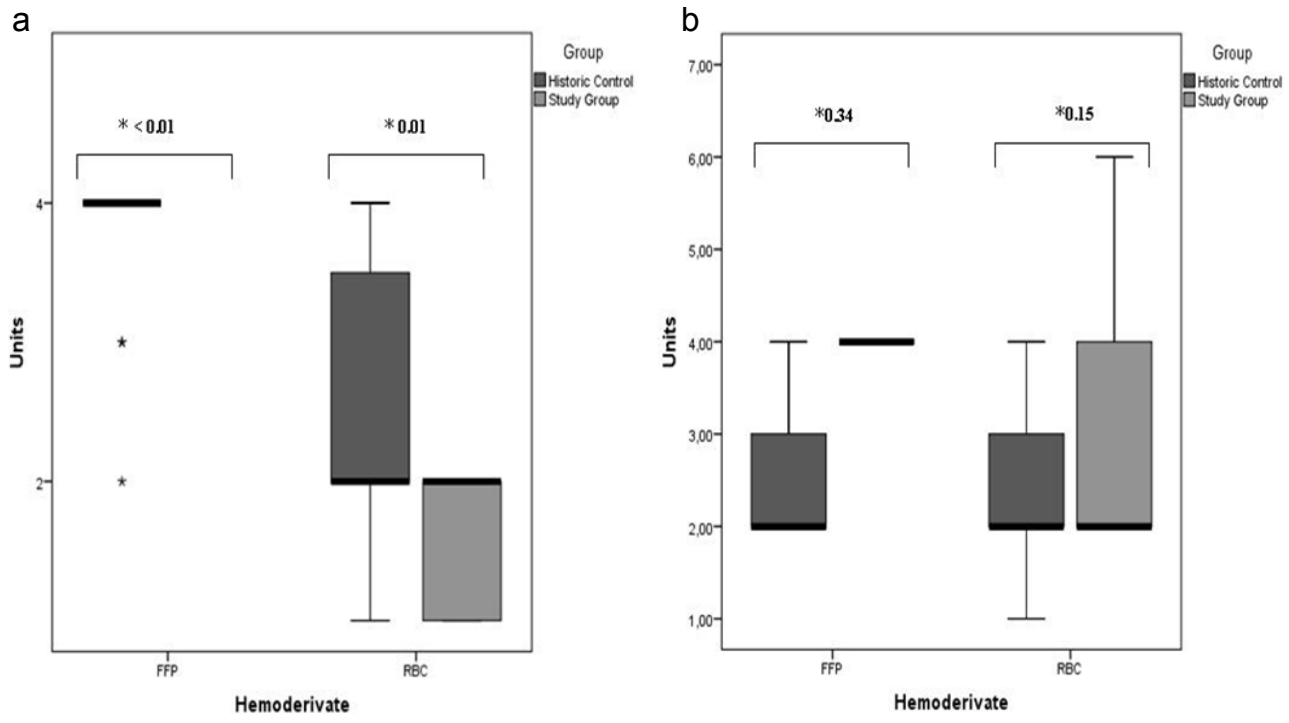

Figure 1: Units of fresh frozen plasma (FFP) and red blood cells (RBC) transfused in patients from historic and study groups during the intraoperative (Figure 1a) and postoperative periods (Figure 1b). Every FFP unit entails a volume of 250 mL in our institution. **1a**, Intraoperatively, 34 patients in historic control group (■) and none in study group (□) received FFP, and 12 patients in historic control group and 6 in the study group (□) received RBC. **1b**, Postoperatively, 3 patients in historic control group (■) and 2 in the study group (□) received FFP, and 10 patients in historic control group (■) and 8 in the study group (□) received RBC. The boxes stand for the median and the lower and upper quartiles; the whispers represent the 95% confidence interval. Statistic Mann Whitney Test. **p* value = statistical significance comparing both groups

of all types of blood products, except for platelets in the study group (Table 2). The percentage of cases with RBC transfusion went from 18% in the historic group to 6% in the study group. None of patients in the study group received FFP during the procedure whereas 50% of patients in the historic group received a mean of 1000 ml of FFP (Figure 1). Considering all perioperative period (surgery and 4 postoperative days), the rate of transfusion of FFP was higher in the historic group and there was also a tendency to higher RBC transfusion (Figure 1). Hemoglobin values at the time of patient discharge were similar in both groups (Table 3).

