

Review of Oncology and Transplant Literature for the Management of Hepatic and Pancreatic Resections in Jehovah's Witnesses

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ABSTRACT

Jehovah's Witnesses undergoing liver or pancreas surgery represent a unique medical and ethical challenge. For hepatic and pancreatic malignancies, resections are currently the only curative treatment. These surgeries pose a risk for significant blood loss, for which blood transfusions are traditionally given. However, blood transfusions are considered unacceptable to many Jehovah's Witnesses patients. As the technology of surgery as well as development of new products continue to evolve, transfusion-less surgery modalities have been utilized for Jehovah's Witnesses. The use of these transfusion-less techniques is not yet standardized for hepatic and pancreatic resections. We aimed to review both oncology and transplant medical literature on pancreatic and hepatic resection to develop guidelines for the management Jehovah's Witnesses patients.

KEYWORDS

Transfusion-free surgery; Pancreatectomy; Jehovah's Witnesses; Hepatic resection

1. INTRODUCTION

Jehovah's Witnesses is a Christian denomination that was founded in the late 1800s. There are currently over 8 million members worldwide [1]. Based on their interpretation of Acts 15:28, 29 and other scriptures, they consider the consumption of blood to be a violation of God's law and consequently often refuse blood transfusions. The willful acceptance of a blood transfusion by an unrepentant member has been grounds for expulsion from the group since 1961. Though Jehovah's Witnesses traditionally do not accept blood transfusions of whole blood, they may accept some blood plasma fractions at their own discretion.

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Liver resection remains the most optimal treatment for primary or metastatic liver malignancies, benign liver tumors, and some biliary diseases [2,3]. Similarly, total or partial pancreatectomy is currently the only potentially curative treatment in patients with pancreatic adenocarcinoma [4]. The medical management of Jehovah's Witnesses raises medical, ethical, and legal issues, especially in the setting of major operative procedures, when the potential for blood loss and the need for blood replacement is significant [5]. The concept of 'bloodless surgery' is developing rapidly and avoiding allogeneic blood transfusion in many types of surgeries is

becoming an increasingly attractive option. This has led to the evaluation and use of optimization of preoperative EPO schedules as well as autologous transfusion through acute normovolemic hemodilution and intraoperative cell salvage. Our paper reviewed eight retrospective and case studies on the use of transfusion free techniques for pancreatic and hepatic resections of Jehovah's Witnesses to identify treatment standards.

2. TRANSFUSION FREE PROCEDURES

Erythropoietin

Erythropoietin (EPO) is a hormone produced primarily by the kidney. Hypoxemia stimulates its production, resulting in erythropoiesis. Recombinant EPO has been used for 30 years in anemic patients undergoing renal dialysis and it is now approved for use in autologous blood donation and to reduce transfusion requirements in patients undergoing major surgery [6-8]. RHuEPO may be an effective alternative to blood transfusion in patients undergoing major surgery and is recommended in patients if their clinical condition permits sufficient time for EPO to promote erythropoiesis (~4 weeks). Erythropoiesis is seen in 3 days, the equivalent of one unit of blood is produced in 7 days, and five units are produced in 28 days [9]. Intravenous iron supplementation is recommended in all patients undergoing EPO therapy.

In the majority of the studies reviewed, patients consented to the use of recombinant erythropoietin therapy. At some institutions, consenting to EPO was a requirement for enrolling in a transfusion free surgery program [10]. Jabbour et al. 2004 administered preoperative EPO to all living donor liver transplant patients from 1998 to 2001, regardless of preoperative hemoglobin levels, but administered postoperative EPO as needed [10]. For more recent living donor liver transplants that took place in 1999 to 2004, Jabbour et al. 2005 did not describe the use of preoperative EPO [11].

In the other four more recent studies, EPO was utilized for malignant pancreatic and hepatic resections. In these publications, its administration was given preoperatively and/or postoperatively based on the patient's hemoglobin levels. The authors usually described supplementing EPO with iron and folate. Konstantinidis et al. reviewed outcomes in Jehovah's Witnesses undergoing pancreatic or hepatic resections from 1996 to 2011. EPO use was consented by 19 of the 25 patients studied and was administered to 6 patients preoperatively [12]. Specific surgery type or morbidities were not stratified against the use of EPO. Lee et al. gave preoperative EPO to 6 of the 11 patients who underwent pancreatic resections [13]. Nishida et al. and Barakat et al. presented case studies of two patients who underwent trisectionectomy procedures for intrahepatic cholangiocarcinoma [14,15]. Both of these patients received EPO without any attributed morbidities.

