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The role of the complement system in liver transplantation

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INTRODUCTION

DCD liver grafts have poorer outcomes compared to DBD liver grafts, specifically ischaemic cholangiopathy is a significant complication. The pathophysiology behind this is poorly understood, with up to 30% of DCD liver grafts suffering from this complication. There has been increasing interest in the role of the complement system in ischaemia-reperfusion injury in transplantation. This study aims to understand the role of complement in liver transplantation.

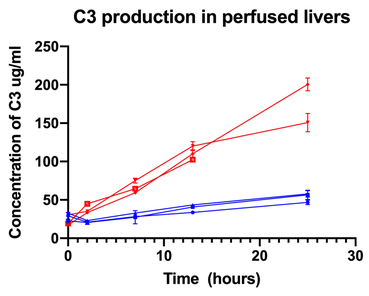
AIM

Investigate the role of the complement system in the pathophysiology of ischaemic cholangiopathy in deceased donor liver grafts.

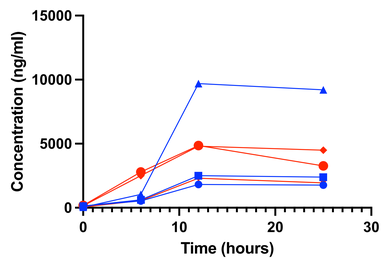
METHOD

- N=6 livers (3 DBD, 3 DCD) were perfused using an in house normothermic machine perfusion circuit
- Red cell based perfusate
- Livers were perfused for up to 10 hours
- Perfusate and tissue samples were taken to investigate the circulating levels of complement, and tissue specific deposition of proteins

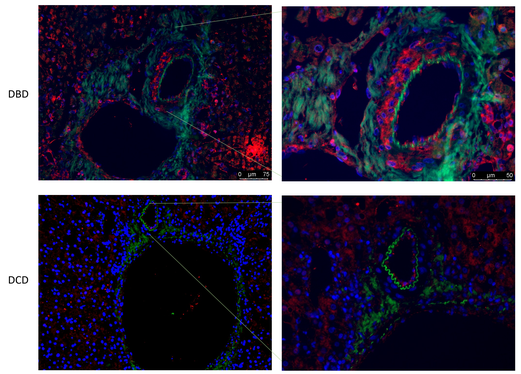
RESULTS



Circulating levels of C3 in machine perfused livers.
p<0.001

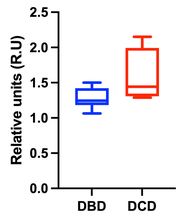


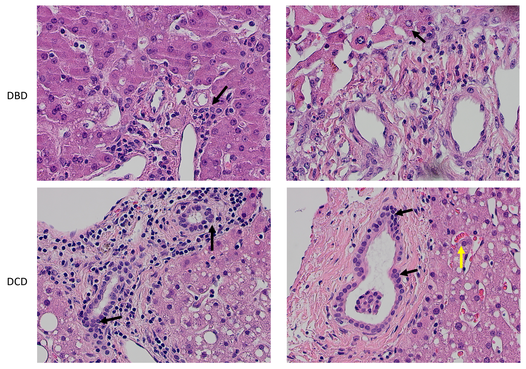
Circulating levels of C5b-9 in machine perfused levels.
p=0.49



Co-localization of membrane attack complex (MAC) deposition within portal arterial endothelium. Red = CD31/PECAM, Green = MAC, Blue = DAPI. Below – Relative intensity of staining of MAC, p=0.09

C5b-9 deposition on arterial endothelium in portal tracts





Haematoxylin & eosin staining of tissue sections taken at 10 hours of normothermic machine perfusion. All sections were images at 20x optical zoom. The DCD liver was more steatotic than the DBD liver in this example, although not seen through the series.

There was infiltration of cholangiocytes seen in the bigger and smaller bile ducts (black arrow). There were also rouleaux formations found within the sinusoids of the DCD liver (yellow arrow). This was seen through the sections for all livers.

Finally, infiltration of immune cells in hepatocytes were noted through all sections.

CONCLUSIONS

- The anaphylatoxin C3 is produced preferentially in DCD livers
- This does not translate to an increased circulating sC5b-9 level
- However, there is a strong trend of increased MAC staining within the portal arterial endothelium noted on immunofluorescence.
- There is activation of complement, preferentially within DCD livers, that is targeting the endothelium of portal arteries. Complement inhibition could ameliorate ischaemia-reperfusion injury in liver transplantation.

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