Outcome data are presented in Table 3. The overall in-hospital

	Historic Controls n=68	Study Group n=104	*p-value*
Hemoglobin at discharge (mg/dL)	10.7(10-12.2)	10.8(9.6-11.8)	0.23
Platelets at 4th postoperative day (x 10^9/L)	128(97-176)	146(106-208)	0.08
Ratio Prothrombin Time at 4th postoperative day	1.30(1.17-1.46)	1.23(1.14-1.34)	0.09
AST/ALT at 4th postoperative day (U/L)	305(158-523)	247(159-432)	0.35
Bilirubin at 4th postoperative day (mg/dL)	1.5(1-2.8)	1.2(0.8-1.9)	0.01
Complication rate stratified by Clavien			
No complications	38(56%)	68(65%)	
I	4(6%)	6(6%)	
II	15(22%)	22(21%)	0.66
III	6(9%)	4(4%)	
IV	4(6%)	3(3%)	
V	1(2%)	1(1%)	
Re-intervention n (%)	6(9)	3(3)	0.01
Re-intervention for bleeding n (%)	1(1,5)	0	0.39
Intensive Care Unit Stay (days)	1(0-3)	1(0-3)	0.49
In hospital Stay (days)			
Overall	10(7-14)	7(5-11)	<0.01
Laparoscopic approach	6 (5-13)	4 (3-7)	0.07
Open surgery	10 (8-15)	9 (6-14)	0.02

Definition of Abbreviations: *p* value = statistical significance comparing both groups. Data expressed as median (25-75%)

Table 3: Comparison of postoperative complications and outcome data between historic controls (2009) and study group (January 2012-June 2013).

major complication rate (≥ 3 Clavien Score) was similar in both groups (16% vs. 8%, $p>0.05$). Nonetheless, notably, the rate of re-intervention was significantly higher in the historic group (9 vs. 3 %, $p=0.01$); being postoperative bleeding the cause of re-intervention only in 1 patients from the historic group ($p=0.39$). None of patients in the study group experienced postoperative bleeding requiring surgery. For the study group, bilirrubin level on 4th postoperative day was lower, whereas hepatic enzymes, ratio prothrombin time and platelet count were similar in both groups. There were no differences in the length of stay in ICU. However, in-hospital stay was longer in the historic group than in the study group (16 ± 22 vs. 10 ± 9 days, $p<0.01$) even when we excluded patients underwent laparoscopy approach (17 ± 23 vs. 12 ± 10 days, p=0.02).

Discussion

The present retrospective study with a historical control supports the thesis that prophylactically transfusion of FFP is neither useful nor necessary for reducing perioperative bleeding during liver surgery resection. We are aware of the limitations of a study of this type, however, based upon the new trends and experience reported on the management of coagulopathy in the setting of liver disease, we considered unethical propose a randomized controlled trial. FFP has been traditionally used during liver surgery for the purpose of hemostatic effect by correction of deficiency of coagulation factors, maintenance of circulating blood volume by supplementation of albumin, in addition to the purpose of prevention of hepatic failure [3,10-12]. However, since FFP transfusion has been associated with adverse effects: transmission of infection, allergic reactions, hemolysis, anaphylaxis, transfusion related acute lung injury (TRALI) [12-14] and even, postoperative hepatocarcinoma recurrence [12,13], the efficacy of FFP should have been proved in this context. We successfully reduced the intraoperative FFP transfusion rate from 50% in our historical patients before 2010 to 0% without increasing perioperative blood losses or morbidity in both cirrhotic and non-cirrhotic patients underwent liver resection.

In our Institution, for more than two decades and regardless the presence of bleeding, we routinely administered FFP during liver surgery (once resection was completed) or in the immediate postoperative period to all cirrhotic patients and those non-cirrhotic who were undergone major liver resections. Historically, patients undergoing liver surgery received prophylactic transfusion of FFP with the aim of normalizing pre-existing (in cirrhotic patients) or expected transient (in non-cirrhotic patients) coagulation abnormalities to minimize the perioperative blood losses. In line with previous experiences reported in the field of liver transplantation [15], our study failed to show any convincing benefit to this routine. Our historic patients did not show a reduction of intraoperative hemorrhage. All currently available criteria for FFP transfusion have been defined retrospectively and generally include a ratio prothrombin time less than 1.5 [16-19]. However several reasons can be argued against this practice specifically in the context of liver resections: 1) liver resection entails a decline in both pro- and anticoagulant factors, 2) an hypercoagulability status assessed by viscoelastic test has been evidenced the first week following surgery [20], and 3) the poor predictive value of the ratio prothrombin time predicting bleeding events has never been proved [7]. Then, taking together these data, haemostatic competence after liver resection is likely better than we may expect, so the need for FFP to improve the prothombin time is questionable. In fact, all our patients, before and after the implementation of the new protocol, showed an almost normal ratio prothrombin time (<1,4) at 4th postoperative day. Moreover, systematic prophylactic use of FFP just to improve or to correct hemostatic function has never been shown any benefit, with exception of massive intraoperative bleeding, and may occasionally be deleterious. Consequently, the administration of FFP during liver resection should be limited to abnormalities of the routine coagulation tests along with bleeding episodes.

