NHS BLOOD AND TRANSPLANT

LIVER ADVISORY GROUP

FIXED-TERM WORKING UNIT – CO-SPONSORED WITH BASL

TOPIC – Acute liver failure

Membership

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Specific (minimum) questions to be addressed:
Is there a transplant survival benefit for patients transplanted for paracetamol-induced acute liver failure at 3 years and beyond?

Conclusions

In completing this exercise the striking lack of data to inform the analysis is apparent, reinforcing the need for the coordinated prospective collection of data for future work. Nonetheless on the basis of the data reviewed a number of conclusions can be drawn, albeit with varying levels of certainty.

1. No formal analysis of the survival benefit of transplantation for paracetmol-induced ALF has been performed to date, but in unwell patients with other forms of liver failure a striking benefit may be seen.
2. Survival after transplantation for paracetamol related ALF does not differ significantly from that seen after transplant for non-paracetamol etiologies.
3. Most deaths occur in the early post-transplant period, and 3 year patient survival would currently be expected to exceed 75%.
4. Whilst survival in patients managed medically have improved in recent years, in specific subgroups mortality remains high.
5. Currently, short term survival in those patients who fulfil KCC but are not transplanted probably lies between 25-35%.

These data would suggest that there is a significant survival advantage to transplantation for selected patients with paracetamol related ALF, with benefit seen at 3 years after surgery. Refinement of the process for identification of patients unlikely to survive with medical management alone would be likely to maximise the advantage gained.

Could patients with sub-acute liver failure be listed sooner?
Remains under consideration at present time.

Can specific circumstances for de-listing patients because of improvement and deterioration, respectively, be agreed?

Conclusions

Delisting because of deterioration.
Currently there are generally accepted indications for liver transplantation in the setting of ALF. No generally accepted contraindications exist to listing patients with ALF. Published medical contraindications when applied dynamically could be used as "criteria" for delisiting because of deterioration on the active transplant waiting list. These might include:

1. Untreated infection or progressive infection despite 48 hours of appropriate antibiotic therapy.
2. Progressive hypotension resistant to vasopressor support.
3. Clinically significant ARDS, FiO2 > 0.8.
4. Fixed and dilated pupils > 1 hour, in the absence of thiopentone therapy.

Delisiting because of improvement.
This clinical situation is significantly more problematic to address than delisting because of deterioration. Currently applying the Kings College poor prognostic criteria to patients with acute liver failure would predict that patients who do not develop these clinical features will have a 90% or higher chance of surviving spontaneously. Two recent meta-analysis of the Kings College criteria have confirmed the high specificity of the criteria: Craig reported pooled specificity of 94.6% in paracetamol induced ALF and McPhail reported specificity of 82% in non-paracetamol induced ALF.

No data exist to inform such clinical decisions. Risk analysis would suggest that patients should be delisted when their risk of death with super-urgent liver transplantation is greater than conservative management (current ELTR data for 1 year mortality for all causes of ALF is reported as 21%). Unfortunately risk analysis of this sort is not available in patients with ALF. Ethically should delisting guarantee survival or accept that there is still a significant risk of mortality? Potential delisting criteria because of improvement might include:

1. Reversal of clinical hepatic encephalopathy
2. Weaning form vasopressor support
3. Recovery of renal function, improving urine output or falling serum creatinine if not on renal replacement therapy.

Current new specific question under consideration "Should ALF have priority over patients with chronic liver disease for allocation of donated livers"