Hemopatch
Sealing Hemostat

HEMOPATCH

Technique-Bicarbonate

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Introduction

HEMOPATCH Sealing Hemostat is a medical device that consists of a bovine collagen pad coated with a thin layer of NHydroxysuccinimide-Polyethylene Glycol (NHS-PEG). HEMOPATCH, now approved in a variety of countries around the world, first received Conformité Européenne (CE) mark approval in Europe in October 2013 as a hemostatic device for surgical procedures when control of bleeding by pressure, ligature or conventional procedures is either ineffective or impractical. This approval was then followed by an expanded CE mark approval as a surgical sealant and as a device to close dural defects in 2016.

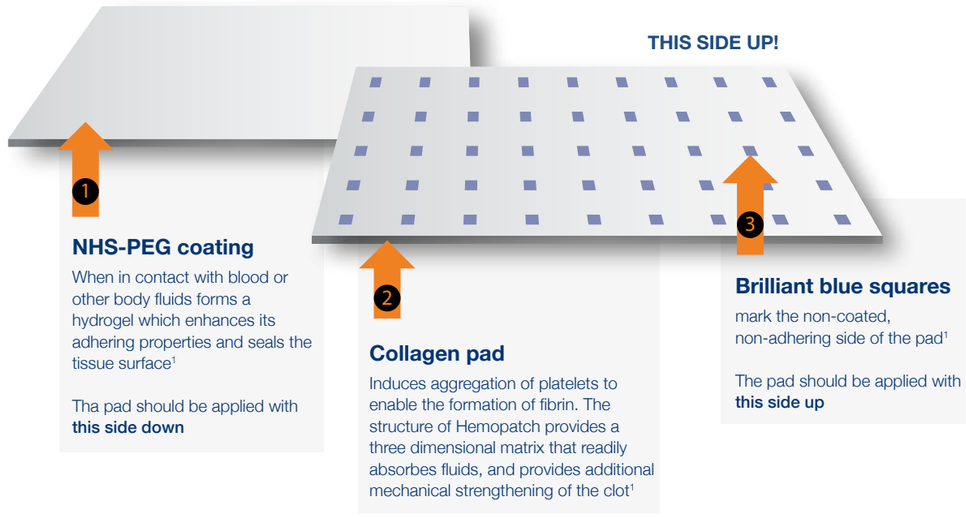
HEMOPATCH and Bicarbonate: Background

During the initial clinical experience with HEMOPATCH, routine conversations with Hepato-pancreato-biliary (HPB) surgeons revealed that in certain clinical scenarios, they saw a less than optimal adherence of the patch to the carbonized liver surface. In these clinical situations, little to no body fluid is present at the carbonized liver wound surface. However, HEMOPATCH needs suitable body fluids, such as blood or lymph fluid, to perform as designed. These fluids (1) quickly dissolve NHS-PEG and (2) have a high enough buffer capacity to increase the pH to slightly basic, which is needed to start the reaction of NHS-PEG with proteins on tissue surfaces.
In the absence of suitable amounts of such body fluids, like in the above clinical scenario, the use of a sodium bicarbonate solution was explored by several HPB surgery thought leaders. This technique demonstrated a clear improvement of the adherence of Hemopatch to the carbonized liver wound surface. Today, many HPB surgeons have adopted this technique in their surgical practice.

HEMOPATCH mode of action

The performance of HEMOPATCH is linked to its mechanism of action, which involves the interaction of the collagen pad and the NHS-PEG. Both components have their own mechanism of action which combined will result in effective hemostasis and/or sealing *(Figure 1)*.
One mechanism results in rapid adherence of HEMOPATCH

