

Temporary abdominal closure and delayed biliary reconstruction due to massive bleeding in patients undergoing liver transplantation: an old trick in a new indication

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Abstract

Background Massive bleeding during liver transplantation (LT) is difficult to manage surgical event. Perihepatic packing (PP) and temporary abdominal closure (TAC) with delayed biliary reconstruction (DBR) can be applied in these circumstances. **Method** A prospective database of LT in a major transplant center was analyzed to identify patients with massive uncontrollable bleeding during LT that was resolved by PP, TAC, and DBR. **Results** From January 2009 to July 2013, 20 (3.6%) of 547 patients who underwent LT underwent DBR. Mean

intraoperative blood loss was 20,500 ml at the first operation. The DBR was performed with a mean of 55.2 h (16–110) after LT. Biliary reconstruction included duct-to-duct ($n = 9$) and hepatico-jejunostomy ($n = 11$). Complications occurred in eight patients and included portal vein thrombosis, cholangitis, severe bacteremia, pneumonia. There was one in-hospital death. In the follow-up of 18 to 33 months we have seen one patient died 9 months after transplantation. The remaining 18 patients are alive and well.

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Conclusions In case of massive uncontrollable bleeding and bowel edema during LT, the combined procedures of PP, TAC, and DBR offer an alternatively surgical option to solve the tough situation.

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Keywords Abdominal wound closure techniques · Biliary tract surgical procedures · Liver transplantations · Surgical hemorrhage

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Introduction

Temporary abdominal closure (TAC) has been created as a surgical option for some of the most challenging situations in surgery. It can be used for difficult to close abdominal wound or for intraabdominal conditions that require re-exploration. A typical indication for TAC is a severely traumatized patient who, after initial surgical maneuvers requires a more definitive procedure after some time. Other indications for TAC include: severe peritonitis, abdominal wall edema, deep wound dehiscence, abdominal compartment syndrome and temporary tamponade of bleeding [1, 2].

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Massive hemorrhage during liver transplantation (LT) is a rare and difficult to manage event. The causes of bleeding can

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be surgical and medical [3]. Surgical bleeding results from the extensive collaterals that form in patients with portal hypertension or by well vascularized adhesions. Medical causes of bleeding include impaired clearance of fibrinolytic enzymes released from damaged cells and tissue thromboplasmin compounds inducing coagulopathy [3, 4]. When medical measures do not correct the bleeding, consumption coagulopathy and secondary fibrinolysis should be suspected [3].

The prolonged surgery and hemorrhagic insult cause an important bowel edema that further complicate situation [3].

Management of the open abdomen is associated with high morbidity and mortality [5, 6]. The concepts related to TAC have evolved significantly over the last 40 years but there is still no universally accepted method. The application of TAC in a LT patient with massive bleeding, although believed by some authors to be a thing of the past [7] can allow to stabilize a patient and perform a delayed biliary reconstruction (DBR) in a safe environment.

In this paper we present our experience with TAC and DBR for LT patients with massive intraoperative bleeding and bowel edema.

Methods

We have reviewed our prospective database of LT and identified all patients in whom a TAC and DBR have been performed during 57 months (from 1 January 2009 to 1 August 2013). All preoperative, intraoperative and postoperative data were analyzed. All patients alive at the time of manuscript preparation were called for a follow-up visit assuring at least 18 months follow-up time for the study group.

Eligibility criteria for temporary abdominal closure and staged biliary reconstruction

The decision to perform perihepatic packing (PP), TAC and DBR was taken by operating surgeon facing uncontrollable bleeding from the raw liver surface resistant to several haemostatic maneuvers. The bleeding typically occurs during the recipient's hepatectomy phase. If it progresses to medical bleeding during the anhepatic phase temporary packing and temporary porto-caval shunt can be installed. However, if after reperfusion the bleeding continued despite aggressive resuscitation and all available hemostatic strategies, the PP and DBR were decided in order to allow for stabilization of the patient and correction of coagulopathy that would allow for a safe biliary reconstruction. The time between the implantation of the graft and the decision to perform PP and DBR differed between surgeons. The decision to perform PP and DBR was taken by the operating surgeon once he felt that his maneuvers aimed at achieving homeostasis were futile.

