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Research Article

LIVER TRANSPLANT SURGERY-AN OVERVIEW

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Abstract:

Introduction: The amazing work of Thomas Starzl, et al and other researchers in the 1950s led to the first ever successful liver transplant in 1963 by Starzl in Denver, et al. 5 years later, Sir Roy Calne, conducted the first European liver transplant programme in Cambridge, UK. In the beginning, the progress was very gradual and the death rates of recipients were very high. It is due to the tribute to the early pioneers that they stayed persistent in overcoming the many challenges and obstacles; advances in surgical and anaesthetic techniques, greater understanding of the physiological, haematological, biochemical, microbiological and immunological variations in liver disease and transplantation led to a multidisciplinary approach that led to better outcomes. The progress made, together with more effective immunosuppressive and anti-microbial agents and enhancements in patient and donor selection, has made liver replacement as a routine surgery with very good long term results

Aim of work: In this review, we will discuss the most recent evidence regarding liver transplant surgery. **Methodology:** We did a systematic search for liver transplant surgery-an overview using PubMed search engine (<http://www.ncbi.nlm.nih.gov/>) and Google Scholar search engine (<https://scholar.google.com>). All relevant studies were retrieved and discussed. We only included full articles. **Conclusions:** Liver transplantation, though currently considered a routine procedure, with known indications and usually excellent results, still has many difficulties. Donor shortage continues to be a major drawback. Transplanted organs are full of risk and could transmit malignancy, infections, metabolic or autoimmune diseases. Methods to solve the donor shortage problem consist of using of organs from donors after circulatory death, from living donors and from those previously infected with Hepatitis B and C and even HIV for selected recipients. Normothermic regional and/or machine perfusion, whether static or pulsatile, normo- or hypothermic, are being studied and will be probably have an essential role in enhancing donation rates and results. The main indications for liver replacement are alcoholic liver disease, HCV, non-alcoholic liver disease and liver cancer. New research have concluded that selected patients with severe alcoholic hepatitis could also get advantages from liver transplant. The advent of new and highly effective treatments for HCV, whether given before or after transplant will have a major impact on outcomes. The role of transplantation for those with liver cell cancer continues to evolve as other interventions become more efficient. Immunosuppression is often needed for life-long and adherence continues to be a huge difficulty, particularly in young adolescents. Immunosuppression with calcineurin inhibitors (primarily tacrolimus), antimetabolites (azathioprine or mycophenolate) and corticosteroids remains standard. Results after transplantation are good but not normal in quality or quantity. Premature death may be due to increased risk of cardiovascular disease, de novo cancer, recurrent disease or late technical problems

Key words: Surgery, liver transplant, an overview, recent advances.

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INTRODUCTION:

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METHODOLOGY:

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The terms used in the search were: Surgery, liver transplant, an overview, recent advances

Organ shortage

As liver transplantation has been a routine procedure and contraindications is little, the numbers of possible recipients are in increasing. In most situations, the waiting, which will underrate the true need, are growing; in the UK, up to eighteen percent of adults listed for a first elective transplant will suffer death or become too ill before a graft is found [1]. This decrease in the number of donors comes at a time when, in most states, the pool of potential donors is decreasing, in part as a result of better health, fewer road traffic incidents and changes in the way of treatment of patients with catastrophic brain injuries. Possible donors are being older and with a higher BMI. Older donors are more expected to have co-morbidities and a raised BMI, coupled with hepatic steatosis, increases the donor risk for the liver. The higher imbalance between need and availability of deceased donors has resulted in surgeons often working at the boundaries of what is

possible within the donor pool. [2]

Using organs from donors with higher risk

All donated organs are coupled with risk however some donors are linked with greater risk. These risks may have relation to either the donor or the organ. The surgeon, with the suitably informed and consented patient needs to make a risk analysis: balancing the risks of accepting an organ from a donor with an estimated risk of disease transmission or poor function with the risks of death awaiting the next suitable offer.

Donor risks include the transmission of disease

Donor transmission of cancer: cancers from donors may be donor-transmitted or donor derived. There are several guidelines indicating the risk of cancer transmission from donors with a history of cancer.

Donor transmission of infections:

A wide variation of infections has been spread by solid organ transplant. Donor characterization will often exclude or recognize a number of infective agents (the screening included Hepatitis B and C, Cytomaglovirus (CMV), Epstein Barr virus (EBV), Human T-lymphotropic virus 1 and 2 (HTLV), Human Immunodeficiency virus (HIV) I and II, Treponema pallidum. Other investigations that could be performed involve but not limited to assessing malaria, West Nile virus and T cruzi. In the latter cases, the serology could become available only after transplantation. Standard serology could miss some patients with active infection, like may occur in the window period, where virus is present in blood however before a detectable antibody response. In other patients, rare infection may be missed, such as a recent case of fatal *Helicophalabus gingivalis* transmission. The advent of rapid nucleic acid technology (NAT) testing could led for a faster and more sensitive assessment of the donor risk. But, the advent of effective and often curative treatments for Hepatitis B and C and HIV may mitigate the impact of such donorderived infections. Currently, organs from selected donors with HIV could be safely utilized for recipients with HIV infection [3]; organs from donors with previous HBV infection may be used in selected recipients and are usually given long-term treatment with lamivudine or other antiviral agent; livers from those donors with HCV can be effectively offered to those with HCV.