The increasingly selective use of EPO may reflect more recent findings about increased risk of thromboembolism and cardiac events with its use [16,17]. EPO use may be given more readily to healthy organ donors while more conservative EPO use may be appropriate for patients with hepatic and pancreatic malignancies.

Autologous transfusion

Jehovah's Witnesses acceptance of autologous donation and reinfusion remains at the discretion of the individual and often hinges on ensuring that the diverted blood is maintained in continuity with the circulatory system at all times. Of the three main techniques for autologous transfusion - preoperative autologous blood donation (PAD), acute normovolemic hemodilution (ANH) and intraoperative and postoperative cell salvage, PAD is unacceptable to Jehovah's Witnesses [18].

ANH is a blood conservation technique and is done by collecting the patient's whole blood at the induction of

anesthesia with simultaneous infusion of a crystalloid or colloid solution to maintain a normovolemic status. Acute normovolemic hemodilution reduces blood viscosity, systemic vascular resistance and enhances cardiac output with reduced myocardial O₂ consumption. Reinfusion of platelets and coagulation factors corrects any coagulopathy that arises out of perioperative blood loss. ANH is acceptable to Jehovah's Witnesses only if it is done in a continuous circuit [19].

Acute normovolemic hemodilution (ANH) involves placement of a large-bore IV with gravity drainage of whole blood into a CPD bag following anesthesia induction. Whole blood is removed while albumin or crystalloid IV restoration of intravascular volume occur simultaneously. This is maintained until the patient's hematocrit drops to a level between 18% - 30%. Any blood loss that occurs during surgery results in the loss of diluted blood. The whole blood collected pre-operatively stays in the operating room and all ANH blood is returned to the patient as needed during the procedure and all is returned by the end of the operation [20].

The major benefits of ANH include: 1) Simplicity - it does not require any preoperative preparation whereas with blood augmentation using erythropoietic drugs there is a time delay for erythropoiesis as well as a pharmaceutical cost increment. 2) ANH contains whole blood including platelets and coagulation factors. It takes advantage of the natural redundancy of the coagulation system which allows removal of a significant portion of the protein pro-coagulant and platelet compartments while preserving 100% platelet and plasma protein clotting system activities. 3) ANH provides a valuable cushion for safety, usually 400 cc - 800 cc, in the event of unexpected blood loss.

The basic principle behind ANH is that isovolumic anemia is a safe condition in most patients that is well

tolerated. ANH builds upon the concept that hematologic redundancy, in this case of the red cell mass, is present and allows manipulation of this red cell mass compartment to the benefit of the patient. Vascular volume is preserved so cardiac output and oxygen delivery are maintained. ANH to a hemoglobin level as low as 5gm/dl in conscious healthy resting humans did not produce inadequate systemic oxygenation. Studies have shown that ANH decreases systemic vascular resistance (SVR), increases heart rate (HR) and increases stroke volume (SV). Plasma lactate levels stay constant over a wide range of hemoglobin [21].

In five of the eight studies reviewed, acute normovolemic hemodilution (ANH) was utilized. In both living donor liver transplant studies by Jabbour et al., ANH was utilized with all donors. For living donor liver transplants from 1998 to 2001, the average blood loss was approximately 1500 mL and ANH reinfusion was 3.5 units [10]. The range of ANH reinfusion was as low as 2 units for 300 mL blood loss and as high as 7 units for 2900 mL blood loss. For living donor liver transplants from 1999 to 2004, average blood loss was 400 mL and ANH reinfusion was 2 units [11]. Their ANH protocol was to remove 10-20% of the patient's blood volume at the beginning of the procedure, which was later refused at the point when further bleeding was not anticipated. In the review of patients who underwent pancreatic and hepatic resections by Konstantinidis et al., ANH use was consented by 17 of the 25 patients studied and used in 5 hepatic resections and 4 pancreatic resections [12]. Each patient received 1 to 4 units of ANH reinfusion. The authors stated that it was unclear why ANH was not used in a higher proportion of the patients they reviewed.

