The Utilization Of Venovenous Bypass And Transfusion In Orthotopic Liver Transplantation

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Citation

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Abstract

Orthotopic liver transplantation (OLT) requires transfusion, and may require venovenous bypass (VVB); with associated risks and cost. This study evaluated the utilization of VVB and transfusion; and relationship between VVB and transfusion requirement in OLT. Electronic anesthesia and perioperative data of 151 adult OLT patients were collected prospectively and analyzed. Data collected included patient demographics, liver failure etiology, coagulation profile, Model for End-stage Liver Disease (MELD) score, ischemia durations of donor liver, VVB use, VVB duration, blood components transfused and cell-saver transfusion. It showed a VVB utilization rate of 12.5%, with a mean duration of 100 ± 35.8 minutes. VVB was associated with higher transfusion of red blood cells and fresh frozen plasma, but not platelets or cryoprecipitate. There was positive correlation between red blood cell, fresh frozen plasma and platelet transfusion. The study confirms that VVB is being utilized less and is associated with increased transfusion.

This work is attributed to the Departments of Anesthesiology and Surgery, University of Michigan, Ann Arbor, USA.

INTRODUCTION

Orthotopic liver transplantation (OLT) in adult patients usually requires blood component transfusion, and sometimes requires venovenous bypass (VVB). Transfusion and venovenous bypass are associated with potentially serious complications; and constitute a significant proportion of perioperative resource utilization and cost in OLT ([1, 2]). Current practice is increasingly being scrutinized and debated. The use of venovenous bypass in OLT is controversial and not supported by adequate or reliable data ([3]). Although venovenous bypass may improve cardiovascular function during vena cava clamping, it is not associated with significant benefit with respect to renal function, transfusion requirement, post-reperfusion syndrome, perioperative morbidity and mortality ([3, 4, 5]). Blood component requirement in OLT is variable, multifactorial, and may be positively or negatively influenced by venovenous bypass ([3, 6, 7, 8]). The objectives of this study were to analyze the utilization of venovenous bypass and blood component transfusion in OLT, and to determine the relationship between venovenous bypass and blood component transfusion requirement.

MATERIALS AND METHODS

Following institutional approval, 151 consecutive adult patients undergoing OLT at the University of Michigan hospital between January 2004 and February 2006 were included in this prospective observational study. Anaesthetic technique and haemodynamic management were standardized. Rapid IV infusor, cell-saver and heating devices were employed. Calcium and magnesium were administered to maintain normal serum levels. Packed red blood cells (PRBC) were infused to maintain haematocrit above 25% and fresh frozen plasma (FFP) was transfused to maintain an international normalized ratio (INR) below 1.7. Platelet transfusion was administered to maintain the platelet count above 70 x 10^9/L. Cryoprecipitate infusion was indicated at fibrinogen level below 150mg/dl. Clinical fibrinolysis, indicated by diffuse hemorrhage of non-surgical origin, was treated with epsilon-aminocaproic acid. VVB was indicated if there was more than 50% reduction in cardiac output or mean arterial pressure after vena cava clamping. VVB was employed to decompress the portal venous system in a bid to minimize bleeding or bowel oedema; in patients who manifested signs of these problems during the initial stages of laparotomy. All the surgeons and anaesthesiologists used the same criteria for instituting venovenous bypass. All the anaesthesiologists used the same haemodynamic management protocol before vena cava

clamping. The protocol included colloid infusion and norepinephrine infusion. VVB involved extracorporeal flow of blood from the femoral vein to the internal jugular vein.

Perioperative data were collected from electronic patient records, including the Centricity anaesthesia information system (Centricity, GE Healthcare Inc, Waukesha, WI). Data included patient demographics, etiology of liver failure, preoperative coagulology, Model for End-stage Liver Disease (MELD) score, ischaemia durations of donor liver, the use of VVB, duration of VVB, amount of specific blood components transfused and amount of cell-saver blood transfused.

