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The use of a NHS-PEG coated, collagen-based sealant in a patient undergoing Associating Liver Partition and Portal vein Ligation for Staged hepatectomy (ALPPS)

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ABSTRACT

INTRODUCTION: ALPPS (Associating Liver Partition and Portal vein Ligation for Staged hepatectomy) is a new two-stage hepatectomy for patients in whom conventional treatment is not feasible due to insufficient future liver remnant (FLR). During stage one of ALPPS, accelerated growth of the FLR is induced by ligation of the portal vein and *in situ* split of the liver, which prevents interlobar collateral portal circulation and attributes to the accelerated hypertrophy response. This can present a risk for postoperative haemorrhage. Furthermore, adhesion of the adjacent resection surfaces might complicate the second stage of the procedure. Hemopatch® is a flexible, NHS-PEG coated, absorbable collagen-based sealant that provides haemostasis. This paper illustrates the use of Hemopatch during ALPPS for hemostasis and prevention of adhesions between the cut-surfaces of the liver.
PRESENTATION OF CASE: An 81-year-old patient requiring right hemihepatectomy for synchronous liver metastases underwent ALPPS. During stage one, Hemopatch was applied according to the manufacturer's instructions to the hepatic resection surfaces. Stage-2 was performed uneventfully, with no adhesions observed in the resection plane 18 days after the first stage. The patient was discharged without any major complications.
DISCUSSION: Hemopatch is a useful tool in prevention of postoperative haemorrhage in patients undergoing ALPPS procedure as well as in the prevention of adhesions between the cut-surfaces after transection. This facilitates stage-2 of the procedure which potentially improves postoperative outcomes.
CONCLUSION: Topic haemostatic agents to cover the transection surface during stage one of ALPPS could help to prevent adverse interstage events.

1. Introduction

The limitations of liver surgery critically depend on the amount of functioning remnant liver, which is one of the causes that only a minority of patients with hepatobiliary malignancies qualify for liver surgery. In 2012 an adaptation of the conventional two-stage hepatectomy was described, in which the portal vein trunc to the tumour-bearing segments is ligated and the liver parenchyma is split *in situ* during the first stage. This combination induces more rapid and extensive liver growth compared to traditional techniques, and allows completion of the resection in the second stage after only 7–14 days (Fig. 1) [1,2]. Associating liver partition and portal vein ligation for stages hepatectomy (ALPPS) renders more patients resectable and can be used as a salvage procedure when portal vein embolization has not resulted in sufficient hypertrophy of the future liver remnant (FLR) [3].

Since the introduction of ALPPS there is an ongoing discussion regarding its safety [4], mainly due to the morbidity (i.e, Clavien-Dindo grade ≥IIIb) and 90-day mortality rates initially reported as high as 59% and 29% respectively [5]. A major predictor of adverse events after stage two of ALPPS is morbidity occurring between the two stages [6], which is why several centers have minimized the first stage, for instance by using partial parenchymal transection [7]. One of the issues in ALPPS is the formation of adhesions between the cut-surfaces of the liver after the in-situ split. As described in the first report on ALPPS [1] a plastic bag can be applied around the FRL in order to prevent adhesions. However, the bag predisposes to the formation of fluid collections and subsequent infection. Furthermore, the plastic bag can become troublesome if stage-2 cannot be performed. The use of plastic bags has therefore been abandoned in most centers. Few reports however, have

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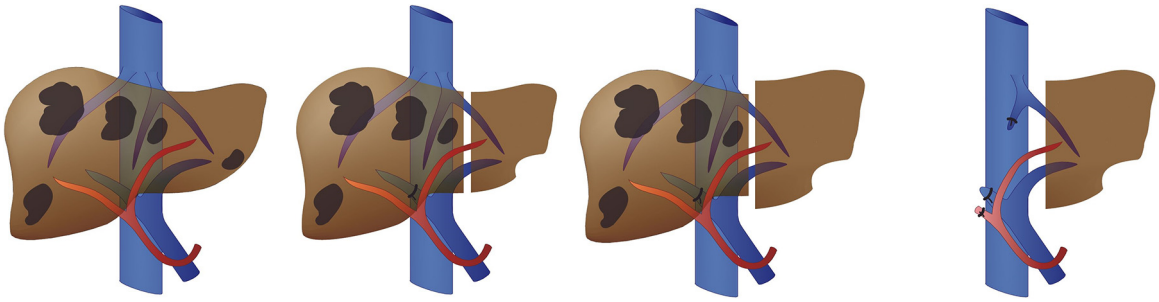