A highest requirement of RBC was observed in those patients who received FFP in absence of bleeding. Given the retrospective nature of the study, it is worthy to note the fact that the starting and final hemoglobin levels are the same for both groups excluding the potential bias of different management. Previous retrospective studies in patients underwent liver transplantation have also shown a link between FFP and RBC transfusion [21]. Dilutional effect of FFP volume as well as the transient hypervolemia through venous congestion could contribute to higher bleeding during liver resection. Hence, the avoidance of FFP volume probably would help to maintain low central venous pressure during liver resection, considered a crucial strategy to prevent bleeding

during invasive procedures, such as liver surgery, in both cirrhotic and non-cirrhotic patients [22].

Prevention of the consequences of temporary hepatic failure, one of the most dreadful complications associated to liver resection, is another purpose of prophylactic use of FFP. However, the use of blood products including FFP has been associated with poorer outcome after liver transplantation and some recent studies suggest that it could also happen in the setting of liver resection [23]. Martin et al. reported the use of FFP after hepatic resection of liver metastasis from colorectal cancer and suggested that postoperative complications were not associated with FFP use [16]. Tomimaru et al. showed that there is no clear benefit of FFP transfusion and postoperative prognosis in cirrhotic population underwent liver resection for hepatocarcinoma [24]. According to those early studies, in our study, which includes both cirrhotic and non-cirrhotic patients, postoperative residual liver function represented by ratio prothrombin time, transaminases and bilirubin, was not better in patients who received FFP. On the contrary, they showed higher bilirubin levels at 4th postoperative day.

In particular, perioperative FFP transfusion has been also used for maintenance of colloid osmotic balance by supplementation of albumin lost during surgery, mainly in order to avoid intractable ascites. Immamura et al. achieved zero operative mortality and low rate morbidity in more than 1000 liver resections by adhering to a policy of transfusing FFP to maintain total serum albumin levels at 3.0 g/dL. However, in the multiple logistic regression analysis, the albumin level was no identified as independent risk factor associated to postoperative complications [2]. Later, Yamazaki et al. prospectively determined a lower safety limit of serum albumin level (2.4 g/dL) to avoid postoperative complications in cirrhotic patients underwent liver resection for cancer [25,26]. The postoperative albumin level was not available in our patients, however we specifically recorded the incidence and severity of postoperative ascites and edema (included in the results as complications), which were similar in both groups. Hence, there is no clear justification for FFP transfusion to treat or prevent complications from hypoalbuminemia and, in any event, the use of albumin products should be considered as safer alternative to FFP.

There are several limitations to this study. Although data were prospectively collected, a retrospective study design using single-center data has well-known limitations. The results may not be applied to other centers since the patient population, indication of surgery, and perioperative strategies vary from center to center. Nonetheless, our center is an experienced, high-volume transplant center, and these data may be of use to other centers. Lastly, during the study period some new surgical devices to control bleeding during liver resection have probably been implemented and may alter the outcome of patients. Even though our data indicate that the avoidance of prophylactic FFP in this setting is not deleterious in any respect and should be considered for prudent risk-benefit analysis in transfusion decision-making.

In conclusion, our results provide substantial support for the proposition that the routine administration of FFP for the liver resection is not necessary and even may have a negative impact, making them extensive to cirrhotic and no cirrhotic population. Considering the inefficacy on avoiding hemorrhagic complications and improving liver function and, the potential adverse effects associated to the use of FFP, we believe that this practice should be strongly discouraged.

