

# Anesthetic Management of Hepatectomy in a Jehovah's Witness Patient with Lynch Syndrome

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## Abstract

The anesthetic management for hepatic resection is a challenging undertaking associated with the potential for major surgical blood loss, often accompanied with hemodynamic instability. That challenge is made more complex and challenging when a patient presents with a genetic predisposition for malignancy and deep-seated religious beliefs that negate the possibility of blood transfusions. This literature review will explore the major considerations associated with a devout Jehovah's Witness patient presenting for hepatectomy carrying a genetic diagnosis of Lynch Syndrome, a unique set of co-presenting circumstances. The review will examine perianesthetic approaches for management and minimization of surgical blood loss during hepatectomy in a patient who refuses blood transfusion. The pathophysiology and implications of Lynch Syndrome, a genetic predisposition to malignancy, will be explored. Implications and impacts of the religious beliefs of Jehovah Witness patients will be examined, especially in a situation that is likely to necessitate blood replacement therapy.

## CASE PRESENTATION

A mid-thirties, devout Jehovah's Witness patient presented for right hepatectomy for metastatic colon cancer, genetically confirmed to be consistent with Lynch syndrome. Diagnosed months earlier with colon cancer, the patient had previously undergone uncomplicated left hemicolectomy for splenic flexure adenocarcinoma and multiple chemotherapeutic cycles of capecitabine in combination with oxaliplatin. Given the patient's young age and response to the chemotherapeutic regimen, potentially curative hepatic resection for metastatic hepatic masses was planned. The unique co-presentation of Lynch Syndrome, Jehovah's Witness beliefs, and presentation for hepatectomy necessitated a review of the literature prior to anesthetic management to ascertain optimal evidence-based modalities for incorporation into the anesthetic plan of care. The purpose of this manuscript is to examine the perianesthetic management techniques for minimizing surgical blood loss during hepatectomy, the pathophysiology and clinical implications associated with Lynch Syndrome, and the impact of religious beliefs associated with Jehovah's Witness patients, especially in a situation that is likely to produce blood loss necessitating blood replacement therapy.

## LYNCH SYNDROME

Colorectal cancer affects over 140,000 patients in the

United States (US) each year and is associated with approximately 50,000 deaths yearly.<sup>1,2</sup> While most colorectal cancers have no readily identifiable cause, an estimated 30% of colorectal cancers are potentially associated with genetic predisposition.<sup>1,2</sup> Lynch syndrome, also known as hereditary nonpolyposis colorectal cancer, is a highly penetrant, autosomal-dominant cancer-susceptibility syndrome that accounts for approximately 3% of all colorectal cancers worldwide.<sup>2,3</sup>

Lynch syndrome is considered the most common inherited colorectal cancer syndrome and arises from germline mutations in one or more DNA mismatch repair (MMR) genes, including, but not limited to, MLH1 (Mut L homologue), MSH2 and MSH6 (Mut S homologues), and PMS2 (Postmeiotic segregation, a Mut L homologue).<sup>1,2</sup> These genes encode proteins that are intricately connected to MMR.<sup>2,3</sup> MMR maintains genetic integrity by correcting nucleotide mismatches that escape DNA polymerase editing.<sup>1,2</sup> Nucleotide single-base mismatches and insertion-deletion loops formed during DNA replication can alter cell growth regulation and incite neoplastic development.<sup>2</sup> Individuals with intact MMR processes utilize proteins to target nucleotide base mismatches and erroneously copied DNA sequences for repair.<sup>2</sup> The MSH2-MSH6 genes encode proteins that recognize and bind single nucleotide mispairs while the MLH1-PMS2 genes encode

proteins that bind to the identified nucleotide mispairings for base removal from the DNA strand, enabling resynthesis of DNA with appropriate nucleotide pairings.<sup>1,2</sup> The lifetime risk of colorectal cancer has been cited as being as high as 80% in these gene mutation carriers, but risk is variable dependent upon which MMR gene is affected.<sup>2</sup> As such, identification of these patients and family members could afford early surveillance, prophylactic therapies, and predictive genetic testing.<sup>2</sup> Annual incidence of Lynch syndrome is reported to be 4100 individuals in the US, or 1 in every 35 patients with newly diagnosed colorectal cancer.<sup>2</sup>

