Original Research Article

Anaesthesia for liver transplantation at King Hussein medical centre: an overview of 70 cases

Ashraf Fadel Mohammad*, Ghazi S. Aldehayat, Qais K. Al-Qusus, Mohammad A. Khasawneh, Yaser A. Alghoul

Department of Anaesthesia and Intensive Care at Jordanian Royal Medical Services, Amman, Jordan

*Correspondence:
Dr. Ashraf Fadel Mohammad,
E-mail: ashraffadel1975@yahoo.com

ABSTRACT

Background: To review the indications, patients' demographics, and anaesthetic protocol and to analyze perioperative complications of liver transplantation surgery.

Methods: Retrospective analysis of 70 cases of LT in the period between June 2004 and October 2020 at King Hussein medical centre. Preoperative factors such as patients' demographics, age, gender, etiology of hepatic pathology, laboratory investigations, model for end-stage liver disease scores, duration of surgery and type of liver donation were recorded. Intraoperative factors such as anaesthetic and surgical protocols, need of blood product transfusions and haemodynamic monitoring were analyzed. Postoperative tracking of patients' complications and outcomes was done.

Results: 68 living donor and two cadaveric LT procedures. Male to female ratio was 2.9:1.The age of LT recipients ranged from 3 to 62 years with an average age of 38.45 years. Their body weights ranged from 13 to 100 kg with mean body weight of 67.03 kg. Most common indication was cryptogenic liver cirrhosis (21.4%), followed by cirrhosis due to viral hepatitis B (15.7%). Autoimmune hepatitis was an indication in 11.4% and hepatitis C liver cirrhosis in 10%. All living donors were closely related. Right hepatic lobe graft was used in 85.7% of transplantations. Average red cells concentrate (RCC) transfused (units) was 3.1±3.97 (mean±SD). Duration of surgery (hours) was 12.5±2.4 (mean±SD). Fast track LT with extubation in theatre was done in 37 LT recipients (52.9%). Readmission to operative theatre was needed in 5 recipients (7.14%). Most common long term complications were biliary leak (20%), biliary stenosis (14.2%) and recurrence of primary disease (12.9%).

Conclusions: Transplantation from living donors was by far more common in our study population. Majority of recipients were male and cryptogenic liver cirrhosis was the most common indication. Right hepatic lobe graft was used mostly. Biliary leak was the most common postoperative complication. Surgical time duration and blood products transfusion decreased significantly over years since the start of LT program.

Keywords: Anesthesia, Indications, Liver, Recipient, Transfusion, Transplantation

INTRODUCTION

LT has become a treatment option for many patients with end-stage liver disease or failure. Nowadays, the liver is the second most commonly transplanted solid organ after the kidney.[1] In 2017, statistics showed that more than eight thousand patients received liver transplantation and more than thirteen thousand patients were on the waiting list for liver transplant in the United States of America alone.[2] In 1958, Francis Moore described the orthotopic liver transplantation technique in dogs.[3] The first cadaveric human liver transplant was performed in

Colorado in 1963 by Thomas Starzl. The first human LT recipient was a 3 year old child with biliary atresia, who unfortunately died intraoperatively as a result of uncontrollable haemorrhage. In the first five cadaveric liver transplantations no patient survived more than 23 days. However, it was not until 1967 when Starzl performed the first successful liver transplantation (LT) on a 19-month-old girl with hepatocellular carcinoma (HCC) that resulted in an extended survival.[4] LT has witnessed enormous progress over the last 50 years and now it can be considered a life-saving procedure for patients with liver failure.

In current study we will review the indications (etiology of hepatic failure) of LT, recipients demographics. We will also present our LT anaesthetic protocol and the perioperative complications of LT.

METHODS

Current study is a single centre, retrospective analysis of medical records of 70 cases of LT at King Hussein medical centre (KHMC), Amman, Jordan in the period between June 2002 and October 2020. Patients' data was collected on special forms designed for the purpose of this study and subsequently tabulated for analysis. Microsoft Excel was used to analyse data. Data is presented as mean, range and standard deviation (SD) or numbers and percentages. Ethical committee approval obtained.

