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Perioperative factors and outcome associated with massive blood loss during major liver resections

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Background

Mortality and morbidity rates from major liver resections have decreased sharply over the past 25 years. This improvement is due to a better understanding of liver anatomy and the introduction of new operative techniques, but also to improved anesthetic perioperative support. Certain cases are still associated with voluminous blood loss. These patients may be at higher risk for postoperative problems and increased length of stay (LOS) in hospital.

Methods

We have retrospectively reviewed 115 patients undergoing major hepatic resections (three or more anatomic segments) with respect to operative blood loss (EBL). Those with an EBL $\geq$ 5000 ml (group 1; $n = 39$) were compared to those with an EBL $\leq$ 2000 ml (group 2; $n = 42$). Type of resection, age ($\geq$70 years), tumor size, mortality, morbidity, and hospital LOS were examined. Operative reports were examined for any explanation for excessive blood loss. Anesthetic support often entailed the use of a rapid infusion system.

Results

The EBL was 7692 $\pm$ 3848 ml for group 1 and 1359 $\pm$ 514 ml for group 2. Primary liver tumors were resected in 20 patients in group 1 and in 18 patients in group 2. The remaining resections were for metastatic tumors, primarily colorectal in origin. In group 1, 13/39 patients had a left hepatectomy compared to 10/42 patients in group 2 ($p = 0.34$). The overall mortality was 5/115. Four deaths occurred in group 1 and one in group 2 ($p = 0.16$). Two deaths in group 1 were intra-operative (hemorrhage, air embolism). There was no difference in the number of patients with complications, 12/39 in group 1 and 8/42 in group 2 ($p = 0.22$). Two patients in group 1 required re-operation for bleeding; there were none in group 2. Largest tumor size did not differ between the two groups ($p = 0.08$), nor did the proportion of patients aged 70 years or older ($p = 0.06$). There was no difference in hospital LOS (10.54 $\pm$ 6.1 vs 8.90 $\pm$ 4.7 days, $p = 0.21$). Review of operative notes in group 1 indicated no unusual problems in 13/39, large tumors or proximity to the inferior vena cava in 10/39, and bleeding from the middle hepatic vein in 7/39. Three patients in group 1 required total vascular exclusion for tumor removal; there were none in group 2.

Discussion

Massive EBL during major liver resection seems to be provoked by tumors near the inferior vena cava or major hepatic veins, or injury to the middle hepatic vein during operation, and not by patient age, tumor size alone, or type of hepatectomy. However, by avoiding prolonged hypotension and hypothermia with the use of rapid infusion devices, the perioperative course of these patients does not differ from those with much less EBL.

Keywords

liver surgery, blood loss, liver resection, liver tumors

The great problem in dealing with resection of the liver has always been the control of hemorrhage, not only at the time of operation, but permanently

G. Grey Turner 1923

In 1899 William Keen [1] reported a successful resection of the left lobe (probably left lateral segments) of the liver for a large malignant neoplasm. He wrote: 'the hemorrhage was not very severe, excepting when I burnt into some larger veins'. These were controlled by finger pressure and suture ligature. Blood loss was estimated at 300 ml although Keen confessed 'I was in constant dread lest alarming and possibly uncontrollable hemorrhage might occur'. The patient made an uneventful recovery. In 1923 Grey Turner [2] removed a large tumor occupying over one-half of the right liver. With the aid of

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large chromic catgut sutures and an intestinal clamp he was able to resect the neoplasm but not without substantial blood loss. He commented:

> '… in the aggregate there must have been a considerable blood loss. Towards the end of the operation, the blood-pressure had fallen considerably, and there were other evidences of grave shock which caused us anxiety.'

How many liver surgeons since then have had similar angst in the course of a difficult hepatectomy! Following the operation and resuscitation there were no further complications and the patient was discharged 24 days later.

Despite advances in our understanding of liver anatomy and refinements in operative technique, to this day blood loss remains a major obstacle in hepatic resection. Current reports still document mean blood losses of over 3 L [3], and a number of patients requiring over 20 units of blood transfused [4]. Blood loss is a major cause of intra-operative death [5] and has been linked to higher postoperative mortality and morbidity rates [6, 7]. We have previously noted an average blood loss during major hepatic resections which approximated 3 L even with anatomic resections and careful inflow (and, often, outflow) control [8]. Through this retrospective review, we have sought to identify factors responsible for massive blood loss during major hepatectomy and to determine the effect on postoperative recovery.