Figure 1: Mechanism of action of HEMOPATCH



1 - HEMOPATCH Sealing Hemostat Instructions for Use - 2016

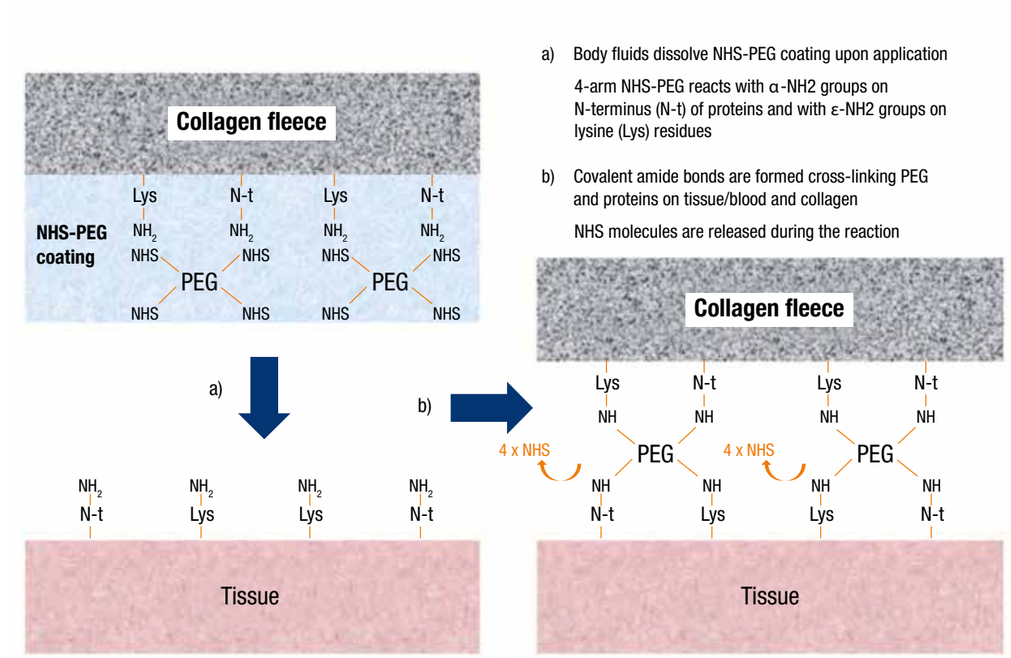


Figure 2: Chemical bonding of NHS-PEG to proteins

to a tissue surface due to the electrophilic cross-linking of NHS-PEG. When in contact with suitable body fluids, such as blood or lymph fluid, NHS-PEG quickly dissolves and reacts with proteins on tissue surfaces and in body fluids, thereby cross-linking HEMOPATCH to the wound surface (Figure 2).1,2 Another outcome of the reaction of NHS-PEG with proteins is the formation of a hydrogel, a water containing matrix that seals the tissue surface.[2]

The other mechanism is triggered by the collagen fleece. Collagen fleece induces the aggregation of platelets when in contact with blood. Platelets deposit in large numbers on the collagen structure, degranulate, and release coagulation factors that together with plasma factors enable the formation of a fibrin clot. The collagen also provides a three dimensional matrix that absorbs fluids and provides additional mechanical strengthening of the clot.[1]

Impact of pH on performance of HEMOPATCH

In order to perform as intended, HEMOPATCH requires an environment that provides a neutral to slightly basic pH. It is in the nature of reactions of NHS esters like the HEMOPATCH NHS-PEG with proteins, that the chemical reactivity and speed is controlled by the pH.4,5 The reason is that NHS esters are virtually non-reactive at an acidic pH. In fact, reconstitution of NHS-PEG in acidic diluents is used for synthetic tissue sealants such as Coseal® and Duraseal® to prevent premature reaction of NHS esters.6,7 To start the desired chemical reaction that culminates in the formation of an adhering hydrogel, these products are mixed upon application with a second solution which changes the pH from acidic to neutral or slightly basic.

In off-the-shelf HEMOPATCH we also find an acidic environment due to the specific manufacturing process of the raw collagen pad material. During a downstream processing step, collagen fibers are dissolved with a solution containing acetic acid. Subsequently, virtually all of the acetic acid is removed during a lyophilizing step. However, minor traces of acetic acid are still present and, as a result, the pH of the final collagen pad is acidic with a specified range of pH 2.8 to 3.43. As outlined above, beside a sufficient amount of fluid to dissolve the NHS-PEG, a neutral to slightly basic pH is needed to start the desired NHS PEG reaction.

This pH usually is encountered in surgery where body fluids such as blood and lymph fluid are present at wound surfaces. Besides their capability to rapidly dissolve the NHS-PEG coating, these fluids have a high enough buffer capacity to quickly change the pH of the collagen so that HEMOPATCH can perform unimpaired. Other body fluids like bile, urine or CSF do not have as strong an effect as blood and lymph fluid, and a decrease in adhesive force was observed in an in vitro study.[2]

Conclusion and Recommendations for Bicarbonate

As outlined above, very dry wound surfaces lacking virtually any suitable body fluid can be encountered during surgery. Under such conditions, the use of a solution which quickly dissolves NHS-PEG and rapidly raises the pH of collagen, such as sodium bicarbonate, can be suitable to start the NHS PEG reaction of HEMOPATCH as intended, and substitute for blood or lymphatic fluid.