Inclusion and exclusion criteria

Inclusion criteria for current study were recipients of LT from all ages. Patients with incomplete or missing data were excluded from current study.

Anaesthetic protocol

Multidisciplinary preoperative assessment that involves gastroenterologists, hepatobiliary surgeons, vascular surgeons, radiologists, cardiologists, anaesthetists and psychologists was done before each procedure. Multidisciplinary meetings and discussions of the LT team were conducted preoperatively. Intraoperatively, haemodynamic monitoring starts before induction of anaesthesia with the basic monitoring of pulse oximetry, electrocardiography, end-tidal carbon dioxide monitoring, non-invasive blood pressure, invasive arterial blood pressure (radial artery cannulation under local anaesthesia) and semi-invasive cardiac output monitoring.

Induction of anaesthesia with fentanyl 2 mcg/kg, propofol 3 mg/kg or etomidate 0.3 mg/kg and a neuromuscular blocker (cis-atracurium). Rapid sequence induction of anaesthesia (RSI) with suxamethonium chloride 1.5 mg/kg was carried out in patients with high risk of aspiration (such as the presence of ascites, gastro-oesophageal reflux or gastric paresis). Vasopressors such

as ephedrine, phenylephrine or diluted noradrenaline were used as boluses or infusions if needed at the time of induction of anaesthesia. General anaesthesia is maintained with a balanced technique that includes an inhalational agent (sevoflurane or isoflurane), neuromuscular blocker infusion (cis-atracurium) and an opioid infusion (remifentanil). The right internal jugular artery is cannulated at with multi-lumen venous catheter and two dilator sheaths (7 French). Pulmonary artery catheter (Swan-Ganz catheter) was introduced through one of the dilator sheaths while the other dilator sheath is connected to a previously primed rapid infusion device. Transesophageal echocardiography (TEE) was used in selected cases.

Stages of surgery

LT is complex surgery that constitute of three phases; each phase has its peculiar anaesthetic considerations: pre-anhepatic phase: This phase spans from skin incision to clamping of the inferior vena cava (IVC), portal vein and hepatic artery. At this phase the liver is being dissected, and significant bleeding can occur. Anhepatic phase: this phase extends from the moment that hepatic venous inflow is being clamped up to graft reperfusion. At this phase the IVC clamping causes a decrease in cardiac output (CO). Neo-hepatic phase: this phase begins from the moment of liver reperfusion and resumption of flow in the portal vein and IVC. This phase is complicated by post-reperfusion syndrome (PRS) or bleeding from sites of vascular anastomosis (IVC, hepatic artery or portal vein).

The main intraoperative anaesthetic considerations are bleeding and haemodynamic instability. Cell salvage devices are routinely used unless contraindicated (the presence of neoplasia or infection represents an absolute contraindications for cell salvage devices). Emergency drugs should be readily available as boluses and infusions during the three phases of LT surgery; and they include: adrenaline, dopamine, noradrenaline, vasopressin and calcium chloride (or gluconate).

The use of short-acting opioids, neuromuscular blockers and anaesthetic agents allows for early recovery after LT surgery. Immediate postoperative extubation in the operating theatre could be safely performed in a large fraction of patients without an increased risk of subsequent reintubation. However, some patients with poor clinical condition preoperatively or patients with complicated intraoperative course may not be eligible for fast tracking protocols and may need stabilization in the intensive care unit before endotracheal extubation.

RESULTS

Recipients' characteristics, demographic data and disease severity are presented in (Table 1). The mean age of the LT recipients was 37.7±16.3 years. Majority of LT recipients were males (74.3%). Adult LT recipients were

59 patients (84.3%) while paediatric recipients were 11 (15.7%). Most common type of liver donation in our study was from living donors (97.1%).

Table 1: Recipients' characteristics.

