

Anesthesia Aspects of Multivisceral Transplantation: A Case Series Study

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Research Article

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Abstract

Background

Multi-visceral transplantation (MVTx) usually refers to the transplantation of more than three intra-abdominal organs. A successful MVT procedure requires strong multidisciplinary teamwork of transplant surgeons, anesthesiologists, and intensivists.

Case presentation:

We present 5 cases of MVT with a history of short bowel syndrome admitted to the Abu-Ali Sina Hospital, Shiraz, Iran between May 2019 and January 2020 and describe anesthetic considerations in MVT. Subjects were identified (4F/1M) with a mean age of 43 years old (range 35–51). The most frequent criterion was Portal vein thrombosis followed by bowel gangrene and short bowel syndrome. The mean \pm SD duration of the operation was 360 ± 60 min. The approximate bleeding volume was 2600 ± 1474 cc and the 4 \pm 1 bag packed red blood cells were transfused.

Conclusion

Careful preoperative planning, vigilant intraoperative anesthetic management, and prevention of postoperative infection are imperative to reach the best outcomes.

Background

Multi-visceral transplantation (MVTx) usually refers to the transplantation of more than three intra-abdominal organs. The liver, stomach, pancreas, duodenum, small intestine, a portion of the colon, are the most common organs transplanted as part of an MVTx procedure (1).

This long-term procedure is associated with significant blood loss, metabolic abnormalities, temperature fluctuations, fluid and electrolyte shifts, and coagulopathy .(2) A successful MVT procedure requires strong multidisciplinary teamwork of transplant surgeons, anesthesiologists, and intensivists (2). Anesthesiologists are an essential part of the MVTx management team, expected to provide safe anesthesia and intraoperative life support and play the role of critical care professional for patients undergoing multi-visceral transplantation (2). However, the anesthetic considerations of MVTs are less detected. In this case series study, the anesthetic aspects of five MVT cases at a referral single center were discussed.

Case Presentation

The authors report five cases of MVT between May 2019 to January 2020 in the Abu-Ali Sina Hospital, Shiraz, Iran. Written consent form was obtained from patients. Anesthesia was induced with intravenous propofol (2 mg/kg), fentanyl (4 micro/kg), and high dose rocuronium (1.2 mg/kg) or succinylcoline1-2 mg/kg. Then, After

intubation, midazolam 50 micro/kg, and morphine 0.1 mg/kg were maintained with propofol infusion (0.1-0.2 mg/kg/min) and oxygen/air.

In these cases, the following information is addressed: demographic data (age, BMI, and sex), comorbidity disease, the etiology of intestinal failure and MVT indications, outpatient department parenteral nutrition, time on the waiting list (WL), ABO compatibility, length of hospitalization before transplantation (days), length of TPN (days), preoperative laboratory data such as hemoglobin, albumin, total and direct bilirubin, and serum creatinine (Table 1).

Information on intraoperative anesthesia such as the number of bleedings, blood products transfusion, albumins and fluids administration, operation time, mean Cold Ischemia Time (CIT), Warm Ischemia Time (WIT) are shown in Table 1.

Postoperative complications like acute and chronic rejection rates, their causes, antibody-mediated rejection, infection (site/pathogens), CMV infection, and other complications that occurred during a 6-months follow-up, were also recorded. Moreover, survival rates were also considered (Table S.1).

Case 1:

She was a 44-year-old woman diagnosed with a well-differentiated neuroendocrine tumor (NET, grade one, Carcinoid Tumor); she had undergone multiple operations, colectomy, and small bowel resection anastomosis at another center. She developed small bowel tumor recurrence, single liver metastasis, short bowel syndrome, and enterocutaneous fistula. The patient was referred to the center while complaining about food intolerance and bowel obstruction symptoms as gastric outlet obstruction. She was admitted and received gastrointestinal rest and TPN for two months. She underwent classic MVT and had a good postoperative period. She survived **the event**.

Case 2:

She was a 52-year-old woman known as a case of celiac and superior mesenteric arteries (SMA) aneurysm admitted to our center. She suffered from severe abdominal pain after the diagnosis. SMA and celiac artery aneurysm reconstructions were performed using saphenous vein interposition graft, but graft thrombosis occurred post-operation. The patient underwent immediate classic MVT. She survived for three months, afterward, she died of GVHD (graft-versus-host disease) and pneumonia in the hospital.

