

Modification of Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy by Hepatic Middle Vein Ligation Improves Hypertrophy and Prevents Critical Ischemia

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Abstract

The Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy (ALPPS) procedure represents a therapeutic option for selected patients with advanced and bilobular hepatic metastasized colorectal cancer. However, this procedure currently has a high rate of perioperative morbidity and mortality. We report of a 45-year-old woman being diagnosed with synchronous Colorectal Liver Metastases (CRLM). A primary ALPPS procedure was performed and in contrast to standard procedures, the Middle Hepatic Vein (MHV) was ligated during stage I. It was well-tolerated by the patient and resulted in an outstanding extent of hypertrophy of 87.2% within six days and 127% within eleven days, visualized by a CT scan. A significantly contrasting ligated right portal vein was seen, after stage I. A ligating MHV during ALPPS stage I is feasible and could lead to a higher extent of hypertrophy. An increased venoportals shunting may help to overcome ischemia in liver tissue and consecutively avoid biliary leaks and necrosis within segment IV between stage I and II. However, this data requires further validation.

Keywords: ALPPS; Future Liver Remnant; Ligation of Middle Hepatic Vein; Modified ALPPS

Introduction

ALPPS has expanded the therapeutic field treating patients with extensive and bilobular colorectal liver metastases. Better surgical management, as well as stricter selection of patients undergoing this procedure has led to the improved safety of patients. However, ALPPS has been criticized for its high rates of morbidity and mortality, due to insufficiently induced hypertrophy and local infection. In this particular case, we report on a modified ALPPS approach, addressing two major points of observation: hypertrophy and ischemia.

Case Report

In June 2018, a 45-year-old woman was presented as an

out-patient in our surgical consultation with a newly diagnosed carcinoma of the colon sigmoideum with synchronous hepatic metastases. Prior to this, the patient had suffered from various cancer entities (such as breast cancer, lung cancer as well as liposarcoma of the left axilla) which had all been treated curatively. The patient had complained about abdominal pain and bloating, and we performed a colonoscopy. An adenocarcinoma of the colon sigmoideum was diagnosed via a tissue biopsy and histological data analysis (grade of differentiation: G3). Further staging included a PET scan, which revealed multiple bilobular liver metastases in segments I, IVa, V and VIII. Furthermore, a mass of 2 cm was identified in the left adrenal gland. The patient's case was discussed at our interdisciplinary tumor conference of the Goettingen Comprehensive Cancer Center (G-CCC). Surgical resection of the primarius as well as resection of the left adrenal gland was recommended, in order to assess the origin of the tumor,

as it was suspected to be a metastasis. The initial plan to remove the primarius and all hepatic lesions entails surgical resection of the rectum and segment I during the first surgery, followed by embolization of the right portal vein and the portal branch of segment IVa to induce hypertrophy of the lesion-free segments II and III.

Surgery was performed as outlined above, including colon resection and resection of segment I. Intraoperatively, a localized suspicious lesion was resected and later turned out as peritoneal carcinosis. The patient recovered from surgery without any postoperative complications. The final histopathological analysis revealed the presence of a 4.3 cm adenocarcinoma of the colon with a perforation of the serosa, one single peritoneal lesion and blood vessel infiltration. The overall TNM stage was: pT4, pN1 (3/30), pM1 (HEP/PER), L0, V1, G3, R0. The lesion of the left adrenal gland showed no signs of malignancy and was subsequently diagnosed as adenoma. Molecular analysis revealed wildtype of

KRAS, *NRAS* and *BRAF* genes as well as a microsatellite stability.

Due to the peritoneal carcinosis, a postoperative chemotherapy with FOLFOX and panitumumab instead of resection was recommended by the tumor conference. After completing four cycles of chemotherapy, the therapy was interrupted due to the patient experiencing diarrhea, chills and loss of appetite. CT scans (Figure 1) showed regressed liver metastases after 2.5 months, however, the volume of liver segments II and III was assessed to be at 211 cm³. The patient's weight was 70 kg at a height of 170 cm. As Future Liver Remnant (FLR) was too low, induction of hypertrophy was inevitable. However, the patient rejected an interventional Portal Vein Embolization (PVE) as she feared subsequent tumor progression. We therefore advised that a primary ALPPS procedure ought to be performed, should no progress of the peritoneal carcinomatosis be found.

