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Peri-hepatic gauze packing for the control of haemorrhage during liver transplantation: A retrospective study

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ABSTRACT

Background: Albeit accepted in the trauma setting, use of peri-hepatic gauze packing has been rarely reported during liver transplantation.
Aims: To assess the results of packing in liver transplantation.
Methods: We reviewed clinical characteristics, intraoperative events and postoperative outcome of consecutive adult liver transplantation recipients between 2003 and 2013. Patients treated with packing were compared to no-packing patients and to matched controls selected using a propensity score.
Results: Of 1396 recipients, 107 were treated with packing for peri-hepatic bleeding (76.6%), allograft damage (12.1%) or partial outflow obstruction (11.2%). Urgent reoperation for ongoing haemorrhage was required in 6 (5.6%). Correction of haemodynamic and coagulation parameters was constantly achieved. Overall, patient (90% vs. 98%, $p < 0.001$) and graft (83.2% vs. 94.7%, $p < 0.001$) 3-month survival was significantly reduced in packing patients. However, after matching, no significant difference was observed in patient (89.3% vs. 95.2%, $p = 0.12$) and graft (83.5% vs. 92.2%, $p = 0.06$) 3-month survival. Patient survival was associated with recipient age (HR 2.59; $p = 0.04$) and donor age × recipient MELD (HR 2.04; $p = 0.02$), but not with packing (HR 1.81; $p = 0.29$).
Conclusions: In our experience, packing was a valuable adjunct to conventional means of haemostasis during liver transplantation and, after accounting for confounding covariates, was not associated with inferior outcomes.

1. Introduction

Peri-hepatic gauze packing (PHGP) is an accepted technique for the control of haemorrhage after severe liver trauma [1,2]. The goal of temporary PHGP is to achieve fast control of bleeding while haemodynamic stability is restored and coagulation disorders are fixed, thus avoiding futile and potentially harmful attempts at achieving haemostasis. Patients experiencing acidosis, hypothermia and coagulopathy (the so-called "killing triad") are more likely to require PHGP.

The physiopathology of haemorrhage occasionally observed in the course of liver transplantation (LT) is similar to that observed after liver trauma. Baseline cirrhosis-related coagulopathy, blood losses, prolonged surgery, anhepatic phase and initial allograft dysfunction may all contribute to trigger the vicious circle of acidosis, hypothermia and coagulopathy [3]. The use of extended criteria grafts, more susceptible to initial dysfunction, may further sustain coagulopathy. In this setting, usual means of haemostasis can be ineffective and reiterate attempts at controlling bleeding can be frustrating or even detrimental. Although this would ideally represent a good indication for PHGP, packing use during LT raises concerns for a potentially increased risk of infections and graft-related complications.

The practice of PHGP is not new in the setting of LT. However, except some small case-control studies [4,5] and one patient series [6,7], the only large reported experience is that of the UCLA group: in a recent article evaluating the impact of intraoperative blood transfusion volume on early LT outcome, they reported a series of 233 consecutive cases between 2006 and 2008 in which the rate of PHGP was roughly 8% [8]. In a subsequent article, they focused

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on the efficacy and outcome of damage control strategy in the setting of liver transplantation, concluding that inferior early outcome observed in patients treated with packing is most likely due to the patients' condition severity rather than to packing itself [9]. The aim of our study was to assess the value of PHGP during LT based on a European single centre experience over a decade. First, focusing on patients treated by PHGP, we evaluated the efficacy of packing in achieving stable haemostasis, the clinical scenarios in which PHGP was applied, and the variations of haemodynamic and metabolic parameters. Second, we compared the patients treated with PHGP to a cohort of controls selected by propensity score matching to assess the influence of the technique on 3-month patient and graft survival and on postoperative complications.

2. Patients and methods

2.1. Patient selection

This retrospective study is based on a consecutive series of 1500 patients transplanted from January 2003 to August 2013 at our institution. The study sample was chosen well after the Centre learning curve in LT was completed, i.e. beyond the 1000th case performed [10]. All transplant operations were personally performed or supervised by one of three experienced senior surgeons. Intraoperative deaths and patients aged <18 years were excluded. Patients treated with PHGP due to uncontrollable haemorrhage during LT were first compared to the whole group of patients undergoing a standard LT procedure. Secondly, two equally numerous cohorts of PHGP and no-PHGP patients selected by propensity-score matching were analyzed. Collected data included baseline patient characteristics, donor features, intraoperative variables, postoperative complications and outcome. Minimum follow-up for surviving patients was 3 months.