Cardinal features of Lynch syndrome include an autosomal dominant inheritance cancer pattern in the family pedigree, earlier onset of colorectal cancer than the general population (mean age of onset is 45 years), accelerated carcinogenesis, high risk of recurrence of colorectal cancer and a significantly increased risk for malignancy at extracolonic sites, such as hepatobiliary tract, pancreas, brain, ovary, urogenital tract and endometrium (with a lifetime risk of endometrial cancer reported as high as 40-60%).<sup>2,3</sup> Colorectal cancers in Lynch syndrome usually affect the proximal (right) colon and characteristically have reported a high recurrence rate near 30%.<sup>1,2,3</sup> Colorectal tumors associated with Lynch syndrome are mucinous, poorly differentiated and display a high level of microsatellite instability.<sup>1,2</sup>

Anesthetic implications associated with Lynch Syndrome are not clearly elucidated in the literature. However, it is incumbent upon the nurse anesthetist to recognize the impact that concurrently (or previously) utilized chemotherapeutic and radiation therapies will have upon the anesthetic plan of care. Some of these impacts are minimal; others can be potentially problematic, such as the pulmonary toxicity associated with bleomycin and cardiotoxicity associated with the anthracyclines (daunorubicin and doxorubicin-analogues, such as doxorubicin). With respect to practicing primary care and specialty advanced nurse practitioners, current recommendations for management of colorectal carcinoma in Lynch syndrome include early identification of individuals and heightened surveillance in patients at risk, including yearly colonoscopy beginning at age 20.<sup>2</sup> The clinical progression of adenomatous polyps, the precursor lesion of colorectal cancer, is accelerated toward malignancy from the typical 8-10 year timeframe seen in sporadic cases of colorectal cancer to 2-3 years in Lynch syndrome, necessitating more intensive surveillance and increased

frequency of screenings.<sup>1,3</sup> Advanced molecular testing and DNA mutational analyses are available.<sup>2</sup> Individualized screenings for the other associated cancers of Lynch syndrome are dependent on the familial history.<sup>2</sup> Genetic counseling is advisable.<sup>3</sup>

### **JEHOVAH'S WITNESS PATIENT**

Jehovah's Witnesses are an international religious organization originating from the biblical study lead by Charles Taze Russell in the early 1870's.<sup>4,5</sup> Followers subscribe to a strict literal interpretation of the Bible, such that non-adherence to biblical commands eliminates the possibility of eternal life.<sup>4</sup> While the exact number of Jehovah's Witnesses is unknown, the official website of the Jehovah's Witnesses indicates that 19 million people have attend Jehovah Witnesses-related conventions and meetings worldwide.<sup>6</sup> Jehovah's Witnesses have members in over 200 countries with over 15,000 congregations in the US, Canada and the Caribbean.<sup>6</sup> Members of the group believe that God's name is Jehovah and pledge allegiance to God's Kingdom, remaining neutral politically without allegiance to, or participation in, any civic government.<sup>4,7</sup>

#### **The blood ban and refusal of transfusions**

In 1945, the governing body of the Jehovah's Witness, the Watchtower Society, prohibited blood transfusions, based on 4 Biblical passages: Genesis 9:4, Leviticus 17:10, Deuteronomy 12:23 and Acts 15:28-29.<sup>4,5,7</sup> These passages describe the sacred nature blood and a prohibition of blood consumption,<sup>5,7</sup> which was literally interpreted to prohibit acceptance of blood that had been "lost" from the body.<sup>8</sup> Blood transfusions were viewed as a "taking in blood to sustain the body" and should blood be transfused, there is elimination of the promise of eternal life - a completely unacceptable prospect for the majority of members of this highly devout group.<sup>7,8</sup> This blood ban included allogenic whole blood and blood components as well as autologous blood that was "separated" from the patient's body.<sup>5,7</sup> By 1961, acceptance of blood transfusions became grounds for member expulsion from the society, with actual societal shunning of members who accepted blood transfusions.<sup>8</sup> Changes to the blood ban guidelines evolved in 2004 with certain blood fractionates (such as albumin, erythropoietin and certain factor concentrates) becoming more acceptable.<sup>5</sup> However, the ultimate decision for acceptance and utilization during medical situations is left up to the discretion and conscience of the individual member.<sup>4,5,8</sup> Variability in observation of

the blood ban is noted among members of the group.<sup>4,5</sup> Certain members willingly accept certain blood fractionates while others will adamantly refuse any blood component under any and all circumstances.<sup>4</sup>

