Postoperative Critical Care in Liver Transplantation

Subjects: Transplantation

Contributor: Fuat H. Saner , Dieter P. Hoyer , Matthias Hartmann , Knut M. Nowak , Dmitri Bezinover

Perioperative care of patients undergoing liver transplantation (LT) is very complex. Metabolic derangements, hypothermia, coagulopathy and thromboses, severe infections, and graft dysfunction can affect outcomes. Advances in pre-transplant evaluation, surgical technique, and an increased understanding of the pathophysiology of cirrhosis significantly improved patient outcome. Due to the increasing demand for organs, a higher number of extended criteria grafts (ECD) are being used for transplantation. The use of ECD grafts has been shown to be associated with a higher rate of early allograft dysfunction (EAD), which results in dysfunction of other organ systems.

liver hemostasis graft dysfunction

1. Infection Prophylaxis

Infection prevention is an important problem in the care of liver transplantation (LT) recipients. The incidence of infection after LT varies from 53% to 79%, with most infections occurring in the first month after transplantation [1].

In 2009, a survey was sent out to all LT centers who are members of the European Liver and Intestine Transplant Association [2]. This survey analyzed the differences in prophylactic antimicrobial regimens used in LT recipients. For elective LT, beta-lactam antibiotics or co-trimoxazole were used as first-line antibiotic prophylaxis in 25% of all centers; third or fourth generation cephalosporins, as well as glycopeptide, carbapenem, or antipseudomonas were used in 73% of centers; and 2% of centers used a 6-month rotation strategy using two different types of broad-spectrum antibiotics. Antifungal prophylaxis was administered in 35% of centers for all LT recipients; only in patients at risk in 53% of centers; and in 12% of centers, antifungal prophylaxis was not used. The duration of antibiotic prophylaxis was also different between centers, from 24 h to 1 week.

In 2019, Berry et al. published a randomized controlled trial (RCT) comparing 72 h of perioperative antibiotic prophylaxis protocols [3]. Their initial hypothesis was that 72 h preoperative prophylaxis would decrease rates of surgical site infection (SSI) in LT patients when compared with intraoperative antibiotic prophylaxis alone. A total of 102 patients were randomized as follows: 51 patients to the extended antibiotic group, and 51 to the intraoperative antibiotic group. Rates of SSI and nosocomial infection were not different between groups. Moreover, ICU and hospital length of stay (LOS), 30-day mortality, and time to infection were also similar in both groups. Patients developing infections had longer ICU and hospital LOS and a higher prevalence of reoperation. These results suggest that intraoperative antibiotic prophylaxis alone is acceptable for LT without increased risk of infection.

There is a general recommendation to use antifungal prophylaxis in high-risk patients with a MELD score above 20 [4][5]. Antifungal treatment is also recommended for patients with MELD scores above 30, patients needing reoperation (for bleeding or bile leak), on renal replacement therapy, receiving pulsed dose cortisone for rejection, or categorized as at high-risk for fungal infection.

In 2006, Cruciani et al. published a meta-analysis that included six RCT evaluating antifungal prophylaxis in LT recipients [6]. They found a reduced rate of colonization, fungal infection, and fungal-related deaths in the groups where antifungal prophylaxis was performed. Compared to controls, however, the rate of resistant *Candida* spp. was higher in the prophylaxis group; although, the overall mortality was not different. In 2014, Evans at al. published a similar meta-analysis encompassing 14 RCT that included echinocandins (a new drug for prophylaxis) [7]. The results were similar: the use of antifungal drugs as prophylaxis was protective against colonization, invasive fungal infection (IFI), and IFI-related deaths, but overall mortality was not affected.

