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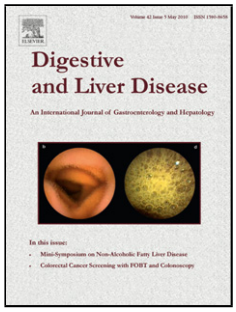

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Peri-hepatic gauze packing for the control of haemorrhage during liver transplantation: a retrospective study

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List of abbreviations: BAR, balance of risk score; D-MELD, donor age * recipient MELD; DReAM, donor recipient allocation model; EAD, early allograft dysfunction; HAT, hepatic artery thrombosis; ICU, intensive care unit; IVC, inferior vena cava; LT, liver transplantation; MELD, model for end-stage liver disease; PHGP, peri-hepatic gauze packing; POD,

postoperative day; PRBC, packed red blood cells; SIRS, systemic inflammatory response syndrome.

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 1,396 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 hemodynamic and coagulation parameters was constantly achieved. Overall, patient (90% versus 98%, p<0.001) and graft (83.2% versus 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% versus 95.2%, p=0.12) and graft (83.5% versus 92.2%, p=0.06) 3-month survival. Patient survival was associated with recipient age (HR 2.59; p=0.04) and donor age x 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.

Keywords: liver transplantation, haemorrhage, peri-hepatic gauze packing, damage control surgery, open abdomen

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 hemodynamic 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 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 hemodynamic 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.

PATIENTS AND METHODS

Patient selection

This retrospective study is based on a consecutive series of 1,500 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.

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 hemodynamic 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 hours 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.

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 gynecological 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 > 2,000 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 > 3X baseline or ≥ 4.5 mg/dL with an acute rise ≥ 0.5 mg/dL, or a urine output < 0.3 mL/kg/hour for 24 hours or anuria for 12 hours[20]. Standard definitions were used for systemic inflammatory response syndrome (SIRS) and sepsis[21].

Study endpoints

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

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 Hosmer-Lemeshow calibration measure using bootstrap resampling (100 runs)[23]. Two equally numerous (1 : 1 matching) coeval cohorts of PHGP and no-PHGP patients were selected using a caliper size equal to one-fifth of the standard deviation of the logit of the estimated propensity score. Finally, a Cox proportional hazards model with robust variance estimation was used to regress the 3-months survival time accounting for potential confounding variables in the matched sample. Interactions between the variables were tested by Wald test. Results of the Cox model are presented as hazard ratios (HR). A two-sided *p* value of less than 0.05

was considered to indicate statistical significance. All analyses were carried out using R version 3.02 (http://www.R-project.org).

RESULTS

Peri-hepatic gauze packing application and efficacy

During the study period five (0.3%) intraoperative deaths and 99 recipients aged less than 18 years were excluded from analysis. Thus, the study population consisted of 1,396 adult patients, among whom 107 were treated with PHGP to control intraoperative bleeding (7.7%). The percentage of patients treated with PHGP ranged between 5.3% and 9.5%, remaining almost stable throughout the study period. Patient, donor and intraoperative features are summarized in Table 1. Compared to controls, patients treated with PHGP had a higher rate of previous LT, previous upper abdominal surgery and portal vein thrombosis. Portal vein thrombosis grade was distributed as follows: grade 1, n = 7 (6.5%); grade 2, n = 5 (4.7%); grade 3, n = 1 (0.9%). PHGP patients also presented with a more advanced liver disease and worse prognostic indexes, as demonstrated by higher MELD, D-MELD, BAR and DReAM scores. As expected, the patients in the PHGP group were also more profusely transfused during the transplant operation, required higher doses of inotropes, and presented an increased end-procedure lactate level.