The following 4 case reports provide examples of these clinical scenarios where the above technique has proven clinically beneficial (Rico Morales, Santiago Lopez) and some where the technique was not required (Uranus, Castell Gomez).

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Case report

Management of liver bed bleeding after cholecystectomy for acute cholecystitis in a patient on antiplatelet treatment

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Optimisation of coagulation and haemostasis in a Klatskin tumour case

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Keywords: Hepatology / Laparoscopy / Cholecystectomy

Background

Diffuse bleeding from the liver bed following cholecystectomy is difficult to control with electrocoagulation alone. In such cases, haemostatic devices that can quickly and effectively stop bleeding are extremely important.

A 74-year-old male patient presented with acute calculous cholecystitis and hydrops. The patient had two coronary stents placed two months before surgery, and was on double antiplatelet therapy with aspirin and clopidogrel. Clopidogrel was stopped three days prior to surgery; the procedure was performed on the third day after admission.

During the laparoscopic removal of the phlegmonous gallbladder, diffuse bleeding from the liver bed occurred as the plane of dissection between the gallbladder and the liver had disappeared due to advanced cholecystitis. Electrocoagulation was not successful in stopping the diffuse bleeding (Figure 1). To that end, a haemostatic pad (Hemopatch; Baxter International, USA) was introduced through a 10 mm trocar, and applied to the liver bed (Figure 2) to successfully stop the bleeding. The post-operative course was uneventful.

Discussion and Conclusion

Hemopatch haemostatic pads can be extremely effective to stop diffuse (non-spurting) bleeding, such as is the case after cholecystectomy for acute cholecystitis. The increasing number of patients with antiplatelet treatment makes additional efforts in stopping initial bleeding, and preventing after-bleeding, necessary.

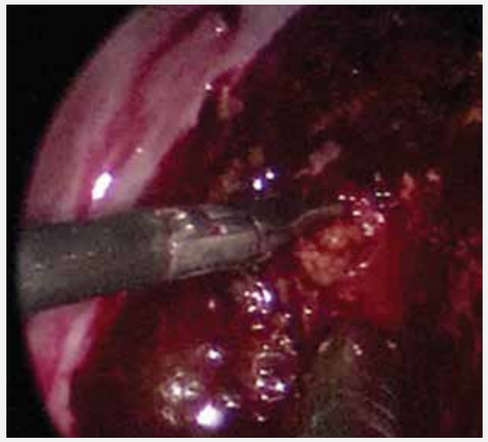

Figure 1: Electrocoagulation alone was not successful in stopping diffuse bleeding after removal of a phlegmonous gallbladder

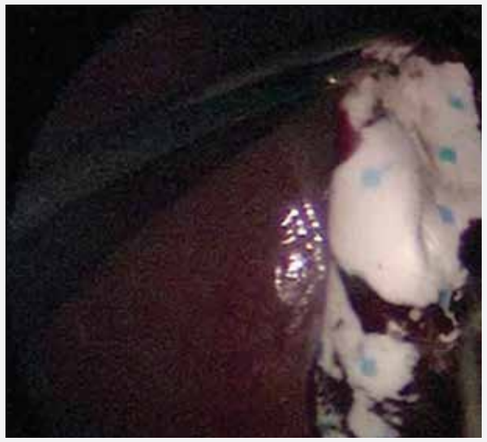

Figure 2: Use of Hemopatch haemostatic pads was able to stop the bleeding

Details of this case are included in: Fingerhut A et al. European initial hands-on experience with Hemopatch, a novel sealing hemostatic patch: Application in general, gastrointestinal, biliopancreatic, cardiac and urologic surgery. Surgical Technology International 2014;25:29-35.