In a multicenter, retrospective study, Raghuram et al. evaluated the rate of fungal infections in high-volume US LT centers over a period of 5 years [8]. They found that the rate of IFI was 11.5%. The main fungus isolated was *non-albicans* (58%), and only 28% were isolated as *C. albicans*, 15% *aspergillosis,* and 3% *Cryptococcus*. Among the *C. albicans,* only 44% were susceptible to fluconazole. One hundred percent of *C. parapsilosis* were resistant to fluconazole. The authors concluded that the use of antifungal prophylaxis did not reduce the rate of IFI. Moreover, infections with fluconazole-resistant *Candida* spp. were associated with a higher mortality. In another cohort study published in 2008, the incidence of IFI was 6.1% [9]. At that time, all patients received antifungal prophylaxis with fluconazole. Thirteen years later, the same group reported an IFI rate of 5.6%, but without antifungal prophylaxis [10]. It is interesting to note that in the second period study, the patients' MELD scores were higher (14 vs. 20).

In conclusion, recent studies have demonstrated that prolonged (more than 24 h) antibacterial prophylaxis is not required. Antifungal prophylaxis should be considered in high-risk patients; however, a clear survival benefit has not been demonstrated.

Viral infections are also a significant problem in the postoperative period, with human cytomegalovirus (CMV) being most common in LT recipients. The main risk factor for developing CMV is a recipient's CMV-seronegative status. Without prophylaxis, the prevalence of CMV has been reported to be 78–88% in seronegative recipients (R-) obtaining a seropositive organ (D+). This incidence decreases to 13% if donor and recipient are CMV-seronegative [11]. Oral valganciclovir and intravenous gancicilor are used for both prophylaxis and treatment [12]. The recommended dose of valganciclovir is 900 mg/day, which should be adjusted when kidney function is impaired. The duration of prophylaxis in high-risk patients (D+/R−) has not been specified, but is generally recommended for 6 months [13]. For R+ recipients, the recommend duration of therapy is 3 months.

The management of chronic hepatitis B infections (HBV) is very complex and beyond the scope of this research. In the absence of prophylaxis, recurrence of HBV cirrhosis after LT is very high [14]. The use of hepatitis B immunglobulin (HBIG), becoming available only within the last 20 years [15], together with antiviral medications

such as lamivudine, entecavir, and tenofovir, improved 5-year survival from 45% to 85% after LT [16]. Based on this success, HBs-Ag-positive or Anti-HBc-positive donor organs are recognized as extended criteria organs and can be used for LT. Prophylaxis with antiviral medication, with or without HBIG, is recommended to prevent transmission of HBV, if these grafts are used for LT [17].

In conclusion, the recommended CMV prophylaxis includes valganciclor or ganciclovir for D(+) and R(−) organs. In patients transplanted due to hepatitis B, or if a HBc-positive donor organ is used, prophylaxis should be performed using HBIG and the antiviral medications, entecavir or tenofovir.

2. Management of Coagulopathy

2.1. Coagulopathy Assessment

The first attempts at human LT were associated with very high mortality. Uncontrolled bleeding (and in few cases, thromboembolism) were the major causes of death in these patients. This was only partially related to surgical expertise. An even greater problem was a lack of experience in the management of coagulopathy in patients with end stage liver disease (ESLD). It was quickly understood that standard laboratory tests (SLTs) do not accurately reflect the coagulation profile in patients with ESLD. In 1981, Ewe et al. published a paper evaluating bleeding after liver biopsy [18]. The authors raised a concern that SLTs did not correlate with the bleeding time after procedure. The number of patients with a completely normal coagulation profile had prolonged bleeding, whereas other patients with an international normalized ratio (INR) above 3 did not have significant bleeding. Several patients with a platelet count above >100/nL had prolonged bleeding, and several patients with a platelet count below 20/nL did not bleed. These observations were confirmed in a meta-analysis performed by Haas et al. [19] They evaluated 53 studies related to the overall management of the bleeding (not just in patients with ESLD), and found that SLTs are not useful in guiding bleeding management. SLTs frequently do not correctly reflect the overall coagulation picture in patients with ESLD because they are designed to assess only procoagulants (in patients with ESLD, levels of both pro-and anti-coagulants are decreased). SLTs are measured in plasma (with the addition of thrombin and calcium) resulting from centrifuged citrated blood. This approach does not reflect the interaction between the different branches of the coagulation cascade. Viscoelastic tests (VET) can be used as an alternative to SLTs. As opposed to SLTs, VETs are performed on whole blood and reflect the interaction between pro- and anti-coagulants, and platelets [20].