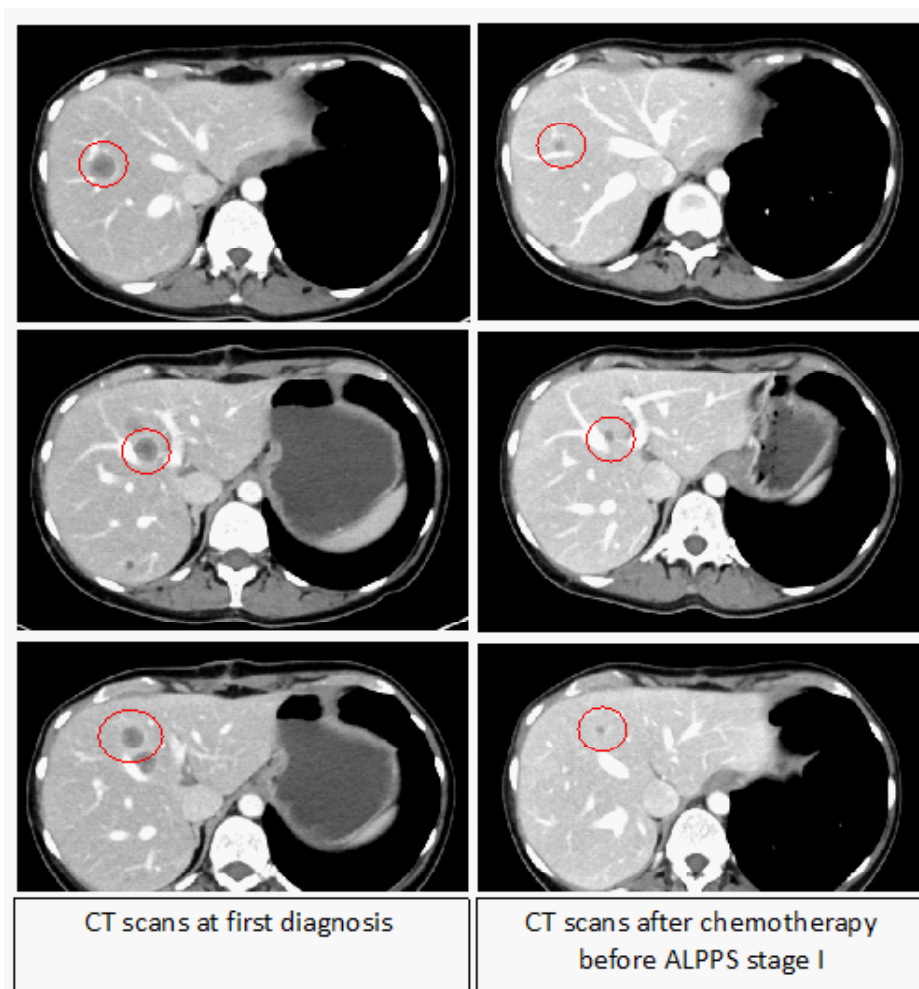


Figure 1: CT scans at first diagnosis (left) and after chemotherapy before ALPPS stage I (right)

During surgery, no peritoneal cancer was found and stage I was performed. The goal of the parenchyma dissection was a complete and save separation of FLR and the remaining liver because of the necessity of an enormous hypertrophy for the remaining segments II and III. In this special case, the simplest way was to dissect the MHV. Following surgery, the patient was transferred to the ICU unit. Postoperative ultrasound showed advanced arterial perfusion in both liver parts. However, a blood flow within the dissected, intrahepatic right portal vein was unexpectedly high. Although this phenomenon had been described previously by Schadde et al. [1], a CT scan was performed to confirm this finding. The scan revealed that the dissection of the extrahepatic portal vein was successful and the ultrasound results of retrograde filling were confirmed (Figure 2).

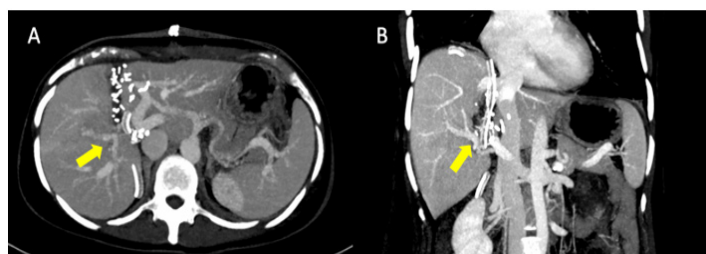


Figure 2: Axial and coronal reconstructions of initial postoperative CT scan reveal residual perfusion of the right portal vein (arrow).

Furthermore, the scan illustrated that hypertrophy of the left liver lobe had increased from 211 cm³ to 309 cm³ which was considerably high on day 2 (hypertrophy about 46.5%; (Figure 3A-C)). In order to verify the diagnostic value of this volumetry, an MRI scan - which was performed five days later after CT scan - confirmed progressive hypertrophy of segments II and III measuring 479 cm³ (127%, (Figure 3D)). Though sufficient hypertrophy was seen via imaging techniques, the usual time period of 12 days between stage I and II was awaited.