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References

1. Mariette D, Smadja C, Naveau S, Borgonovo G, Vons C, et al (1997) Preoperative predictors of blood transfusion in liver resection for tumor. Am J Surg 173: 275-279.
2. Imamura H, Seyama Y, Kokudo N, Maema A, Sugawara Y, et al. (2003) One thousand fifty-six hepatectomies without mortality in 8 years. Arch Surg 138: 1198-1206.
3. Makuuchi M, Takayama T, Gunvén P, Kosuge T, Yamazaki S, et al. (2014) Restrictive versus liberal blood transfusion policy for hepatectomies in cirrhotic patients. World J Surg 13: 644-648.
4. Melendez JA, Arslan V, Fischer ME, Wuest D, Jarnagin WR, et al. (1998) Perioperative outcomes of major hepatic resections under low central venous pressure anesthesia: blood loss, blood transfusion, and the risk of postoperative renal dysfunction. J Am Coll Surg 187: 620-625.
5. Youssef WI, Salazar F, Dasarathy S, Beddow T, Mullen KD (2003) Role of fresh frozen plasma infusion in correction of coagulopathy of chronic liver disease: a dual phase study. Am J Gastroenterol 98: 1391-1394.
6. Stanworth SJ, Brunskill SJ, Hyde CJ, McClelland DBL, Murphy MF (2004) Is fresh frozen plasma clinically effective? A systematic review of randomized controlled trials. Br. J Haematol 126: 139-152.
7. Segal JB, Dzik WH, Network TMCT (2005) Paucity of studies to support that abnormal coagulation test results predict bleeding in the setting of invasive procedures: an evidence-based review. Transfusion 45: 1413-1425.
8. Poon RT (2004) Recent advances in techniques of liver resection. Surg. Technol. Int. 13: 71-77.
9. Makuuchi M, Imamura H, Sugawara Y, Takayama T (2002) Progress in surgical treatment of hepatocellular carcinoma. Oncology 62 Suppl 1:74-81.
10. Franco D, Smadja C, Kahwaji F, Grange D, Kemeny F, et al. (1988) Segmentectomies in the management of liver tumors. Arch Surg 123: 519-522.
11. Makuuchi M, Kosuge T, Takayama T, Yamazaki S, Kakazu T, et al. (2014) Surgery for small liver cancers. Semin Surg Oncol 9: 298-304.
12. Isbister JP (1993) Adverse reactions to plasma and plasma components. Anaesth. Intensive Care 21: 31-38.
13. MacLennan S, Barbara JAJ (2006) Risks and side effects of therapy with plasma and plasma fractions. Best Pract Res Clin Haematol 19: 169-189.
14. Bux J, Sachs UJH (2007) The pathogenesis of transfusion-related acute lung injury (TRALI). Br J Haematol 136: 788-799.
15. Ozier Y, Tsou MY (2008) Changing trends in transfusion practice in liver transplantation. See comment in PubMed Commons below Curr Opin Organ Transplant 13: 304-309.
16. Martin RCG, Jarnagin WR, Fong Y, Biernacki P, Blumgart LH, et al. (2003) The use of fresh frozen plasma after major hepatic resection for colorectal metastasis: is there a standard for transfusion? J Am Coll Surg 196: 402-409.
17. (1994) Practice parameter for the use of fresh-frozen plasma, cryoprecipitate, and platelets. Fresh-Frozen Plasma, Cryoprecipitate, and Platelets Administration Practice Guidelines Development Task Force of the College of American Pathologists. JAMA 271: 777-781.
18. (1996) Practice Guidelines for blood component therapy: A report by the American Society of Anesthesiologists Task Force on Blood Component Therapy. Anesthesiology 84: 732-747.
19. Massicotte L, Lenis S, Thibeault L, Sassine MP, Seal RF, et al. (2005) Reduction of blood product transfusions during liver transplantation. Can J Anaesth 52: 545-546.
20. Cerutti E, Stratta C, Romagnoli R, Schellino MM, Skurzak S, et al. (2004) Thromboelastogram monitoring in the perioperative period of hepatectomy for adult living liver donation. Liver Transpl 10: 289-294.
21. Jones RM, Moulton CE, Hardy KJ (1998) Central venous pressure and its effect on blood loss during liver resection. Br J Surg 85: 1058-1060.
22. Moller S, Bendtsen F, Henriksen JH (1995) Effect of volume expansion on systemic hemodynamics and central and arterial blood volume in cirrhosis. Gastroenterology 109: 1917-1925.

23. Rana A, Petrowsky H, Hong JC, Agopian VG, Kaldas FM, et al. (2013) Blood transfusion requirement during liver transplantation is an important risk factor for mortality. J Am Coll Surg 216: 902-907.

24. Tomimaru Y, Wada H, Marubashi S, Kobayashi S, Eguchi H, et al. (2010) Fresh frozen plasma transfusion does not affect outcomes following hepatic resection for hepatocellular carcinoma. World J Gastroenterol 16: 5603-5610.

25. Yamazaki S, Takayama T, Kimura Y, Moriguchi M, Higaki T, et al. (2011) Transfusion criteria for fresh frozen plasma in liver resection: a 3 + 3 cohort expansion study. Arch Surg 146: 1293-1299.

26. Llovet JM, Fuster J, Bruix J; Barcelona-Clínic Liver Cancer Group (2004) The Barcelona approach: diagnosis, staging, and treatment of hepatocellular carcinoma. Liver Transpl 10: S115-120.