Case 3:

She was a 35-year-old woman had undergone laparoscopic right hemicolectomy due to the colonic polyp and subsequent GI bleeding. She was discharged from the hospital; however, a few days later, she presented with abdominal pain, leukocytosis, and thrombocytosis in the laboratory data. Doppler ultrasonography showed the portal vein thrombosis (PVT), and exploratory laparotomy revealed extensive bowel gangrene. Small bowel resection and anastomosis failed three times in the local hospital.

She was admitted with short bowel syndrome, TPN-associated liver failure, and fistula. She received some TPN and then established a GI continuity by deudeno-colic anastomosis surgery. TPN continued, and MVT

was performed 79 days later. Klebsiella pneumonia and severe sepsis deteriorated her condition during her hospital stay; unfortunately, she died two months after MVT.

Case 4:

She was a 39-year-old woman, known case of diabetes mellitus, opium-addicted, non-cirrhotic portal hypertension, and protein C deficiency developed with extensive Porto mesenteric thrombosis. She was admitted to the hospital with severe abdominal pain, food intolerance, lack of response to band ligation, and repeated upper gastrointestinal bleeding. She received TPN for 25 days and was then scheduled for classic MVT. She had one episode of acute graft rejection on the 8th days post-operation which was resolved with high-dose steroids; she was finally discharged from the hospital 25 days after MVT, and she was well at the follow-up 6 months later.

Case 5:

A 47-year-old man who was suffering from a klatskin tumor with obstructive jaundice admitted to the hospital. PTBD (percutaneous transhepatic biliary drainage) was inserted, and a left hepatectomy was performed. He received an entire course of adjuvant chemotherapy and then returned with recurrent tumor and GOO (Gastric outlet obstruction) one year later. TPN started, and metastatic workup revealed no distant metastasis. Afterwards, Cluster MVT was performed, and he had an uneventful postoperative period until he had a high-output fistula. TPN, octreotide, and GI rest decreased his fistula drain to <1100cc in 24 hours. Finally, he developed pneumonia, severe sepsis and died two months later in the hospital.

Discussion

Multivisceral transplantation (MVTx) have gained acceptance as therapeutic modalities for patients with: intestinal failure with life-threatening complications of parenteral nutrition (PN), rare cases of vascular abdominal catastrophes and some cases of low-grade neoplastic tumors and desmoids involving the mesenteric root. This prolonged procedure, associated with significant blood loss, metabolic abnormalities, temperature fluctuations, fluid and electrolyte shifts, and coagulopathy. Malnutrition, dehydration, reduced physiologic reserves due to long-standing intestinal failure, and liver dysfunction make these challenges more difficult to overcome (3). These pathophysiologic considerations underpin the anesthetic plan for the patients undergoing multi-visceral transplantation (4). In this case series, the anesthetic aspects of five MVT cases at a referral single center were discussed.

Patients' monitoring:

In addition to peripheral access, a large-bore introducer should be embedded in the right internal jugular vein for fluid resuscitation, blood products transfusion and vasopressor infusion. Patients presenting for multi-visceral transplantation are critically ill, and long-term parenteral nutrition increases the risk of prior venous thrombosis. Therefore, using bedside ultrasound is recommended to identify the target vein (5). A radial arterial catheterization is suggested for the beat-to-beat evaluation of mean arterial blood pressure, measurement of systolic pressure variations in estimating intravascular volume status, and the continuous evaluation of blood gasses, hemoglobin, and electrolytes (6, 7). During MVT, wide

temperature fluctuations secondary to prolonged exposure of the viscera is common, so the maintenance of normothermia is essential, which prevents coagulopathy and cardiac instability followed by hypothermia (5, 8). Accordingly, we measured core body temperature through the esophageal probe and considered pre-warming of resuscitation fluids. Blood glucose (BS) monitoring is necessary in all cases recently had undergone TPN, and supplemental dextrose is required to prevent hypoglycemia following abrupt discontinuation of TPN.