2.2. Peri-hepatic gauze packing indication and technique

In all cases, the decision to use PHGP was made after failure of all other available means of haemostasis, including administration of coagulation factors, fibrinogen and activated factor VII, and local application of fibrin and thrombin glues. Most patients were treated with temporary packing during the same operation. PHGP was carried out placing gauzes behind the liver allograft along the inferior vena cava, in the Morrison space and around the hepatic pedicle. Any compression or torsion of the vascular structures was carefully avoided. As previously described [11], biliary anastomosis was systematically delayed in any case of profuse bleeding clearly requiring packing, and also in patients requiring a hepaticojejunostomy when bowel oedema precluded a safe suturing. In selected cases, when bleeding initially seemed controllable by temporary packing without the need for a 2-stage procedure, the biliary anastomosis was performed while temporary packing was in place. In these patients the decision to use prolonged packing was made due to persistence of bleeding after completion of the biliary anastomosis. After positioning two or three large bore drains, only the skin was closed to prevent abdominal compartment syndrome. The patient was then transferred to the intensive care unit (ICU) to restore haemodynamic stability and correct metabolic and coagulations disorders. Packing removal and definitive abdominal wall closure were considered when acidosis, hypothermia and coagulopathy had resolved, normally 48 h after the transplant operation. Packing was re-positioned in case persistent bleeding was observed during second-look operation after packing removal. Piperacillin/tazobactam and continuous-infusion vancomycin were administered until 10th postoperative day (POD) after packing removal; liposomal amphotericin B was administered until central venous line removal. Immunosuppression included steroids, a calcineurin inhibitor (Cyclosporin A was preferred in patients with hepatitis C virus) and mycophenolate mofetil (introduced as soon as platelet count was >50,000/μL and white blood cell count was >3000/μL). No modification to the immunosuppression protocol was made according to PHGP status.

2.3. Definitions

Packing failure was defined as the need for urgent reoperation for ongoing bleeding despite PHGP. Most widely adopted prognostic scores in LT, including model for end-stage liver disease (MELD) [12], donor age × recipient MELD (D-MELD) [13,14] and balance of risk (BAR) [15] were calculated as previously described. Donor-recipient allocation model (DReAM) is a recently described prognostic score of 3-month graft survival based on both donor and recipient variables; it was calculated using the updated formula including supplementary variables (allograft steatosis) and coefficients derived from our own Centre [16]. Previous abdominal operations were defined as any supra-mesocolic operation (excluding laparoscopic cholecystectomy) or any laparotomy. Appendectomy, hernia repair and any pelvic or gynaecological operation were not considered. Portal vein thrombosis was classified according to Yerdel et al. [17]. Early allograft dysfunction (EAD) was defined according to Olthoff et al. [18] as the presence of one or more of the following: bilirubin >10 mg/dL on postoperative day (POD) 7, international normalized ratio >1.6 on POD 7, alanine or aspartate aminotransferases >2000 UI/mL within the first 7 PODs. The Clavien–Dindo classification [19] was used to grade postoperative complications; grade 3 and 4 complications were defined as severe. Renal failure was defined as a serum creatinine >3× baseline or ≥4.5 mg/dL with an acute rise ≥0.5 mg/dL, or a urine output <0.3 mL/kg/h for 24 h or anuria for 12 h [20]. Standard definitions were used for systemic inflammatory response syndrome (SIRS) and sepsis [21].

2.4. Study endpoints

The primary endpoint was 3-month patient survival. Secondary endpoints were 3-month graft survival and postoperative complications.

2.5. Statistical analysis

Continuous data are presented as medians and interquartile ranges or means and standard deviations. Discrete data are given as counts and percentages. Chi-square test or, where appropriate, Fisher exact test were performed to compare groups of categorical data; the Mann–Whitney *U* test was used to compare continuous data.

Following a stepwise selection procedure, a predictive model was constructed to identify patients prone to require a PHGP during the transplant operation. Demographic and clinical patient variables possibly associated with the PHGP procedure were entered into the model.

Three-month survivals were compared between the PHGP and control groups by using the log-rank test and are presented as Kaplan–Meier curves. Multivariate Cox proportional hazards models were applied to assess the effect of PHGP on 3-month survival, with the effect of the PHGP choice adjusted by the propensity to undergo the packing procedure [22]. Briefly, clinical characteristics associated with the probability to undergo PHGP were entered into a multivariate logistic regression model to derive the propensity score. The model goodness of fit was evaluated using graphical examination of the residual diagnostics, discrimination and Brier score, the Somer's Dxy rank correlation index and the