Optimisation of coagulation and haemostasis in a Klatskin tumour case

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Keywords: Klatskin tumour / Intraoperative haemorrhage / Coagulation

Background

The only potentially curative treatment for Klatskin tumours is R0 oncologic resection.[1,2] Surgically, the patient should be prepared so that the possibility of peri- and postoperative complications can be reduced. Of the complications that may occur, haemorrhage requiring allogeneic transfusion has been associated with an increased incidence of surgical site infections, pneumonia, tumour recurrence and mortality.
Certain additional risk factors are associated with Klatskin tumours, such as obstructive jaundice which can affect platelet function, and extensive liver resection, which may give rise to peri- or postoperative haemorrhage and liver failure. As such, awareness of haemorrhage as a possible complication is crucial. Pre- and perioperative measures need to be presented to optimise the coagulation system and surgical haemostasis in patients undergoing R0 oncologic resection for Klatskin tumours.[3-6]

A 62-year-old woman with painless obstructive jaundice underwent clinical examination. Initial clinical tests revealed total bilirubin of 5.39 mg/dL (direct 4.73 mg/dL); gamma glutamyl transferase of 1459 IU/L; alkaline phosphatase of 588 IU/L; and transaminases GOT 157 IU/L and GPT 344 IU/L. Following further tests (Figure 1) a Klatskin IIIA tumour was diagnosed. The initial residual liver volume was 22.1%. Percutaneous transhepatic cholangiography was performed, followed by internal-external drainage of the left liver lobe with subsequent radiologic embolisation of the right portal vein and S4. The final residual liver volume was 31.6%. Indocyanine green retention after 15 minutes was 8%. The patient's nutritional and immunologic situation was optimised through the use of IMPACT® supplements (Nestlé Health Science, Lausanne, Switzerland; omega-3 fatty acids, arginine and nucleotides). The Tumour Committee suggested to treat this tumour with right trisection and S1 segmentectomy, using the Neuhaus "no-touch" technique 2 (Figures 2 and 3), with resection of the portal bifurcation and perioperative biopsy of the left biliary resection margin. The Pringle manoeuvre was not performed. The reconstruction is illustrated in Figures 4 and 5: the main portal vein left branch and hepatico-jejunal anastomosis. The resection surface was covered with a HEMOPATCH (Baxter Healthcare Corporation, Deerfield, IL) (Figure 5). A blood transfusion was not necessary. The resected tumour was staged as T2N0M0, R0.

Discussion

Haemorrhage is a complication that determines patient morbidity and mortality, and may also determine the oncologic outcomes.[4] Haemorrhagic control should start preoperatively by optimising liver function, controlling jau-

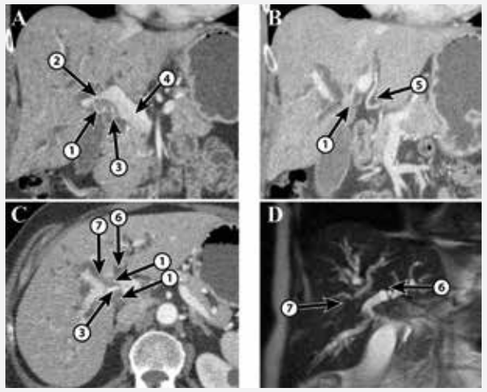

Figure 1. The tumour is in close contact with the right portal vein and encapsulates the right hepatic artery. In A, the tumour is affecting the right hepatic artery and the right portal branch. The portal vein is not affected. In B, the non-affected left hepatic artery is shown. In C, the affected right hepatic artery surrounded by the tumour is shown. D is a cholangio-MRI of the tumour and shows its relation to the left and right hepatic duct (without affecting secondary branches). (1) Tumour; (2) right portal; (3) right hepatic artery; (4) portal vein; (5) left hepatic artery; (6) left hepatic duct; (7) right hepatic duct.

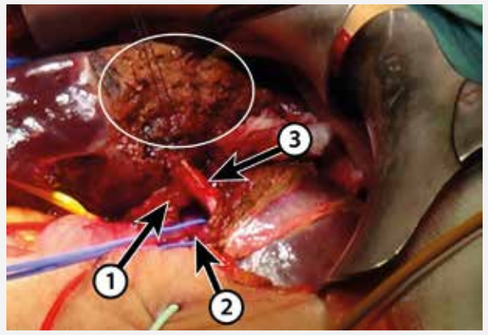

Figure 2. In the Neuhaus technique the tumour zone should not be dissected. (1) Tumorous zone; (2) left portal; (3) left hepatic duct; hepatic section in white ellipse.