Data analysis was performed with the SPSS program (v 13.0, SPSS Inc, Chicago, IL). Bivariate analysis was performed using the Student's t-test for equality of means and the Levene's test for equality of variances. Results are expressed as mean ± SD. Correlation of variables was achieved using Pearson's correlation coefficient. A P value <0.05 was considered statistically significant.

RESULTS

A total of 151 adult orthotopic liver transplantation cases were analyzed. The patient demographic data is shown in Table 1.

Figure 1

Table 1

Age	Number of cases	Percentage
18-64years	139	92
65-71years	12	8
Gender	**Number of cases**	**Percentage**
Male	104	69
Female	47	31

The etiology of liver failure was hepatitis-C in 34%, alcoholic liver cirrhosis in 15%, cholangitis in 12%, cryptogenic cirrhosis in 9%, biliary atresia in 7%, non-alcoholic steato-hepatitis in 7%, fatty liver in 5%, autoimmune hepatitis in 5% and other etiologies in 6% of patients. About 93% of the patients had never had previous abdominal surgery or orthotopic liver transplantation.

Nineteen patients (12.5%) required venovenous bypass, with a mean duration of 100 ± 35.8 minutes (range 55-200 minutes). The primary reason for instituting venovenous bypass (VVB) during the anhepatic phase in all the 19 patients was a severe reduction (usually greater than 50%) in cardiac output or mean arterial pressure after vena cava clamping. All the 19 patients who required VVB had severe pre-transplant cardiovascular insufficiency in the form of low cardiac output, low mean arterial pressure and high central venous pressure. VVB significantly improved haemodynamic parameters, with average mean arterial pressures of 50mmHg, in 13 of the 19 cases in which it was employed. The secondary reason for VVB in a small fraction of this group was to decompress the portal venous system in a bid to minimize bleeding or bowel oedema.

The average patient MELD score was 18. Forty-nine percent of patients had INR ? 1.2 and 51% had INR > 1.2. Ninety-four percent of donor livers had a normal healthy appearance, and 6% appeared congested. The cold ischaemia time range of the donor livers was 151-785 minutes with a mean of 500 minutes; and the warm ischaemia time range was 21-100 minutes with a mean of 42 minutes. All these parameters, including the demographic data and diagnoses, were similar in the VVB group and the non-VVB group of patients; without a significant difference.

All the patients received PRBC and FFP transfusion; 78.4% received platelets; and 23.9% received cryoprecipitate. The relationship between VVB and blood component transfusion indicated that patients in the VVB group required significantly higher transfusion of PRBC (p=0.006) and FFP (p=0.009), but VVB did not show any significant association with platelet and cryoprecipitate transfusion (Table 2).

Figure 2

Table 2

Blood component type	Units transfused: Mean ± SD	*p* value
PRBC -VVB	21.33 ± 15.89	*p*=**0.006**
-No VVB	9.39 ± 8.82	
FFP -VVB	27.42 ± 14.88	*p*=**0.009**
-No VVB	17.04 ± 11.88	
Platelets-VVB	17.60 ± 9.18	*p*=0.249
-No VVB	14.60 ± 8.03	
Cryoprecipitate -VVB	8.60 ± 6.80	*p*=0.239
-No VVB	12.05 ± 8.77	

PRBC=Packed red blood cells. FFP=Fresh frozen plasma. VVB = Venovenous bypass. SD = Standard deviation.

The inter-relationship between the different blood components transfused showed a significant positive correlation between PRBC and FFP; and between PRBC and platelets (Table 3). The data on cell-saver blood transfusion was considered unreliable and thus was excluded from analysis.

Figure 3

Table 3: Correlation between blood components transfused

	FFP	PRBC	Platelets	Cryoprecipitate
FFP - Pearson Correlation - Significance: 2-tailed	r = 1	R=0.839 p=0.0001	r=0.286 p=0.003	r = -0.288 p = 0.109
PRBC-Pearson Correlation -Significance: 2-tailed	r=0.839 p=0.0001	R = 1	r =0.256 p=0.009	r = -0.320 p = 0.079

PRBC = Packed red blood cells. FFP = Fresh frozen plasma.