These fundamental beliefs present great dilemmas for the nurse anesthetist managing the Jehovah's Witness patient, especially during major, complicated surgical procedures. The clinical consequences of transfusion refusal, in acute massive blood loss, are self-evident. While the majority of surgical procedures carry little risk for the need of blood transfusion, larger and more complex surgical procedures, such as hepatectomy, are quite likely to necessitate blood component therapy. Approaching these patients prior to major surgical procedures requires a straight-forward, honest, non-judgmental approach. The patient should be informed of the risks of blood component refusal, to include an open discussion about the potential for death. Additionally, Jehovah's Witness patients, when presenting for major surgical procedures where blood transfusions are likely to be needed, may occasionally be accompanied by a spiritual advisor, often an elder of the congregation.<sup>4,5</sup> Discussion regarding the risks associated with refusal of blood components should occur with the patient confidentially as some patients may be reticent to openly consent to blood component therapy in the presence of the spiritual advisor.<sup>4,5</sup> Regardless of the decision of the patient, the nurse anesthetist must accept the patient's right to self-determination and maintain the confidentiality of discussions and patient decisions.<sup>4</sup>

Several studies have demonstrated no increase in morbidity or mortality associated with Jehovah's Witness refusal of transfusion therapy.<sup>4</sup> However, it is reported that an estimated 1000 Jehovah's Witnesses may experience premature death after abstaining from blood component therapy.<sup>8</sup> In the healthy patient, several chronic adaptive mechanisms to anemia – including increased cardiac output and enhanced tissue oxygen extraction – are activated.<sup>8</sup> Acute anemia related to ongoing or uncontrolled hemorrhage, however, is a more critical prospect with limited compensatory physiologic mechanisms available. While the terminal human hemoglobin level remains unknown, some sources indicate that the terminal hemoglobin level may be as low as 3 grams per deciliter (g/dL).<sup>4,8</sup> Case reports demonstrating the survival of Jehovah's Witnesses with operative hemoglobin levels and postoperative hemoglobin levels of 2.2 g/dL and 1.4 g/dL, respectively, can be found.<sup>8</sup>

### **ANESTHETIC IMPLICATIONS OF HEPATIC RESECTION**

Hepatic resections for metastatic disease carry a multitude of anesthetic implications. While this section will describe the more profound anesthetic implications of hepatic resections, particularly methods, techniques, and adjuncts to minimize blood loss, a complete description of all anesthetic implications for hepatic resection is beyond the scope of this manuscript.

Since the liver is divided into 8 Couinaud segments, resection of 3 or more segments is defined as a major hepatic resection.<sup>9</sup> Hepatic resections are performed for benign and malignant hepatic tumors, either primary hepatic tumors or metastatic lesions.<sup>9</sup> One source estimates that there are approximately 11,000 hepatic resections performed in the US annually.<sup>9</sup> Fifty to sixty percent of colorectal cancer patients develop hepatic metastases with approximately 20-30% of these metastases confined to the liver, making these metastatic lesions suitable for surgical resection.<sup>9</sup> Hepatic resection is considered the curative approach for colorectal hepatic metastases, providing a 5-year survival rate in excess of 40%.<sup>9</sup>

With regard to anesthetic management of hepatic resection, no anesthetic technique has been proven to be superior to another.<sup>10,11</sup> General anesthesia is generally the technique of choice, even though hepatic metabolism and clearance of drugs can be depressed following resection.<sup>10,11</sup> No evidence-based consensus can be found that suggests any particular anesthetic agent is better suited for management of the hepatic resection.<sup>11</sup> All of the volatile inhalational anesthetics have been utilized successfully in hepatic resections. While a theoretical concern with sevoflurane use does exist due to its partial hepatic metabolism, one study demonstrated that sevoflurane potentially provides ischemic preconditioning before inflow vascular occlusion techniques (the so-called Pringle maneuver), thereby limiting postoperative liver injury.<sup>11,12</sup> While cisatracurium and atracurium would likely be considered the ideal neuromuscular relaxants due to their unique non-hepatic metabolism, all muscle relaxants have been utilized with success in hepatic resection.<sup>11</sup> To reduce the risk of increased duration of action secondary to impaired metabolism of neuromuscular relaxants, the use of muscle relaxants should be guided, as is standard practice, by peripheral neuromuscular junction monitoring.

