

# Liver transplantation

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James talks to Anastasia Volovets about liver transplantation, a final treatment option for patients who would otherwise die of their liver disease.

Dr Anastasia Volovets is a consultant gastroenterologist and hepatologist. After completing her advanced training at Royal Prince Alfred Hospital, she took off for the green pastures of Edinburgh in Scotland to complete a fellowship in advanced liver disease and liver transplantation. On return she did some more liver transplantology as a consultant before settling into a part time staff specialist duties at RPA as well as some private practice locally.

Anastasia loves teaching patients, nurses, medical students and other doctors almost as much as she loves the liver. She is currently involved in developing a state wide curriculum on gastrostomy feeding in her spare time and can often be found wondering the hospital with a cup of coffee and a toxicology textbook.

## Liver Transplantation

*With Dr Anastasia Volovets, Gastroenterologist and Hepatologist, Royal Prince Alfred Hospital, Sydney, Australia*

### Introduction

A liver transplant is the final treatment option for patients who would otherwise die of their liver disease. Not only does it require a donor liver and a suitable patient but post-operatively is challenging for the patient, in both the immediate and longer term due to the immunosuppression and related complications.

### 1. Common indications for liver transplant

- Acute liver failure
  - This is rare, it usually occurs in the setting of drug toxicity or viral infections
- End stage chronic liver disease
  - Chronic liver disease is irreversible and progressive

- Once chronic liver disease is end stage, there is no alternative treatment to liver transplantation
- When chronic liver disease decompensates patients suffer a constellation of signs and symptoms, including portal hypertension, ascites, jaundice, encephalopathy, malnutrition, muscle wasting and inability to work
- The aim is to offer these patients transplants before they become too unwell to handle a transplant, selection at the right time is difficult
- The MELD (Model of End stage Liver Disease) score is used to calculate the prognosis of patients with end stage liver disease, it looks at bilirubin, INR and creatinine
- A MELD score greater than 14 suggests the patients should be worked up for liver transplant
- Liver cancer
  - Only in suitable cases - patients have to be within a criteria based on characteristics of the cancer

## 2. Contraindications for liver transplant

### Absolute contraindications:

- Incurable or non-correctable disease that will prevent the patient surviving the operation or recovery, such as severe triple vessel disease ischaemic heart disease or severe Chronic obstructive pulmonary disease (COPD)
- Active infection or metastatic malignancy which will flare on immunosuppressive medications
- Patients who are unable to look after their transplant organ, such as those with severe brain injury

### Relative contraindications include:

- Active malignancy that can't be easily treated
- Issues that will make surgery technically difficult, including previous abdominal surgery or severe obesity
- Complications of end stage liver disease such as severe hepatopulmonary syndrome, pulmonary hypertension or cirrhotic cardiomyopathy
- Alcohol dependence with a high risk of relapse. Worldwide patients must have demonstrated at least 6 months of abstinence from alcohol before being considered for transplant by an addiction specialist and a psychiatrist
- Poor social supports

## 3. Overview of the work up for liver transplant

Patients are usually worked up as outpatients, the process can take several weeks to months. Occasionally the patient is more acutely unwell, in these cases they can be worked up as an inpatient in roughly a week.

- Test cardiopulmonary function, transthoracic echocardiogram, carotid dopplers, pulmonary lung function tests, arterial blood gas and if indicated dobutamine stress echocardiogram, cardiac angiogram and right heart catheter
- Test for liver cancer, CT 3 phase liver plus a CT chest
- Test for EtOH brain damage, with CT brain
- Baseline bloods to identify other issues that may be exacerbating their liver disease or might make recovery difficult
- Test for dormant infections, serology
- Test for osteoporosis/osteopenia, DEXA and a skeletal survey
- Test for poor dentition, dental review and OPG
- Variceal surveillance, gastroscopy
- Assess cancer risks including colonoscopy, pap smear/mammogram and skin checks
- MDT
  - Drug and Alcohol specialists
  - Psychiatry review
  - Social Work assessment of support network
- Surgical and anaesthetic review
- Patients own specialists need to be involved as well

#### 4. How long do people spend on the list and how do you follow them up?

- Time spent on the waiting list is variable, depending on the patients risk of dying from their liver disease in the following 3 months - i.e. those who are sickest, get priority
- Duration also fluctuates depending on the number of sick people on the list
- On average people wait 6-9 months on the list, but the waiting can be several years
- While on the waiting list, patients are reviewed every 6 weeks

#### 5. Does everyone who is on the list get to transplant eventually?

- No, 10-33% are delisted
- This can be due to disease progression or a new disease process that makes them unsuitable for a transplant
  - HCC
  - New contraindication e.g. new cancer
  - Death while waiting