Intraoperative concerns

Fluid resuscitation is crucial because of the prolonged operation time, significant blood loss, and excessive third-space losses. Therefore, conservative fluid management and application of a pulse counter cardiac output (PICCO) system are the recommended fluid management strategies to restore intravascular volume (9). In this study, PICCO was used to evaluate pulse pressure variation (PPV) and stroke volume variation (SVV) which predict the preload volume and fluid responsiveness.

Colloid solutions are more effective plasma volume expanders than crystalloids and reduce the severity of bowel edema. Studies suggest that the optimal crystalloid-to-colloid volume ratio is approximately 60:40. A balanced fluid strategy is a well-directed technique to maintain mean arterial pressure (MAP) > 60 mm Hg and target CVP $> 10\text{--}12$ mm Hg), it aims to stabilize hemodynamic status and improve organ perfusion (10). To prevent bowel edema, we considered a conservative fluid strategy that maintains the target CVP < 10 mm Hg with the concomitant administration of vasopressor infusions (norepinephrine, vasopressin, and/or epinephrine) if the MAP was < 60 mmHg. It should be noted that the mean \pm SD of total volume administration was 15 ± 1 cc/kg/h which were given as normal saline solution 0.9% /albumin 20% (60%/40%).

Some researchers have suggested that Rotational thromboelastometry (ROTEM) can be applied for the evaluation of coagulation status in MTX (6). Using intra-operative ROTEM analysis in our center revealed that the majority of patients were in a 'hypercoagulable status' and there was no need for fresh frozen plasma (FFP), cryoprecipitate ,and platelet except the fourth case, whom we transfused FFP, cryoprecipitate ,and platelet to correct microvascular bleeding after massive transfusion.

Bleeding during the MVTx procedure would be either surgical or coagulopathic or both. It might be more severe in patients with adhesions from previous abdominal surgeries, portal hypertension, or portal vein thrombosis (PVT) (11).We had an average of 2600 cc blood loss during these MVTx procedure. To achieve adequate tissue oxygenation, the hemoglobin level should be maintained at the range of 7-10 g/dl. On the other hand, overcorrection of hemoglobin may enhance the risk of vascular graft thrombosis and should be avoided (12). In our study, the average Hb level was 10.62 g/dl and the average transfusion of packed red blood cells was 4 ± 1 bag in the series.

About 47% of patients undergoing small bowel transplants experience post-reperfusion syndrome (PRS) (13). PRS is the largest hemodynamic disorder due to the amount of reperfused organs. It is characterized by marked decreases in MAP, and systemic vascular resistance, as well as moderate increases in pulmonary arterial pressure and central venous pressure. This syndrome may also develop when the mean arterial pressure (MAP) is less than 60 mm Hg or 30% below the pre-unclamping baseline value, lasting for at least 1 min, within 10 min after unclamping (8, 14, 15). The PRS occurred among all these five cases but severe PRS which needed continuous vasopressin and norepinephrine infusion happened in only one case. It is well-documented that several factors contribute to PRS development (i.e., hyperkalemia, acidosis, sudden hypothermia, vasoactive substances like free radicals, endotoxin, inflammatory cytokines, and acidotic compounds produced by the graft or intestine) (15) Aortic cross clamp and PRS may also contribute to renal injury. Studies suggested that the risk of post-transplant renal failure was 50% in MVTx (16). We did not observe any case of CRRT or dialysis-requiring acute kidney injury. It might be related to maintaining MAP > 60 mmHg and improving kidney perfusion pressure with infusion minimum dose of vasopressor during the clamping and unclamping phase (16, 17).

Indeed, TPN supplement contain potassium, on the other hand, concomitant liver graft reperfusion may enhance the intensity of hyperkalemia. *Serial measurements* of plasma potassium have suggested to keep the potassium level below 4 mmol/L before un-clumping phase and revascularization (18). Treatment options for hyperkalemia include the simultaneous administration of insulin and hypertonic-glucose, calcium gluconate, insulin, sodium bicarbonate, and diuretics (19-21).

In this study, methylprednisolone was administered simultaneously in the beginning of vascular anastomosis. A Wide range of antibiotics are a part of our center's protocol to prevent infection and immunosuppression infusion (thymoglobin), but MVTx procedure are associated with considerable risk of immunomodulation and immunosuppression, so patients are more likely to experience a postoperative infection. Recent advances in surgical techniques and immunosuppressive treatments, have increased knowledge about immunologic responses, and critical post-operative services have made MVTx an effective lifesaving intervention for cases having already adopted other treatment interventions.