Surgical technique

The technique was applied in patients with the graft in situ, after completion of all vascular anastomoses. Both sides of the common duct were left open. PP was achieved with surgical pads introduced around the liver to induce compression. The introduction of the pads has been very gentle and slow in order not to damage recently performed vascular anastomosis of the inflow and outflow vessels, prevent its kinking and prevent interposition of the vessels of the anterior segment of the graft. An absorbable haemostat (SURGICEL, Johnson & Johnson, Neuchatel, Switzerland) was applied between the pads and hepatic surface to prevent adhesions and to allow a relatively easy unpacking. An area without pads was left on the hepatic surface to create a "sonographic window" for postoperative ultrasound surveillance (Fig. 1). One Jackson-Pratt (JP) drain (connected to vacuum ball only) was inserted into the subhepatic space for bile drainage. The bile duct was usually left without cannulation and without tie in order not to compromise the viability of the stump.

The fascia was left open with the vacuum pack technique to prevent abdominal compartment syndrome. A 3-L normal saline bag was cut open to cover the viscera surface with the edges tugged under the abdominal fascia. The saline bag was sutured to the fascial edge topped with two gauze pads and two JP drains. Afterwards a piece of 3M Ioban antimicrobial incise drape was used to cover the wound including gauze and JP drains, which were connected to constant negative pressure (connected to low pressure suction system) to dry wound (Fig. 1).

Once the PP and TAC were performed, the transfusion and resuscitation protocols were installed in the Intensive Care

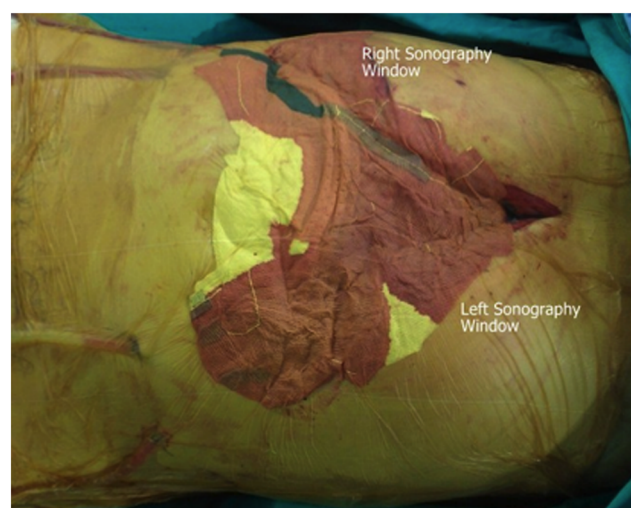


Fig. 1 Window for performing Doppler ultrasonography and vacuum pack technique with constantly negative pressure through drain tubes

Unit. The second-look operation was performed after the fulfillment of hemodynamic criteria: mean arterial pressure (MAP) >65 mmHg, urine output >0.5 ml/kg per h, portal vein flow >10 cm/s, <250 ml/100 g liver tissue; hepatic artery (HA) flow >35 cm/s RI >0.65, and perfusion criteria: SVO₂ >70%, lactate >10% clearance. The second-look operation had to be performed within the timeframe of 48 h to avoid infectious complications.

Emergent second look was decided when there was ongoing bleeding despite optimal resuscitation and blood products, and unstable vital signs in spite of maximum medical intensive care.

The criteria for performing a DBR during the second-look operation were no active oozing and stable hemodynamics. If the bile duct in the recipient was found to be ischemic then a hepatico-jejunostomy by Roux-en-Y reconstruction was performed; otherwise a duct-to-duct anastomosis was preferred. In all patients the definitive biliary reconstruction has been performed by an experienced microsurgeon using operative microscope. In four patients during the second-look operation the operative field was judged as unacceptable thus requiring re-packing and re-TAC.

The anesthetic management of patients was objective-directed. Colloid and crystalloid solutions were used to maintain the intravascular volume with low infusion volume (1 ml/kg per h) during the hepatectomy phase, later augmenting it gradually in the anhepatic and reperfusion phase. Dopamine 2 µg/kg per min was given continuously throughout the operation for renal sparing and hemodynamic effect. Metabolic acidosis was corrected with 7% sodium bicarbonate when the base excess was greater than -5 mEq/L and 5% calcium chloride was administered to treat ionized hypocalcaemia when serum calcium was lower than 0.8 mmol/L. Dextrose infusion was used to maintain a glucose level of 180–200 mg/dL. When intense bleeding was seen during the hepatectomy phase, and hypotension ensued MAP <65 mmHg the resuscitation protocol was implemented which consisted of crystalloid fluids (lactate Ringer) and packed red blood cells (PRBCs), leukocyte-poor PRBCs (LPR), leukocyte-poor plasma (LPP) and cryoprecipitates that were transfused to maintain stable hemodynamics with the aid of norepinephrine.