The use of VET for managing hemorrhagic shock and other bleeding disorders is recommended by the European Society of Anesthesiology [21]. In two RCTs, the use of VET to guide transfusion in patients with ESLD was significantly associated with decreased blood product use without increasing spontaneous or procedure-related bleeding [22][23]. The use of VET for managing coagulopathy during LT was recently recommended in the ERAS project performed by the ILTS [24].

2.2. Thromboembolism in End Stage Liver Disease

The coagulation system in ESLD patients is in a delicate balance between bleeding and clotting. It can be easily tilted in either direction [25]. One of the first papers confirming that patients with ESLD are prone to thromboses was based on the Danish National Registry and published in 2009 [26]. The authors evaluated over 99,000 patients with venous thromboembolism (VTE) compared to over 400,000 controls. Patients with both cirrhotic and non-cirrhotic liver disease had an elevated relative risk for thromboses (1.74 and 1.87, respectively). Similar results were demonstrated later in the US [27]. The causes of hypercoagulability in ESLD are mostly related to endothelial dysfunction [28][29], with release of von Willebrand factor (vWF), factor VIII, and plasminogen activator inhibitor-1 [20][30][31][32] from the endothelium combined with a simultaneous decrease in hepatic production of ADAMRS13 (a cleaving protease regulating vWF) [33]. Other causes of hypercoagulability include overproduction of thrombin due to thrombomodulin resistance [34] and increased clot stability [35]. There is also number of genetic mutations predisposing patients with ESLD to thromboses [36][37].

2.3. Use of Coagulation Factor Concentrates

As an alternative to fresh-frozen plasma (FFP), coagulation factor concentrates are available. The most commonly used products in hepatic surgery or in cirrhotic patients are prothrombin complex concentrates (PCC), which include factor II, VII, IX, and X. Additionally, four-factor PCC contains heparin, and proteins C and S, which makes this a well-balanced compound. In vitro, PCC has been demonstrated to improve thrombin generation in patients with ESLD significantly better than FFP [38]. The use of factor concentrates appears safe when used in bleeding patients if it is monitored and guided by VET [39][40].

2.4. Preemptive Management of Coagulation

Hemostasis treatment should only be performed in case of bleeding [41]. In patients with ESLD, bleeding rarely occurs solely due to factor deficiency, and is usually associated with portal hypertension [41]. Volume expansion prompts an increasing portal venous pressure and related risk of bleeding. This is the reason why prophylactic fresh-frozen plasma (FFP) transfusion should be avoided. It has been demonstrated that transfusion of six units of FFPs will increase the portal pressure by 15 mmHg, which correlates well with increased bleeding risk [42]. FFP transfusion has only a limited effect on either correcting factor deficiencies or improving thrombin generation [43][44].

It has also been demonstrated that prophylactic fibrinogen administration in LT recipients did not affect transfusion requirements [45].

A recent paper prepared as a part of an ILTS ERAS project did not recommend the use of prophylactic antifibrinolytics in LT recipients [24]. Antifibrinolytics should be used only in the case of fibrinolysis-related clinical bleeding as diagnosed with VET.

3. Thrombotic Microangiopathy

Thrombotic microangiopathy (TMA) is a very complex condition. Clinical signs of TMA include microthrombotic hemolysis, thrombocytopenia, and organ injury [46]. The most frequent manifestation of TMA is thrombotic thrombocytopenic purpura (TTP), first reported in 1924 [47]. Moschcowitz described a case of a 16-year-old girl initially presenting with weakness, fever, and hemiparesis. Her condition deteriorated and she died 14 days after admission. Autopsy demonstrated massive thrombi in arterioles and capillaries in the kidneys. TTP can be hereditary or acquired. Hereditary TTP is due to a mutation in ADAMTS 13, and acquired TTP is associated with autoantibody production against ADAMTS 13. Both lead to an increased concentration of von-Willebrand factor (vWF) [48]. TMA presents as microthrombotic hemolytic anemia with thrombocytopenia. Patients develop kidney failure and neurologic deficits. TMA can also present as an atypical hemolytic-uremic syndrome (HUS). HUS is principally caused by Shiga-toxin producing *E. coli* [49]. Cell damage occurs when Shiga binds to globotriaosylceramide (GB3) on endothelial, mesangial, and tubular cells. This results in an inflammatory reaction and cell apoptosis with subsequent release of vWF from endothelial cells [48]. Atypical HUS is complement-mediated.