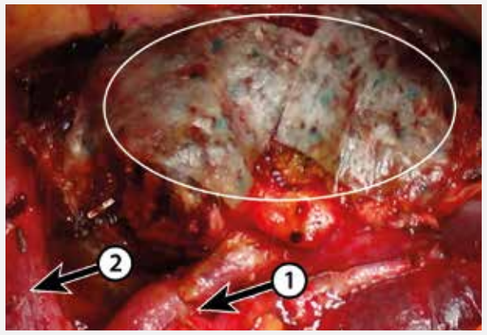

Figure 4. Venous reconstruction. (1) Vascular suture between the portal vein and the left portal branch; (2) cava vein; HEMOPATCH in white ellipse.

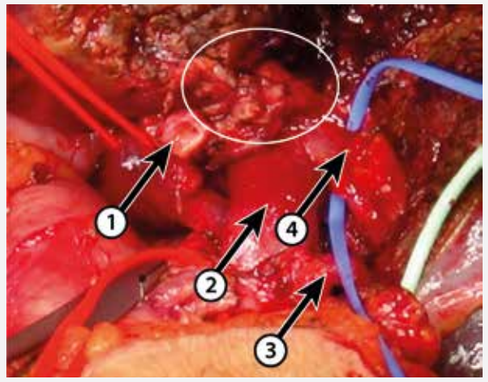

Figure 3. The distal biliary margin should be biopsied perioperatively. (1) Left hepatic artery; (2) portal right branch, (3) portal vein; (4) sectioned hepatic duct; tumour in white ellipse.

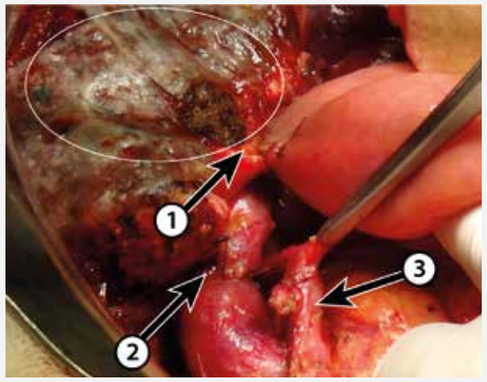

Figure 5. Final image with biliary and venous reconstruction. (1) Hepato-jejunal anastomosis; (2) venous anastomosis; (3) left hepatic vein; HEMOPATCH in white ellipse.

ndice and adjusting liver volume. A satisfactory nutritional status is also important. Perioperatively, local haemostatic agents reduce the incidence of peri- and postoperative haemorrhage, together with an appropriate surgical technique and anaesthesia (CVP control and use of antifibrinolytic agents).[5] Although the use of haemostatic agents is not supported by high levels of evidence, a reduction in transfusions of 15% has been observed alongside an increase of the application of haemostatic agents in liver surgery.[6]

Conclusions

During extensive liver resection, a local haemostatic agent must be able to stop haemorrhage and act as an "active sealer" in the presence of bile to avoid postoperative biliary fistulas. The use of HEMOPATCH is a good alternative in this kind of procedure, acting both as a haemostatic agent and sealer.

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Use of the HEMOPATCH in complex cases of laparoscopic cholecystectomy

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Keywords: Chronic cholecystitis / Perivesicular abscess / Exposed cholecystectomy bed / HEMOPATCH / Haemostasis

Background

Haemorrhaging is one of the most serious complications of laparoscopic cholecystectomy leading to increased rates of complications and transfusions. Furthermore, intraoperative haemorrhaging can increase the risk of mortality during surgery by up to 15%.[1] The risk of haemorrhage is especially high during surgical interventions treating acute cholecystitis, cirrhosis and portal hypertension. Management of intraoperative haemorrhage depends on the degree and location of the event. Traditionally, sutures, ligatures, compression and electrocautery have been used as haemostatic measures for more than 20 years; today, topical haemostatic agents are also available.[2]