Considering the limited and retrospective nature of the data herein discussed, there may be some concerns regarding the potential bias or overestimation of management. However, to the best of our knowledge, this is the first study in Iran presenting a series of patients undergoing MVTx and future studies are still recommended to assay other aspects of this technique.

Conclusion

Each phase of the MTVx procedure has its own unique cautions. Careful preoperative planning (patient selection, nutritional status and optimization of patient's condition), intraoperative vigilant anesthetic consideration (hemodynamic and fluid management) and postoperative infection prevention are imperative to reach the best outcomes.

Abbreviations

MVTx

Multi-visceral transplantation

WL

waiting list

WIT

Warm Ischemia Time

SMA

superior mesenteric arteries

CIT

Cold Ischemia Time

GVHD

graft-versus-host disease

PVT

portal vein thrombosis

PTBD

percutaneous transhepatic biliary drainage

GOO

Gastric outlet obstruction

PN

parenteral nutrition

Declarations

Ethics approval and consent to participate: Written consent form was obtained from patients. This study approved by Ethics Committee of Shiraz University of Medical Sciences

Consent for publication: Written informed consent was obtained from the patient or the patient's next of kin for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal

Availability of data and materials: All data will be available on request.

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Data Access and Responsibility: The principal investigator, Dean Khalili, had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Author contribution: MB.Kh, MA.S, and MH.E: Anesthesia management and post operation care, H.N: surgeon, F.Kh, V.NB, P.V, and S.GhT: study design, manuscript preparation, manuscript writing, manuscript revise. all

authors have read and approved the manuscript.

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Tables

Table1: Demographic, Preoperative, and Intraoperative data.

	case 1	Case 2	Case 3	Case4	Case 5
Demographic and Preoperative data					
age	44	51	35	39	47
sex	F	F	F	F	M
BMI	19.6	20	17.5	14.5	19
Cause of intestinal failure	NET(carcinoid)with liver metastasis	Abdominal aneurysm	PVT after laparoscopic colectomy	Diffuse mesenteric &PVT	Klatskin tumor
ABO typing	A+	A+	A-	A+	O+
Comorbidity	-	-	IFLAD	DM , Addiction	-
Waiting time (days)	62	2	101	197	30
Length of hospitalization before TX (days)	62	2	79	25	30
Outpatient department PN	yes	No	No	No	No
Length of TPN (days)	62	-	110	24	20
Hemoglobin (gr/dl)	11.9	12.7	9.3	9.4	9.8
Albumin(mean)	2.3	2.6	2.9	3.9	3.5
Total bilirubin(mean)	0.58	2.59	3.9	1.8	2.5
Direct bilirubin(mean)	0.25	0.34	2.25	0.4	1.3
Serum creatinine (mean)	0.7	0.8	0.9	0.7	0.8
Intraoperative data					
Ringer lactate (ml)	500	-	-	500	500
N/S (ml)	2500	2500	5500	2500	5500
Gelatin (ml)	1000	1000	-	2000	-

Fluid cc/kg/h	17	13	15.5	14.5	15.5
Albumin 5% (gr)	20	30	40	30	30
Packed cell transfusion	5bag	3bag	5 bag	7bag	4bag
cryoprecipitate	-	-	-	5 bag	-
approximate Blood loss (ml)	1500	1500	3000	5000	2000
Hco3, before reperfusion	13.6	15.5	12.5	22.6	15.9
K serum before reperfusion	3	3.4	2.6	3.4	3.5
BE, before reperfusion	-13	-11.7	-13.9	-1.7	-9.7
Hco3,30 min after reperfusion	21.6	20.3	14.2	19.2	21
BE, 30 min after reperfusion	-3.3	-5.1	-6.4	-6.5	-3.5
K serum, 30 min after reperfusion	3.9	3.2	2.7	2.7	2.7
Operation time(min)	300	300	420	360	420
CIT(min)	240	270	120	180	160
WIT(min)	60	30	35	60	45