Barakat et al. was the only case report reviewed that documented the use of ANH [15]. To treat a large intrahepatic cholangiocarcinoma in a 49-years-old female Jehovah's Witness patient, they performed a combined

left trisegmentectomy and caudate lobectomy, along with resection of the inferior vena cava. The patient consented to the administration of EPO and activated factor VII, ANH, and the use of cell salvage. She declined to receive fresh frozen plasma, human albumin, and cryoprecipitate. During this initial phase of preparation, the patient's hematocrit was 41.4%. One unit of blood was withdrawn before surgical incision and was maintained at room temperature during the procedure. During the surgery, she lost approximately 450 mL of blood. While preoperative EPO, factor VII, and cell salvage were ultimately not needed, the patient received one unit of ANH reinfusion during the surgery. Postoperative hematocrit was 35%. The patient developed a pleural effusion and biliary leak that resolved with treatment and she was discharged on postoperative day 16. The patient was alive at 4 months follow up.

Lee et al. in a study from Korea shared their experience with transfusion-free pancreatic resections in Jehovah's Witnesses [13]. There were four cases of Whipple's operation, 4 of pylorus-preserving pancreaticoduodenectomy, 2 radical antegrade modular pancreatectomy and 1 of laparoscopic distal pancreatectomy. All were performed by one surgeon. Six of the 11 patients included in the study received intraoperative ANH of 2 to 3 units. The anesthesiologist determined whether ANH would be carried out based on the following criteria: anticipated blood loss, preoperative hemoglobin, and patient's overall physiologic status. Average preoperative hemoglobin was 12.52 g/dl and postoperative hemoglobin was 11 g/dl. There were postoperative complications in 4 patients: Wound infection, pneumonia, and two cases of ileus.

Even in the event of significant blood loss, postoperative anemia is safe. A study presented at the American Society of Hematology found that 6 out of 7 patients (85.7%) with a hemoglobin as low as 2.5 g/dL - 3.0 g/dL survived. Out of a total of 128 patients with profound anemia

(hemoglobin ranging from 2.5 g/dL - 7.0 g/dL), 95.3% survived [22]. Patients with profound postoperative anemia treated without blood transfusions have a high survival rate. In a randomized control trial of 130 patients undergoing major hepatic resection, ANH has been shown to reduce the need for allogeneic red blood cell transfusion by 50% [23]. In an RCT of 160 patients undergoing major gastrointestinal surgery, 8 of whom underwent Whipple's surgery, ANH was not shown to reduce the need for allogeneic red blood transfusion [24]. Additional controlled trials on the use of ANH for patients undergoing pancreatic resections were not found.

With the cell salvage technique, shed blood is suctioned from the wound, centrifuged, washed, mixed with an additive/anticoagulant solution and then re-infused via a filter (leucocyte depleted) as required. It may be acceptable to some Jehovah's Witnesses if the blood is not stored and the circuitry is in continuity with the patient's own circulation. It is used when the expected blood loss is more than 20% of total body volume [25]. One of the advantages of cell salvage is that the returned blood is warm and has normal concentrations of 2,3-diphosphoglycerate. It is contraindicated in situations, where the blood is likely to be contaminated (e.g. sepsis, contamination with intestinal contents) as well as cases of sickle-cell anemia and thalassemia [25].

Cell salvage was prepared in 6 of the studies reviewed, however, blood loss was often too low for autotransfusion to occur. For all living donor liver transplant patients described, Jabbour et al. utilized a Cell Saver setup. While their first publication does not discuss Cell Saver yield, in their second publication, 6 of the 13 patients yielded blood from Cell Saver [11]. The authors concluded that ANH and Cell Saver may eliminate the need for transfusion in general surgery patients when the risk of cardiovascular events is low and there is sufficient red blood cell mass.

Cell salvage was consented by 17 of the 25 hepatic and pancreatic resections reviewed by Konstantinidis et al. [12]. While Cell Saver was set up for all patients who consented to it, blood was only returned in 3 of the patients. The first of these patients underwent a right hemi-hepatectomy, lost approximately 1500 mL of blood, and had blood return of 225 mL. The second patient also underwent a right hemi-hepatectomy, lost approximately 500 mL of blood, and had blood return of 125 mL. The final patient underwent a pancreaticoduodenectomy that was abandoned due to perioperative bleeding. The patient lost approximately 2,270 mL blood and, in addition to 2 units of ANH, received 405 mL from Cell Saver.