Postoperative management

All patients received immunosuppressants that include tacrolimus, low-dose steroid, and mycophenolate mofetil as standard immunosuppressant regimen. As for prophylaxis for postoperation bacterial and *Candida* infections, combination of either cefepime or ceftazidime (20 mg/kg per 8 h) and teicoplanin (400 mg/day) was started immediately before

operation and lasted for 3–5 days depending upon post-transplant conditions, and fluconazole 100 mg/day was started after transplantation and was used during post-operation stay at ICU. Daily trimethoprim 80 mg/sulfamethoxazole 400 mg was started after operation and was used indefinitely as prophylaxis for *Pneumocystis jiroveci*. Ganciclovir (5 mg/kg per 12 h) was used when cytomegalovirus infection was clinically suspected or upon detection of CMV antigenemia [8].

Results

During the study period there were 547 LT performed at the Kaohsiung Chang-Gung Memorial Hospital. In 20 patients (3.6%) a PP, TAC, and DBR was deemed necessary.

The baseline characteristic of the study group is shown in Table 1. There were seven patients with Child–Pugh score A, four with B and nine with C. Mean Model of End-Stage Liver Disease (MELD) score was of 15 points (6–35). Mean ascitic fluid volume was 2,700 ml (0–13,150). Mean preoperative Hb was 11.1 (6.8–14.8) g/dl. Mean preoperative platelet count was 106 (12–271) × 10³ µL and mean preoperative international normalized ratio (INR) was 1.29 (1–1.81). Four patients had a history of previous hepatic resection and one had been previously transplanted.

Mean blood loss during primary surgery in the presented group was as high as 20.5 L (1.8–86). The details on the amount and type of blood derived products transfused in the perioperative period are presented in Table 2. One recipient with planned choledocho-jejunostomy had estimated 1,800 ml blood loss. The biliary reconstruction was delayed due to edematous bowel which made primary anastomosis impossible.

The type of biliary reconstruction was duct-to-duct anastomosis in nine patients and a hepatico-jejunostomy by Roux-en-Y reconstruction in 11 patients.

The DBR was performed after a mean of 55.2 h (16–110) after LT. The mean duration of the delayed surgery was 285 min. The mean blood loss during second surgery was 491 ml. Severe complications after second-look laparotomy and DBR occurred in eight patients (40%) and included portal vein thrombosis, cholangitis, severe bacteremia, pneumonia, and intraabdominal infection. One patient died in the postoperative period. We have not seen clinically sound biliary strictures or bile leaks. Only one case of cholangitis was successfully treated with antibiotics. Nineteen patients in the presented group were discharged home and remained in the follow-up for at least 18 months. There was one death recorded 9 months after surgery due to sepsis arising from intraabdominal abscess.

Table 1 Preoperative characteristic of patients

Patient no.	Age	Sex	Diagnosis	MELD score	Child-Pugh score	Hgl gm/dl	INR	Ascites (ml)
1.	53	M	HBV CIR	17	B	9.9	1.02	11,800
2.	61	M	HCV HCC	7	A	14.5	1.02	100
3.	56	M	HBV HCC	7	A	13.8	1.13	50
4.	57	F	HCC CIR ALC	27	C	6.8	1.62	1,275
5.	51	M	HBV ALC CIR	6	B	8.2	1.33	4,560
6.	48	M	HCC HCV	7	A	13.0	1.02	1,600
7.	59	M	HCV HCC	21	C	12.2	1.32	50
8.	48	F	HCV ALC CIR	19	C	7.8	1.64	50
9.	65	M	HBV	19	C	10.3	1.39	4,650
10.	59	F	HBV	26	C	11.4	1.68	5,500
11.	62	F	Polycystic liver disease	7	B	12.5	1.02	500
12.	50	F	HCV	23	C	9.4	1.44	2,900
13.	54	M	HCV	22	A	13.8	1.25	700
14.	54	M	ALC	7	C	9.0	1.23	13,150
15.	35	F	HCC	7	A	14.8	1.02	0
16.	59	M	HBV	25	C	8.6	1.81	5,700
17.	61	F	Intrahepatic stone	10	B	13.0	1.01	300
18.	50	M	Intrahepatic stone	13	A	10.2	1.61	0
19.	63	M	Recurrent cholangitis	14	A	10.0	1.20	200
20.	62	F	HBV	35	C	13.2	1.42	100