Supplementary table 1: Complications during 6 month post operation

	case 1	Case 2	Case 3	Case4	Case 5
Infection (site/pathogenesis)	Esophagitis (HSV)	Sputum (kelebsiella)	BSI & pneumonia (kelebsiella)	BSI (VRE)	pneumonia (kelebsiella)
CMV infection	-	-	-	-	-
Other complication	Entrocotaneous fistula	Pancreatitis & small bowel obstruction	-	Pancreatitis & small bowel obstruction	Entrocotaneous fistula
Patient status	alive	expired	expired	alive	expired
Cause of death	-	GVHD	Sever sepsis	-	Sever sepsis
Time of death	-	3 month later	2month later	-	2month later

Figures

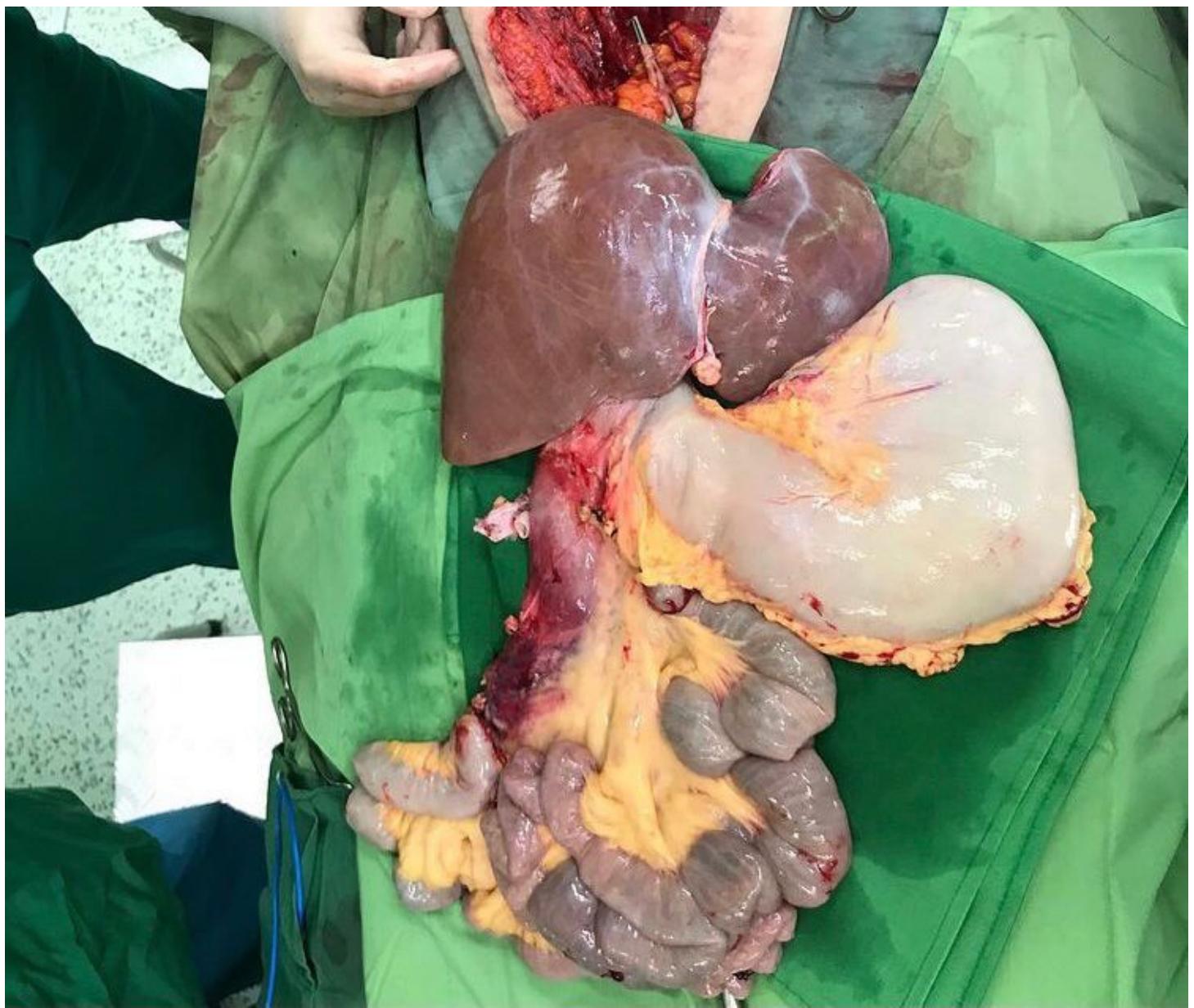


Figure 1

Recovered organs before implantation.