Characteristics	Observation
Age, mean ±SD	37.7±16.3 years
Adults, N (%)	59 (84.3)
Adults, average age ±SD	42.5±12.9 years
Paediatric, N (%)	11 (15.7)
Paediatric, average age ±SD	12±4.1 years
Males, N (%)	52 (74.3)
Female, N (%)	18 (25.7)
Redo-liver transplantation, N (%)	1 (1.4)
Living donor liver transplantation (LDLT), N (%)	68 (97.1)
Cadaveric donor liver transplantation (CDLT), N (%)	2 (2.9)
Two solid organs transplantation, N (%)	1 (1.4) (liver and kidney transplantation)
Average MELD* score ±SD	20.4±7.1

*MELD: model for end stage liver disease

The leading cause of liver failure necessitating LT was cryptogenic liver cirrhosis (21.43%), followed by viral hepatitis B (15.71%). Etiological factors of liver failure in this study population and their relative frequencies are shown in (Table 2). Recipients' intraoperative characteristics and perioperative complications are presented in (Table 3). Duration of LT procedure averaged 12.5±2.4 hours (ranged from 8 hours to 20 hours). Blood salvage techniques were used in 61 patients (87.14%). Massive blood transfusion was needed in 8 recipients (11.4%). Theatre extubation was possible in 37 recipients (52.9%) and 5 patients needed theatre readmission for surgical re-exploration (7.14%). Most common late postoperative complication was biliary leak (20%). Surgical time duration and blood products transfusion are presented in (Figures 1-2). Surgical time duration varied but showed gradual decline over years (Figure 1). In general, the amount of blood products transfused decreased also over the 16 years of the study.

DISCUSSION

Liver transplantation is a therapeutic option of choice for acute and chronic end-stage liver disease.[5] The LT programme was introduced in Jordan at King Hussein medical centre (KHMC) in 2004. Between 2004 and 2009 a LT team from Turkey was invited to perform the procedure at KHMC. From 2009 all LT procedures were done by our staff. In most part of the world, the main source of liver for transplantation remains the donation after brain death (DBD), but due to shortage of cadaveric organs and high mortality of patients awaiting LT other options such as split liver transplantation, living donor

liver transplantation (LDLT), and donation after cardiac death (DCD) have been used. LDLT has been accepted as an alternative option especially in view of scarcity of cadaveric organs due to cultural beliefs in the middle-eastern societies.

Likewise, due to shortage of deceased donor liver transplantation (DDLT) at KHMC in Jordan, LDLT is the most common source of hepatic grafts for patients with ESLD. Only two of the seventy cases reviewed in this survey had cadaveric hepatic grafts. The majority of donors for LDLT were first degree relatives (parent to offspring or offspring to parent). Ethical quandary of exposing healthy living donors to major surgery exists. This mandates careful selection of the LDLT donors and very meticulous surgery and anesthesia.

Table 2: Recipients' etiology of liver failure.

Indication	N	%	Age range	Mean age
Cryptogenic liver cirrhosis	15	21.43	11-60	43.5
Viral hepatitis B	11	15.71	40-62	50.75
Viral hepatitis C	7	10	49-58	54.5
Autoimmune hepatitis	8	11.43	12-30	22.5
Hepatocellular carcinoma	9	12.86	26-62	43.83
Primary sclerosing cholangitis (PSC)	3	4.28	39-42	40.5
Progressive familial intrahepatic cholestasis	2	2.86	12-23	17.5
Biliary atresia	2	2.86	6-19	12.5
Re-transplantation (Redo)	1	1.43	52	52
Congenital hyperbilirubinemia	1	1.43	17	17
Budd-Chiarry Syndrome	1	1.43	17	17
Secondary biliary cirrhosis	1	1.43	49	49
Wilson disease	1	1.43	-	-
Primary biliary cirrhosis (PBC)	1	1.43	3	3
Histiocytosis	1	1.43	37	37
Hyperoxaluria (causing ESRD)*	1	1.43	21	21
Congenital hepatic fibrosis	1	1.43	10	10
Alcoholic liver cirrhosis	1	1.43	49	49
Secondary sclerosing cholangitis	1	1.43	40	40
Criggler-Najjar	2	2.86	12	12
Total cases	70	100	-	-