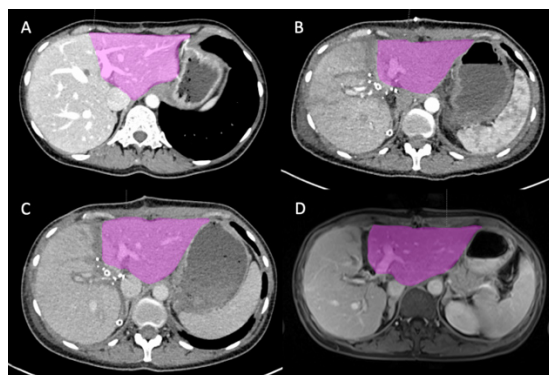


Figure 3: Preoperative CT imaging (A). Volumetric analysis reveals a FLR volume of 211 cm³. Postoperative CT- (B, C) and MRI-imaging (D) shows subsequent increase of FLR volume from 395 cm³ (B) to 479 cm³ (D).

Hereupon, ALPPS stage II was completed without any incidents. No signs of ischemia, which is frequently found in segment IVb, were found in this case. The patient made a smooth recovery.

Discussion

ALPPS still remains an individualized therapeutic option for selected patients due to high rates of perioperative complications. Our unplanned modification of the standard procedure retrospectively addresses two major concerns in ALPPS: low extent of hypertrophy of FLR and high risk of ischemia of segment IV with consecutive necrosis or biliary leaks. The occlusion of portal vein (surgical ligation or interventional embolization) is associated with only a moderate amount of hypertrophy of 30-40% in four to six weeks, while hepatectomies of more than 50% shows rapid hypertrophy of 80-90% within ten days [2,3]. The high rate of hypertrophy performing ALPPS (compared to portal vein embolization only) can perhaps be correlated to the changes of portal vein hemodynamics, leading to rapid liver regeneration by additionally obliterating intrahepatic shunts and collaterals, resulting in a hyper flow in the portal vein [1,4]. Due to this, a “buffer response” of hepatic artery is observed as a decreased arterial flow in order to sustain a constant sinusoidal blood flow [1,5]. Since oxygenation of liver tissue is largely dependent on the hepatic artery, it is hypothesized that ALPPS is associated with hypoxia, which may represent a main stimulus for increased regeneration. Recently, this phenomenon was demonstrated on a rat model [1].

In this case report, a hypertrophy of 127% was reached within 11 days, respectively, after ALPPS stage I including hepatic vein ligation. By comparison, the average hypertrophy of other patients who prior underwent ALPPS procedure in our department without ligation of MHV was measured at 48.5% within 11 days. Therefore, it is reasonable to conclude that the ligation of MHV additionally increases the extent of hypertrophy. The hypothesis that dissecting a hepatic vein increases hypertrophy in ALPPS is supported by findings from Schadde et al [6]. who, by use of a pig model, reveal that an intraoperative simultaneous double ligation of portal and hepatic veins induced a hypertrophy three times higher, compared to only portal vein ligation within seven days. The mechanisms behind this increased hypertrophy remain unclear. Additional MHV ligation could further reduce the blood flow and oxygen supply within the liver tissue, which is planned to be resected in stage II of the surgery and therefore would increase the hypertrophy effects in FLR. However, further investigation and molecular analysis is needed. The exact mechanisms behind the standard hypertrophy due to classic ALPPS are not yet clear. The question was raised whether this phenomenon is based on steatosis, edema or true proliferation [7,8]. Schlegel et al. state that

inflammatory reaction and growth factors such as IL-6 or TNF- α could mediate the liver regeneration [9,10].

Besides the increased hypertrophy, we observed absence of necrosis in segment IV after performing ALPPS stage I, including MHV ligation. With respect to the blood supply of segment IV and the common problem of ischemia during both steps of ALPPS, it is important to note that this segment is supplied arterially by both the Right Hepatic Artery (RHA) and Left Hepatic Artery (LHA) [11]. Thus, parts of segment IV being supplied by the LHA could potentially become ischemic, due to the separation process. The ischemia then gives rise to higher risks of postoperative complications [12]. Ligation of MHV could overcome the critical ischemic area of segment IV on the resection surface and prevent necrosis and biliary leaks, leading to increased blood flow between arteriportal branches. As outlined above, a strong portal blood flow was observed postoperatively in ultrasound examination as well as via a CT scan, two days after stage I. This phenomenon was previously revealed in another case report whereby a standard ALPPS procedure was performed [13]. This could be explained by retrograde filling of portal veins from hepatic sinusoids, arterial shunting or retrograde filling of the right and inferior hepatic veins [14,15]. Furthermore, this retrograde filling could have been strengthened by ligating MHV resulting in fewer ischemic areas of segment IV.

Conclusion

In this case report, we demonstrate a modified approach of ALPPS by ligating MHV, which addresses perioperative aspects such as extent of hypertrophy and critical ischemia in future ALPPS procedures. If this effect is reproducible and animal data can further support this modification, it may help to reduce perioperative morbidity and mortality and subsequently increase the safety of the patients.

Acknowledgement

The authors declare no conflict of interest.

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