While invasive hemodynamic monitoring modalities are

determined based on underlying patient comorbidities and the extent of resection, adequate vascular access must be obtained for rapid fluid and blood administration with invasive arterial blood pressure monitoring almost universally indicated.<sup>10</sup> The choice of fluid replacement for surgical blood loss is a more complex decision. No clear evidence supports the utilization of either colloids over crystalloids or crystalloids over colloids for general surgical fluid resuscitation, much less complex surgical procedures such as hepatectomy. While the literature is often conflicting about whether colloid use, such as albumin and hydroxyethyl starches, in fluid resuscitation may impact mortality, the majority of these studies are in critically ill patients with varied comorbidities in intensive care unit (ICU) settings.<sup>13,14,15,16</sup> Both colloids and crystalloids possess benefits while posing potential risks. Aggressive crystalloid replacement may induce hemodilution and hepatic congestion, which could be especially problematic in the described case. Colloids do have beneficial properties, such as the maintenance of plasma oncotic pressure. However, hydroxyethyl starches have often been implicated in coagulopathy and hepatic and renal dysfunction, especially in ICU studies.<sup>15,17</sup>

Clearly, no one fluid is superior to the other for volume replacement. As such, a limited and balanced use of both crystalloids and colloids could be beneficial in fluid management during hepatic resection, as long as replacement was guided and/or targeted. In the management of the presented case, a combination of crystalloids, low molecular weight hydroxyethyl starch, and albumin was utilized in a goal-directed fluid management approach. Fluids were titrated to maintain euvolemia with a targeted central venous pressure (CVP) of less than 5 mmHg with continuous intraoperative stroke volume variation (SVV) monitoring utilized to guide fluid resuscitation. A lower molecular weight starch, Voluven® - 6% hydroxyethyl starch 130/0.4 in 0.9% sodium chloride, was selected as it has a higher maximum daily dose of 50 mL/kg/day<sup>18</sup> than does conventional 6% hetastarch.

### **Management of blood loss**

In hepatic resections, bleeding results not only from the hepatic artery and hepatic/portal vein but also from liver mobilization, dissection of biliary structures, parenchymal transection, and the inferior vena cava.<sup>11,19</sup> Major hepatic resections may result in significant blood loss and a need for transfusion in approximately 30% of patients.<sup>11</sup> Large intraoperative blood loss correlates with increased

postoperative complications and decreased long-term survival rates.<sup>20</sup> Bleeding in hepatic resections is the major intraoperative complication and cause of death. This concern is further elevated in a patient refusing transfusion as operative mortality in such situations approaches 7.1% for patients with hemoglobin levels greater than 10 g/dL versus 61.5% for patients with hemoglobin levels less than 6 g/dL.<sup>11</sup>

Blood loss can also be reduced by utilization of various surgical resection instrumentation and technologies (argon beam coagulation, water jet dissection, radiofrequency coagulation, and lasers) and other techniques that are outside the control of the nurse anesthetist and beyond the scope of this manuscript.<sup>20</sup> However, the utilization of vascular occlusion techniques and hemodynamic management also reduce the amount of surgical hemorrhage during resection. While vascular occlusion is also outside of the control of the nurse anesthetist, these techniques do carry relevant anesthetic implications that will be discussed later in this manuscript. Maintaining certain hemodynamic parameters, as will be discussed, is also utilized to reduce intraoperative blood loss.

### **Blood conservation strategies**

Traditionally, blood conservation strategies have been employed to various extents in hepatic resections. Among the more prominent strategies are acute normovolemic hemodilution, and intraoperative cell salvage techniques.

#### **Acute normovolemic hemodilution**

In acute normovolemic hemodilution, a quantity of whole blood is removed with the lost volume replaced with crystalloids and/or colloids.<sup>4,5,19</sup> This technique reduces the red blood cell mass lost during acute surgical hemorrhage while maintaining intravascular volume.<sup>4,5,19</sup> An additional positive aspect of this technique is improvement of microcirculation and tissue perfusion.<sup>5,19</sup> Upon attainment of surgical hemostasis, or need for blood cell replacement, the patient receives the withdrawn autologous whole blood containing all essential clotting factors and viable platelets.<sup>4,19</sup> Additional efforts may need to be undertaken to maintain continuity of phlebectomized blood with systemic circulation (using a closed loop circuit) upon employment of this modality, as required by certain devout Jehovah's Witness sects.<sup>4,5</sup>