ALC alcoholic cirrhosis, CIR cirrhosis, HBV hepatitis B virus infection, HCC hepatocellular cancer, HCV hepatitis C virus infection, INR international normalized ratio, MELD Model of End-Stage Liver Disease

Table 2 Perioperative blood loss and blood derived products transfusion

Patient no.	Perioperative blood loss (ml)	LPR (units)	PRBC (units)	FFP units/ml	PLT units/ml
1.	25,000	106	0	40	60
2.	9,000	28	6	24	24
3.	18,600	58	0	18	24
4.	5,000	24	0	24	36
5.	1,800	14	0	12	0
6.	11,800	34	16	20	24
7.	9,250	46	24	20	36
8.	15,300	44	0	16	24
9.	16,300	52	14	26	12
10.	43,900	236	12	78	60
11.	37,000	106	6	60	60
12.	12,450	42	0	36	36
13.	20,000	72	12	24	24
14.	8,600	12	0	12	0
15.	40,750	62	68	36	36
16.	19,600	72	0	58	60
17.	6,600	38	0	20	24
18.	86,600	226	12	50	72
19.	8,000	42	12	24	12
20.	8,800	30	20	24	48

FFP fresh frozen plasma, LPR leukocyte poor red blood cells, PLT platelet, PRBC packed red blood cells

Discussion

The techniques of TAC were developed in the second part of the twentieth century to treat some of the most complicated and dreadful situations in surgery. In the beginning, the idea consisted basically of simple packing of the abdominal cavity. The first report in 1979 by Steinberg consisted of packing the abdominal cavity with sterile surgical towels [9]. The reoperation could be performed quickly and access to the abdomen was very easy – just removing the towels. To limit the risk of infection some form of closure has been added to the packing. At first it was either just skin closure [10] or zipper closure allowing for several re-operations [11]. A major advance in the temporary closure of the abdomen designed to treat severely traumatized patients was a “Bogota bag” technique used by Columbian surgeons [2]. It is simple, cheap and effectively protects the viscera. The modification of this technique with the use of suction drains [12] has been used in our study. More recently, two more sophisticated and expensive techniques have been proposed: the Wittman patch [13] and VAC techniques [14].

The safety and effectiveness of every innovative technique in TAC is constantly challenged [15]. In a review of 106 publications spanning a period of 35 years and reporting the results of 4,000 patients the authors concluded that in the absence of sepsis, Wittmann patch and VAC offered the best outcome, while in the presence of septic conditions VAC offered the highest closure and the lowest mortality rates [1]. The outcomes in different techniques are shown in Table S1. The technique used in our center can be considered a bridge between the “Bogota bag” and VAC technique.

The problem of abdominal closure is relatively frequent after pediatric liver transplantation [16] and after intestinal and multivisceral transplantation [17]. However, the difficulty encountered in these situations is a definitive closure of abdominal wall due to deficit in abdominal wall tissue. We could not find in the literature a description of the delayed abdominal closure used as a bridge to perform a safe biliary reconstruction after stabilizing an abundantly bleeding transplant patient as in our study.

Regardless of the indication for the TAC the management of these patients is complex and differs significantly depending on the indications.

In patients with an open abdomen the major cause of mortality is a multi-system organ failure [18]. The pooled mortality is estimated for 26% [5]. This may be due to the primary insult or to secondary complications [14]. The formation of intestinal fistula has been until recently believed to be linked to the use of meshes but the data from systematic reviews [1, 5] suggest that fistulas occur independently of the applied technique. In one series it was shown that mortality doubled

when a fistula had developed [19]. Also the use of VAC was suggested to cause fistulation [20]. However, in more than half of the more recently published series the negative pressure is used [1]. Once again, data from systematic reviews indicate that it is the patient condition rather than a particular technique that is responsible for fistula formation. Our data support this statement as in our series we have not seen an intestinal fistula formation and all the complications were related rather to the underlying disease.

The experience of our team in the field of LT can be considered fair. By the year 2013 we have performed over 1,000 liver transplants [21]. But even with this kind of technical proficiency we still encounter difficult cases that are salvaged by TAC, PP and DBR.