Nishida et al described a case report of Jehovah's Witness patient, a 33 year old Hispanic female with a history of epilepsy who had intrahepatic cholangiocarcinoma [15]. She underwent a right trisectionectomy with bile duct resection, lymph node dissection, and Roux-en-Y hepatico-jejunostomy without blood transfusion. The patient lost 300 mL of blood, although it is unclear if the cell saver ultimately yielded blood return. The patient developed a postoperative wound infection but was otherwise in good health after the operation. She was discharged on postoperative day 8 and her liver eventually grew back to an optimal size and volume.

Cell salvage has been shown to save an average of 0.68 units of allogeneic RBC per patient [26]. A randomized control trial on the use of cell salvage in 96 patients undergoing hepatectomy found that patients randomized to the cell salvage group had a 36% reduction in the need for allogeneic blood transfusion [27]. The rate of complication rates between both groups was comparable. Similar randomized control trials on cell salvage and allogenic blood transfusion in patients undergoing pancreatectomies were not found in the literature.

The use of Cell Saver in the context of malignancy is debated. There is a theoretical concern that the reinfusion of tumor cells may produce worse outcomes. However, studies on pancreatic and hepatic resections have shown that the leuko filtration device reliably depleted cancer cells prior to reinfusion [28]. Meta-analysis of oncology patients who received cell saver transfusions found that there was not an increased risk for cancer recurrence or metastasis [25].

Surgical technique

In three of the publications reviewed, EPO, ANH, and Cell Saver were either unutilized or did not return blood to the patient. In addition to or in the absence of these blood augmenting and blood salvaging conserving methods, the surgical approach is crucial for minimizing blood loss. The use of meticulous dissection, hemostasis, and low central venous pressure was described by several of the authors reviewed.

Lim et al. [29] studied Jehovah's Witnesses who underwent liver resection for liver tumors between 2014 and 2017. 10 patients were included in the study and major hepatectomy was performed in 4 patients. None needed preoperative EPO. Low central venous pressure and hemodialysis were maintained during the surgeries and the Pringle maneuver was prepared for all patients. The median estimated blood loss was 200 mL. A Cell Saver was installed in 2 patients but none received saved blood. Nine complications occurred in 4 patients but no postoperative hemorrhage occurred and in-hospital mortality was nil. Similarly Nishida et al. [14] concluded that bloodless liver transection techniques with inflow clamping, meticulous dissection, and hemostasis should be utilized for major hepatectomy in a Jehovah's Witnesses. They performed 55 minutes of effective inflow clamping.

In a series of case reports, Fernandes et al. reported the Brazilian experience in Jehovah's Witnesses undergoing pancreatic resections with vascular reconstructions [30]. The first case involved a 64-years-old woman with a history of Crohn's disease, and multiple episodes of acute cholangitis and pancreatitis with repeated hospital admissions for percutaneous drainage of peripancreatic collections. She presented jaundice three months after the initiation of treatment for tuberculosis. Computerized tomography showed a lesion in the head of the pancreas with involvement of the portal vein. After transection of the pancreas 3 cm from the pancreatic neck, tumoral infiltration of the portal vein was evidenced, partial resection of the vein and its reconstruction were performed, without the need for grafting. The surgical margin of the pancreatic border was positive for malignancy at the freezing test. Thus, total pancreatectomy was performed. The patient did not receive blood products and Cell Saver recovered 192 ml of blood, which reinfusion was not indicated. Hemoglobin fell from 14.8 mg/dl to 10.7 mg/dl at the end of the operation. The second case involved a 69-years-old woman on rivaroxaban, with a lesion in the head of the pancreas with involvement of the superior mesenteric vein. Surgical exploration involved pancreaticoduodenectomy with resection of the involved segment of the SMV with primary anastomosis. The patient received no blood products and the cell saver did not aspirate enough volume to be processed. Hemoglobin did not fall after the operation.

In order to perform a complex left trisegmentectomy, caudate lobectomy, and inferior vena cava resection, Barakat et al. [15] utilized meticulous dissection as well as total vascular isolation, in situ hypoperfusion, and venovenous bypass.

For hepatic malignancies that involve the vasculature, they recommended total vascular isolation for the resection, in combination with in situ hypoperfusion and venovenous bypass. The authors cautioned the use of vascular isolation be limited to an hour in duration, as there are often complications beyond this time point [31].