The indication to PHGP was peri-hepatic bleeding, liver allograft damage and bleeding related to a partial obstruction of the venous outflow in 82 (76.6%), 13 (12.1%) and 12 (11.2%) patients, respectively. Allograft damage was due to traumatic liver injury before donor death or consequent to allograft handling during retrieval or implant in 4 (30.8%) and 9 (69.2%) cases, respectively. Inferior vena cava (IVC) anastomosis technique was as follows: “classic” technique with IVC replacement (n = 12, 11.2%), standard piggy-back using recipient’s

hepatic veins cuff (n = 88, 82.2%) or modified piggy-back technique with side-to-side IVC anastomosis (n = 7, 6.6%). Veno-venous by-pass was not used in any patient. There was no association between IVC anastomosis technique and indication for packing or outcome. In most cases, the decision for PHGP was made after temporary packing (mean duration = 100 ± 52 minutes) had demonstrated to be ineffective.

PHGP was effective in achieving stable control of haemostasis in all but 6 patients (5.6%) who required an urgent reoperation within 24 hours due to ongoing bleeding. However, after further haemostasis and packing re-positioning, all these patients were managed in the usual way. In 92 patients (86%), PHGP could be removed during the first second-look operation, which took place at a median interval of 48 hours after the transplant operation. The remaining patients required 2 (n=13, 12.1%), 3 (n=1, 0.9%) or 4 (n=1, 0.9%) second-look operations to achieve haemostasis. Median overall PHGP duration was three days. A mean of 1,084 ± 1,601 mL packed red blood cells, 1,109 ± 2,036 mL fresh frozen plasma and 0.7 ± 0.9 platelet units were transfused between the end of the transplant operation and the first second-look operation.

Severe hypothermia, coagulopathy and acidosis were constantly observed during the transplant operation at the time of PHGP positioning. However, all the considered indicators of coagulopathy significantly improved at the moment of the second-look operation (Table 2).

Outcome of patients treated with PHGP

Twelve PHGP patients died in the 3-month postoperative period (11.2%). Causes of death were sepsis (n = 9), delayed allograft non-function (n = 2) and acute myocardial infarction (n = 1). At least one severe complication was observed in 33 (30.8%) patients in the PHGP group. Three (2.8%) patients developed primary allograft non-function requiring early retransplantation. EAD was observed in 68 (63.6%) patients. In the unmatched cohort, both

patient (90% vs. 98%, HR 5.32, p<0.001) and graft (83.2% vs. 94.7%, HR 3.3, p<0.001) 3-month survival were significantly reduced in patients undergoing PHGP (Figure 1).

No differences in terms of patient and graft survival were observed according to the indication for packing (Figure 2). Primary non-function rate was 2.4%, 0% and 8.3% (p=0.42) in patients undergoing PHGP for peri-hepatic bleeding, graft damage and outflow obstruction, respectively. EAD was more frequently observed (p<0.001) in patients undergoing PHGP for outflow obstruction (100%) and allograft damage (84.6%) compared to peri-hepatic bleeding (54.9%).

In 78 (72.9%) patients biliary anastomosis was delayed. There was no difference between patients having a delayed or immediate biliary anastomosis in terms of postoperative (7.7% versus 3.4%, p = 0.67) and long-term (23% versus 24.1%, p = 1.0) biliary complications.

Predictive model for peri-hepatic gauze packing

A predictive model was constructed to elucidate which patients were more prone to require PHGP during the transplant procedure. Due to the huge disequilibrium in packed red blood cells (PRBC) transfusions among the treatment groups, this continuous variable was dichotomized based on the 80th centile (4,000 mL). Previous upper abdominal surgery (OR=3.19, p<0.001), previous transplantation (OR=1.85, p=0.09), PRBC transfusion above the 80th centile (OR=26.3, p<0.001) and higher DReAM score (OR=1.25, p=0.14) were the variables associated with the likelihood to require PHGP, which were entered into the multivariate logistic regression model to calculate the propensity score.

Analysis after propensity score matching

After selection by individual propensity score, 103 patients in the PHGP group were matched to 103 controls; thus, only four outliers were excluded from the PHGP group, preserving the vast majority of the patients in the treatment group for analysis.