Cyclosporine and tacrolimus may also induce TMA by inhibiting prostacyclin and vascular-endothelia growth factor (VEGF). This results in damage to endothelial cells and TMA in glomeruli. Treatment includes discontinuing cyclosporine or tacrolimus.

Outcomes with TMA after LT have been described by Takatsuki et al. [50]. The authors reported on 98 LDLT patients who developed TMA soon after transplantation. The 1-, 3-, and 5-year survival were 66.9%, 64.6%, and 62.2%, respectively. The only independent risk factor for mortality was dialysis-dependent kidney failure.

References

1. Safdar, N.; Said, A.; Lucey, M.R. The role of selective digestive decontamination for reducing infection in patients undergoing liver transplantation: A systematic review and meta-analysis. Liver. Transpl. 2004, 10, 817–827.
2. Vandecasteele, E.; De Waele, J.; Vandijck, D.; Blot, S.; Vogelaers, D.; Rogiers, X.; Van Vlierberghe, H.; Decruyenaere, J.; Hoste, E. Antimicrobial prophylaxis in liver transplant patients--a multicenter survey endorsed by the European Liver and Intestine Transplant Association. Transpl. Int. 2010, 23, 182–190.
3. Berry, P.S.; Rosenberger, L.H.; Guidry, C.A.; Agarwal, A.; Pelletier, S.; Sawyer, R.G. Intraoperative Versus Extended Antibiotic Prophylaxis in Liver Transplant Surgery: A Randomized Controlled Pilot Trial. Liver. Transpl. 2019, 25, 1043–1053.
4. Pappas, P.G.; Kauffman, C.A.; Andes, D.; Benjamin, D.K., Jr.; Calandra, T.F.; Edwards, J.E., Jr.; Filler, S.G.; Fisher, J.F.; Kullberg, B.J.; Ostrosky-Zeichner, L.; et al. Clinical practice guidelines for

the management of candidiasis: 2009 update by the Infectious Diseases Society of America. Clin. Infect. Dis. 2009, 48, 503–535.