A 63-year-old patient with type 2 diabetes was hospitalized for conservative treatment of acute cholecystitis of six days' duration. The patient was treated with antibiotics and was discharged seven days after admission. Eight days post-discharge, the patient was rehospitalized due to a flare-up of pain. A cholecystectomy was scheduled during the second admission. For the cholecystectomy, the patient was positioned in the decubitus recumbent position with the legs closed. Four trocars were used. During surgery acute-phase chronic cholecystitis was discovered, along with an inflammatory fibrotic mass that was difficult to dissect. The structures of Calot's triangle were then identified, and a decision was taken to proceed in detaching the gallbladder from the liver bed. Multiple abscesses were found, but the dissection plane was not able to be clearly delineated. As an exposed bed remained, the decision was made to use HEMOPATCH (Baxter Healthcare Corporation, Deerfield, IL), to avoid bleeding in the post-operative period. The HEMOPATCH was introduced wrapped in a gauze dressing to avoid adherence to the walls of the 12-mm trocar (Figure 1-3) and the cholecystectomy bed was dampened with bicarbonate to facilitate its adhesion to the cauterized tissue (Figure 4, 5). No other post-operative procedures were performed; follow-up consisted of regular analytical tests. No bleeds were observed and the patient's response was satisfactory.

Figure 1. HEMOPATCH is wrapped in a gauze dressing.

Figure 2. The wrapped HEMOPATCH.

Discussion

Haemorrhaging is one of the most feared complications in laparoscopic surgery.1 The difficulty in finding the cleavage plane between the gallbladder and the liver bed

increases the likelihood of an haemorrhagic event. The presence of superficial veins in the cholecystectomy bed as a consequence of inflammation, and the attempt of electrocoagulation, may produce profuse bleeding.[1,2] When electrocoagulation is not sufficient, the use of local haemostatic agents may be effective. Some studies claim that the haemostatic agents have improved clinical and surgical results in serious situations.[2,3]

Conclusions

In a diabetic patient presenting cholecystitis, surgery may be the best option during the first 48 hours after assessment. Surgery may reduce the complications associated with a long hospital stay and the extended use of antibiotics.
The use of HEMOPATCH may be limited by the reduced adherence to cauterized tissue. This is rapidly resolved by dampening the tissue with bicarbonate. In our case, the HEMOPATCH was protected with a gauze to avoid the material sticking to non-target tissues; the cholecystectomy bed was dampened with a few drops of bicarbonate. The sealing effect of HEMOPATCH was rapid and appropriate for this procedure.

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Figure 3. The wrapped HEMOPATCH is introduced via the 12-mm trocar and spreads out inside the abdomen.

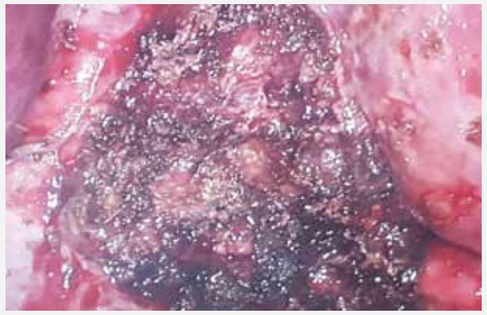

Figure 4. The cholecystectomy bed is dampened with a few drops of bicarbonate to support HEMOPATCH adherence to the cauterized tissue.

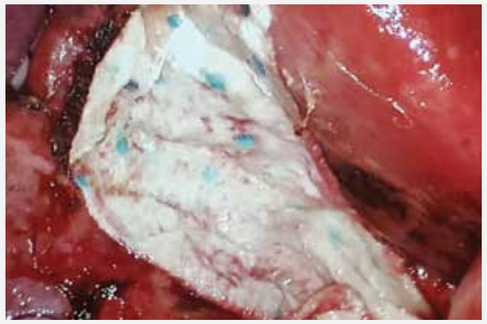

Figure 5. Pressure is applied with a dry gauze dressing for two minutes resulting in adherence of the HEMOPATCH and bleeding cessation.

HEMOPATCH Technique-Bicarbonate

HEMOPATCH in laparoscopic left hepatectomy with extensive vascular exposure

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Keywords: Laparascopic hepatectomy / Haemostasis

Background

It has taken longer to implement a laparoscopic approach to liver surgery than for other disciplines of digestive surgery (e.g. colorectal or bariatric surgery), possibly due to surgeon's fear of intraoperative or postoperative bleeding.1 Despite advances in technology and anaesthetics that allow for liver transection, there are resections in which extensive vascular exposure can increase the risk of bleeding and fistula, which may result in the need to use adjuvant methods to reinforce haemostasis and biliostasis. We present the case of a totally laparoscopic left hepatectomy sealed with HEMOPATCH (Baxter Healthcare Corporation, Deerfield, IL).

