Goal-Directed Fluid Therapy Using Stroke Volume Variation for Resuscitation after Low Central Venous Pressure-Assisted Liver Resection: A Randomized Clinical Trial

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BACKGROUND: The optimal perioperative fluid resuscitation strategy for liver resections remains undefined. Goal-directed therapy (GDT) embodies a number of physiologic strategies to achieve an ideal fluid balance and avoid the consequences of over- or under-resuscitation.

STUDY DESIGN: In a prospective randomized trial, patients undergoing liver resection were randomized to GDT using stroke volume variation as an end point or to standard perioperative resuscitation. Primary outcomes measure was 30-day morbidity.

RESULTS: Between 2012 and 2014, one hundred and thirty-five patients were randomized (GDT: n = 69; standard perioperative resuscitation: n = 66). Median age was 57 years and 56% were male. Metastatic disease comprised 81% of patients. Overall (35% GDT vs 36% standard perioperative resuscitation; p = 0.86) and grade 3 morbidity (28% GDT vs 18% standard perioperative resuscitation; p = 0.22) were equivalent. Patients in the GDT arm received less intraoperative fluid (mean 2.0 L GDT vs 2.9 L standard perioperative resuscitation; p < 0.001). Perioperative transfusions were required in 4% (6% GDT vs 2% standard perioperative resuscitation; p = 0.37) and boluses in the postanesthesia care unit were administered to 24% (29% GDT vs 20% standard perioperative resuscitation; p = 0.23). Mortality rate was 1% (2 of 135 patients; both in GDT). On multivariable analysis, male sex, age, combined procedures, higher intraoperative fluid volume, and fluid boluses in the postanesthesia care unit were associated with higher 30-day morbidity.

CONCLUSIONS: Stroke volume variation-guided GDT is safe in patients undergoing liver resection and led to less intraoperative fluid. Although the incidence of postoperative complications was similar in both arms, lower intraoperative resuscitation volume was independently associated with decreased postoperative morbidity in the entire cohort. Future studies should target extensive resections and identify patients receiving large resuscitation volumes, as this population is more likely to benefit from this technique. (J Am Coll Surg 2015;221:591−601. © 2015 by the American College of Surgeons)

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Perioperative fluid management has been recognized as an important factor with an impact on postoperative morbidity and recovery.[1,2] An ideal balance between under- and over-resuscitation, which lead to hypoperfusion or overload and tissue edema, respectively, is difficult to achieve using standard parameters (eg, heart rate, blood pressure, central venous pressure, or urine output) that poorly estimate preload and preload responsiveness. Goal-directed fluid therapy (GDT) represents a spectrum

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Abbreviations and Acronyms

CO = cardiac output
DO_2 = oxygen delivery
GDT = goal-directed fluid therapy
LCVP = low central venous pressure
PACU = postanesthesia care unit
SV = stroke volume
SVI = stroke volume index
SVV = stroke volume variation

of strategies that aim for optimal perioperative fluid management to ensure adequate end-organ perfusion, by monitoring arterial pressure and blood flow parameters including cardiac output (CO), cardiac index (CI), stroke volume index (SVI), stroke volume variation (SVV), and oxygen delivery (DO_2). Goal-directed therapy has been shown to be useful for optimizing hemodynamic status using dynamic physiologic end points of resuscitation.[3,4] Although the ideal end point and optimization strategy remain elusive, this physiologic approach has led to improved postoperative recovery and decreased complication rates in different surgical patient populations.[1,5-8]

Improvements in operative techniques and perioperative care during the last 2 decades have led to reduced mortality after liver resection. On the other hand, perioperative morbidity remains an important issue, with as many as 40% of patients experiencing significant complications, even at high-volume centers.[9-12] In addition, postoperative morbidity has been linked with worse long-term oncologic outcomes in patients undergoing resection for cancer, which remains the most common indication for liver resection.[13-17] Although operative- and patient-specific factors are related to postoperative morbidity, there are few modifiable factors associated with the development of postoperative morbidity in these patients.

Stroke volume variation, which is the percentage of change between the maximal and minimal SVs during a period of time divided by their mean value, reflects variation in left ventricular output secondary to intrathoracic pressure changes induced by mechanical ventilation. Stroke volume variation has been shown to be an accurate predictor of fluid responsiveness, that is, the ability of the left ventricle to increase SV (and subsequently CO) in response to administration of fluids.[18]

Using SVV as a resuscitation end point after low central venous pressure (LCVP)-assisted liver resection, the present randomized controlled study evaluates the impact of GDT on the development of postoperative complications and postoperative recovery milestones in adult patients undergoing resection of primary and metastatic liver tumors.

METHODS

Trial design, participants, and intervention

This was a prospective, single-blinded, single-institution, randomized trial evaluating the potential benefit of GDT in patients undergoing hepatic resection. Patients were allocated in a 1:1 ratio to undergo resuscitation after LCVP-assisted liver resection to predetermined hemodynamic end points (GDT arm) or standard management, as reported previously.[19,20] Randomization was stratified by diagnosis (metastatic liver disease compared with primary disease, where primary disease encompassed liver cancer and extrahepatic biliary cancer including hilar cholangiocarcinoma with bile duct resection and reconstruction). All adult patients scheduled to undergo an open, elective liver resection (including those initially approached laparoscopically but converted to an open resection and those undergoing additional procedures) were assessed for eligibility and approached for participation in the preoperative clinic. Exclusion criteria included active coronary, cerebrovascular, or congestive heart disease; atrial fibrillation or flutter; clinically significant pulmonary insufficiency with a resting oxygen saturation $<90\%$; active renal dysfunction (serum creatinine >1.8 mg/dL); evidence of severe hepatic dysfunction or portal hypertension (coagulopathy, thrombocytopenia, hypoalbuminemia, ascites); pregnancy; extreme BMI (>45 or <17 kg/m^2).

Interventions

The Department of Anesthesiology and Critical Care at Memorial Sloan Kettering Cancer Center has a hepatobiliary team of anesthesiologists and nurse anesthetists who perform >90% of all scheduled hepatobiliary cases at our institution. This allows for complete homogeneity in the anesthetic technique, particularly as it pertains to LCVP. All participants in the study received anesthesia from one of these practitioners, all of whom had had earlier experience with the FloTrac sensor and SVV monitoring. All patients had continuous arterial waveform monitoring from the beginning of the operation and their SVV after induction (baseline) was recorded using the FloTrac sensor and EV1000 clinical platform (Edwards Lifesciences). Stroke volume variation provides a measure of the patient's intravascular volume and fluid responsiveness. Specifically, a large SVV (>15%) predicts the ability of the left ventricle to increase the SV and CO in response to administration of IV fluid.

The details of the LCVP technique have been published previously.[19-21] Briefly, LCVP consists of 2 phases: a prehepatic resection that takes advantage of strict fluid restriction (overnight fluid replacement is withheld and