5. Saliba, F.; Delvart, V.; Ichai, P.; Kassis, N.; Botterel, F.; Mihaila, L.; Azoulay, D.; Adam, R.; Castaing, D.; Bretagne, S.; et al. Fungal infections after liver transplantation: Outcomes and risk factors revisited in the MELD era. Clin. Transpl. 2013, 27, E454–E461.
6. Cruciani, M.; Mengoli, C.; Malena, M.; Bosco, O.; Serpelloni, G.; Grossi, P. Antifungal prophylaxis in liver transplant patients: A systematic review and meta-analysis. Liver. Transpl. 2006, 12, 850–858.
7. Evans, J.D.; Morris, P.J.; Knight, S.R. Antifungal prophylaxis in liver transplantation: A systematic review and network meta-analysis. Am. J. Transpl. 2014, 14, 2765–2776.
8. Raghuram, A.; Restrepo, A.; Safadjou, S.; Cooley, J.; Orloff, M.; Hardy, D.; Butler, S.; Koval, C.E. Invasive fungal infections following liver transplantation: Incidence, risk factors, survival, and impact of fluconazole-resistant Candida parapsilosis (2003–2007). Liver. Transpl. 2012, 18, 1100–1109.
9. Saner, F.H.; Olde Damink, S.W.; Pavlakovic, G.; van den Broek, M.A.; Rath, P.M.; Sotiropoulos, G.C.; Radtke, A.; Canbay, A.; Paul, A.; Nadalin, S.; et al. Pulmonary and blood stream infections in adult living donor and cadaveric liver transplant patients. Transplantation 2008, 85, 1564–1568.
10. Karadag, H.I.; Andacoglu, O.; Papadakis, M.; Paul, A.; Oezcelik, A.; Malamutmann, E. Invasive Fungal Infections After Liver Transplantation: A Retrospective Matched Controlled Risk Analysis. Ann. Transpl. 2021, 26, e930117.
11. Lautenschlager, I.; Halme, L.; Hockerstedt, K.; Krogerus, L.; Taskinen, E. Cytomegalovirus infection of the liver transplant: Virological, histological, immunological, and clinical observations. Transpl. Infect. Dis. 2006, 8, 21–30.
12. Paya, C.; Humar, A.; Dominguez, E.; Washburn, K.; Blumberg, E.; Alexander, B.; Freeman, R.; Heaton, N.; Pescovitz, M.D.; Valganciclovir Solid Organ Transplant Study Group. Efficacy and safety of valganciclovir vs. oral ganciclovir for prevention of cytomegalovirus disease in solid organ transplant recipients. Am. J. Transpl. 2004, 4, 611–620.
13. Lizaola-Mayo, B.C.; Rodriguez, E.A. Cytomegalovirus infection after liver transplantation. World J. Transpl. 2020, 10, 183–190.
14. Burra, P.; Germani, G.; Adam, R.; Karam, V.; Marzano, A.; Lampertico, P.; Salizzoni, M.; Filipponi, F.; Klempnauer, J.L.; Castaing, D.; et al. Liver transplantation for HBV-related cirrhosis in Europe: An ELTR study on evolution and outcomes. J. Hepatol. 2013, 58, 287–296.
15. Samuel, D.; Muller, R.; Alexander, G.; Fassati, L.; Ducot, B.; Benhamou, J.P.; Bismuth, H. Liver transplantation in European patients with the hepatitis B surface antigen. N. Engl. J. Med. 1993, 329, 1842–1847.

16. Kim, W.R.; Poterucha, J.J.; Kremers, W.K.; Ishitani, M.B.; Dickson, E.R. Outcome of liver transplantation for hepatitis B in the United States. Liver. Transpl. 2004, 10, 968–974.
17. Cholongitas, E.; Papatheodoridis, G.V.; Burroughs, A.K. Liver grafts from anti-hepatitis B core positive donors: A systematic review. J. Hepatol. 2010, 52, 272–279.
18. Ewe, K. Bleeding after liver biopsy does not correlate with indices of peripheral coagulation. Dig. Dis. Sci 1981, 26, 388–393.
19. Haas, T.; Fries, D.; Tanaka, K.A.; Asmis, L.; Curry, N.S.; Schochl, H. Usefulness of standard plasma coagulation tests in the management of perioperative coagulopathic bleeding: Is there any evidence? Br. J. Anaesth. 2015, 114, 217–224.
20. Saner, F.H.; Gieseler, R.K.; Akiz, H.; Canbay, A.; Gorlinger, K. Delicate balance of bleeding and thrombosis in end-stage liver disease and liver transplantation. Digestion 2013, 88, 135–144.
21. Kozek-Langenecker, S.A.; Ahmed, A.B.; Afshari, A.; Albaladejo, P.; Aldecoa, C.; Barauskas, G.; De Robertis, E.; Faraoni, D.; Filipescu, D.C.; Fries, D.; et al. Management of severe perioperative bleeding: Guidelines from the European Society of Anaesth.esiology: First update 2016. Eur. J. Anaesthesiol 2017, 34, 332–395.
22. Kumar, M.; Ahmad, J.; Maiwall, R.; Choudhury, A.; Bajpai, M.; Mitra, L.G.; Saluja, V.; Mohan Agarwal, P.; Bihari, C.; Shasthry, S.M.; et al. Thromboelastography-Guided Blood Component Use in Patients With Cirrhosis With Nonvariceal Bleeding: A Randomized Controlled Trial. Hepatology 2020, 71, 235–246.
23. De Pietri, L.; Bianchini, M.; Montalti, R.; De Maria, N.; Di Maira, T.; Begliomini, B.; Gerunda, G.E.; di Benedetto, F.; Garcia-Tsao, G.; Villa, E. Thrombelastography-guided blood product use before invasive procedures in cirrhosis with severe coagulopathy: A randomized, controlled trial. Hepatology 2016, 63, 566–573.
24. Yoon, U.; Bartoszko, J.; Bezinover, D.; Biancofiore, G.; Forkin, K.T.; Rahman, S.; Spiro, M.; Raptis, D.A.; Kang, Y.; Group, E.R. Intraoperative transfusion management, antifibrinolytic therapy, coagulation monitoring and the impact on short-term outcomes after liver transplantation-A systematic review of the literature and expert panel recommendations. Clin. Transpl. 2022.
25. Saner, F.H.; Bezinover, D. Assessment and management of coagulopathy in critically-ill patients with liver failure. Curr. Opin. Crit. Care 2019, 25, 179–186.
26. Sogaard, K.K.; Horvath-Puho, E.; Gronbaek, H.; Jepsen, P.; Vilstrup, H.; Sorensen, H.T. Risk of venous thromboembolism in patients with liver disease: A nationwide population-based case-control study. Am. J. Gastroenterol. 2009, 104, 96–101.
27. Wu, H.; Nguyen, G.C. Liver cirrhosis is associated with venous thromboembolism among hospitalized patients in a nationwide US study. Clin. Gastroenterol. Hepatol. 2010, 8, 800–805.