#### **Cell salvage techniques**

Intraoperative cell salvage involves the filtering, washing, and concentration of shed surgical blood (removed via surgical site evacuation) into a red blood cell suspension with a hematocrit near 60%, which can then be transfused.<sup>5,19</sup> Cell salvage techniques have been life-saving in cases of massive surgical blood loss.<sup>19</sup> Since the shed blood is autologous in nature, cell salvage techniques have been demonstrated, and utilized, to decrease the amount and necessity of transfused allogenic blood.<sup>5,19</sup> Historically, only 2 contraindications to the use of cell salvage techniques exist - in procedures where contamination or infection may occur and in cases involving malignancy.<sup>5,19</sup> While the former contraindication is easily understood since the reinfusion of potentially contaminated surgical blood may lead to bacteremia/septicemia, the latter contraindication is more problematic. The concern with use of this modality in malignancy is that blood shed from a site of malignancy may potentially contain malignant cells that could be systematically reinfused and driven to distant sites inducing metastatic spread. A recent meta-analysis calls this dictum into question.<sup>21</sup> Evidence suggests that the use of a leukocyte-depletion (leukocyte-reduction) filter, during transfusion of the "salvaged" red cell suspension, effectively eliminates any active malignant tumor cells.<sup>21,22</sup> Additionally, recent studies have not found associations with cell salvage techniques and tumor recrudescence, while noting that patients receiving cell salvage autologous blood demonstrate improved survival compared to patients receiving allogenic blood transfusions.<sup>21,22</sup> While the studies called for more robust clinical trials, the development of potentially catastrophic intraoperative hemorrhage, especially in clinical situations described earlier in this manuscript, can trigger the urgent necessity of cell salvage utilization. Again, special efforts and equipment may be required to maintain continuity of shed blood with systemic circulation (using closed loop circuitry) upon employment of this modality for certain Jehovah's Witness sects.<sup>4,5</sup> Should cell salvage become necessary, leukocyte-depletion filters should be utilized to minimize tumor cell contamination of re-infused shed blood as described in the literature.<sup>19,21,22</sup>

It should be noted that a previously cited systematic review indicated that neither hemodilution nor cell salvage improved mortality and morbidity in hepatic resections, although hemodilution was useful in decreasing transfusion requirements.<sup>9</sup> However, none of the included trials in that systematic review were sufficiently powered to detect differences in mortality and morbidity from standard control care.<sup>9</sup>

Adjuncts to reduce blood loss

Additional non-pharmacologic and pharmacologic adjuncts are often incorporated into the anesthetic plan of care for the major hepatic resection patient. Maintenance of normothermia during the perioperative period, known to assist in reducing intraoperative blood loss by protecting platelet function, is an example of a nonpharmacologic adjunctive mechanism utilized perioperatively.<sup>19</sup> Active forced air warming equipment and active warming of intravenous fluids are often the mainstays of this approach.<sup>23</sup> Detection and aggressive management of acidosis and electrolyte imbalances, particularly hypocalcemia, during active hemorrhage also assists in reducing additional blood loss related to hemostatic disruptions, well known to be produced by acidemia and hypocalcemia.

Pharmacologic modalities

Administration of pharmacologic adjuncts such as antifibrinolytics (aprotinin or tranexamic acid) and desmopressin have also been utilized to reduce operative blood loss, although substantial complications are occasionally associated with these adjunctive agents.<sup>4,5,8,11,19,20</sup> Safety concerns, such as prothrombotic phenomenon, with the use of antifibrinolytics, do exist. Hepatic resection may produce states of hyperfibrinolysis.<sup>20</sup> Antifibrinolytic agents, in particular aprotinin and tranexamic acid, have been proposed and utilized to reduce intraoperative blood loss in hepatectomy and hepatic transplantation.<sup>5,8,11,19,20,23</sup> In 2008, aprotinin, a serine protease inhibitor, was removed from the market by the manufacturer in response to concerns of increased mortality related to renal and cardiac sequelae.<sup>5,8</sup> Currently, the only antifibrinolytic agents available for clinical use are the lysine analogues, aminocaproic acid and tranexamic acid.<sup>5,8,20</sup> A 2006 study by Wu et al. demonstrated that tranexamic acid reduced the amount of perioperative blood loss and blood transfusion requirements in hepatic resections.<sup>24</sup> Tranexamic acid (10 milligrams per kilogram [mg/kg]) can be considered and administered intravenously after induction of anesthesia (prior to surgical start) over a 30 minute time period.<sup>24</sup> While the dosing can be repeated in 3 to 6 hours and continued in the postoperative phase, consideration of additional doses of tranexamic acid can be guided by thromboelastography to minimize the possibility of serious prothrombotic effects.<sup>24</sup> As discussed, safety concerns with antifibrinolytics must be considered; however, the circumstances described in the case

presentation justify the consideration and appropriate utilization of antifibrinolytic agents.

