

Outcome of liver transplant patients at the University Hospital Centre Zagreb

ANA VUJAKLIJA BRAJKOVIĆ¹, JAKŠA BABEL¹, VESNA VEGAR², MARINA PREMUŽIĆ³, DAVOR RADIĆ³, VLADIMIR GAŠPAROVIĆ¹

¹ Department of Intensive Care Medicine, University Hospital Centre Rebro, Kispaticeva 12, Zagreb 10 000, Croatia

² Department of Anaesthesiology, Reanimatology and Intensive Care, University Hospital Centre Rebro, Kispaticeva 12, Zagreb 10 000, Croatia

³ Department of Gastroenterology, University Hospital Centre Rebro, Kispaticeva 12, Zagreb 10 000, Croatia

Corresponding author:

Ana Vujaklija Brajković

Kispaticeva 12

Zagreb 10 000

Phone: +385 1 2367 481

E-mail: avujaklija@gmail.com

ABSTRACT

At the University Hospital Centre Zagreb, 37 patients underwent liver transplantation in the period from 2010 to 2014. Six patients had fatal complications in the early post-transplantation period and decesses in the surgical intensive care unit (ICU). All other patients (31) were transferred to the medical ICU and later to the medical ward. The most common indications for liver transplantation were alcoholic liver disease (9 patients) and hepatitis C (8 patients). Two-thirds of the patients were male (67.7%) with an average age of 51 years. Thirty patients were discharged alive from the hospital. Infections developed in nine patients, mostly pneumonia and peritonitis. Only one patient experienced infection caused by multi-drug resistant bacteria, namely peritonitis due to methicillin-resistant *Staphylococcus aureus* (MRSA). All infections were successfully treated with antibiotics and none of them caused graft rejection.

Key words: liver transplantation, infection, outcome assessment

INTRODUCTION

There are numerous causes of liver disease that can result in cirrhosis, either by causing chronic hepatic inflammation or cholestasis. In developed countries, the common causes of cirrhosis include chronic viral hepatitis (hepatitis B, C), alcoholic liver disease, hemochromatosis and nonalcoholic fatty liver disease. (1) Infectious complications are the major causes of morbidity and mortality after

liver transplantation. Infection can be caused by bacteria, fungi, viruses and parasites. Bacterial infections are predominant during the first two months, post-transplantation. These may cause surgical site infections, bacteremia, pneumonia, catheter-related infections and urinary tract infections. (2)

Here we present indications for liver transplantation, patient characteristics, infective complications and the outcomes at a single hospital centre.

MATERIALS AND METHODS

We reviewed the medical records of liver recipients between January 1, 2010, and December 31, 2014, at the Department of Intensive Care Medicine at the University Hospital Centre Zagreb.

We analysed indications for transplantation, demographic data, and infective complications in the early post-transplantation period. Nosocomial infection was defined as an infection that was absent during preadmission assessments, but detected at least 48 hours after admission to the hospital.

All subjects received immunosuppression comprising of corticosteroids, mycophenolate mofetil and tacrolimus.

The follow-up time of all liver recipients was minimally six months. Descriptive statistics is used.

RESULTS

In the period from January 2010 to December 2014, thirty seven patients underwent liver transplantation (figure 1). Six patients

had fatal complications in the early post-transplantation period and decesses in the surgical intensive care unit; therefore they are not described in this report. Thirty one patients were transferred to the medical ICU after completion of surgical treatment.

The indications for transplantation were: alcoholic liver disease, hepatitis C and B, hepatocellular carcinoma, Wilson's disease, primary biliary cirrhosis and primary sclerosing cholangitis (table 1). Four patients with hepatitis C also had hepatocellular carcinoma.

The MELD score for the entire population was 24 (interquartile range 17-25). Two thirds of transplanted patients were males with an average age of 51 years. Thirty patients were discharged from the hospital. One patient died in the medical ward as a consequence of severe cerebral ischaemia due to cardiac arrest that occurred on the first postoperative day.

Three patients developed thrombosis of the hepatic artery and one had retroperitoneal haemorrhage due to coagulopathy. All patients underwent surgical revision, were stable afterwards and transferred to our unit.

The median of lengths of stay in the surgical ICU, medical ICU and gastroenterology ward were: 5 days surgical ICU, 11 days medical ICU, 15 days medical ward. The simplified Acute Physiology Score (SAPS II) at admission to the medical ICU was 21, and was 15 at the moment of transfer of the patient to the medical ward.

All patients received antibiotic prophylaxis before transplantation according to local guidelines, namely piperacillin and tazobactam, metronidazole and fluconazole. Three patients had positive swabs (two

laryngeal swabs - *Candida* species, perianal swab - *Staphylococcus* species) and one positive urine culture (*Citrobacter freundii*) before transplantation. Nine patients had infective complications after the procedure; five had pneumonia and four had peritonitis (table 2). All patients with pneumonia had chest X- ray infiltrate. In addition, all infections were nosocomial. Five patients had CMV infections after their ICU stay that was well controlled with antiviral drugs. None of the infections caused rejection of the graft.

