Occult fibrin in deceased donor livers is associated with transplant failure and cholangiopathy

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INTRODUCTION

Ex situ normothermic liver perfusion (NMP) enables preservation, assessment and treatment of livers before transplantation. Evidence to date suggests that, like HOPE, untreated livers undergoing NMP still develop non-anastomotic biliary strictures (NAS).

We have previously shown that fibrin within peribiliary vessels is associated with biliary necrosis, and that treatment with alteplase and FFP during NMP appears to prevent NAS (1).

AIMS

To determine:

1. the prevalence of intravascular fibrin by measurement of D-dimers in perfusate
2. the kinetics of D-dimer release
3. whether fibrin is present before NMP
4. the significance of fibrin load on liver outcomes
5. whether livers recovered after normothermic regional perfusion (NRP) have similar fibrin burdens as livers recovered by static cold storage alone.

METHODS

1. The OrganOx *metra* was used for NMP.
2. D-dimer concentrations were measured in stored serial perfusate samples taken during NMP.
3. Prior to being placed on the *metra*, some livers were flushed with 2 litres of Hartmann's compound sodium lactate solution; D-dimers were measured on the effluent.

CONCLUSIONS

- Livers accumulate fibrin during cold storage
- Large amounts of fibrin are associated with non-anastomotic biliary strictures and worse transplant survival.
- Livers recovered using NRP have least fibrin, explaining the low incidence of NAS?

RESULTS

1. D-dimer release over time (figure 1)

D-dimer release increased over the first hour of NMP before plateauing. More D-dimers were released when the livers were treated with alteplase + FFP during the perfusion.

2. D-dimer release by donor type (Fig 2)

There was no significant difference in D-dimer release between DCD and DBD livers, but there was significantly less D-dimer released by livers recovered by NRP.

For reference, the laboratory diagnostic threshold for PE or DVT is a D-dimer >250ng/ml.

3. D-dimers were released by flushing liver with Hartmann's solution (figure 3)

2 litres of Hartmann's solution were flushed through the liver *before* placing it on NMP. The effluent D-dimer concentration was variable but some livers had a large amount, suggesting fibrin was present in the livers during cold storage.

4. Cholangiopathy & D-dimer release (fig 4)

Transplant recipients were ordered by the amount of d-dimer measured in the 2 hour perfusate samples, and divided into quartiles. Those livers with the highest quartile of D-dimers had the highest incidence of NAS.

5. Transplant survival & D-dimer release

Livers with the highest 2-hour D-dimer release had the worst transplant survival. The common causes of transplant failure were NAS and sinusoidal obstruction.