A 63-year-old woman was treated for sigmoid colon adenocarcinoma one and a half years prior to presentation. The patient was still in follow up following treatment, when she presented with hepatic metastasis involving the left lobe. The Multidisciplinary Committee proposed a left hepatectomy. A full laparoscopic left hepatectomy was performed with control and section of the left pedicle by the extra-Glissonian method.[2] The medial hepatic vein was approached dorsally 3 with complete exposure at the transection surface. Parenchymal dissection was carried out by combining the CUSA (Integra, Plainsboro, New Jersey, USA) with THUNDERBEAT (Olympus Medical Systems, Tokyo, Japan), performing biliostasis with bipolar coagulation. Given the extensive vascular exposure, a decision was made to seal the surface with 2 patches of HEMOPATCH using bicarbonate to dampen the liver surface. The postoperative period occurred without incident, allowing discharge within 72 hours of surgery.

Discussion

Perioperative bleeding can lead to morbidity and mortality after hepatectomy. There are numerous factors that influence perioperative bleeding, such as haemodynamic factors, the type of surgical technique and the type of resection. The pressure exerted by the pneumoperitoneum during the laparoscopic approach helps reduce venous bleeding during transection, but may favour delayed ble-

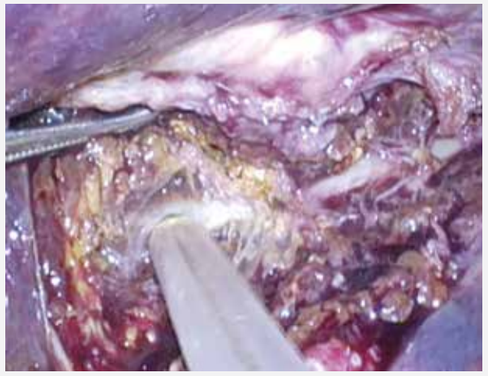

Figure 1. Dorsal approach to the medial hepatic vein

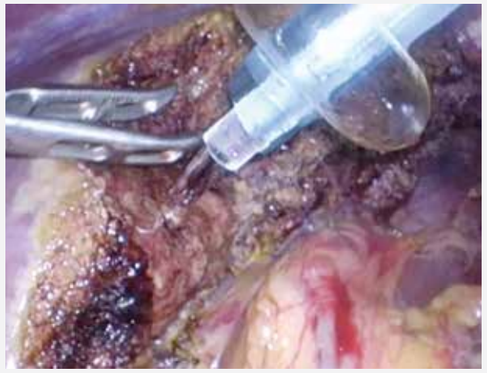

Figure 2. Dampening the exposed liver surface with bicarbonate

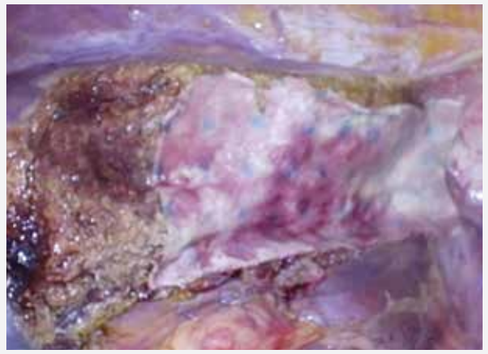

Figure 3. Application of the first HEMOPATCH

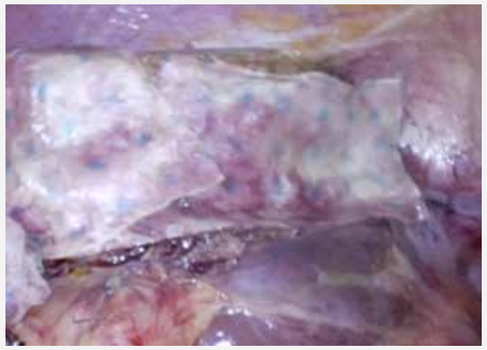

Figure 4. The second HEMOPATCH has been cut to fit the exposed surface

eding when it is removed at the end of the procedure. Additionally, major resections may present frequently with deterioration of clotting parameters, and when combined with the required extensive vascular exposure, the haemorrhagic risk increases. Furthermore, vascular pedicle exposure increases the risk of biliary fistula.[4]

Conclusions

The patient described in this case required a laparoscopic approach for major hepatectomy and extensive vascular and pedicular exposure. The use of haemostats with sealing capabilities, such as HEMOPATCH, can decrease the biliary and haemorrhagic complications of major hepatectomies.[5]

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