DISCUSSION

This study revealed a low VVB utilization rate of 12.5%, and confirms the decreasing use of VVB in OLT. Previous studies reported VVB utilization rates of 18% to 40% ([9], [10], [11], [12]). Many studies have shown that the limited benefits of VVB in orthotopic liver transplantation do not appear to outweigh the risks and cost ([1], [2], [3], [5]). A recent study of 72 living-donor liver transplant recipients showed that patients who had VVB required significantly more red blood cells, FFP, and platelet infusion; had lower intraoperative temperature; had worse postoperative hepato-renal function; required longer postoperative ventilatory support; and had significantly higher mortality ([12]). Our study is larger and is the first in orthotopic liver transplant patients to show that VVB is associated with significantly higher FFP and red cell transfusion. This contests previous reports of significant reduction in blood component transfusion with VVB ([13], [14]). A previous study published more than a decade ago reported no difference in transfusion requirements during liver transplantation with or without VVB ([15]). These previous reports may have been influenced by inadequate surgical and anesthesia technique or expertise in the period prior to the last decade.

Despite advances in surgical and anesthetic care, bleeding remains a major problem during OLT. The increased blood transfusion associated with VVB in our study may be due to increased platelet adhesion, haemolysis and fibrinolysis in the bypass tubing ([3]). Our study result suggests that red cell transfusion had a positive correlation with FFP transfusion. Furthermore, red cell and FFP transfusion were associated with increased platelet transfusion. These positive correlations in blood component transfusions are mainly due to coagulopathic bleeding and efforts to correct it by administration of appropriate blood components. The problem of coagulopathic bleeding may be minimized by avoidance of VVB, adequate platelet function, fibrinogen adequacy and antifibrinolysis ([7], [8]). Our routine practice includes the correction of coagulopathy before the commencement of the transplantation procedure. Although we used epsilon-aminocaproic acid infusion to treat clinical fibrinolysis that presented in the form of non-surgical diffuse haemorrhage, the data limitations of our retrospective study do not allow conclusive analysis of the antifibrinolytic efficacy of epsilon-aminocaproic acid in orthotopic liver transplantation.

There are many factors that may affect bleeding during OLT. These include the length of the cold ischemia time and quality of the donor liver ([16]). Our practice involves the use of high-quality donor grafts and the limitation of cold ischemia to a minimum. The preoperative MELD score and coagulation profile have been identified as predictors of bleeding during OLT ([17]). Our practice includes improving thrombocytopenia and coagulopathy before the commencement of the transplantation procedure. Coagulopathy is also corrected aggressively during transplantation. However, despite all the above measures, bleeding and blood transfusion during orthotopic liver transplantation may be very variable and unpredictable ([1], [6], [15]).

The risks of VVB include vascular injury, cardiac failure, haematoma, seroma, thrombosis, and embolism. Although this study is prospective observational and may have data limitations, it confirms that venovenous bypass is now utilized less and suggests that it may be associated with increased transfusion. The risks and cost of venovenous bypass and blood transfusion in orthotopic liver transplantation are potentially significant such that utilization should be judicious and minimized whenever possible. Our current practice is to limit the use of venovenous bypass to patients who manifest persistent severe intraoperative cardiovascular insufficiency in the form of low cardiac output and low systemic arterial blood pressure despite normovolaemia and cardiovascular support with low-dose infusion of a vasopressor or inotrope. Our clinical observations show that this technique is reliable and reduces the need for venovenous bypass during orthotopic liver transplant surgery. Further studies are required to clearly determine the best type, optimal dose range and most appropriate clinical applications of vasopressor or inotrope support during orthotopic liver transplantation.

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