Frontiers of Liver Surgery

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Question 1: In patients requiring extended liver resection, when would you consider associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) as opposed to preconditioning by portal vein embolization (PVE)? Does the underlying disease matter in your differential approach?

Oldhafer: In my opinion, the first-line technique to obtain a sufficient future liver remnant (FLR) is PVE. It is very well established, and morbidity and mortality rates of the intervention are low. However, there are two important factors which need to be taken into consideration: First, a very low standardized FLR (sFLR), and second, a non- or low responder after PVE. In the first case, e.g. 15% FLR, I believe that a combination of PVE and ALPPS (so-called ‘Hybrid-ALPPS’) is a good tool to obtain a sufficient FLR. In my experience, the problem of a very low sFLR combined with a patient who underwent multiple cycles of chemotherapy will not be solved by PVE alone. In this case, dissection of the collaterals will greatly improve the regenerative capacity of the liver without increasing morbidity or mortality. Regarding the second factor, there are patients in daily clinical practice who will not respond adequately to PVE (also with segment 4 embolization). Therefore, the so-called ‘Rescue-ALPPS’ can achieve the desired volume.

As always, there are exceptions to the first statement in the first sentence. When considering ALPPS or PVE, metastases in the FLR will be an argument to perform a Hybrid-ALPPS. In this setting, we are able to free the FLR from tumor and transect the liver in one step and perform a PVE later.

Regarding the underlying cause, I refer to the second question and answer. However, the disease itself does not determine whether PVE or ALPPS is used.

Schadde: In my opinion, there is an absolute contraindication to use ALPPS in hepatocellular carcinoma (HCC) and cholangiocarcinoma, both intra- and extrahepatic, based on the evidence of catastrophic outcomes in the literature. From a medico-legal standpoint, its use for primary liver tumors cannot be justified at the moment. In contrast, it may be helpful in metastatic disease, in colorectal liver metastases (CRLM), in neuroendocrine tumors (NETs), and in NON-CR-NON-NET metastases.

The indications are extremely rare. 90% of patients can be appropriately treated with PVE or double embolization of the portal and hepatic veins. Its use may be justified for monosegment or double-segment FLR with a volume of less than 18%. In my opinion, its use is never justified to accelerate the resection, but only to increase the FLR volume. The second stage should not be done before 10 days have elapsed, and a HIDA scan to assess the function of the remnant liver is obligatory. I would not do a second stage with an Amsterdam index less than 3%/min/m². If you have a metastasis that is running away because it is not responding to chemotherapy or because it is growing too fast, then ALPPS will not save your patient. Surgery is not effective against tumor biology.

Yamamoto: I would select ALPPS when the cancer aggravation is impending. So far, I have tried ALPPS twice. The first case was in a patient with a giant HCC of 2,490 ml in the right liver. The volume of the liver remnant was only 350 ml (26.7%), and ICG-Krem was 0.037. The tumor was in a state of impending rupture, and the puncture route for percutaneous transhepatic PVE was difficult to obtain due to the huge tumor mass. One week post step 1 procedure, ICG-Krem had increased to 0.053. The second case was also in a patient with HCC of 774 ml in the right liver. The tumor was in a location broadly adhering to the inferior vena cava, and it

looked like the tumor was going to develop a tumor thrombus in the short hepatic veins soon.

I think that another indication for the ALPPS procedure is a patient in whom ICG-Krem is less than 0.04 because such patients often fail to increase ICG-Krem to over 0.05 even after PVE [1].

Question 2: In your practice, where do you see contraindications to extended liver resection by ALPPS or resection following PVE? When do you choose not to operate on patients, namely those suffering from hilar cholangiocarcinoma?

Oldhafer: After the ALPPS meeting in 2015 in Hamburg, the data pointed clearly against liberal application of ALPPS in non-colorectal carcinoma (NCRC) patients. However, the first ALPPS itself was performed on a patient with an NCRC. Therefore, I think that ALPPS may play a role in patients with NCRC (e.g. hilar cholangiocarcinoma). Nevertheless, we need to think about the correct selection of patients.

Unfortunately, in daily practice, patients who suffer from hilar cholangiocarcinoma and who require extended right hepatectomies and PVE are often caught up in a diagnostic and interventional loop. Before thinking about hypertrophy concepts, they need to be drained (either by a percutaneous or endoscopic approach). The procedure itself can cause morbidity and mortality (cholangiosepsis, insufficient drainage). The time between drainage/PVE and resection can be very long and so much extended that at the time of the exploration, the tumor has already progressed.

This somehow answers the second part of the question: A patient with insufficient drainage, progress of the tumor, or low FLR will not be resected. Due to the insidious nature of hilar cholangiocarcinoma, however, surgical exploration will often be necessary to confirm the irresectability. In this setting, a palliative drainage operation can be considered.

Schadde: Absolute contraindications to ALPPS: all primary liver tumors, CRLM with progression on chemotherapy, breast, ovarian and testicular cancer metastases with progression on chemotherapy, neuroendocrine carcinoma (grade III NETs), NETs grade 1 and 2 with more than 10 lesions (complete resection too much, debulking suffices to prolong survival), fibrosis, cirrhosis, sinusoidal obstruction syndrome (SOS), chemotherapy-associated steatohepatitis (CASH), immune deficiency (e.g. s/p transplantation), history of more than 9 cycles of fluorouracil/platinum/irinotecan-based chemotherapies (those patients are eligible only to parenchymal-sparing resections).