Fig. 1. Schematic overview of ALPPS procedure: (a) baseline liver with colorectal liver metastases in both hemi-livers, (b) ligation of right portal vein, *in situ* transection of the liver and excision of the metastases in the future remnant liver (FRL), (c) hypertrophy response of the FRL following liver partition, (d) remnant liver after the second stage of the procedure in which the deportalized liver is removed. Figure by Darryll Atema.

focused on alternative strategies to isolate the two resection planes to prevent formation of adhesions. Effective therapies in this regard could reduce interstage morbidity and thereby the outcomes of ALPPS altogether [8].

Hemopatch is a flexible, NHS-PEG coated, absorbable collagen-based sealant that attaches to tissue owing to the pentaerythirol polyethylene glycol ether tetra-succinimidyl gyltarate (NHS-PEG) layer, thereby providing haemostatic properties. The indication for its use during surgical procedures is control of bleeding when pressure, ligature or conventional procedures are ineffective or impractical. We herein report the use of Hemopatch in a patient who underwent ALPPS procedure in accordance with the SCARE criteria [9].

2. Material and methods

2.1. Patient

An 81-year-old female patient was referred to our surgical outpatient clinic with synchronous colorectal liver metastases (CRLM). Colonoscopy examination revealed a distal rectal tumour 7 cm ab ano. Biopsy confirmed well-differentiated adenocarcinoma. At staging (Contast enhanced computer tomography and magnetic resonance imaging), two liver metastasis in segments 7 and 8 were identified which led to radiological tumor staging of cT3cN2M1 (Fig. 2).

At the multidisciplinary team meeting it was decided to treat the patient with curative intent using neoadjuvant radiotherapy