The results of matching are summarized in Table 3: matched groups were comparable in terms of recipient age, sex, previous transplant, previous upper abdominal surgery, portal vein thrombosis, blood transfusion requirement and most widely adopted prognostic scores. In the matched sample, no significant difference in 3-month patient (89.3% vs. 95.2%, p=0.12) and graft (83.5% vs. 92.2%, p=0.06) survival was observed between PHGP and no-PHGP patients (Figure 1). Cox survival analysis showed that the only variables significantly associated with 3-month patient survival were D-MELD (Δ 714 – 1,476, HR 2.04, p=0.02, i.e. moving from 714 to 1,476 D-MELD values leads to a risk which is 2.04 times higher) and recipient age (Δ 47 – 60, HR 2.59, p=0.04), whereas PHGP was not (Δ no – yes, HR 1.81, p=0.29).

Postoperative complications in the matched sample are summarized in Table 4. Overall, the rate of grade ≥ 3 postoperative complications was comparable among study groups (p=0.10). Noteworthy, the rate of EAD, primary non-function, re-LT, abdominal abscess and pneumonia was not significantly increased after packing. Rejection rate was also comparable. Nonetheless, patients in the PHGP group presented a significantly increased rate of reoperation (29.1% vs.15.5%, p=0.03), hepatic artery thrombosis (HAT; 7.8% vs.1%, p=0.04), SIRS (33% vs.18.5%, p=0.02) and sepsis (22.3% vs.10.7%, p=0.02). The difference in the reoperation rate was not due to an increased rate of haemorrhage or abdominal sepsis in the PHGP group, but was related to an increased rate of reoperation for other indications, including re-LT (n=5), wound complications (n=3), vascular complications (n=2), complicated inguinal hernia (n=1), bowel occlusion (n=1) and positioning of a feeding jejunostomy (n=1). In the PHGP group, HAT was diagnosed in four cases (50%) during the second-look operation and was treated by thrombectomy, whereas it occurred as a consequence of an end-stage delayed non-function in two patients (25%) who were considered unfit for re-LT. In

the remaining 2 cases (25%), HAT occurred after depacking and abdominal wall closure; one case was successfully managed by surgical thrombectomy, whereas the other was treated by hyperbaric oxygen therapy. No case of HAT recurrence was observed in the subsequent follow-up; one patient with a patent hepatic artery developed ischemic cholangiopathy and a right liver abscess 6-months after LT, finally leading to death due to carbapenemase-producing *Klebsiella pneumoniae*-related sepsis. The patient treated with hyperbaric oxygen therapy is currently alive and well; Doppler ultrasonography shows an intra-parenchymal post-occlusive arterial flow in the liver allograft due to the presence of small collateral arteries, most likely an issue of hyperbaric therapy.

DISCUSSION

The main finding of this study is that, despite about 6% of patients experienced an initial failure of the technique, PHGP was finally effective in all patients, allowing achievement of haemostasis and correction of coagulation and haemodynamics prior to packing removal. Moreover, after adjusting for confounding covariates through propensity score matching, PHGP did not appear *per se* to impact on 3-month patient and graft survival.

The paramount importance of bleeding control during LT cannot be overemphasized. Previous studies have identified volume of blood transfusion as a strong predictor of postoperative mortality[8, 24-27]. The patients who present adhesions from previous major abdominal operations and those with a more advanced liver disease are more prone to require high transfusion volumes[8, 24, 26]. This is even more frequently observed in the current MELD era, in which sicker patients have a higher priority in organ allocation to avoid drop-out from the waiting list. Veno-venous by pass has been introduced as a strategy to avoid inferior vena cava and portal hypertension during the transplant operation, thus reducing

haemorrhage. However, its use should be weighed against potential complications and its efficacy in terms of reduction of intra-operative haemorrhage is controversial [28, 29]. Thus, in spite of meticulous surgical technique and optimal anaesthesiological management, massive haemorrhage during LT remains today far from infrequent.