Relative contraindications: age > 60 years (except for patients with a very good performance) as well as comorbidities that are prohibitive for major hepatectomies.

As far as hilar cholangiocarcinoma is concerned, extended resections are necessary in only a minority of patients in my opinion. Extended resections are only necessary in type IIIa/IIIb tumors with wide extension to the right and left side as well as type IV or

intrahepatic cholangiocarcinomas in a hilar location, which in my opinion are not true Klatskin tumors. As long as the middle vein can be preserved (i.e., there is no tumor invasion into the middle hepatic vein), there is no reason to perform an extended resection.

ALPPS is contraindicated in cholangiocarcinoma; PVE always suffices to induce enough function in the FLR. I always perform a HIDA scan; bilirubin should be less than 1.5 mg/dl, otherwise resection is too risky.

Yamamoto: In my opinion, hilar cholangiocarcinoma is not a good indication for ALPPS because the manipulation of the hepatic hilum during the step 1 procedure hampers the non-touch isolation of the tumor. I choose PVE for hilar cholangiocarcinoma. If the patient does not gain an ICG-Krem > 0.05 by PVE, I will give up extended liver resection.

Question 3: In your pre- and intraoperative decision making, when would you consider expanding your procedure by either vascular resection and reconstruction or multivisceral resection (e.g. hepatopancreatoduodenectomy) as opposed to aborting the procedure as an exploration?

Oldhafer: First, the physical performance and age of the patient play a pivotal role in extending the operation. However, an extended resection with vascular involvement will not be performed with certain tumor entities. Currently, in my opinion, if faced with a pancreatic carcinoma with vascular involvement, the patient needs to receive neoadjuvant therapy and to be included into a study, if eligible. If the extension of the vascular infiltration was underestimated preoperatively, the exploration needs to be terminated and we would refrain from resecting the tumor. Primary liver tumors, such as hilar cholangiocarcinomas, are usually associated with vascular infiltration; therefore, concomitant vascular resection can be anticipated. As stated before, the two most important aspects to extend the resection, either pre- or intraoperatively, are to consider the physical condition and performance of the patient and the tumor biology.

Schadde: Vascular resection: I have performed portal vein intra- and extrahepatic resections for hilar cholangiocarcinoma and metastatic disease. As a matter of principle I do not perform arterial resections and reconstructions in either hilar cholangiocarcinoma or CRLM, but I sometimes had to shave tumor off the artery. These are of course R1 resections except if there has been a complete response to chemotherapy. I have performed vena cava reconstructions with a 22 mm Gore-Tex ring graft, but these need to be planned ahead; that is never a matter of intraoperative decision making, especially when the hepatic veins are involved, due to veno-venous bypass and cooling. Imaging of the liver with magnetic resonance imaging as well as vascular and liver-specific contrast is so good that there is no need for intraoperative decision making here.

Extension into the duodenum is sometimes difficult to detect on imaging. I would never extend a major liver resection to a Whipple, but rather abort the procedure at the level of the exploration. The pancreatic head resection potentiates the risk of post-hepatectomy liver failure, and the liver resection potentiates the risk of Whipple complications. Both together are an explosive combination.

Part of the duodenum can on occasion be excised and closed when the liver tumor only invades the duodenum, but a Whipple is too much.

Yamamoto: When there is any possibility of R0 resection and tolerability of the patients, I usually try to expand the procedure. Vascular resection and reconstruction is usually not problematic, but I am cautious about hepatopancreatoduodenectomy due to possible serious complications.

Question 4: Where do you see the future of laparoscopic and robotic liver surgery?

Oldhafer: I firmly believe that minimally invasive surgery in hepatobiliary surgery will be the future and needs to be trained and taught extensively. In diseases in which we are not sure whether the oncological outcome will reach that of the open procedure, the development of new technology and techniques will maybe even surpass the oncological open surgery in the years to come. However, in order to improve those two important factors, minimally invasive surgery needs to be implemented in high-volume centers. Then it will be possible to gather more prospective data and answer the questions regarding oncological equality.

Schadde: I think, if hepato-pancreato-biliary centers would stay up to date with existing skills and technology in 2017, 80% of all liver resections would be done laparoscopically in 2017, which is realistic, and that is what we currently do in Winterthur. That includes of course right and left hemi-hepatectomies, extended resections, resections after PVE and non-anatomic resections in seg-

ments 7, 8, 4a and 2 and biliary procedures like Roux-en-Y hepatico-jejunostomies. That should not be the future, but should be the present.

Big tumors, hilar tumors, and tumors requiring vascular reconstruction or bypass/cold perfusion will still be performed in an open fashion in 20 years from now.

The robotic technology will evolve. Eventually, everything that we are doing laparoscopically today will be done robotically in 20 years from now. Jumping from open to robotic without collecting experience with laparoscopy first is not a good idea in my opinion. Ultimately, however, I am sure that 90% of all surgery will be done robotically, like 90% of all airplanes are nowadays landed with the help of automatic landing systems.

Yamamoto: For complex liver resections, I do not see so much an advantage of laparoscopic surgery as the promoters say, but it will surely be incorporated as a trend of times. As to robotic surgery, apart from laparoscopic surgery, it might occupy an important position for reconstructing small vessels in liver surgery.

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