

8.1. Summary

Orthotopic liver transplantation (OLT) is a surgical procedure aimed at prolonging and improving the quality of life of patients with liver failure (LF) and/or its neoplastic disease. OLT is a high-risk procedure, therefore the employment of a thorough and efficient diagnostic protocol during the recipient qualification process is justified so that the benefits of this procedure outweigh the risks associated with surgery and chronic immunosuppression. The main cause of mortality for patients after OLT are cardiovascular (CV) diseases, i.e., myocardial infarction, stroke, cancers, severe infections, hemorrhage, and thrombotic complications.

Early identification and reduction of risk factors for these diseases may increase the survival of patients after OLT. Despite the complexity of OLT as a medical procedure, currently no unified qualification standards for liver transplantation recipients have been designed for all centers in Poland, based on the analysis of pre-, peri- and postoperative risk factors. Patient qualification thus far has been based on regional procedures, referring mainly to the experience of one center and scanty literature reports.

The main aim of this work was to analyze diagnostic algorithms utilized during the qualification process of OLT recipients at the Bydgoszcz Liver Transplantation Center (BLTC) in the years 2017-2021 and to demonstrate their impact on the outcomes following transplantation of this organ.

The specific objectives of the undertaken research were as follows:

1. To determine the impact of the application of a standardized, modified qualification form created at the BLTC on mortality and survival rates of patients following OLT.
2. To evaluate the usefulness and impact of the cardiac diagnostic algorithm developed at the BLTC on the reduction of CV risk.
3. To initiate multicenter work on the development of uniform guidelines in Poland in the OLT qualification process, thus facilitating the exchange of experience and conducting joint research work. The main goal of such work would be to design standards useful in everyday medical practice.

This work presents the results of a retrospective study of 54 BLTC patients qualified for OLT, for whom a complex, multidisciplinary, detailed analysis of risk factors for pre-, peri- and postoperative complications was performed. The study population was divided into two groups: patients qualified for OLT (64.8%) and patients not qualified for transplantation. These groups were compared, and the comparison involved statistical analyses of the collected results, including laboratory blood tests, imaging tests, and consultations with physicians representing various specialties. The analysis was performed based on the data required in the qualification process for OLT at the BLTC. In order to monitor patient outcomes and the graft function, the results were analyzed 1, 6 and 12 months following the transplantation procedure.

The shortest waiting time for OLT (since the time of qualification for surgery) was 5 days, the longest 460 days, 25% of patients received a transplant within 41 days, 50% of patients within 90 days, and 75% within 172 days. The likelihood of long-term survival after OLT was higher, at the level of statistical significance, after the introduction of the modified qualification form compared to the period before its introduction ($p=0.0658$). The results evidenced that the main reason for disqualification in the BLTC, apart from the lack of abstinence from alcohol in the case of patients with alcoholic liver disease (ALD), was the presence of extrahepatic tumors.

Of the 26 liver recipients, 9 (34.6%) died during the follow-up period. As regards the cause of LF, in the BLTC the highest mortality rate was observed among patients who required transplantation due to hepatitis C-related LF. The causes of death in the early period after OLT (5/9 patients) were diverse: hemorrhage from surgical anastomoses, sudden cardiac arrest, venous thrombosis, sepsis, pneumonia. The remaining deaths (4/9 patients) in the period from 30 to 180 days after OLT were mainly infection related. Among patients who died after OLT, no deaths from CV causes, i.e., stroke or myocardial infarction, or cancer occurred during the follow-up period, which may confirm the accuracy of the employed diagnostic protocol and the adequate design of the qualification form as a dense "diagnostic sieve", increasing the chance of identifying cancer in a location other than the liver.

Based on several-year experience gained by the transplantation team (TT), close cooperation with cardiologists, who served as consultants, and obtained test results, an algorithm for cardiac diagnostics was designed and presented in this work. The algorithm aims

to assess the risk of CV risk in patients qualified for OLT at the BLTC. It is mainly based on the assessment of the risk of acute coronary ischemia during and after OLT.

Then, the control parameters of graft efficiency after OLT during the one-year follow-up period were collected and analyzed using the results of laboratory and imaging tests.

It was revealed that ALT (alanine aminotransferase) and AST (aspartate aminotransferase) levels in patients who died during the follow-up period remained elevated one month after OLT, contrary to the levels of these parameters in survivors, in whom a short-term increase was followed by a decrease and their relative normalization. Similar correlations were found as regards GGTP (gamma-glutamyl transpeptidase) levels and total bilirubin. This indicates the strong prognostic value and sensitivity of these parameters as markers of graft function.

Based on the conducted research, the following conclusions were drawn:

1. Meticulous and systematized diagnostic procedures, analysis of indications and contraindications as well as a qualification process for liver recipients conducted by an interdisciplinary team based on consultations have a significant impact on OLT outcomes. The diagnostic algorithms used in the BLTC during the qualification process reduced the mortality rate and the number of complications after OLT.
2. The modified qualification form created at the BLTC contributed to reduced mortality rates and number of complications after OLT, consequently increasing the opportunity of identifying risk factors for surgery failure. As confirmed by post-OLT deaths, its application at the BLTC reduced the risk of death due to myocardial infarction, stroke, and cancer - the most common causes of mortality in this patient population.
3. The algorithm of cardiac diagnostics designed at the BLTC for OLT qualification turned out to be a useful tool in reducing CV risk and CV mortality among OLT recipients.
4. It is advisable to develop multicenter, unified qualification guidelines for OLT in Poland in order to facilitate the exchange of experiences, as well as the development of multicenter clinical and research cooperation.

The presented work can serve as a contribution to initiate and incentivize further discussion and research concerning the optimization of diagnostic algorithms in qualification for OLT.