The utilization of recombinant factor VIIa (rFVIIa) in the management of life-threatening surgical and traumatic hemorrhage is well-described in the literature.<sup>4,8</sup> rFVIIa binds to both exposed tissue factor and platelets at the site of vascular injury and induces a thrombin burst.<sup>4,23,25</sup> Thrombin plays a major role in the conversion of fibrinogen to fibrin, a necessary product for stable clot formation.<sup>23,25,26</sup> rFVIIa is cloned, recombinant human coagulation factor VII protein derived in baby hamster kidney cells and cultured in calf serum. No human proteins or serum are utilized in its manufacture, often making it acceptable to populations averse to blood component therapy. Randomized controlled trials, using various dosages of rFVIIa, exploring its safety and efficacy in reducing blood transfusion requirements in hepatectomy have met with mixed results.<sup>25,27</sup> While no overt safety issues were identified, the use of recombinant factor VIIa has not been statistically demonstrated to reduce transfusion requirements in hepatectomy patients.<sup>25,27</sup> However, a trend toward reduction in the number of patients requiring blood transfusion was noted.<sup>26</sup> The potential risk of rFVIIa inducing catastrophic arterial thrombosis and its use must be carefully considered. However, rFVIIa may be considered in situations where life-threatening hemorrhage develops and conventional approaches, namely, blood component transfusion, for management of hemorrhage/coagulopathy are limited, unavailable, or unacceptable.

### **Inflow vascular occlusion**

Surgical techniques have evolved to limit blood flow through the liver during parenchymal resection in an effort to minimize hemorrhage. While a number of surgical techniques can be utilized, including some techniques that produce total vascular exclusion of the liver (thus isolating the liver from systemic circulation), inflow vascular occlusion techniques are the more commonly utilized in hepatic resections.<sup>11,20</sup> Inflow vascular occlusion techniques, such as the Pringle maneuver, limit antegrade hepatic blood flow through clamping of the portal triad in the hepato-duodenal ligament.<sup>20</sup> During the Pringle maneuver, the hepatoduodenal ligament is ensnared with a surgical rubber tape with a vascular clamp placed in such a fashion as to tension the tape until perfusion through the hepatic artery disappears.<sup>20</sup> The Pringle maneuver can be applied intermittently for up to 15-20 minutes at a time followed by at least 5 minutes of reperfusion.<sup>20</sup> This

maneuver increases the total hepatic ischemic time that can be tolerated but can involve substantial bleeding during periods of unclamping, as well as, increasing surgical resection time.<sup>20</sup> However, inflow vascular occlusion techniques are effective in reducing blood loss during hepatic parenchymal resection.<sup>11</sup>

Application of inflow vascular occlusion techniques is associated with clinically significant hemodynamic perturbations, such as increases in systemic vascular resistance by up to 40%, reduction of cardiac output by 10%, and increased mean arterial pressure by approximately 15%.<sup>11</sup> Release of occlusion (via unclamping) causes hemodynamic parameters to slowly return to baseline values.<sup>11</sup> The nurse anesthetist must be attuned to the application of surgical hepatic vascular occlusion, as well as length of time of application, and the resultant hemodynamic perturbations potentially associated with hepatic vascular occlusion surgical techniques. Total hepatic vascular occlusive techniques can produce substantial hemodynamic manifestations.<sup>20</sup>

### **Hemodynamic management**

In 1998, Melendez et al. and Jones et al. demonstrated that maintenance of low central venous pressure (CVP) during anesthesia was effective in reducing surgical hemorrhage and blood transfusion requirements during hepatectomy.<sup>28,29</sup> Since then, most reviews of anesthetic management of hepatectomy have incorporated the maintenance of a low CVP to reduce operative blood loss and improve survival during hepatic resection.<sup>9,11,20</sup> A reduced CVP decreases hepatic venous pressure, reducing bleeding during parenchymal resection.<sup>9,28</sup> Maintaining the CVP below 5 mmHg produces very low blood loss during major hepatic resections.<sup>11,19,20,28,29</sup> Smyrniotis et al. also noted that the effectiveness of the "Pringle" maneuver is negatively impacted by elevated CVP and CVP fluctuations.<sup>30</sup>

To attain low CVP anesthesia for hepatectomy, the hemodynamic effects of volatile inhalational anesthetics, in concert with maintenance of normovolemia, are usually sufficient for achieving a CVP of less than 5 mmHg. Venodilators, such as nitroglycerin, may be employed, as necessary, to facilitate this endeavor.<sup>11</sup> Maintaining the CVP at such a point, requires strict monitoring and maintenance of hemodynamic parameters.<sup>20</sup> Systolic arterial blood pressure must be maintained over 90 mmHg and urine output must exceed 0.5 milliliters per kg per hour

(mL/kg/hr) to ensure vital organ perfusion and appropriate volemic reserve.<sup>11,20</sup> Upon completion of hepatectomy and attainment of hemostasis, volume expanders and blood products are then administered to restore vascular volume while achieving a hemoglobin value above 8 g/dL, in the usual patient population.<sup>20</sup>