Donors for LDLT in our centre will usually have a thoracic epidural catheter inserted preoperatively. The use of thoracic epidural analgesia (TEA) in conjunction with general anaesthesia is associated with reduction of intraoperative anaesthetic requirements; blood loss and lung atelectasis.[6] It also has positive effects on postoperative pulmonary function and provides excellent postoperative pain relief.[7] Such benefits for epidural anaesthesia in donors for LDLT have also been demonstrated in many studies.[8-10] On the other hand the use of TEA in LT recipients is a debatable issue due to coagulation profile derangements and bleeding tendency in patients with liver failure.[11,12] Li et al. demonstrated significantly increased risk of major bleeding after invasive procedures in cirrhosis.[13] None of the recipients in our cohort received TEA as patients may suffer coagulation derangements perioperatively, which may expose patients to risk of developing epidural hematoma. Nevertheless, recent publication by Hausken et al in a 10-year study demonstrated the selected use of TEA in 327 recipients (out of 685) without any serious complications.[14]

Table 3: Recipients intraoperative characteristics and complications.

Intraoperative characteristic	N (%)
Duration of surgery (hours), mean ±SD	12.5±2.4
Patients who had autologous blood transfusion (Cell saver)	61 (87.14)
Patients who had homologous (allogenic) blood transfusion	62 (88.6)
Patients who needed massive blood transfusion	8 (11.4)
Average red cell concentrate (RCC) transfused (units): mean ±SD	3.1±3.97
Average fresh frozen plasma (FFP) transfused (units): mean ±SD	4.59±4.75
Average platelets transfused (units): mean±SD	2.1±3.5
Use of pulmonary artery catheter (Swan-Ganz)	69 (98.6)
Use of semi-invasive cardiac output measurement device	70 (100)
Use of transesophageal echocardiography (TEE)	5 (7.14)
Need of Intraoperative vasopressor/inotrope infusion	55 (78.6)
Intraoperative mortality	1 (1.4)
Extubation in theatre (fast-tract surgery)	37 (52.9)
Readmission to theatre (Re-exploration)	5 (7.14)
Long term complications	
Biliary leak	14 (20)
Biliary stricture (stenosis)	10 (14.3)
Recurrence of disease	9 (12.9)
Acute rejection	5 (7.14)
Wound infection	4 (5.71)

Most of the recipients for LT in our study were males (74.3%) (Table1). Similar results of sex disparity were noted in literature by Sarkar et al and Darden et al.[15,16] Both aforementioned studies explained this sex disparity by size differentials between men and women as well as differences in liver compartment size. Moreover, Allen et al. explained the reduced access to liver transplantation in women by underestimation of disease severity by model for end-stage liver disease (MELD) score.[17] Orthotopic LT can be marked by significant hemodynamic instability (in LT recipients), which mandates the use of a variety of hemodynamic monitors to navigate intraoperative and early postoperative management.[18] Advanced haemodynamic monitoring is used to guide optimal fluid balance, assessment for the need and choice of inotrope or a vasopressor.[19] Our protocol includes the use of pulmonary artery catheter (PAC, Swan-Ganz), cardiac output based on arterial waveform analysis in all patients and the use of transesophageal echocardiography (TEE) in selected patients. Although that the use of PAC does have significant diagnostic limitations; it is still one of the most precise means of CO measurement and an essential monitor in patients with significant pulmonary vascular disease.[20] Another benefit is the measurement of mixed venous oxygen saturation (SvO_2) via PAC which indirectly allows assessment of CO.[21] The use of PAC facilitates for the measurement of CO via intermittent thermo-dilution.[22] Although often considered as the gold standard for CO measurements, its accuracy depends on several user-dependent techniques such as speed of injection, volume of injectate and temperature of injected saline.[23] Accuracy can also be limited by the presence of tricuspid regurgitation or intracardiac shunts.[24] A new generation of PACs can allow for continuous CO measurement.[25] This new technology utilizes heat instead of cold thermodilution via a thermal filament connected to a specialized PAC and a distal thermistor.[25] However, this new generation PACs is still not available at our unit. Several less invasive commercial devices for continuous cardiac output based on arterial waveform are currently available PiCCO (pulse contour cardiac output), LiDCO (lithium dilution cardiac output) and flowtrac/vigileo system).[26,27] We use the flowtrac/vigileo system because it uniquely does not require intermittent CO bolus calibration. The CO waveform technology allows for the continuous beat-to-beat measurements of stroke volume variation (SVV) and pulse pressure variation (PPV) which are valuable tools for fluid responsiveness assessment.[28] Patients with liver cirrhosis are known to have hyper-dynamic circulation characterised by low systemic vascular resistance and high cardiac output.[29] This observation was evident in current study. Patients with hepatic failure have impaired production of pro-coagulant and anticoagulant factors which results in severe derangements in clotting. Our protocol includes the use of thromboelastography (TEG) in addition to the traditional coagulation investigations. TEG is a viscoelastic test that allows rapid evaluation of clot formation, clot strength and fibrinolysis from a sample of whole blood.[30,31] Evidence exist that utilization of TEG