28. Violi, F.; Ferro, D.; Basili, S.; Lionetti, R.; Rossi, E.; Merli, M.; Riggio, O.; Bezzi, M.; Capocaccia, L. Ongoing prothrombotic state in the portal circulation of cirrhotic patients. Thromb. Haemost. 1997, 77, 44–47.
29. Clapp, B.R.; Hingorani, A.D.; Kharbanda, R.K.; Mohamed-Ali, V.; Stephens, J.W.; Vallance, P.; MacAllister, R.J. Inflammation-induced endothelial dysfunction involves reduced nitric oxide bioavailability and increased oxidant stress. Cardiovasc. Res. 2004, 64, 172–178.
30. Hollestelle, M.J.; Geertzen, H.G.; Straatsburg, I.H.; van Gulik, T.M.; van Mourik, J.A. Factor VIII expression in liver disease. Thromb. Haemost. 2004, 91, 267–275.
31. Leebeek, F.W.; Kluft, C.; Knot, E.A.; de Maat, M.P.; Wilson, J.H. A shift in balance between profibrinolytic and antifibrinolytic factors causes enhanced fibrinolysis in cirrhosis. Gastroenterology 1991, 101, 1382–1390.
32. Lisman, T.; Bongers, T.N.; Adelmeijer, J.; Janssen, H.L.; de Maat, M.P.; de Groot, P.G.; Leebeek, F.W. Elevated levels of von Willebrand Factor in cirrhosis support platelet adhesion despite reduced functional capacity. Hepatology 2006, 44, 53–61.
33. Mannucci, P.M.; Canciani, M.T.; Forza, I.; Lussana, F.; Lattuada, A.; Rossi, E. Changes in health and disease of the metalloprotease that cleaves von Willebrand factor. Blood 2001, 98, 2730–2735.
34. Tripodi, A.; Mannucci, P.M. The coagulopathy of chronic liver disease. N. Engl. J. Med. 2011, 365, 147–156.
35. Hugenholtz, G.C.; Macrae, F.; Adelmeijer, J.; Dulfer, S.; Porte, R.J.; Lisman, T.; Ariens, R.A. Procoagulant changes in fibrin clot structure in patients with cirrhosis are associated with oxidative modifications of fibrinogen. J. Thromb. Haemost. 2016, 14, 1054–1066.
36. Walker, A.P. Portal vein thrombosis: What is the role of genetics? Eur. J. Gastroenterol. Hepatol. 2005, 17, 705–707.
37. Qi, X.; Yang, Z.; Bai, M.; Shi, X.; Han, G.; Fan, D. Meta-analysis: The significance of screening for JAK2V617F mutation in Budd-Chiari syndrome and portal venous system thrombosis. Aliment. Pharm. Ther. 2011, 33, 1087–1103.
38. Abuelkasem, E.; Hasan, S.; Mazzeffi, M.A.; Planinsic, R.M.; Sakai, T.; Tanaka, K.A. Reduced Requirement for Prothrombin Complex Concentrate for the Restoration of Thrombin Generation in Plasma From Liver Transplant Recipients. Anesth. Analg. 2017, 125, 609–615.
39. Kirchner, C.; Dirkmann, D.; Treckmann, J.W.; Paul, A.; Hartmann, M.; Saner, F.H.; Gorlinger, K. Coagulation management with factor concentrates in liver transplantation: A single-center experience. Transfusion 2014, 54 Pt 2, 2760–2768.