Drawbacks to the low CVP management approach during hepatic resection are noted in the literature. Maintenance of low CVP must be withdrawn should uncontrolled surgical hemorrhage develop or if total hepatic vascular occlusive techniques become necessary.<sup>20</sup> The potential for the development of venous air embolism associated with maintenance of low CVP during inflow vascular occlusion techniques is also noted in the literature.<sup>11,20</sup> During hepatic parenchymal resection with low CVP, air can become mobilized into open hepatic venous structures, especially in right hepatectomies where resection occurs in close proximity to the inferior vena cava.<sup>11</sup> Low CVP and inflow vascular occlusive techniques create a negative pressure gradient at the surgical site as compared to the right atrium, enhancing the potential for air entrainment through open venous structures.<sup>11</sup> Morbidity and mortality associated with venous air embolism is dependent on the volume and rate of air entrainment.<sup>11</sup> Awareness of the clinical signs of venous air embolism during anesthesia for hepatic resection is necessary. Despite the utility of low CVP in reducing blood loss in hepatic resection, a recent systemic review concluded that this technique did not reduce red blood cell transfusion requirements in hepatic resection, but did decrease the need for fresh frozen plasma.<sup>9</sup>

## CLINICAL APPLICATION AND CONCLUSION

Following an extensive pre-anesthetic discussion in which the risks involved with regard to refusal of blood products were discussed, the patient remained adamant regarding refusal of blood component transfusions, even indicating acceptance of death should necessary blood transfusions be withheld in accordance with the refusal. Most of the literature-based approaches described herein were discussed, in detail, with the patient along with enumeration of benefits and risks. All were acceptable to the patient and many were utilized to minimize blood loss, including acute normovolemic hemodilution, maintenance of a CVP below 5 mmHg during resection, perioperative cell salvage and anti-fibrinolytic therapy, during a successful right hemi-hepatectomy of Couinaud hepatic sections 5-8 under general endotracheal anesthesia. Despite extensive

blood loss resulting in an extremely low postoperative hemoglobin and hematocrit, the patient made an uneventful recovery and was released home within a week of surgery. No allogenic blood products were utilized.

This case and review clearly illustrate some very important points regarding anesthetic management of such complicated patients undergoing challenging surgical procedures. The importance of individualized patient management approaches and the utilization of available evidence to efficiently and effectively guide clinical practice must be a foremost consideration in all anesthetics. Secondly, the impact of genetic phenomena, as well as the beliefs and health of populations, cannot be overlooked in clinical anesthesia practice.

## References

1. Kastrinos F, Syngal S. Inherited colorectal cancer syndromes. *Cancer J*. 2011;17(6):404-415. doi: 10.1097/PPO.0b013e318237e408.
2. Kastrinos F, Stoffel E. The history, genetics and strategies for cancer prevention in Lynch syndrome. *Clin Gastroenterol Hepatol*. 2013, in print. doi: 10.1016/j.cgh.2013.06.031
3. Lynch HT, Lynch PM, Lanspa SJ, Snyder CL, Lynch JF, Boland CR. Review of the Lynch syndrome: history, molecular genetics, screening, differential diagnosis, and medicolegal ramifications. *Clin Genet*. 2009;76:1-18. doi: 10.1111/j.1399-0004.2009.01230.x
4. Hughes D, Ullery BW, Barie PS. The contemporary approach to the care of Jehovah's Witnesses. *J Trauma*. 2008;65:237-247. doi: 10.1097/TA.0b013e318176cc66
5. Lin ES, Kaye AD, Baluch AR. Preanesthetic assessment of the Jehovah's Witness patient. *Ochsner J*. 2012;12:61-68.
6. About Jehovah's Witnesses. Watch Tower Bible and Tract Society of Pennsylvania. <http://www.jw.org/en/jehovahs-witnesses/>. Accessed November 8, 2013.
7. Frequently asked questions about Jehovah's Witnesses. Watch Tower Bible and Tract Society of Pennsylvania. <http://www.jw.org/en/jehovahs-witnesses/faq/jehovahs-witnesses-medical-treatment/>. Accessed November 8, 2013.
8. Berend K, Levi M. Management of adult Jehovah's Witness patients with acute bleeding. *Am J Med*. 2009;122:1071-1076. doi: 10.1016/j.amjmed.2009.06.028.
9. Gurusamy KS, Li J, Vaughan J, Sharma D, Davidson BR. Cardiopulmonary interventions to decrease blood loss and blood transfusion requirements for liver resection. *Cochrane Database Syst Rev*. 2012. doi: 10.1002/14651858.CD007338.pub3