Materials and methods

All patients who underwent a major hepatic resection (three or more contiguous segments) by the senior author between 1979 and 2002 were reviewed. Operative records were examined to assess intra-operative blood loss. Intra-operative blood loss was determined by the attending anesthesiologists after examination of canister (aspirated) blood and blood-soaked laparotomy pads. All irrigation fluids were, of course, subtracted from the total. Assessed blood loss of $\geq$5 L was determined to be 'massive blood loss', as this generally represents replacement of one blood volume. These patients were designated group 1. As a comparison group, patients who lost $\leq$2000 ml of blood during operation were also examined. These patients were designated group 2. Patient and tumor factors thought to contribute to excessive blood loss were: occurrence of intra-operative hypotension, type of resection, age, tumor size, tumor location (proximity to major vessels). Outcome measures examined were death, complications, and hospital length of stay (LOS). Individual dictated operative reports were reviewed to look for explanations for excessive blood loss.

Measures used to control bleeding varied during the 23-year time-span. Control of inflow and, often, outflow was routinely done before parenchymal dissection, particularly for right hepatectomies. Intermittent portal clamping was used on selected patients but not routinely. Total vascular exclusion was used on three occasions. Over the past 14 years the ultrasonic dissector was used to facilitate parenchymal dissection. More recently, the Harmonic Scalpel™ was used during this part of the operation as well. Blood products were administered via a rapid infusion system (R.I.S.™ Rapid Infusion System, Haemonetics®), which can deliver up to 1500 ml of blood per minute at supernormal (40 °C) temperatures depending on the size of infusion catheter. No attempt was made to induce hypotension to reduce bleeding. Routine intra-operative ultrasonography of the liver was performed to identify occult lesions not seen on preoperative imaging and to define intraparenchymal vascular anatomy.

Statistical analysis was performed using the student's t-test, Pearson's χ^2 determination, or Fisher's exact test with significance determined at the $p < 0.05$ level. Values are expressed as mean $\pm$ standard deviation.

Results

During the study period 115 patients underwent a major hepatectomy. Overall mortality was 5/115 patients (4%). There were 39 patients with an EBL $\geq$ 5000 ml (group 1) and 42 patients with an EBL $\leq$ 2000 ml (group 2). Mean EBL for group 1 was 7692 $\pm$ 3848 ml and for group 2 it was 1359 $\pm$ 514 ml. Primary liver tumors, benign or malignant, were resected in 20 patients in group 1 and 18 patients in group 2. The remaining resections were for metastatic tumors, primarily of colorectal origin. A left hepatectomy was performed in 13/39 patients (33%) in group 1 and 10/42 patients (24%) in group 2 ($p = 0.34$). Three patients in group 1 required total vascular exclusion for removal of tumors; there were no patients in group 2 who needed this maneuver.

All five deaths occurred in one of these two groups (no deaths occurred in the 34 patients with an EBL between 2000 and 5000 ml). Four deaths occurred in group 1 and were due to intra-operative hemorrhage (1), intraoperative air embolism (1), and postoperative liver failure (2). One patient in group 2 died of a postoperative myocardial infarction. The difference was not statistically significant ($p = 0.16$). Twenty patients suffered one or more postoperative complications, 12 in group 1 and eight in group 2 ($p = 0.22$). Re-operation was performed for bleeding in two patients in group 1, but none in group 2. The number of patients aged $\geq$70 years was no different between the two groups (4/34 in group 1, 11/42 in group 2, $p = 0.06$). Largest tumor size averaged 9.74 ± 7.82 cm in group 1 and 7.17 ± 3.67 cm in group 2 ($p = 0.08$). Hospital LOS was 10.54 ± 6.1 days in group 1 and 8.90 ± 4.7 days in group 2 ($p = 0.21$). Inspection of operative notes for patients in group 1 indicated no unusual problems in 13/39 patients, large tumors or proximity to the inferior vena cava (IVC) in 10/39 patients, and bleeding from the middle hepatic vein (MHV) in 7/39 patients. Operative notes of patients in group 2 detailed an uneventful operation, as expected.

Discussion

Advances in hepatic surgery have made operations on the liver safer and less likely to cause excessive hemorrhage. Pringle, in his published report of 1908 [9], described a technique of inflow occlusion by pinching the portal triad, which seemed to reduce bleeding in cases of trauma. He wrote: '… the method acted admirably, perfect control of the bleeding areas of the liver was obtained and a clear field for operating'. The lobar arrangement of intrahepatic vessels was proposed by Cantlie [10] and segmental anatomy championed by Couinaud [11] that defined avascular planes along which hepatectomy could more safely proceed. In fact, the anatomist JE Healey, writing in 1954, felt that the failure to improve operative mortality with liver resection was due primarily to an unawareness of the intrahepatic course and distribution of larger vascular and biliary channels [12].