While most of the Jehovah's Witnesses found EPO to be acceptable, and many found ANH and cell salvage acceptable, some JH patients refused to consent the use of EPO and autotransfusion. Eight percent of the hepatic and pancreatic resection patients that Konstantinidis et al. [12] reviewed refused EPO, ANH, and cell salvage (Table 1).

Red blood cell substitutes

The problems associated with the supply, storage and safety of blood has led to the research for RBC alternatives. Two major groups of Red cell substitutes are perfluorocarbons and Hb solution. Hb based oxygen carriers (HBOCs) are chemically modified Hb solutions containing polymerized, conjugated, or liposome-encapsulated Hb.

Currently, HBOCs are not approved by the U.S. Food and Drug Administration (FDA) and remain in phase III clinical trials. While reports showed that HBOCs may improve chances of survival from anemia secondary to acute bleeding or hemolysis, studies also found an increased chance of adverse events, including myocardial infarction and pulmonary hypertension. Case reports have described the use of HBOC on compassionate grounds as a bridge in severely anemic Jehovah's Witnesses before erythropoiesis recovers, although cases of HBOC use for pancreatic or hepatic surgeries were not found [32].

First author	Date	Study design	Study size	Surgical indications	Surgery type	Transfusion free procedures	Morbidity and mortality
Lim et al.	2018	Retrospective review	10	Hepatocellular carcinoma (n=3) Metastases to liver (n=5) Benign disease (n=2)	Hepatic resection (n=10) Laparoscopic approach (n=2) Hepatectomies (n=4) Vascular control (n=7)	PVE, preop (n=1) Cell salvage (n=2); No blood return Surgical technique: Low central venous pressure, Pringle maneuver, hemostasis	Postoperative morbidity Pneumonia and cardiac arrhythmia (n=1) Pulmonary embolism (n=1) Biliary fistula, abdominal abscess, pleural effusion, and jaundice (n=1) Wound infection (n=1) 9 patients were alive at 13 months (median follow-up)
Lee et al.	2016	Retrospective review	11	Pancreatic ductal adenocarcinoma (n=5) Bile duct cancer (n=2) Ampulla of Vater cancer (n=2) Intraductal papillary tumor (n=1) Autoimmune pancreatitis (n=1)	Pancreatectomy (n=11) Whipple's (n=4) Pancreatocephaloduodenectomy (n=4) Pancreatosplenectomy (n=2) Laparoscopic approach (n=1)	EPO: preoperative (n=6) ANH (n=9) EPO and iron: postop (n=unk)	Wound infection (n=1) Pneumonia (n=1) Bile leak (n=3) Pancreatic fistula (n=1)
Fernandes et al.	2016	Case Report	2	Ductal adenocarcinoma of the pancreas (n=2)	Duodenopancreatectomy (n=2)	Cell salvage (n=2); blood returned in 1 Surgical technique: Meticulous hemostasis	
Konstantindis et al.	2013	Retrospective review	25	Pancreatic diagnoses (n=10) Pancreatic endocrine tumors (n=3) Ductal adenocarcinoma (n=3) Cholangiocarcinoma (n=2) Leiomyosarcoma (n=1) GIST (n=1) Benign disease (n=1) Hepatic diagnoses (n=15) Metastases to liver (n=10) Hepatocellular carcinoma (n=2) Gallbladder cancer (n=2) Hilar cholangiocarcinoma (n=1) Benign disease (n=3)	Pancreaticoduodenectomy (n=6) Distal pancreatectomy/splenectomy (n=4) Segmentectomy or bi/trisectionectomy (n=9) Hemi-hepatectomy or extended hepatectomy (n=6)	Consented to use of blood products for life-threatening bleeding (n=5). 1 patient received blood products EPO and iron: preoperative (n=6) ANH (n=9) Hemodilution Cell salvage (n=17). Blood return in 3 patients. Surgical technique: Low central venous pressure, inflow clamping Surgery discontinued due to blood loss (n=3)	Wound infection (n=6) UTI (n=1) Ascites (n=1) Delayed wound healing (n=1) Bleeding (n=1) Nausea/vomiting (n=6) Lymphedema (n=1) Bleeding/re-exploration (n=1) Abdominal abscess (n=1) ARDS (n=1) No in hospital mortality
Nishida et al.	2007	Case Report	1	Intrahepatic cholangiocarcinoma	Trisectionectomy	EPO, folic acid, vitamins, and iron: preoperative and postoperative Cell salvage Surgical technique: Low central venous pressure, inflow clamping, meticulous dissection, hemostasis	Wound infection
Barakat et al.	2007	Case Report	1	Intrahepatic cholangiocarcinoma	Trisectionectomy, caudate lobectomy, and IVC resection	EPO, folic acid, and iron: postoperative ANH Surgical technique: Meticulous dissection, total caval ligation (60 minutes), venous bypass, in situ hypoperfusion	Pleural effusion Biliary leak No mortality at four months followup
Jabbour et al.	2005	Retrospective review	13	Living donor liver transplantation (n=13)	Right lobectomy (n=9) Left lateral segmentectomy (n=4)	ANH (n=13) Cell salvage (n=13); Blood return in 6 patients Factor VII	Ventral hernia (n=1) No mortality at approximately 3 years follow up
Jabbour et al.	2004	Retrospective review	8	Living donor liver transplantation (n=8)	Right lobectomy (n=8)	EPO, iron, and folic acid: preoperative (n=8), postoperative (n=unk) Cell salvage (n=8) ANH (n=8) Individual component therapies (n=unk) No changes in surgical technique	Reoperation (n=2) No mortality at approximately 2 years follow up