Peri-hepatic gauze packing is an accepted technique to control haemorrhage from liver injuries following abdominal trauma[1, 2, 30-33]. The rationale for PHGP is to avoid futile attempts at haemostasis in a patient suffering from coagulopathy and acidosis. Due to the similarities with the liver injury scenario, the application of PHGP in case of life-threatening persistent haemorrhage during LT has been already proposed; yet, the reported experience is scarce. In the series by Xu et al.[5], LT patients treated with PHGP suffered from an increased postoperative mortality, mostly due to pulmonary infections and renal failure. Results of PHGP were more encouraging in the series by Rodriguez-Montalvo et al.[4], comparing patients treated with PHGP with those requiring early re-laparotomy for bleeding: indeed, they showed that, compared to PHGP, the control group presented a higher infection (20% vs. 33%) and mortality (13% vs. 24%) rate. Allard et al.[7] reported the use of PHGP in 7 patients suffering from partial outflow obstruction during LT or hepatic resection, after failure of conventional means of haemostasis. Control of bleeding was invariably achieved, allowing the correction of haemodynamic and coagulation disorders; all the patients were alive at the end of follow-up. Authors concluded that the practice of PHGP could be implemented. Finally, a recent paper by Di Norcia et al. reported the experience of the UCLA group[9]. In their series, 30-day outcomes were inferior in patients treated with packing even after matching based on preoperative and intraoperative variables. However, they observed that 1-, 3- and 5-year patient survival was similar between packing patients having a single reoperation and 1-stage liver transplant recipients having one reoperation for any reason. Both these groups

experienced better survival compared to patients having multiple reoperations, regardless of the need to recur to a damage control strategy. Accordingly, Authors argued that worse survival observed in the damage control group was due to patients' severity rather than to the damage control strategy itself.

The results of our study are in keeping with their findings. In the context of LT, persistence of bleeding can be even more prejudicial than in the trauma patient, as it can jeopardize the functional recovery of the liver allograft. In our experience, haemorrhage control by PHGP broke the vicious circle of bleeding → hypothermia → acidosis → coagulopathy → bleeding, allowing haemodynamic stabilization and correction of coagulation disorders. This is of special interest given the widespread use of extended criteria donors, more prone to early dysfunction favouring intraoperative haemorrhage[34]. Since comparing patients treated with PHGP with all other LT recipients in our series would have been of scarce interest, we used propensity score matching to select two cohorts of patients having the same probability to undergo PHGP (Table 3). After matching, differences in 3-month patient and graft survival among the study groups were no longer significant and, most importantly, the only variables significantly associated with 3-month patient survival were recipient age and D-MELD, whereas PHGP was not. Thus, PHGP did not appear to have *per se* a detrimental effect on early patient and graft survival. Given these results, we believe that PHGP could be proposed as a valuable haemostasis technique at an earlier stage, i.e. before the onset of haemorrhage-related hypothermia, acidosis and coagulopathy. This would allow sparing blood products transfusions and, hopefully, translate into a reduction of postoperative morbidity.

The association of patient survival with higher recipient age and D-MELD is not surprising. Profuse haemorrhage may more markedly affect survival of older patients or of those who

present a combination of advanced liver disease and older donor. The lower prognostic value exhibited by the BAR score in our matched sample is probably due to the analytical process we applied, selecting a very specific subset of the whole LT population.

