The American Journal of Surgery xxx (2017) 1–11

Contents lists available at ScienceDirect

The American Journal of Surgery

journal homepage: www.americanjournalofsurgery.com

Analysis of the biliostatic potential of two sealants in a standardized porcine model of liver resection

H. Fonouni*, A. Kashfi, O. Stahlheber, L. Konstantinidis, T.W. Kraus, A. Mehrabi, H. Oweira

Department of General, Visceral and Transplantation Surgery, University of Heidelberg, Germany

ARTICLE INFO

Article history:
Received 18 January 2017
Received in revised form
28 May 2017
Accepted 13 June 2017

Keywords:
Biliostasis
Sealant
Fibrin glue
Liver resection

ABSTRACT

Background: Improved resection techniques has decreased mortality rate following liver resections(LRx). Sealants are known as effective adjuncts for haemostasis after LRx. We compared biliostatic effectiveness of two sealants in a standardized porcine model of LRx.
Material and methods: We accomplished left hemihepatectomy on 27 pigs. The animals were randomized in control group(n = 9) with no sealant and treatment groups (each n = 9), in which resection surfaces were covered with TachoSil® and TissuFleece®/Tissucol Duo®. After 5 days the volume of ascites(ml), bilioma and/or bile leakages and degree of intra-abdominal adhesions were analysed.
Results: Proportion of ascites was lower in TissuFleece/Tissucol Duo® group. The ascites volume was lower in TachoSil® group. In sealant groups, increased adhesion specially in the TachoSil® group was seen. A reduction of the "bilioma rate" was seen in sealant groups, which was significantly lower in TissuFleece®/Tissucol Duo® group.
Conclusion: In a standardized condition sealants have a good biliostatic effect but with heterogeneous potentials. This property in combination with the cost-benefit analysis should be the focus of future prospective studies.

1. Introduction

Since liver resection has been shown to be the only curative option in oncological cases, the indication range of liver resection has been steadily extended in recent years.[1,2] Liver resection can now be applied to a wide range of pathological disorders including benign primary tumors such as liver cell adenoma or hemangioma, and primary malignant tumors such as hepatocellular carcinoma, and hepatic trauma. However, the most frequent application is in liver metastases, resulting in higher survival rate especially for metastases of colorectal carcinomas.[3] The scope of liver resection varies from anatomical liver resections to extended resections up to 80% of the liver volume. In the classification of the French Gastroenterological Cancer Society, two classes of liver resections have been reported: Class I (≤4 segments, ≥40% liver residual volume) and Class II (>4 segments, <40% liver residual volume). The mortality rate of class I and class II resections is now <3% and <8%, respectively. The morbidity varies between 15 and 60%,[2,4,5] depending on the extent of the liver resection, the underlying disease and the co-morbidity. Recent series of major hepatectomy reported postoperative mortality rates varying between 0.7% and 2.6%,[6,7,8] while morbidity ranges remained up to 56.4%.[9,10] Because of the exact knowledge of the segment boundaries, improved resection techniques and advancements in surgical armamentariums, a reduced mortality is now achievable.[11–13]

Despite improvements in surgical armamentariums, even the most advanced devices facilitating hepatic parenchymal transection including the Cavitron Ultrasonic Surgical Aspirator, Hydrojet, Stapler and dissecting sealer using radiofrequency energy have not eliminated the complications (bleeding and bile leakage) of liver resection.[14–16] Whatever the technical procedure used, surgeons cannot isolate and secure all small vascular and biliary leakage, and it is impossible, in most cases, to eliminate blood loss and biliary leakage,[17,18] which are the major determinant of morbidity after liver surgery.[18] On the other hand, more patients undergoing liver surgery are affected by pathological underlying liver diseases, such as chemotherapy-associated steato-hepatitis, sinusoidal obstruction syndrome or fibrosis/cirrhosis.[19]

The incidence of bile leakage in reported large series ranges

* Corresponding author. Department of General, Visceral and Transplantation Surgery, University of Heidelberg, Im Neuenheimer Feld 110, 69120, Heidelberg, Germany.
E-mail address: hamidreza.fonouni@med.uni-heidelberg.de (H. Fonouni).

http://dx.doi.org/10.1016/j.amjsurg.2017.06.038
0002-9610/

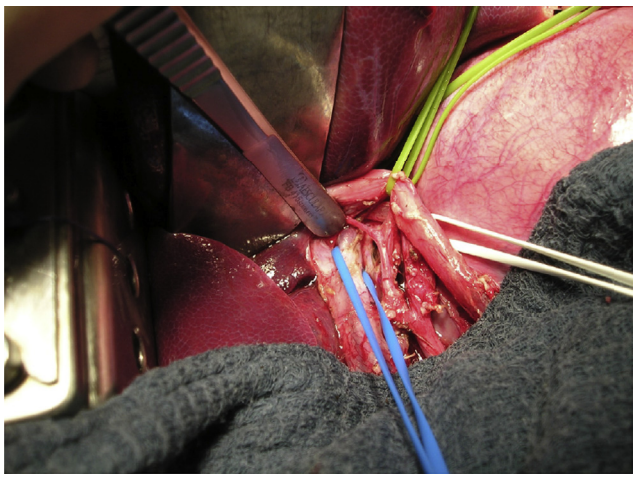

Fig. 1. Preparation of the left pedicle in liver hilum. The left hepatic artery, portal vein and bile duct are separated with white, blue and yellow vessel loops.