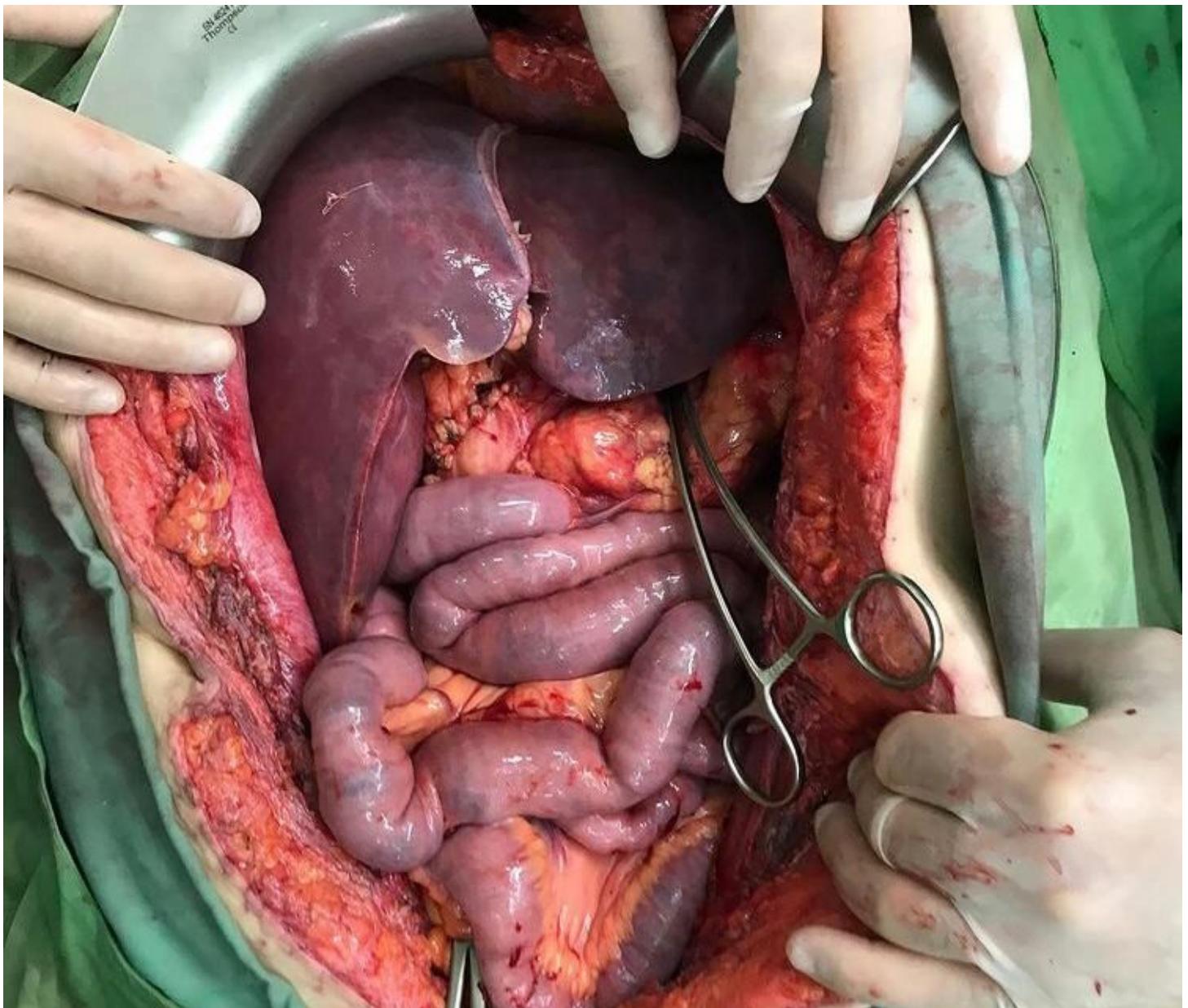


Figure 2

Implanted organs after reperfusion