Finally, the analysis of postoperative complications showed a comparable rate of grade ≥ 3 complications, primary allograft non-function, re-LT and EAD. The analysis of individual complications showed that the rate of SIRS, sepsis and reoperation was increased after packing. This was rather expected and probably reflects the complexity of patients treated by PHGP. However, it should be noted that the increased reoperation rate was not related to an increased incidence of abdominal bleeding or sepsis and that these complications did not negatively affect short-term survival. This was probably achieved thanks to careful patient management by the ICU team and close microbiological monitoring, allowing timely diagnosis and treatment of infections. Hepatic artery thrombosis was the only graft-related complication more frequently observed after PHGP. This could be explained either by the technical difficulties inherent to these challenging operations, or by a possible role of intra-abdominal hypertension determining graft compression. Unfortunately, intra-abdominal pressure was not routinely measured throughout our experience, so we could not assess the incidence of abdominal compartment syndrome after PHGP. Due to the possible role of abdominal compartment syndrome in favouring hepatic artery thrombosis, the need for close monitoring of intra-abdominal pressure and hepatic artery patency by Doppler ultrasound should be emphasized. However, in all four cases in which HAT was somehow attributable to PHGP, arterial continuity was successfully restored during the second-look operation and no graft was lost due to this complication in the short-term. In this regard, the possibility of a systematic check of hepatic vessels patency during the second-look operation adds further value to the PHGP surgical strategy.

Although it represents one of the largest and most comprehensive analyses of patients treated with PHGP during LT to date, our study has the limit of being retrospective and based on a single-centre experience. The analysis by propensity score matching also has limitations. A frequent problem is that matching may lead to a significant reduction in sample size; in our series, however, this problem was almost completely avoided as only four outliers in the packing group were excluded from analysis. Another limitation is the fact that propensity score analysis cannot account for confounding due to unmeasured variables, a problem which is tackled in randomized trials by effect of randomization itself. However, a prospective randomized trial on the use of PHGP in case of persistent haemorrhage during LT would be impractical and raise ethical concerns. It is also worth noting that the possibility that intraoperative events leading to need for packing were not completely recapitulated by the propensity score matching adds even more strength to our findings.

In conclusion, we reported a large consecutive series based on a decade-long experience with PHGP in the setting of LT. Peri-hepatic gauze packing was highly effective in achieving haemostasis, allowed the correction of hemodynamic parameters and coagulation disorders and was not linked *per se* to reduced 3-month patient and graft survival. Although associated with relevant morbidity, PHGP can be suggested as a valuable technique to be included in the armamentarium of the surgeon facing a situation of life-threatening persistent bleeding during a liver transplant operation.

Conflict of interest: none declared

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FIGURE LEGENDS

Figure 1. Kaplan-Meier curves showing 3-month patient and graft survival.

Panel A. Whole series. Patients treated with packing experienced significantly worse patient and graft survival compared to controls.

Panel B. Matched sample. After matching, no significant difference was observed in patient or graft survival.

PHGP: peri-hepatic gauze packing

Figure 2. Kaplan-Meier curves of patient and graft survival according to the indication for packing. No differences in patient or graft survival were found among groups.

Panel A. Patient survival.

Panel B. Graft survival.

PHGP: peri-hepatic gauze packing

TABLE 1. Baseline recipient, donor and transplant operation features in the whole series

	Packing (N = 107)	**No packing (N = 1,289)**	**p**
Sex (Male)	85 (79.4%)	997 (77.3%)	0.71
Recipient age	52.5 (9.1)	53.1 (9.3)	0.35
Main etiology of liver disease			
Hepatitis C virus	47 (43.9%)	514 (39.9%)	0.47
Hepatitis B virus	16 (14.9%)	311 (24.1%)	0.04
Cholestatic or autoimmune	7 (6.5%)	101 (7.8%)	0.76
Cryptogenic or NASH	8 (7.4%)	93 (7.2%)	0.92
Alcoholic	12 (11.2%)	170 (13.2%)	0.66
Fulminant hepatic failure	0	13 (1%)	0.29
Others	17 (15.9%)	87 (6.7%)	0.001
Hepatocellular carcinoma	27 (25.2%)	537 (41.7%)	0.001
Re-LT	27 (25.2%)	85 (6.6%)	<0.001
Portal vein thrombosis	13 (12.1%)	85 (6.6%)	0.031
TIPS	12 (11.2%)	126 (9.8%)	0.63
Previous upper abdominal surgery	60 (56.1%)	250 (19.4%)	<0.001
Type of graft			
Whole liver	101 (94.4%)	1,247 (96.7%)	0.15
Right split	6 (5.6%)	34 (2.6%)	
Left split	0	8 (0.6%)	
Recipient BMI	23.9 (±2.9)	24.8 (±3.2)	0.005
MELD	20.6 (±8.2)	17 (±7.4)	<0.001
D-MELD	1,158 (±578)	972 (±513)	<0.001
BAR	14.9 (±8.2)	11.2 (±8.3)	<0.001
BAR class			
0 – 9	35 (32.7%)	653 (49.9%)	0.004