10. Walia A. Anesthetic management for liver resection. *J Gastrointest Surg.* 2006;10:168-169. doi: 10.1016/j.gassur.2005.09.024.
11. Tympa A, Theodoraki K, Tsaroucha A, Arkadopoulos N, Vassiliou I, Smyrniotis V. Anesthetic considerations in hepatectomies under hepatic vascular control. *HPB Surg.* 2012. doi: 10.1155/2012/720754
12. Beck-Schimmer B, Breitenstein S, Urech S, et al. A randomized controlled trial on pharmacological preconditioning in liver surgery using a volatile anesthetic. *Ann Surg.* 2008;248:909-916.
13. The Albumin Reviewers (Alderson P, Bunn F, Li Wan Po A, et al). Human albumin solution for resuscitation and volume expansion in critically ill patients. *Cochrane Database Syst Rev.* 2011. doi: 10.1002/14651858.CD001208.pub3.
14. Perel P, Roberts I, Ker K. Colloids versus crystalloids for fluid resuscitation in critically ill patients. *Cochrane Database Syst Rev.* 2013. doi: 10.1002/14651858.CD000567.pub6.
15. Zarychanski R, Abou-Setta AM, Turgeon AF, et al. Association of hydroxyethyl starch administration with mortality and acute kidney injury in critically ill patients requiring volume resuscitation. *JAMA.* 2013;309(7):678-688.
16. Annane D, Siami S, Jaber S, et al. Effects of fluid resuscitation with colloids vs. crystalloids on mortality in critically ill patients presenting with hypovolemic shock: the CRISTAL randomized trial. *JAMA.* 2013;310(17):1809-1817
17. Bagshaw S, Chawla LS. Hydroxyethyl starch for fluid resuscitation in critically ill patients. *Can J Anesth.* 2013;60:709-713.
18. Voluven® [package insert]. Lake Forest, IL: Hospira, Inc.; 2012
19. Hofland J, Henny CP. Bloodless (liver) surgery? The nurse anesthetist's view. *Dig Surg.* 2007;24:265-273. doi: 10.1159/000103657.
20. Romano F, Garancini M, Uggeri F, et al. Bleeding in hepatic surgery: sorting through methods to prevent it. *HPB Surg.* 2012. doi: 10.1155/2012/0169351
21. Waters JH, Yazer M, Chen Y, Kloke, J. Blood salvage and cancer surgery: a meta-analysis of available studies. *Transfusion.* 2012;52:2167- 2173. doi: 10.1111/j.1537-2995.2011.03555.x
22. Trudeau JD, Waters T, Chipperfield K. Should intraoperative cell-salvaged blood be used in patients with suspected or known malignancy? *Can J Anaesth.* 2012;59:1058-1070. doi: 10.1007/s12630-012-9781-x
23. Silva MA, Muralidharan V, Mirza D.F. The management of coagulopathy and blood loss in liver surgery. *Semin Hematol.* 2004;41(suppl 1):132-139.
24. Wu C, Ho W, Cheng SB, et al. Perioperative parenteral tranexamic acid in liver tumor resection: a prospective randomized trial toward a "blood transfusion"-free hepatectomy. *Ann Surg.* 2006;243:173-180.
25. Shao YF, Yan, JM, Chau GY, et al. Safety and hemostatic effect of recombinant activated factor VII in cirrhotic patients undergoing partial hepatectomy: a multicenter, randomized, double-blind, placebo-controlled trial. *Am J Surg.* 2006;191: 245-249.
26. Lodge JP. Hemostasis in liver resection surgery. *Semin Hematol.* 2004;41(suppl 1):70-75.
27. Lodge JP, Jonas S, Oussoultzoglou E, et al. Recombinant coagulation factor VIIIa in major liver resection. *Anesth.* 2005;102:269-275.
28. Melendez JA, Arslan V, Fischer ME, et al. Perioperative outcomes of major hepatic resections under low central venous pressure anesthesia: blood loss, blood transfusion, and the risk of postoperative renal dysfunction. *J Am Coll Surg.* 1998;187:620-625.
29. Jones RM, Moulton CE, Hardy KJ. Central venous pressure and its effect on blood loss during liver resection. *Br J. Surg.* 1998;85:1058-60.
30. Smyrniotis V, Kostopanagiotou G, Theodoraki K, Tsantoulas D, Contis, JC. The role of central venous pressure and type of vascular control in blood loss during major liver resections. *Am J Surg.* 2004;187:398-402.



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