Figure 1: D-dimer release over time

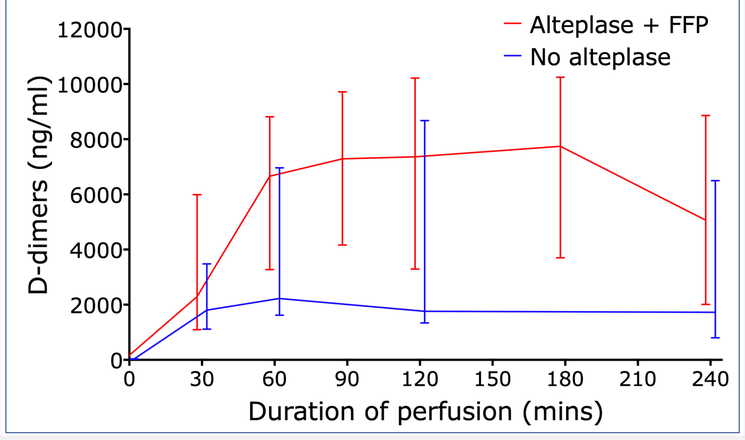


Figure 2: D-dimer release by donor type

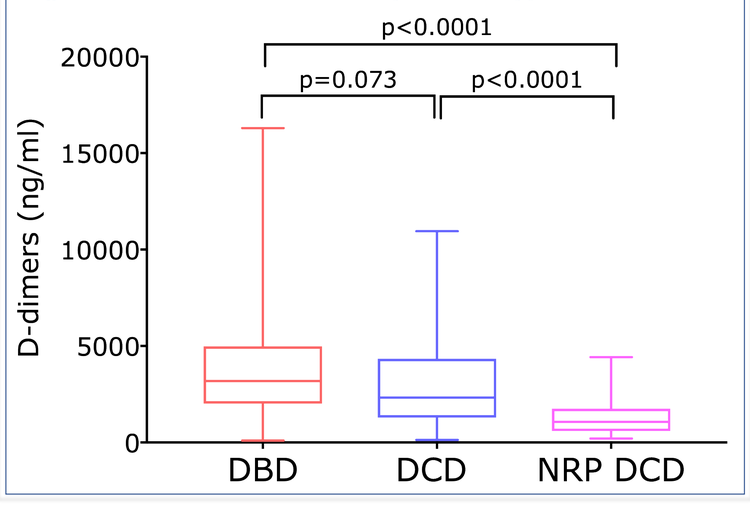


Figure 3: Effluent d-dimer release

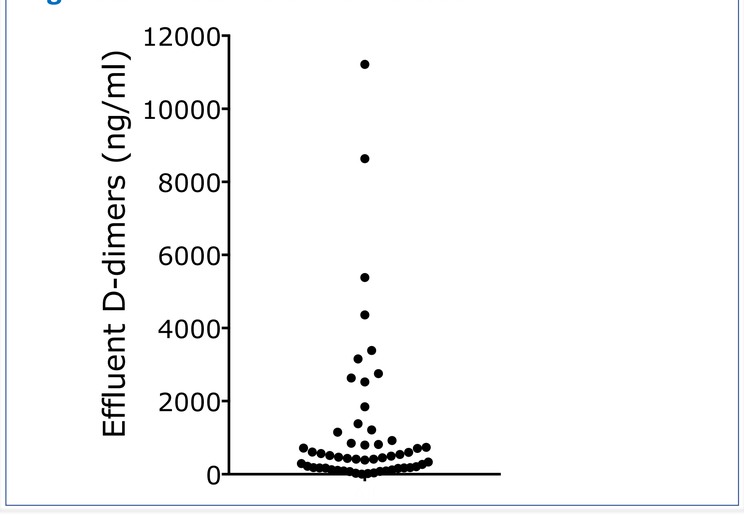


Figure 4: Cholangiopathy by 2-hour D-dimer quartile

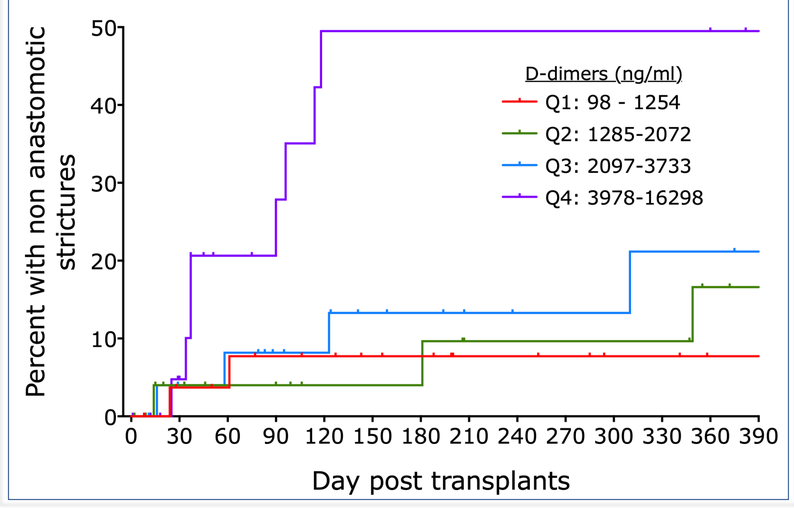
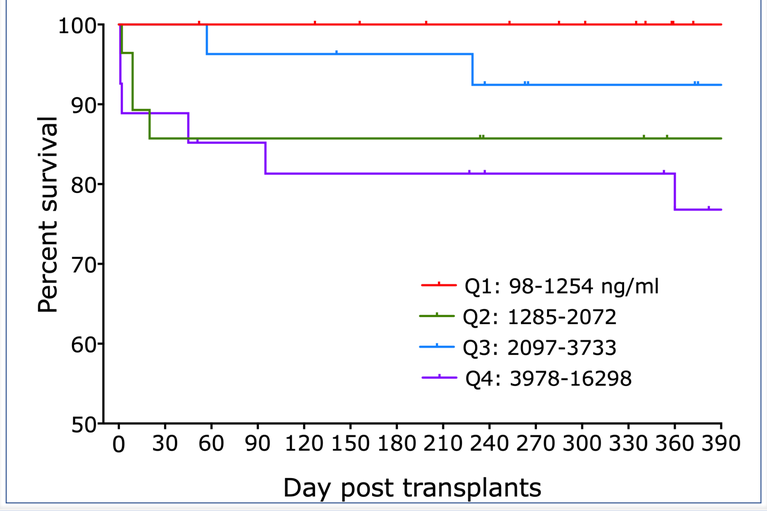


Figure 5: Transplant survival by 2-hour D-dimer quartile



REFERENCE

1. Watson CJE *et a*l. Peribiliary intravascular fibrin occlusions and bile duct necrosis in DCD livers during ex situ perfusion: Prevention with tissue plasminogen activator and fresh frozen plasma. *Transplantation* 2021;105:e401

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