from 2.6% to 8.1%.[20–23] Since bile is both cytotoxic and fibrinolytic it can impair wound healing or result in peritonitis.[24–26] The presence of bile, blood, and devitalized tissues in the dead space after liver resection may provide the ideal environment for bacterial growth and impair the normal host defence mechanisms.[11,20,27] Biliary complications may lead to sepsis, liver failure, and even death.[28] In best cases, the biliary fistula can be self-limited with gradually reduction of secretion until spontaneous cessation, which could be a consequence of post resection liver regeneration. In some cases, it should be treated with an interventional drainage, and in rare cases even an operative revision may be necessary. This leads to considerable costs and a reduction in the revenue of the responsible centre. Fibrin glues have been used for decades in the management of bleeding or sealing resection surfaces of parenchymatous organs in surgery.[18,29,6,15,30] If the limitation of the use was initially because of the uncertainty about the transmission of infectious diseases and the high costs, the main focus now has to be placed on the efficiency, and therefore, on the evidence of the use of these products. At the same time, economic concerns, including direct and indirect costs, which significantly influence the cost/benefit ratio, continue to play an important role.[18,31,32,20]

The ideal topical haemostatic agent should have the capacity to seal or occlude small vessels and bile ducts, and has to be safe and user friendly.[33] The use of modern sealants has already been established in liver surgery and has been recognized as a positively evaluated tool for haemostasis after liver resection. Three classes of topical haemostatic agents are currently available; agents which provide a matrix for endogenous coagulation (collagen, cellulose or gelatine) without active components, the second group contains active components (fibrin sealants) mimicking endogenous coagulation.[33] The third group are a few products that combine both above mentioned properties in a ready-to-use tool. These products contain fibrinogen, coagulation factors such as thrombin and antithrombolytic agents, also called as carrier-bound fibrin sealants[33–35]).

The extent to which the sealants lead to a biliostasis or to a reduction in biliary leakage after liver resection has not been sufficiently investigated in standardized conditions.[18,36] In this work we established a standardized experimental model to evaluate the efficacy of two fibrin-based sealants as a method for sealing resected surface of liver against bile leakage in a short-term postoperative phase.

2. Materials and methods

We have investigated the biliostatic potentials of two modern sealants in a standardized porcine model of chronic liver resection. The liver resection area was covered with one of the two defined and commercially available sealants. The biliary fistula and/or bilioma rate were then recorded after an observation period of five days. After this period, the animals underwent re-laparotomy, and the site of liver resection was analysed for macroscopic changes (adhesions, bilioma, and bile staining). The data obtained were compared with the data of the control group on which no sealant was used.

2.1. Anaesthesia protocol

All operations and subsequent investigations were performed under general anaesthesia. After premedication (azaperone 1–2 mg i.m.), anaesthesia was induced with ketamine (10 mg/kg i.v.), midazolamine hydrochloride (0.25 mg/kg i.v.), pancuronium bromide (0.08 mg/kg i.v.), and continued with fentanyl (0.05 mg/kg/h

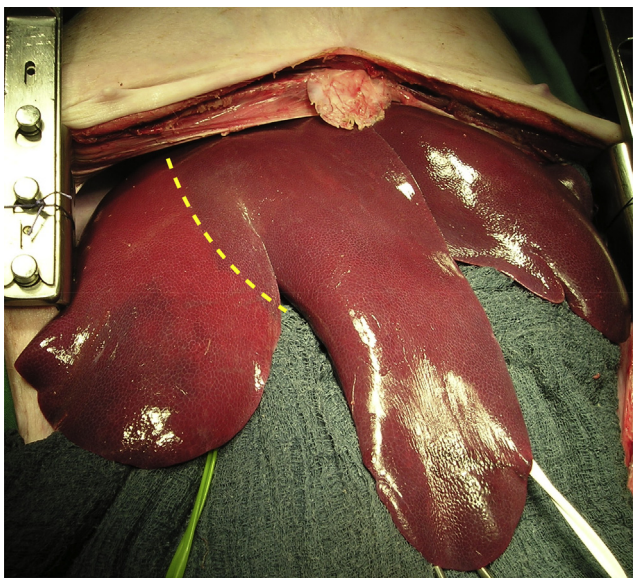

Fig. 2. After ligating the left pedicle, the demarcation zone (yellow line) is used as the resection line for left hemihepatectomy. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

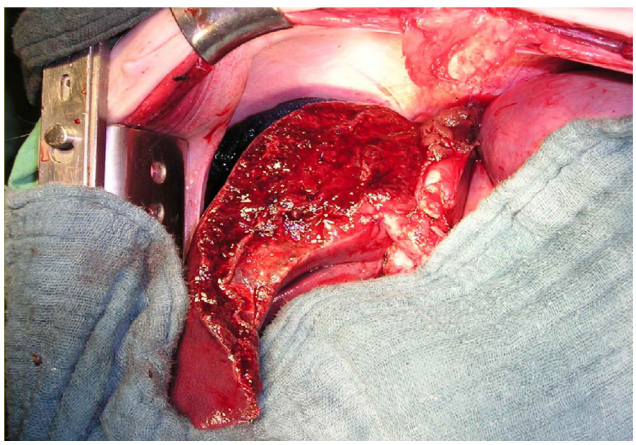

Fig. 3. Liver resection plane after doing left hemihepatectomy.

Please cite this article in press as: Fonouni H, et al., Analysis of the biliostatic potential of two sealants in a standardized porcine model of liver resection, The American Journal of Surgery (2017), http://dx.doi.org/10.1016/j.amjsurg.2017.06.038