The criteria we have adopted to perform a TAC and DBR are subjective. It was the surgeon who decided whether to consider the bleeding uncontrollable by traditional measures and not any laboratory nor clinical finding. One of the objective measures that theoretically could help such a decision is thromboelastography [22]. It has been shown to reduce the blood transfusion requirements [22] but is still used by only 33% of the US centers [23], and the benefit of its usage is under debate as it has not been proved to decrease blood loss or impact survival [24, 25].

The bleeding predisposes the release of fibrinolytic enzymes including tissue type plasminogen activator that induces coagulopathy that may quickly shift the balance to an overall fibrinolytic state [3, 26]. The continuous surgical insult in a hemodynamically unstable patient produces an acidic medium, which also contributes to perpetuate the coagulopathy [27]. After the reperfusion phase a flush of free radicals is circulating and with a stunned implanted liver regaining its function, it may take some time to rebalance the coagulation abnormalities.

Studies show conflicting results on the risk factors for bleeding during LT. Some authors suggest that MELD score, preoperative Hb <10, INR >1.6, and previous surgery influence transfusion requirements but other researchers fail to find such associations [7, 28, 29]. The presented group had surprisingly good preoperative levels of Hb and INR and a low MELD score. Based on the available data, it was impossible for us to determine any triggering factor for a massive bleed that occurred during LT. At the same time it has to be underlined that this group of patients has been selected from a series of 547 LT patients based on our inability to achieve hemostasis using conventional techniques. The definition of a massive bleeding in liver transplantation ranges from 6 to 10 units of RBC in 24 h to the exchange of one blood volume with RBC [30, 31]. All of the patients in the presented group fulfilled all of these criteria although it is a reflection of the experience of our team rather than of using any definition of massive bleeding. Finally, in these severely bleeding patients

the transfusion ratio of RBC to fresh frozen plasma was 1:1 to 4:1. In the trauma setting the ideal rate is 1:1; in transplant recipients this value has not been validated and its use is not related to the amount of bleeding and depends on individual transfusion practices and there is always concern about thrombotic complications [32, 33].

Management of patients undergoing temporary closure is usually left to the discretion of the operating surgeon or ICU team and is not following an agreed protocol. This finding is understandable given the relative rarity of TAC. The indication for the open abdomen technique is sometimes not clear. The authors of the majority of series does not describe whether it was part of a damage control strategy or was decided because of the inability to close the abdomen. TAC systems are subject to a number of technical variations, which in turn makes retrospective analysis complicated [1]. In our study, the PP proved to be useful to control the bleeding until the coagulopathy was corrected. The days spent in the ICU increased the number of bacterial abdominal infections but were readily treated with antibiotic treatment. This highlights the importance of proactive surveillance of these patients.

The rationale for DBR is based on the propensity of biliary tract to ischemic damage [34]. However, blood loss during LT is not always identified as a risk factor for biliary stricture [35]. In case of duct-to-duct anastomosis the recipient bile duct may be ischemic due to the unstable condition of the patient and anastomosis in this situation carries a greater risk of complications [34]. In duct-to-mucosa anastomosis besides the ischemic insult, the bowel is edematous due to the resuscitation fluids making this anastomosis unsafe. Since our group of patients had significant bowel edema it may be speculated that these anastomoses, if performed without delay, would be prone to failure. The newly implanted graft is stressed by the new metabolic demand so additional hemorrhage may force graft dysfunction. This is why it is sound to stop the operative insults and continue to correct the hemodynamic and metabolic disturbances in the ICU. As stated before, another indication for DBR could be severely edematous bowel. Delaying the reconstruction can not only lead to a more secure anastomosis but probably is able to diminished some bile related vascular complications, as one of our patients required changing from a duct to duct to a Roux-en-Y reconstruction because of bile duct stump necrosis recognized during second-look operation.

We have seen only one (5%) in-hospital death. One patient died 9 months after surgery. Given the often dramatic surgical situation that leads to the decision to perform a TAC, the overall survival in this small group of patients can be considered fair.

Conclusion

PP, TAC, and DBR are viable options for massive uncontrollable bleeding, secondary coagulopathy and important bowel edema during LT.

Conflict of interest None declared.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Table S1 Results of the selected methods of abdominal packing (based on Quyn et al. [1]).