rather than traditional coagulation studies results in the administration of fewer blood products.[32] All patients in this study received one gram of tranexamic acid during the first stage of surgery (pre-anhepatic phase). The safety and efficacy of use of tranexamic acid intraoperatively in liver recipients was demonstrated by Badenoch et al and Boylan et al.[33,34] Immediate postoperative extubation after LT is expected to have many clinical and economic benefits.[35] However, LT recipients often present with various preoperative co-morbidities, long duration of surgery, large intraoperative fluid shifts, and delayed correction of metabolic and coagulation derangements by the transplanted liver which may make theatre extubation difficult or unfavorable.[36] More than half of LT recipients (52.9%) in this survey were extubated in theatre.
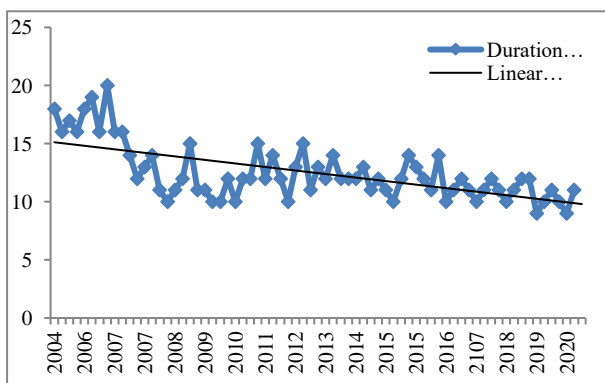

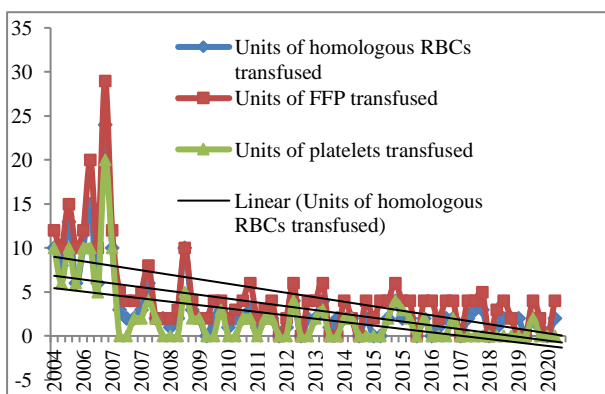**Figure 1: Duration of recipients' surgery.**

Figure 2: Recipients' blood products transfusion requirements.

Although the duration of recipients' surgery and the amount of intraoperative blood loss varied in correlation with several factors such as preoperative coagulation status, presence of previous abdominal surgery, previous hepatectomy or redo LT procedure the overall trend (Figure 1-2) showed gradual decrease in the duration of surgery and the amount of blood (and products) transfusions which can be explained by the increase in experience of our LT team over the last 16 years and the implementation and better use of newer technologies in haemodynamic and neurological intraoperative

monitoring, TEG and intraoperative cell salvage (cell saver).