DISCUSSION

In this report we analysed a relatively small and heterogeneous cohort of patients after liver transplantation at one centre. Overall results show a good survival rate. In the presented population, both surgical and medical (and primarily infective) complications were solved successfully. Despite improved surgical techniques and post-transplant care systems, infections are still the major causes of morbidity and mortality after liver transplantation. Liver transplant recipients are more likely to develop bacterial infections than other transplant recipients because of the complexity of the surgical procedure, which includes penetration of the hepatobiliary system. (3) Moreover, clinical presentation of the infection is less typical in the transplanted patients. Their inflammatory response is impaired, which results in diminished clinical and radiological findings. Thus, an early diagnosis is much more difficult, but it is the key to successful therapy. Moreo-

ver, graft rejection may be confused with infections. New pathogens and new manifestations of infections in compromised hosts are also problems: pathogens common to individuals with prolonged defects in their cellular immune function and neutropenic hosts have been identified in transplant recipients. Another problem is antimicrobial resistance, for instance vancomycin-resistant *Enterococcus*, methicillin-resistant *Staphylococcus aureus*, *Pseudomonas*, *Stenotrophomonas*, fungi (both yeasts and moulds) and ganciclovir-resistant cytomegalovirus. (4, 5) Even though all patients received prophylactic antibiotic treatment, nine patients (29%) developed early infection (during the first postoperative month). All infections were bacterial, including pneumonia and peritonitis as the primary site of the infection.

Liver transplant recipients are vulnerable to respiratory infections because of the long surgical duration, frequent use of posttransplant mechanical ventilation, immunosuppression, massive transfusions, frequent edema with fluid overload, difficulty coughing after surgery and underlying malnutrition. (6) According to some data bacterial pneumonia occurs in 11-28% of liver transplant recipients, mostly nosocomial pneumonia. (7) Surgical site infections (SSI) and intra-abdominal infections are common bacterial infections among liver transplant patients. Currently, the overall incidence of SSI ranges from 18-37%. (8) The incidence of SSIs ranged from 9-21.5% as wound infections, from 6-18% as cholangitis, from 6.3-9% as peritonitis, and from 4-12.9% as abscess. (9, 10)

In this population causative agents were both Gram positive and Gram negative bacteria. Only one patient had infection caused by multi-drug resistant bacteria, namely peritonitis due to methicillin-resistant *Staphylococcus aureus* (MRSA). Infection rates differ across countries, and also from centre to centre. Some authors reported four episodes of bacterial infection during the first post-transplantation month per patient per year in liver recipients. (11) Soongs and colleagues reported early infection in 60% of liver recipients. (12) Kim et al reported a rate of 30.2% during the first month and 67.9% during the total follow-up period (mean, 672 d). (13)

To prevent post-transplant infectious complications, epidemiology, risk factors and clinical characteristics of bacterial infections should be monitored and controlled.

CONCLUSION

Liver transplant recipients in our hospital centre show an overall good survival rate. Excluding early post transplantation surgical complications, main medical complications were nosocomial infections which when approached timely and with appropriate early empirical antibiotic treatment did not show a negative effect on overall outcome. Thus the strategies to obtain the full implementation of available prevention measures and early clinical suspicion of infection are essential to improve safety in liver transplant recipients.

Table 1. Patients' characteristics.

Indication for transplantation, MELD (median, IQR)	
Alcoholic liver disease and cryptogenic cirrhosis	9, 21 (17-26)
Hepatitis C ± hepatocellular carcinoma	8, 23 (11-23)
Wilson's disease	5, 23 (15-29)
Primary sclerosing cholangitis	4, 22 (16-27)
Primary biliary cirrhosis	3, 23 (21-27)
Hepatitis B	1, 21
Sex Male (N/%)	21 (67.7)
Age (median/ IQR)	51 (45-58)
Discharged from hospital (N/%)	30 (96.7)
Alive after six months (N)	29

Table 2. Infective complications in the early postoperative period.

Number	Site of infection	Specimen	Infective agent	Treatment
1	Pneumonia	Tracheal aspirate	Streptococcus viridans, Saprophyte neisseria	Meropenem, Teicoplanin, Fluconazole
2	Pneumonia	Tracheal aspirate	Staphylococcus aureus, Stenotrophomonas maltophilia	Linezolid, Cefepime, Fluconazole, Trimethoprim-sulfamethoxazole
3	Pneumonia		Not isolated	Meropenem, Linezolid, Fluconazole
4	Pneumonia	Tracheal aspirate	Pseudomonas aeruginosa, Candida glabrata	Colistin, Caspofungin, Meropenem
5	Pneumonia	Tracheal aspirate	Staphylococcus epidermidis, Staphylococcus haemolyticus	Meropenem, Linezolid, Caspofungin
6	Peritonitis	Ascites culture	Enterococcus faecium	Teicoplanin, Fluconazole
7	Peritonitis	Ascites culture	E. coli, Staphylococcus aureus	Piperacillin and tazobactam, Teicoplanin, Fluconazole
8	Peritonitis	Ascites culture	Methicillin resistant Staphylococcus aureus	Linezolid
9	Peritonitis	Ascites culture	Staphylococcus epidermidis	Meropenem, Vancomycin



Figure 1. Number of transplanted patients during period from 2010 to 2014.

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