10 – 18	22 (20.6%)	237 (18.4%)	
> 18	50 (46.7%)	408 (31.6%)	
DReAM	7.8 (±8.21)	4.5 (±7.4)	<0.001
DReAM class			
NA	4 (3.7%)	66 (5.1%)	0.036
≤ 15	86 (80.4%)	1,113 (86.3%)	
> 15	17 (15.9%)	110 (8.5%)	
Donor age	57 (±19)	58 (±17)	0.71
Donor BMI	25.6 (±4.5)	25.5 (±4.1)	0.74
Macrovesicular allograft steatosis			
< 15%	85 (79.4%)	1,084 (84.1%)	
15 – 30%	15 (14%)	126 (9.8%)	0.34
> 30%	3 (2.8%)	19 (1.5%)	
NA	4 (3.7%)	60 (4.6%)	
Total ischemia time (min)	506 (±126)	501 (±114)	0.79
Cold ischemia time (min)	480 (±127)	476 (±114)	0.81
Warm ischemia time (min)	26.3 (±10.3)	24.4 (±6.6)	0.15
PRBC transfusions (ml)	8,023 (±5081)	2,244 (±1991)	< 0.001
Plasma transfusions (ml)	8,937 (±4427)	3,329 (±2444)	< 0.001
End-procedure lactate (mmol/L)	3.8 (±2)	2.6 (±1.5)	< 0.001
End-procedure noradrenaline (γ/kg/min)	0.3 (±0.43)	0.2 (±0.2)	< 0.001

Data are expressed as frequency (percentage) or mean (± standard deviation). Abbreviations: NASH, non-alcoholic steato-hepatitis; LT, liver transplantation; TIPS, trans-jugular porto-systemic shunt; BMI, body mass index; MELD, model for end-stage liver disease score; D-MELD, donor age * MELD; BAR, balance of risk score; DReAM; donor-recipient allocation model score; NA, not available; PRBC, packed red blood cells

TABLE 2. Intra-operative variables in the 107 patients treated with peri-hepatic gauze packing

	Start	Packing	End procedure	Depacking	p*
pH	7.44 (7.42 – 7.46)	7.27 (7.25 – 7.28)	7.42 (7.2 – 7.58)	7.42 (7.41 – 7.44)	< 0.001
Temperature (°C)	35.3 (35.1 – 35.4)	34.8 (34.5 – 35)	36.7 (36.5 – 36.9)	36 (35.6 – 36)	< 0.001
Lactate (mmol/L)	1.3 (1.1 – 1.4)	4.9 (4.7 – 5.3)	3.3 (2.9 – 3.7)	0.95 (0.8 – 1.2)	< 0.001
INR	1.6 (1.5 – 1.7)	2.77 (2.5 – 3)	1.86 (1.75 – 1.9)	1.48 (1.42 – 1.53)	< 0.001
Platelets (x1,000/mL)	59 (52 – 57)	20 (17 – 22)	34 (32 – 40)	32 (28 – 35)	< 0.001
aPTT (sec)	44.7 (43 – 46.8)	98.1 (83.9 – 112.4)	57.9 (52.8 – 64.9)	37.2 (36.2 – 38)	< 0.001
Fibrinogen (mg/dL)	214 (185 – 241)	94 (85 – 101)	147 (139 – 153)	284 (269 – 307)	< 0.001
Hemoglobin (g/dL)	10 (9.6 – 10.3)	6.3 (5.9 – 6.4)	8.3 (8.1 – 8.7)	8.7 (8.4 – 9)	< 0.001