Table 1: Summary of studies on transfusion free pancreatic and hepatic resections.

3. DISCUSSION

Improvements in surgical techniques and anesthesia have been crucial to the success of transfusion-less hepatobiliary and pancreatic surgery. The management of Jehovah's Witnesses with complex liver and pancreatic tumors requires a multidisciplinary, tailored strategy compatible with their religious beliefs to achieve good outcomes. Discussing various transfusion-free techniques with the patient before surgery is crucial to planning a management strategy that conforms with the patient's beliefs, because individual Jehovah's Witnesses may consent to receive different types of blood products. Some of the Jehovah's Witnesses patients reviewed consented to the use of allogenic blood transfusion in the case of life-threatening bleeding while others did not consent to EPO, ANH, or cell saver.

An important step in blood preservation is limiting blood sampling by both reducing the frequency and volume of

blood draws. The Jehovah's Witnesses reviewed were moderately accepting of EPO supplementation. In the

cases reviewed, EPO given with iron and folate was able to effectively raise hemoglobin levels. EPO use should be restricted in patients who are at high risk for thrombolytic or cardiovascular events [16,17]. Jehovah's Witnesses patients were more receptive to ANH and cell salvage, as long as the blood stayed in a continuous circuit. Since ANH depletes clotting factors and red blood cells, there is a risk of bleeding, hypotension, and tachycardia [33]. However, this was not apparent in the cases reviewed. ANH was well tolerated and returned 1 to 7 units of blood. Cell salvage is appropriate when significant blood loss is anticipated, although several authors set up cell saver for all surgical procedures. Cell Saver typically returned less than a unit of blood. While several patients had postsurgical wound infections, there were no cases of major contamination or sepsis.

Transfusion-less hepatic and pancreatic surgeries are complex procedures that should be performed in high-volume centers. A skilled anesthetic and surgical team are crucial for maintaining hemodynamics and performing meticulous dissections, respectively. For hepatic resections, the use of low central venous pressure and inflow clamping help minimize blood loss. Meta-analysis comparing low and high central venous pressure during surgery showed no difference in morbidity [34]. Inflow clamping techniques should be varied based on the tumor involvement and limited to prevent ischemia [35]. More complex approaches, such as total venous isolation, venovenous bypass, and *in situ* hypoperfusion may be utilized if there is significant vascular involvement [15].

Achieving optimal hemostasis is crucial for pancreatic and hepatic resections of Jehovah's Witness patients. While surgical hemostasis approaches were well described, the use of topical hemostasis and systemic hemostatic agents was not described in any of the studies used. As absorbable topical agents, tranexamic acid, and E-aminocaproic acid are generally well tolerated, studies on their use in blood-less hepatic and pancreatic resections may be appropriate [36-38] (table 2).