40. Dotsch, T.M.; Dirkmann, D.; Bezinover, D.; Hartmann, M.; Treckmann, J.W.; Paul, A.; Saner, F.H. Assessment of standard laboratory tests and rotational thromboelastometry for the prediction of postoperative bleeding in liver transplantation. Br. J. Anaesth. 2017, 119, 402–410.
41. Saner, F.H.; Abeysundara, L.; Hartmann, M.; Mallett, S.V. Rational approach to transfusion in liver transplantation. Minerva Anestesiol. 2018, 84, 378–388.
42. Giannini, E.G.; Stravitz, R.T.; Caldwell, S.H. Correction of hemostatic abnormalities and portal pressure variations in patients with cirrhosis. Hepatology 2014, 60, 1442.
43. Rassi, A.B.; d'Amico, E.A.; Tripodi, A.; da Rocha, T.R.F.; Migita, B.Y.; Ferreira, C.M.; Carrilho, F.J.; Farias, A.Q. Fresh frozen plasma transfusion in patients with cirrhosis and coagulopathy: Effect on conventional coagulation tests and thrombomodulin-modified thrombin generation. J. Hepatol. 2020, 72, 85–94.
44. Chowdary, P.; Saayman, A.G.; Paulus, U.; Findlay, G.P.; Collins, P.W. Efficacy of standard dose and 30 mL/kg fresh frozen plasma in correcting laboratory parameters of haemostasis in critically ill patients. Br. J. Haematol. 2004, 125, 69–73.
45. Sabate, A.; Gutierrez, R.; Beltran, J.; Mellado, P.; Blasi, A.; Acosta, F.; Costa, M.; Reyes, R.; Torres, F. Impact of Preemptive Fibrinogen Concentrate on Transfusion Requirements in Liver Transplantation: A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial. Am. J. Transpl. 2016, 16, 2421–2429.
46. Moake, J.L. Thrombotic microangiopathies. N. Engl. J. Med. 2002, 347, 589–600.
47. Moschcowitz, E. Hyaline thrombosis of the terminal arterioles and capillaries: A hitherto undescribed disease. Proc. N. Y. Pathol. Soc. 1924, 24, 21–24.
48. George, J.N.; Nester, C.M. Syndromes of thrombotic microangiopathy. N. Engl. J. Med. 2014, 371, 654–666.
49. Pennington, H. Escherichia coli O157. Lancet 2010, 376, 1428–1435.
50. Takatsuki, M.; Eguchi, S.; Yamamoto, M.; Yamaue, H.; Takada, Y. Japanese Society of Hepato-Biliary-Pancreatic S. The outcomes of thrombotic microangiopathy after liver transplantation: A nationwide survey in Japan. J. Hepatobiliary Pancreat. Sci. 2022, 29, 282–292.

Retrieved from https://encyclopedia.pub/entry/history/show/61372