Quattlebaum and Quattlebaum [13], in 1959, outlined the technical principles of hepatic resection acknowledging that 'control of hemorrhage gives greatest concern'. They advocated adequate exposure, complete mobilization of the liver, dissection of the porta hepatis with individual ligation of inflow structures, division of the liver substance along anatomic planes with a blunt instrument rather than sharply, ligation and division of larger vessels and suture ligation of smaller structures, and adequate drainage. Nevertheless, they pointed out that 'adequate blood replacement throughout the operative procedure is mandatory and may require 4,000 to 6,000 cc'. Despite these advances, situations exist in which copious bleeding occurs. Published series of hepatic resections still contain anecdotal reference to intra-operative exsanguination [4, 14, 15]. In Foster and Berman's 1974 Liver Tumor Survey [16], 15 of 621 patients died in the operating room of uncontrollable bleeding. Moreover, operative blood loss has been identified as a predictor of postoperative problems. Didolkar and colleagues [17] found that the EBL in nonsurvivors following partial hepatectomy was significantly higher (9700 ml vs 4933 ml) than in survivors. Ekberg and co-authors [4] noted that patients with postoperative complications had a larger amount of bleeding during operation than those who had no complications. Similarly, Sitzman and Greene [3] found that EBL tended to be higher in patients with postoperative complications (3983 ml) than in those without (2529 ml).

We have identified two groups of patients, those whose intraoperative EBL was modest ($\leq$2000 ml) and those whose EBL was 'massive' ($\geq$5000 ml). However, in a comparative evaluation, in contrast to others, we have failed to detect obvious statistically significant differences between the two groups including preoperative factors (age, type of hepatectomy – right or left, size of tumor) and postoperative outcome: mortality, complications, and hospital LOS. Rather, location of tumors may have played a more significant role. In reviewing operative reports, mention was often made of tumors near the origins of the major hepatic veins or, anecdotally, large tumors that impaired adequate mobilization of the liver for controlled resection. Very likely, even in these instances, avoidance of serious intra-operative or postoperative problems might have been attributed to the ability of the anesthesiologists to rapidly infuse large volumes of warmed blood and other volume expanders via a rapid infusion system. Maintaining perfusion (and avoiding metabolic acidosis) and maintaining euthermia therefore provided protection against the lethal effects of acidosis, hypothermia, and coagulopathy found in profound and prolonged hemorrhagic shock. This gain must be balanced against the dangers of over-resuscitation, which results in bowel edema and can shrink the operative field, making exposure of the liver difficult.

An important component of intra-operative blood loss has been controlling hepatic inflow. Liver resections using the Pringle maneuver produce a decrease in portal and hepatic artery bleeding and better visualization of the operative field. Hepatectomies employing hepatic pedicle clamping have resulted in fewer transfused cases and fewer transfusions per case [18]. In fact, some surgeons [19] have found the Pringle maneuver superior to total vascular isolation (inflow *and* outflow control) in lessening blood loss. Other strategies to reduce blood loss include maintaining low central venous pressure, the use of aprotinin (a serine protease inhibitor), and the use of the ultrasonic dissector [20].

Bleeding from the middle hepatic vein, particularly when tumors are located near its origin, can be voluminous. This was a problem mentioned in a number of patients experiencing massive blood loss in our series. Identification and mapping of the vein by intraoperative ultrasonography is helpful. Additionally, encirclement of the vein extraparenchymally before liver dissection allows for later control should bleeding be encountered. There may even be a role for total vascular isolation in these cases if sudden hemorrhage obscures the operative field as these tumors are approached. Outflow control may also lessen the chance for air embolism that can occur at low central venous pressures.

For large tumors in which mobilization is difficult and even hazardous, the anterior hepatectomy has been described [21, 22]. This technique is performed without mobilization of the right hemi-liver and with intrahepatic control of the hepatic pedicle and major hepatic veins. Once again, an important component of this method is careful identification of the right and middle hepatic veins by intra-operative ultrasonography. This approach minimizes the risk of tumor spillage and bleeding from mobilization of bulky right-sided tumors.

In summary, when performing liver resections basic tenets should be kept in mind, namely, adequate exposure and mobilization, familiarity with intraparenchymal anatomy, and inflow (and, where possible, outflow) control. Nevertheless, when blood loss is expected, in patients with large tumors or tumors near the origins of the major hepatic veins, the ability to infuse warmed blood rapidly may be critical. Not every liver resection will require this technology, but with it blood loss can be quickly replaced, intra-operative hypotension and hypothermia minimized, and, by our findings, outcome unaffected. We have demonstrated no difference in mortality, complications, or LOS with excess blood loss despite what has previously been reported, but we attribute this to our ability to replace shed blood quickly and avoid the pitfalls of prolonged hypotension and hypothermia.

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