Limitations

Limitation of current study was it is a single centre study with retrospective and descriptive design.

CONCLUSION

LDLT is more common in our centre. Most of LT recipients are males. Surgical time duration and blood products transfusion decreased significantly over years since the start of LT program. Fast tract LT was feasible and immediate postoperative extubation was accomplished in majority of patients.

REFERENCES

1. Mahmud N. Selection for Liver Transplantation: Indications and Evaluation. Curr Hepatology Rep. 2020;19:203-12.
2. Kim WR, Lake JR, Smith JM, Schladt DP, Skeans MA, Harper AM, et al. OPTN/SRTR 2016 annual data report: liver. Am J Transplant. 2018;18(1):172-253.
3. Meirelles RF, Salvalaggio P, Rezende MB, Evangelista AS, Guardia BD, Matielo CE, et al. Liver transplantation: history, outcomes and perspectives. Einstein (Sao Paulo). 2015;13(1):149-52.
4. Starzl TE, Marchioro TL, Vonkaulla KN, Hermann G, Brittain RS, Waddell WR. Homotransplantation of the liver in humans. Surg Gynecol Obstet. 1963;117:659-76
5. Song AT, Avelino-Silva VI, Pecora RA, Pugliese V, D'Albuquerque LA, Abdala E. Liver transplantation: fifty years of experience. World J Gastroenterol. 2014 May 14;20(18):5363-74.
6. Atalan HK, Gucyetmez B, Donmez R, Kargi A, Polat KY. Advantages of epidural analgesia on pulmonary functions in liver transplant donors. Transplant Proc. 2017;49(6):1351-6.
7. Koul A, Pant D, Rudravaram S, Sood J. Thoracic epidural analgesia in donor hepatectomy: An analysis. Liver Transpl. 2018;24(2):214-21.
8. Esteve N, Ferrer A, Sansaloni C, Mariscal M, Torres M, Mora C. Epidural anesthesia and analgesia in liver resection: Safety and effectiveness. Rev Esp Anestesiol Reanim. 2017;64(2):86-94.
9. Clarke H, Chandy T, Srinivas C, Ladak S, Okubo N, Mitsakakis N, et al. Epidural analgesia provides better pain management after live liver donation: a retrospective study. Liver Transpl. 2011;17(3):315-23.

10. Feltracco P, Brezzi ML, Barbieri S, Serra E, Milevoj M, Ori C. Epidural anesthesia and analgesia in liver resection and living donor hepatectomy. Transplant Proc. 2008;40(4):1165-8.

11. Blonski W, Siropaides T, Reddy KR. Coagulopathy in liver disease. Curr Treat Options Gastroenterol. 2007;10(6):464-73.

12. Intagliata NM, Davis JPE, Caldwell SH. Coagulation pathways, hemostasis, and thrombosis in liver failure. Semin Respir Crit Care Med. 2018; 39(5):598-608.

13. Li J, Han B, Li H, Deng H, Méndez-Sánchez N, Guo X, Qi X. Association of coagulopathy with the risk of bleeding after invasive procedures in liver cirrhosis. Saudi J Gastroenterol. 2018;24(4):220-7.

14. Hausken J, Haugaa H, Hagness M, Line PD, Melum E, Tønnessen TI. Thoracic epidural analgesia for postoperative pain management in liver transplantation: A 10-year study on 685 liver transplant recipients. Transplant Direct. 2021;7(2): e648.

15. Sarkar M, Watt KD, Terrault N, Berenguer M. Outcomes in liver transplantation: does sex matter? J Hepatol. 2015;62(4):946-55.

16. Darden M, Parker G, Anderson E, Buell JF. Persistent sex disparity in liver transplantation rates. Surgery. 2021;169(3):694-9.

17. Allen AM, Heimbach JK, Larson JJ, Mara KC, Kim WR, Kamath PS, et al. Reduced access to liver transplantation in women: role of height, meld exception scores, and renal function underestimation. Transplantation. 2018;102(10): 1710-6.

18. Rudnick MR, Marchi LD, Plotkin JS. Hemodynamic monitoring during liver transplantation: A state of the art review. World J Hepatol. 2015;7(10):1302-11.