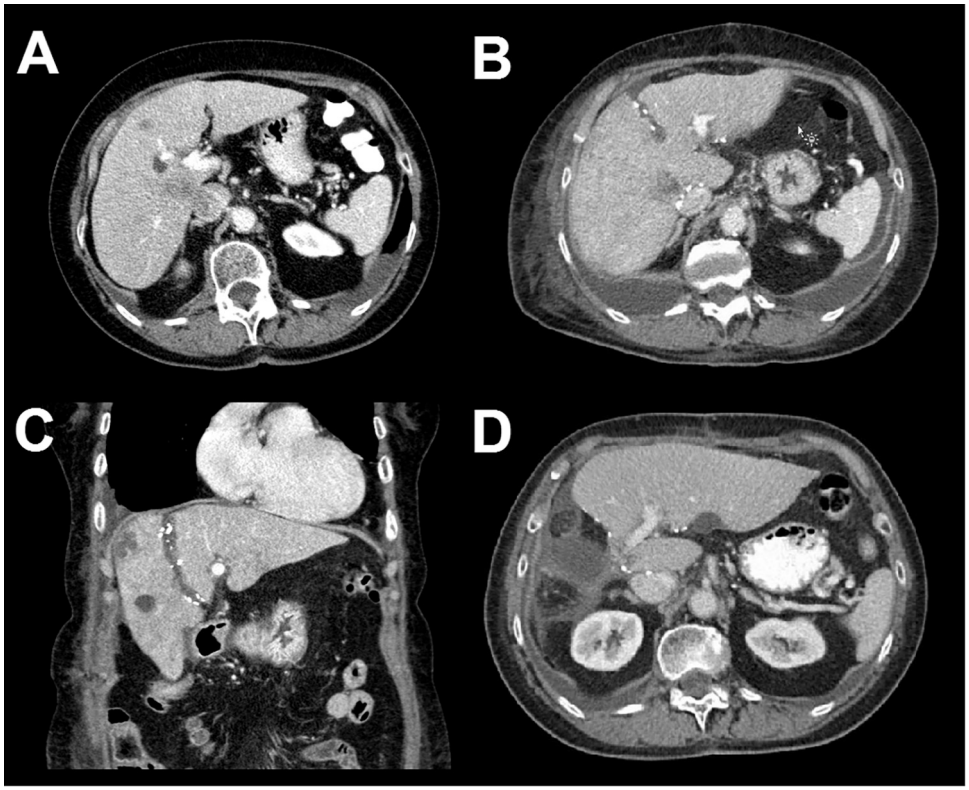

Fig. 2. (A) Preoperative CT image with metastasiin segments 7 and 8. Intra-operative ultrasound however, identified two additional metastases in segments 8 and 3 necessitating extension of the planned resection. (B) Transverse CT −image after the first stage of ALPPS procedure showing the *in situ* partial transection of the liver according to the planned, extended right hemihepatectomy. The right portal vein has been ligated while the right hepatic artery and right hepatic vein are preserved together with the right bile ducts. (C) Coronal, reconstructed CT image after the first stage of ALPPS demonstrating the split liver. The deportalized right liver lobe shows atrophy while the FRL has markedly hypertrophied. (D) CT image at follow-up after stage-2 demonstrating the completed right hemihepatectomy with the hypertrophied remnant liver.

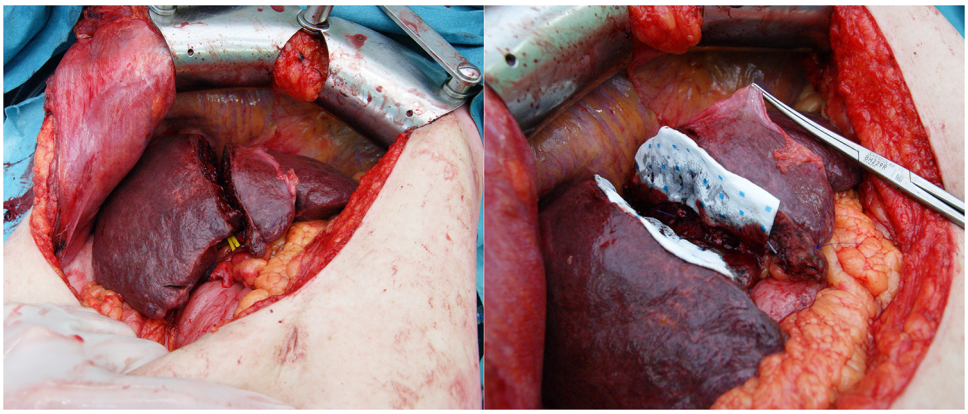

Fig. 3. Operative images during stage-1 of the ALPPS procedure. The left panel shows the *in situ* split of the liver. The right panel illustrates the application of Hemopatch on both the transection surfaces in order to provide haemostasis and prevent adhesions between the two liver lobes.

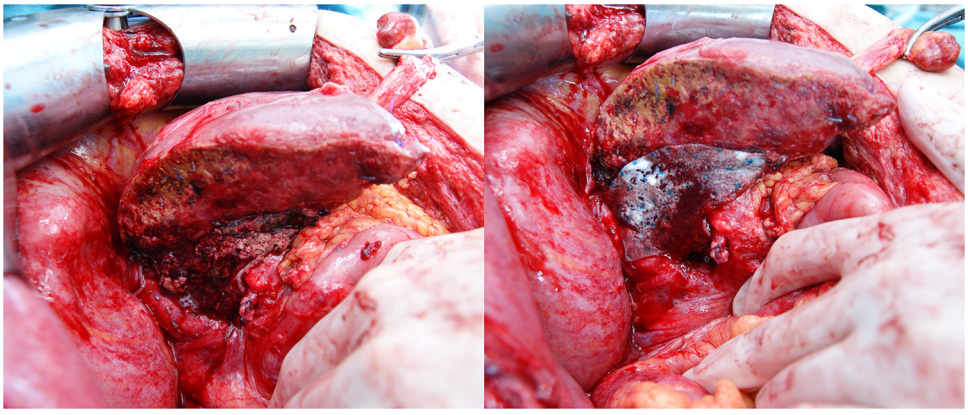

Fig. 4. Operative images during stage-2 of the ALPPS procedure. In the left panel the right hemi-liver has been removed. The image illustrates the partially absorbed Hemopatch applied at the first stage and the new, posterior parenchymal transection surface at completion of transection. The right panel shows the application of Hemopatch on the fresh surface of the last part of the transection.

for the rectal tumour (5 × 5 Gy) and upfront resection of the liver metastases after which an abdominoperineal resection would be planned. Neoadjuvant chemotherapy was not advised because of the patient's age, performance, and co-morbidity. The patient was scheduled for an open resection of liver segments 7 and 8, however, the intra-operative ultrasound identified two additional metastases in segments 8 and 3, respectively. The required right hemihepatectomy with excision of the metastasis in segment 3 was deemed unfeasible due to insufficient volume and function of the FRL. Therefore, it was decided during the operation to switch to an ALPPS procedure in this patient. The first stage of the ALPPS procedure was performed with metastasectomy of segment 3, ligation of the right portal vein and partial transection of the liver between segments 2, 3 and 4. To secure haemostasis and at the same time prevent adhesions between the liver transection surfaces, Hemopatch was applied to both cut-surfaces after completion of the in-situ split (Fig. 3). Using this technique, blood loss at stage-1 was estimated at 250 cc.