- Alternatively, patients might clinically improve
  - Most commonly seen in hepatitis C patients after direct acting antiviral (DAA) treatment

## 6. What happens during the operation? 16-1753

- This requires two long and complex operations, one for the donor and one for the recipient
- Donor
  - Hepatic structures dissected
  - Liver pre-cooled
  - After removal, cold liver is then flushed with cold fluid again and stored on ice
  - Preservation time can be roughly 18 hours on ice
- Recipient ~ 8-20hour operation
  - Preservation fluid is flushed out of donor liver
  - Portal vein thromboses excluded
  - IVC, PV, HA and then biliary tree are re-constructed
  - There is excessive blood loss requiring transfusion and use of cell savers to allow some of the patient's blood to be saved
    - Venovenous bypass is used during anhepatic phases
  - If recipient bile duct is diseased a roux loop with bowel will be formed to replace it

## 7. What is the immediate management post transplantation?

- All patients go to ICU post-operatively
- Patients are usually extubated day 1, but this is occasionally prolonged if they need further surgery
- All patients have a hepatic artery USS day 1 to exclude thrombosis
- Immunosuppressive therapy is started as soon as the patient is transferred to the ICU with methylpredisone
- 5-10 % of post-transplant patients require dialysis in ICU for several days
- Patients are usually stable enough to leave ICU day 1-3 post op

## 8. What medications are patients usually on?

- Transplant patients require a complex combination of immunosuppressive therapy
  - High dose steroids (Started straight after the operation)
    - IV methylprednisolone, then changed to oral steroids
  - Calcineurin Inhibitor (Within 24-48 hours)
    - Tacrolimus (first line)
    - Cyclosporin
  - Anti-metabolite (1 week post-operatively)
    - Azathioprine
    - Mycophenolate
  - IL-2 receptor antibody (Not as routinely as the above classes)
    - Basiliximab
- In addition, immunosuppressed transplant patients will also require antimicrobial therapy
  - Short term broad spectrum IV antibiotics e.g. tazocin
  - To prevent PJP, a one year course of bactrim
  - If at risk of CMV from previous exposure valganciclovir for 3 months
  - If at risk of fungal sepsis fluconazole
- The high dose steroids used for immunosuppression often cause a secondary diabetes requiring insulin or oral hypoglycaemic agents
- Long acting opioids for post-operative analgesia
- Once the transplanted liver is functioning well patients are able to have medications that are toxic in non-transplanted liver failure patients, including paracetamol
- Don't forget regular meds!

## 9. What is the hospital management of these patients?

- Daily blood tests, FBC, EUC, LFTs and tacrolimus levels
- Fluid balance assessments, weights and blood pressure
- Titration of immunosuppression to target levels while minimising toxicity
- Nutrition if malnourished
- Glycaemic control
- Physiotherapy
- Patient education on medication regimes and follow up

## 10. What are the complications we are worried about?

- Short term
  - Day 1-3: primary non-function and hepatic artery thrombosis - rare but may require another transplant
  - Day 3-5: sepsis
  - Day 5-10: rejection, hepatic artery stenosis, bile leaks/strictures, portal vein thrombus/stenosis and intra-abdominal collections
  - Week one onwards: HCV reactivation, CNS toxicity, biliary stricture, ischemic biliopathy, renal impairment
- Medium term
  - 60-80% will have rejection requiring a biopsy and up titration of immunosuppressive therapy
  - Infection
    - Bacterial
    - Atypical organisms: nocardia, fungal infections, aspergillus, PJP

## 11. How often are patients followed up post-transplant?

- Initially on discharge, 1-2 times a week
- At one month, fortnightly
- As they stabilise, monthly
- At 1 year, 2-3 monthly if no complications
- 5-6 years post-transplant, six monthly

## 12. What are the long term complications post liver transplantation?

- Malignancy, 20% of post-transplant patients will develop cancer in 5-10 years post-transplant
  - Most commonly skin cancer, also post-transplant lymphoproliferative disease
- Metabolic syndrome
- Chronic Rejection
- Recurrence of their original disease e.g. NASH, autoimmune hepatitis

## 13. What is the survival of patients post transplantation?

- Over 90% at 1 year
- 70% at 5 years
- This is improving as we have better understanding of transplantation and post-transplant medications

## Take home messages

- Graft and patient survival depends on the careful management of immunosuppressive medications and timely recognition of complications
- The presentation of complications of liver transplantation, including sepsis, can be atypical and patients must be very carefully monitored and followed up in the post-operative stage
- Check all drug interactions when charting medications, especially if altering immunosuppressive or antimicrobial therapy, if concerned double check with the team

## Related Podcasts

- [Chronic liver disease](#)
- [Stress Steroids](#)
- [Liver Function Tests](#)

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