The patient must be assured at their initial team meeting that the goal of the medical team is to formulate a plan for surgery that complies with the patient's beliefs and wishes. The team should carefully explain that no attempt will be made to frighten them or place them under duress. Initially, open ended questions may be appropriate to gain a general understanding of the patient's beliefs and understanding about their illness and surgery. It is important to assess each Jehovah's Witnesses patient individually, as there is heterogeneity in the medical treatments and procedures that different patients may find acceptable. The patient should be informed of each of the therapeutic options available including allogenic blood transfusion, EPO, fractionated products, ANH, and cell

saver. In discussing these modalities, it is important to discuss the risks associated with each treatment and the risks of not using the treatment.

The findings of the study must be interpreted in the context of its limitations. We provide a comprehensive review of the world literature available on this topic; however, there are still some questions and limitations that need to be addressed. Firstly, none of the study are randomized trials. All studies are small size retrospective studies therefore selection bias may have a role to play in outcomes. The studies discussed are heterogeneous in terms of demographics, the management protocols instilled at their institute, and the type of surgical techniques that were used.

An interdisciplinary approach is crucial for the success of transfusion-free hepatic and pancreatic resections. The surgeon outlines the proposed operation, describes possible complications that may result in bleeding, and reminds the patient of the ever-present risk of bleeding with any surgery. They guide the patient through the anticipated and unanticipated surgical outcomes as well as establish a general blood loss threshold at which the surgery will be abandoned if allogenic blood transfusion is not acceptable to the patient. The anesthetist outlines techniques used to avoid blood transfusion. The hematologist discusses the therapeutic agents available to support blood volume and/or hemostatic function in the event of bleeding. If clinically appropriate, the hematologist explains the technique of preoperative hemoglobin enhancement using recombinant EPO and supplements. The patient's informed consent to each transfusion-less technique should be obtained and documented. If the patient has made an advance directive, it should be reviewed with the patient and a copy placed in the notes.

Technique		Recommended indication	Adverse events and contraindications
Blood preservation and augmentation	Limited blood sampling	Limit frequency and amount of blood sampling for all JW patients	—
	EPO supplemented with iron and folic acid	Anemia, indication not required	EPO: thrombolytic and cardiovascular events; Iron: gastrointestinal complaints Folic acid: allergic reaction
Autologous transfusion	Acute normovolemic hemodilution	All Jehovah's Witnesses patients	Anemia Hypotension Tachycardia Sepsis
	Cell salvage	Anticipated blood loss is equal to or greater than 20% of total blood volume	Contamination Sepsis Sickle-cell anemia Thalassemia
Operative strategies	Meticulous dissection	All Jehovah's Witnesses patients undergoing pancreatic and hepatic resections	—
	Low central venous pressure	All Jehovah's Witnesses patients undergoing hepatic resections	No increase in morbidity compared to high central venous pressure
	Inflow clamping	Selective clamping or Pringle maneuver based on tumor size and location Intermittent clamping may be appropriate if liver parenchyma is abnormal	Ischemic injury
	Total venous isolation, venovenous bypass, and <i>in situ</i> hypoperfusion	Hepatic malignancy that involves the vasculature	Hepatic malignancy that involves the vasculature
Hemostasis	Surgical <ul style="list-style-type: none"> • Diathermy • Harmonic scalpel 	All Jehovah's Witnesses patients	—
	Topical <ul style="list-style-type: none"> • Bone wax • Absorbable cellulose or collagen 	Surgical hemostasis is insufficient Discuss acceptable topical hemostasis agents with Jehovah's Witnesses patient	Intravascular application may lead to thrombosis Application in confined spaces may lead to compression
	Systemic agents <ul style="list-style-type: none"> • Tranexamic acid • E-aminocaproic acid • Eptacog 	Surgical hemostasis is insufficient Discuss acceptable systemic hemostasis agents with Jehovah's Witnesses patient	Tranexamic acid: Uncertain thrombotic risk, well tolerated E-aminocaproic acid: Gastrointestinal complaints Eptacog: High risk of thrombosis

Table 2: Guidelines for transfusion free techniques for pancreatic and hepatic resections of Jehovah's Witnesses.

Jehovah's Witnesses patients should be reassured that they are in a partnership with the medical team to determine a therapeutic regimen that meets their values and beliefs. With advancing medical treatments and

techniques, transfusion-less pancreatic and hepatic resections are both safe and feasible. Transfusion-less surgeries may not only meet the spiritual requirements of Jehovah's Witnesses but may also inform efforts to help reduce the need for blood transfusions more broadly.

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