Editorial Commentary

Preoperative 1-week diet can markedly decrease blood loss during hepatectomy

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Great effort has been paid to decrease blood loss during hepatectomy. Excessive blood loss and/or allogeneic blood transfusion can cause an increased risk of perioperative morbidity and mortality and may lead to a greater risk of early tumor recurrence (1-4). Hepatic steatosis or steatohepatitis is present in 30–50% of patients in the Western countries and can increase blood loss and morbidity in patients undergoing hepatectomy for colorectal liver metastases (5-7). Steatotic livers are hypertrophic and delicate and are therefore more difficult to mobilize or transect compared to nonsteatotic livers. Bariatric surgeons routinely prescribe a low-fat diet for 2 weeks before laparoscopic bariatric surgery to make it easier to retract the liver (8). To date, no studies have described whether preoperative diet can improve the difficulty of liver surgery. The author's study group previously demonstrated the effect of a 1-week low-calorie and low-fat diet on histological findings of hepatic steatosis and the surgical outcomes after liver resection in a retrospective comparative study (9).

We congratulate Dr. Richard J. Barth Jr and colleagues for their recent study entitled "Short-term preoperative diet decreases bleeding after partial hepatectomy: Results from a multi-institutional randomized controlled trial" in *Annals of Surgery* (10). This randomized controlled trial (RCT) clearly demonstrated the usefulness of preoperative diet in terms of decreasing blood loss during liver resection.

The most surprising issue is that an only 1-week diet can decrease intraoperative blood loss without any adverse events. In the diet group, an 800 kcal, a 20 g fat, and a 70 g protein diet consisting of 5 units of Optifast 800 (Nestle Nutrition, Vevey, Switzerland) plus an unlimited volume of calorie-free fluids was preoperatively administered. Ninety-three percent of the patients completed the Optifast solely diet. On the other hand, in the non-diet group, no special meal was given. In a previous RCT for bariatric surgery, a very low-calorie diet was given for 2 weeks preoperatively (8). Preoperative low-calorie diets were proven to be safe with no adverse effects on immune parameters or wound healing (8,11). To obtain better compliance, Barth *et al.* (10) applied a very low-calorie diet for only 1 (not 2) week. Recent studies reported that prehabilitation might improve the perioperative parameters, including cardiopulmonary exercise testing, quality of life, a 6-minute walk distance, and total muscle/fat ratio (12,13). It is fascinating whether exercise therapy can provide additional effects on the diet monotherapy. I am convinced that a continued postoperative diet is as important as a short-term preoperative diet. In the post-hepatectomy period, liver regeneration is poorer in patients with liver steatosis than in those without liver steatosis (14).

The patients in this study had a very high body mass index (mean, approximately 32 kg/m^2). Among the factors influencing intraoperative blood loss, the proportion of preoperative chemotherapy, liver cirrhosis, major hepatectomy, laparoscopic approach, and Pringle maneuver cases was similar in the two groups. In this RCT, background factors were fairly allocated. The indication for surgery was liver metastases in 85% of cases (colorectal 70%, miscellaneous 15%), gallbladder cancer in 12%, and cholangiocarcinoma in 3%. Fourteen patients received induction chemotherapy, thirteen received 5-fluorouracil (5-FU) and leucovorin, six received oxaliplatin, three received irinotecan, and one received imatinib. Administration of 5-FU, oxaliplatin, and irinotecan can mainly cause liver steatosis, sinusoidal obstruction, and steatohepatitis, respectively (15).

With regard to the primary endpoint, intraoperative blood loss was significantly lesser in the diet group than in the non-diet group among the overall and major hepatectomy cohorts (≥2 segments). Remarkably less hepatocyte glycogen was observed in the diet group. As every gram of glycogen binds to 4 g water, a decrease in hepatocyte glycogen may result in a marked decrease in water content and liver volume (16). This mechanism may be a reason for decreased bleeding. Although an obvious decrease in blood loss was investigated, unfortunately, it is unknown which procedure had decreased bleeding. The amount can decrease in all situations (mobilization, manipulation, and transection of the liver) and is thus one of the most interesting points to be clarified.

Secondary endpoints consisted of clinical and pathological points. The former included intraoperative liver mobility, morbidity and mortality, and length of stay, and the latter included steatosis, steatohepatitis, and hepatocyte glycogen level. A unique method to evaluate the difficulty of liver mobility is the use of a 1 to 5 Likert scale (1= easy, 5= hard). Liver mobilization and manipulation was significantly easier in the diet group than in the non-diet group. One potential mechanism for improved liver mobility is decreased steatosis. After 6 weeks of an Optifast diet, the liver fat content decreased by 43% on magnetic resonance imaging (MRI) (17). A weak point of the current study was that the investigators did not perform a pre-diet liver biopsy. Based on the previous study of pre- and post-diet liver biopsies, 6 weeks of an Optifast diet dramatically decreased the degree of steatosis from a mean of 29% to 5% (18). Computed tomography (CT) and MRI have emerged as useful diagnostic imaging modalities for noninvasive and accurate evaluation of hepatic steatosis (19). In addition, they can cover the entire liver and are widely available. CT liver-to-spleen (L/S) attenuation ratios seem to be useful in screening liver steatosis and selecting the best timing for operation. In fact, the investigators suspected that 1 week of the very low-calorie diet may be insufficient to decrease steatosis.

The second mechanism evaluated was decreased liver volume mainly due to loss of hepatocyte glycogen (16). In fact, hepatocyte glycogen was significantly less in the diet group compared with the non-diet group. Short-term calorie restriction recently has been demonstrated to decrease intrahepatic triglycerides without significant weight loss by magnetic resonance spectroscopy (20). Although this general method has not been established, hepatocyte glycogen can be reliably measured using conventional MRI scanners. Moreover, although the specific mechanism is unknown, it could be related to decreased circulating insulin and increased lipolysis seen in the early stages of fasting (21). Further, I would like to not only know the changes in liver volume but also know the functional liver volume before and after the diet. The former is assessed by conventional CT and the latter is assessed correctly by ^{99m}Tc-galactosyl human serum albumin (GSA) scintigraphy single photon emission (SPECT) CT and dynamic MRI with gadoxetate-ethoxybenzyl-diethylenetriamine penta-acetic pentaacetic acid (Gd-EOB-DTPA) (22,23). The third factor consists of liver stiffness and liver tension, which can be evaluated by vibration-controlled transient elastography (VCTE) and magnetic resonance elastography (MRE) (24,25). It has been reported that fibroScan, acoustic radiation force impulse (ARFI), and especially supersonic shear imaging postulate high diagnostic values for liver fibrosis in patients with nonalcoholic fatty liver disease. If we can noninvasively assess the changes in the parameters of fatty liver, hepatocyte glycogen storage, (functional) liver volume, and liver stiffness, a more suitable timing of the operation can be selected.

Although the postoperative complication rates were similar, the median length of stay was significantly shorter in the diet group. Considering medical economy, an inexpensive preoperative diet and shorter hospital stay are potent advantages of this therapeutic strategy. The 1-week, low-fat, low-calorie diet can make liver surgery easier and can significantly decrease intraoperative blood loss. We strongly recommend a feasible and low-cost intervention with no increased perioperative risk.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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