Living donation

The degree to which living liver donation is supported differs between nations. In the Far East, where lower donation rates are very low, the main bulk of donors are living. The surgeries for checking

the donor are well recognized and regulatory frameworks are in place to help ensure that the donor is fully informed about the risks, there is no coercion or financial inducement to donate.

Results for recipients are often at least, if not better, than for recipients of lower donor livers, in part linked to the short waiting time and the cold ischemic times. There still ambiguity over the effect of living donation on recurrence of autoimmune disease. The major concern with living liver donation remains with the risk to the donor: accurate figures for mortality are scarce since there is clear under-reporting of death.

Other serious risks involve the need for liver transplantation in a very few, biliary issues and infections but major complications are described in up to forty percent of right lobe donors. There is not much data on the long-term impact on the physical and mental health of the donor but studies to date show excellent results for most [4].

Organs from donors infected with HCV, HBV or HIV

The use of organs from donors who have been infected with HCV or HIV could be safely transplanted into recipients who are already infected with the virus, with very good results [5]. Livers from donors who have antibodies to HB core antigen could bring potentially severe HBV infection in the recipient. Without intervention, this will occur in around seventy percent of non-immune recipients and up to fifteen percent immune recipients. In general, livers from such donors must be used for those who are immune and prophylaxis with lamivudine and anti-HBV immunoglobulin should be given for at least 1 year [6].

Indications for transplant

These are now relatively well established and broadly relate to a quality of life that is unacceptable to the patient and can be treated with liver replacement or reduced length of life.

3.1. Specific indications

The major indications for liver transplantation are HCV infection, liver cell cancer and alcohol related liver disease. Non-alcoholic liver disease (NAFLD) is becoming the main indication. Alcohol related liver disease (ALD): the role of liver transplantation for patients with liver disease secondary to alcohol is now well recognized, with outcomes similar to or better than for other indications [7] however this indication remains to bring attention. Indications for those with alcohol-associated cirrhosis are as for

other indications however additional considerations can apply. Recidivism continues to be a main worry however graft loss from recidivism is less than for many autoimmune and viral indications [8]. The need for a defined six months period of documented abstinence, a legal obligation in some countries.

Severe alcoholic hepatitis:

Severe alcoholic hepatitis was considered an exclusion for transplantation. Patients from seven centers were meticulously selected; inclusion criteria encompassed a first presentation, severe disease, supportive family, no severe co-morbidities and a commitment to future abstinence. Only twenty-six, which represent two percent of those admitted with alcoholic hepatitis, fulfilled their criteria. 6 months survival rates were seventy seven percent for those who received a transplant and twenty three percent for those who did not.

Hepatitis C

Till recently, results after liver transplantation for patients with HCV were inferior to many other indications, largely because of the impact of HCV recurrence. Management of transplant candidates, even with stepped approaches, was limited by poor outcomes and a high rate of adverse-effects. Management of the recipient was effective in some however, sustained virological response rates were low and side-effects often severe. The beginning of effective second-generation treatments associated with high rates of sustained virological response is having a huge influence on the need for and outcome of liver transplantation.

HIV

HIV infection is not considered an indication for liver replacement however some of those with HIV infection could be candidates for liver replacement for example, co-infection with HCV or from the effects of alcohol. Whilst indications vary, most will require absence of HIV viremia, of AIDS defining illness and options of anti-retroviral treatment and a CD4 cell count of more than 200 cells/mL A retrospective analysis of data held by SRTR concluded that HIV infected recipients had a more than one fold increased risk of death and graft loss, independent on HCV status. [9]

Liver cell cancer

The treatment choices for patients with liver cancer and involve not only transplantation and resection but also chemotherapy, radio frequency ablation, percutaneous alcohol injection and trans arterial chemoembolisation. These treatment options could be indicated alone, in combination or in sequence.

Follow-up and survival

Results after transplantation are great for the most of recipients but survival is decreased both in quality and quantity. Only approximately half will return to work [10]. Children and their families, in spite of improving results, remain to have mental problems: a multidisciplinary approach may be needed to help improve the quality of life [11]. Adults who survive the first postoperative year will, overall, lose seven life-years compared with sex and age matched controls but the life-years lost is greatest in younger recipients, males and those grafted for cancer and HCV [12].

Metabolic and cardiovascular complications:

Liver allograft recipients have a two to three fold higher risk of cardio- and cerebrovascular disease and death, in comparison with age and sex matched population. As well as offering recipients general life-style advice, many centers offer recipients statins, in spite of the lack of clear evidence for a clear benefit so far. Doctors should be aware of possible interactions between statins and calcineurin inhibitors; pravastatin has fewer interactions than simvastatin. [13]

The future

The future of liver transplantation is very promising however it will still be limited by the availability of suitable organs for donation [14]. The need is increasing, and new technologies will go some way at least to help overcome this growing gap. There are many difficulties, physiological, immunological, ethical, legal and microbiological, to be overcome before xenotransplantation will reach the clinical arena.

CONCLUSIONS:

Liver transplantation though currently considered a routine procedure, with known indications and usually excellent results, still has many difficulties. Donor shortage continues to be a major drawback. Transplanted organs are full of risk and could transmit malignancy, infections, metabolic or autoimmune diseases. Methods to solve the donor shortage problem consist of using of organs from donors after circulatory death, from living donors and from those previously infected with Hepatitis B and C and even HIV for selected recipients. Normothermic regional and/or machine perfusion, whether static or pulsatile, normo- or hypothermic, are being studied and will be probably have an essential role in enhancing donation rates and results.

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