19. Krenn CG, De Wolf AM. Current approach to intraoperative monitoring in liver transplantation. Curr Opin Organ Transplant. 2008;13(3):285-90.

20. Della Rocca G, Brondani A, Costa MG. Intraoperative hemodynamic monitoring during organ transplantation: what is new? Curr Opin Organ Transplant. 2009;14(3):291-6.

21. Whitener S, Konoske R, Mark JB. Pulmonary artery catheter. Best Pract Res Clin Anaesthesiol. 2014; 28(4):323-35.

22. Vilchez-Monge AL, Tranche Alvarez-Cagigas I, Perez-Peña J, Olmedilla L, Jimeno C, Sanz J, Bellón Cano JM, et al. Cardiac output monitoring with pulmonary versus transpulmonary thermodilution during liver transplantation: interchangeable methods?. Minerva Anestesiol. 2014;80(11):1178-87.

23. Robin E, Costecalde M, Lebuffe G, Vallet B. Clinical relevance of data from the pulmonary artery catheter. Crit Care. 2006;10(3):S3.

24. Schmid B, Fink K, Olschewski M, Richter S, Schwab T, Brunner M, et al. Accuracy and precision of transcardiopulmonary thermodilution in patients with cardiogenic shock. J Clin Monit Comput. 2016; 30(6):849-56.

25. Quintana-Villamandos B, Barranco M, Fernández I, Ruiz M, Del Cañizo JF. New advances in monitoring cardiac output in circulatory mechanical assistance devices. A validation study in a porcine model. Front Physiol. 2021;12:634779.

26. Lamia B, Kim HK, Severyn DA, Pinsky MR. Cross-comparisons of trending accuracies of continuous cardiac-output measurements: pulse contour analysis, bioreactance, and pulmonary-artery catheter. J Clin Monit Comput. 2018;32(1):33-43.

27. Mehta Y, Arora D. Newer methods of cardiac output monitoring. World J Cardiol. 2014;6(9): 1022-9.

28. Willars C, Dada A, Hughes T, Green D. Functional haemodynamic monitoring: The value of SVV as measured by the LiDCORapid™ in predicting fluid responsiveness in high risk vascular surgical patients. Int J Surg. 2012;10(3):148-52.

29. Blendis L, Wong F. The hyperdynamic circulation in cirrhosis: an overview. Pharmacol Ther. 2001; 89(3):221-31.

30. Whiting D, DiNardo JA. TEG and ROTEM: technology and clinical applications. Am J Hematol. 2014;89(2):228-32.

31. Hawkins RB, Raymond SL, Hartjes T, Efron PA, Larson SD, Andreoni KA, et al: The perioperative use of thromboelastography for liver transplant patients. Transplant Proc. 2018;50(10):3552-8.

32. Wang SC, Shieh JF, Chang KY, Chu YC, Liu CS, Loong CC, et al. Thromboelastography-guided transfusion decreases intraoperative blood transfusion during orthotopic liver transplantation: randomized clinical trial. Transplant Proc. 2010; 42(7):2590-3.

33. Badenoch A, Sharma A, Gower S, Selzner M, Srinivas C, Wąsowicz M, et al. The effectiveness and safety of tranexamic acid in orthotopic liver transplantation clinical practice: a propensity score matched cohort study. Transplantation. 2017; 101(7):1658-65.

34. Boylan JF, Klinck JR, Sandler AN, Arellano R, Greig PD, Nierenberg H, et al. Tranexamic acid reduces blood loss, transfusion requirements, and coagulation factor use in primary orthotopic liver transplantation. Anesthesiology. 1996;85(5):1043-8.

35. Wu J, Rastogi V, Zheng SS. Clinical practice of early extubation after liver transplantation. Hepatobiliary Pancreat Dis Int. 2012;11(6):577-85.

36. Aneja S, Raina R. Immediate postoperative extubation after liver transplantation at our centre: A report of two cases. Indian J Anaesth. 2011;55(4): 392-4.