Postoperative functional assessment of the FRL was performed using ^{99m}Tc-mebrofinin hepatobiliary scintigraphy. Three days after stage-1, FRL function was 1.6%/min/m^2 which was considered insufficient to proceed to stage two [10]. At day 10, the function had increased to 2.1%/min/m^2 and at day 17, it further increased to 2.5%/min/m^2 which was considered enough for safe resection, allowing stage-2 to take place. Eighteen days after stage one, the patient underwent the second procedure. There were no adhesions across the plane of transection while remarkably, the pieces of Hemopatch had been partially absorbed on both planes of the transected parenchyma. Right hemihepatectomy was completed with ligation of the right hepatic artery and closure of the right hepatic venous junction. After transection of the last part of the parenchyma posterior to the liver hilum, a new piece of Hemopatch was applied to the new resection plane on the side of the liver remnant. The procedure was uncomplicated with 800 cc blood loss (Fig. 4).

The postoperative course was uneventful. The patient was discharged 10 days after stage-2. The total hospital stay was 29 days. Pathologic examination confirmed the metastases while the resection margins were negative. The patient is currently scheduled for rectal resection.

3. Discussion

The more rapid hypertrophy observed after ALPPS has redefined resectability of hepatic malignancies and sparked both experimental and clinical research into the mechanisms of the accelerated, interstage liver hypertrophy. ALPPS allows surgical resection of extensive disease, however the technique is burdened by the reported rates of adverse perioperative outcomes. Especially morbidity after stage-1 is predictive of severe morbidity and mortality after stage-2. Preventing the formation of adhesions between the liver transection surfaces could be key to decrease the incidence of complications since these adhesions could hamper the second stage and increase operative time and haemorrhage.

Although the outcomes of ALPPS have improved in experienced centers [11], the overall morbidity and mortality rates after ALPPS

are still high when compared to liver resection after preoperative portal vein embolization or in the setting of a conventional two-stage liver resection [12]. The technically demanding first stage and early second stage are debit to the high mortality. Furthermore, blood loss is associated with unfavourable postoperative outcomes and therefore, reduction of haemorrhage is advantageous for the patient and should be the goal of performing a safe liver resection.

In the current report, we describe the application of Hemopatch on the transection surfaces during the first stage of ALPPS. Hemopatch was applied to provide haemostasis as well as prevent the formation of adhesions between the adjacent cut-surfaces. The second stage was uncomplicated in this patient 18 days after stage-1, with no apparent adhesions found in the plane of transection and nearly complete absorbtion of the pieces of Hemopatch applied at stage-1. In our center, insufficient experience exists in order to establish the impact of using haemostatic agents on outcomes in ALPPS patients, this data is probably unavailable wordwide. Nonetheless, the application of haemostatic agents does subjectively facilitate stage two of ALPPS for the operating surgeon which could positively affect outcomes for both patient and surgeon.

Based on this experience, Hemopatch application on the transection surfaces during the first stage of the ALPPS procedure seems superior to the use of plastic bags or other described techniques [1,13,14]. Hemopatch is superior to a plastic bag since it provides haemostasis as well as prevents the formation of adhesions, whereas additional devices might be required for haemostasis when using a plastic bag. Furthermore, plastic bags are prone to fluid accumulation and infection and cannot be left in situ if stage-2 cannot be carried out. Application of an absorbable sealant such as Hemopatch during ALPPS, therefore helps to prevent adverse outcomes of ALPPS.

Conflicts of interest

None.

Sources of funding

None.

Ethical approval

The need for ethical approval exempted for case-reports by the medical ethical committee.

Consent

Informed consent present.

Author contribution

All authors designed the study collected data and interpreted data. Olthof wrote the paper and the others (Rassam and van Gulik) revised.

Guarantor

All authors.

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