Data are expressed as median (95% Confidence interval). *Mann-Whitney non-parametric test between packing and depacking variables. Abbreviations: INR, international normalized ratio; aPTT, activated partial thromboplastin time

TABLE 3. Baseline recipient, donor and transplant operation features in the study sample selected by propensity score matching

	Packing (N = 103)	**No packing (N = 103)**	**p**
Sex (Male)	82 (79.6%)	80 (77.7%)	0.86
Recipient age (years)	52.6 (± 9.2)	53.6 (± 8.6)	0.44
Re-LT	27 (26.2%)	19 (18.4%)	0.24
Re-LT timing (months)	31.5 (± 47.6)	20.7 (± 25.6)	0.38
Early Re-LT (<1 month)	4 (14.8%)	6 (31.6%)	0.27
Previous abdominal surgery	58 (56.3%)	53 (51.4%)	0.57
PRBC transfusion > 80th percentile	87 (84.5%)	87 (84.5%)	1
MELD	20.9 (± 8.2)	19.1 (± 7.3)	0.09
D-MELD	1,169 (± 583)	1,070 (± 524)	0.2
BAR	15.2 (± 8.1)	13.9 (± 8.3)	0.27
DReAM	7.76 (± 8.21)	8.31 (± 8.03)	0.62
Portal vein thrombosis	12 (11.6%)	8 (7.8%)	0.48

Data are expressed as frequency (percentage) or mean (± standard deviation). Abbreviations: LT, liver transplantation; PRBC, packed red blood cells; MELD, model for end-stage liver disease score; D-MELD, donor age * recipient MELD; BAR, balance of risk score; DReAM, donor-recipient allocation model score.

TABLE 4. Postoperative complications in the study sample selected by propensity score matching

	Packing	**No packing**	p
	(N = 103)	**(N = 103)**	
Dindo-Clavien grade			0.10*
1-2	43 (41.7%)	55 (53.4%)	
3a	2 (1.9%)	5 (4.8%)	
3b	14 (13.6%)	9 (8.7%)	
4a	10 (9.7%)	10 (9.7%)	
4b	3 (2.9%)	1 (0.9%)	
5	12 (11.6%)	4 (3.9%)	
Primary non-function	3 (2.9%)	3 (2.9%)	1
Early allograft dysfunction	65 (63.1%)	53 (51.5%)	0.12
Re-LT within 90 days	6 (5.8%)	4 (3.9%)	0.74
Reoperation**	30 (29.1%)	16 (15.5%)	0.03
Reoperation < 48 h	4 (3.9%)	0	0.12
Reoperation for bleeding	4 (3.9%)	3 (2.9%)	1
Reoperation for abdominal sepsis	16 (15.5%)	10 (9.7%)	0.51
Reoperation for other indication	13 (12.6%)	3 (2.9%)	0.016
Renal failure	28 (27.2%)	19 (18.5%)	0.18
Dialysis	11 (10.6%)	8 (7.7%)	0.63
Hepatic artery thrombosis	8 (7.8%)	1 (1%)	0.04
Portal vein thrombosis	1 (0.9%)	1 (0.9%)	1
Hemorrhage	11 (10.7%)	6 (5.8%)	0.31

Biliary leak	6 (5.8%)	5 (4.8%)	1
Abdominal abscess	16(15.5%)	8 (7.8%)	0.12
Pneumonia	30 (29.1%)	19 (18.4%)	0.1
SIRS	34 (33%)	19 (18.5%)	0.02
Sepsis	23 (22.3%)	11 (10.7%)	0.02
Acute cellular rejection	17 (16.5%)	17 (16.5%)	1

Data are expressed as frequency (percentage). *Chi-square test for grade ≥ 3 complications; **Programmed relaparotomies in packing patients excluded. Abbreviations: LT, liver transplantation; SIRS, systemic inflammatory response syndrome.