

NHS BLOOD AND TRANSPLANT
CARDIOTHORACIC ADVISORY GROUP
CLINICAL AUDIT GROUP: CHAIRMAN'S REPORT

SUMMARY

- 1 This paper provides an overview of the work of the CTAG Clinical Audit Group since the last CTAG meeting. I am grateful to the Audit Group members and our colleagues in NHSBT Statistics for their work.

INTRODUCTION

- 2 The Clinical Audit Group held teleconferences on 11 August and 29 September 2016. A planned face-to-face meeting was cancelled because of industrial action. The attendance of members over the last 2 years is shown in **Appendix C**

CLINICAL AUDIT FELLOWS

- 3 Summaries of the work carried out by Aravinda Page (NHS England Clinical Fellow) and Sanjeet Singh (NHS Scotland Clinical Fellow) are provided in the **Appendix A**.

DATA APPLICATIONS

- 4 Prof John Dark, Freeman Hospital, Newcastle: *'Post-transplant renal injury and long term function after adult heart and lung transplantation'*
The aim of the project is to address the issue of long-term dysfunction. Locally at Newcastle there is an increasingly relaxed view of pre-operative renal dysfunction since much of this is affected by pre-transplant condition, and the centre has demonstrated no huge effect on the need for post-transplant haemofiltration or mortality. However, if there were long-term effects, the centre may modify their selection criteria. Haemofiltration in the first 30 days will be used as a marker of acute kidney injury. **This application was approved** by the Audit Group.

NHSBT ORGAN SPECIFIC REPORTS

- 5.1 The NHSBT Annual Cardiothoracic Organ Specific Report was published in July 2016. The report is downloadable from: <http://www.odt.nhs.uk/uk-transplant-registry/organ-specific-reports/>
- 5.2 The publication of the NHSBT Annual VAD Report has been delayed due to concerns about data completeness. A report has been included in the CTAG Heart agenda detailing the concerns of NHS England.

- 5.3 Aravinda Page has designed a survey to collect feedback on the content and use of all NHSBT Organ Specific Annual Reports. NHSBT will circulate a link to this survey in the near future.

PRESENTATIONS AND PUBLICATIONS

- 6.1 A Taylor and colleagues. Comparison of the Clinical Outcomes after De-Novo Heart Transplantation between Adults with and without Congenital Heart Disease. Presented at *ISHLT 36th Annual Meeting and Scientific Sessions, Washington, DC*.
- 6.2 R.V. Venkateswaran and colleagues. The Interval between Brain Stem Death and Cardiac Assessment Influences the Retrieval of Hearts for Transplantation. Presented at *ISHLT 36th Annual Meeting and Scientific Sessions, Washington, DC*.
- 6.3 J Evans and colleagues. Socioeconomic deprivation and survival after heart transplantation in England: an analysis of the United Kingdom Transplant Registry. Accepted by *Circulation: Cardiovascular Quality and Outcomes*

UPDATE ON AUDIT PROJECTS

- 7.1 Progress reports from the project leaders are provided in **Appendix B**.

MEMBERSHIP OF THE CLINICAL AUDIT GROUP

- 8.1 Steven Tsui, CTAG Chair, has asked Nick Banner to continue as CTAG Audit Chair.
- 8.2 The Heart Transplantation representative is due for election. Dr Banner will not be standing for re-election. An election for a 3 year term will now be held.
- 8.3 The LVAD representative is due for election (Dr Parameshwar is eligible for re-election).
- 8.4 The Paediatric position is due to rotate from GOS to Newcastle (by agreement between the 2 paediatric centres).
- 8.5 The Donor Management and Organ retrieval position will be due for election in autumn 2017.
- 8.6 The Lung Transplantation position will be due for election in autumn 2018.
- 8.7 Nominations for the Heart and LVAD positions should be emailed to Dr Banner by 4th November. Depending on the number of nominations, the election rules may need fine tuning; this will be the responsibility of the CTAG Chair, Steven Tsui. The election will be conducted by NHSBT and the electorate will be the CTAG voting members.

- 14 Any outgoing member of the Audit Group will continue as an associate member until the projects that they have been involved in have been completed.

Nick Banner
2016
CTAG Audit Chair

6 October

Appendix A

Aravinda Page – NHS England Clinical Fellow (Supervisor S Tsui)

Stream One: Scout Project Phase II

One of the big challenges we faced in Phase II was incomplete data. However, within the limits of the data that we have had we were able to draw meaningful conclusions to guide further management. This together with the individual opinions from the respective centres led to a consensus opinion that scouting should continue.

In order to validate the data we have and further develop our findings, it was decided that it be peer reviewed externally. This is to be presented to the working group and NHSBT in September.

Stream Two: Advanced optimisation of poorly functioning donor hearts

Together with my supervisors we have designed an experimental protocol to investigate the effect of circulatory support in optimising poorly functioning donor hearts. This research protocol investigates two aspects, firstly, the use of extra corporeal membrane oxygenation (ECMO) in the brain dead donor in an attempt to offload the donor heart and allow for a period of recovery while limiting the use of deleterious pharmacological support. Secondly, the protocol investigates the effect of normothermic machine perfusion compared to cold storage. The novel strategy we propose will combine these two circulatory support technologies to allow poorly functioning donor hearts a chance to recover, as well as minimize the ischaemic insult sustained as a result of the retrieval process.

We have been fortunate in successfully applying for a research grant from Heart Research UK for nearly £250,000 and intend to start our experimental work in the next couple of months.

General

Over the period of the last 7 months I have attended heart and lung retrievals from both DBD and DCD donors. This has given me the opportunity to gain insight into the retrieval process as well as learn how to perform this operation. This has benefitted me both personally and professionally. It has been a privilege to be a part of the retrieval team and has contributed significantly to my training towards my aspiration of becoming a transplant surgeon. Furthermore, it has educated me about the retrieval process and put the research and audit element that I am undertaking into a clinical context.

Following the publication of the cardiothoracic organ specific report, I have designed a survey to help NHSBT review the content of the report and to understand its audience. This has subsequently been adapted to cater to all the organ specific reports and will be distributed by NHSBT.

I have also had the opportunity to write a review article on DCD heart transplantation
- Page, A. A., Messer, S., Tsui, S. S., & Large, S. R. (2016). Early Results Using Donation After Circulatory Death (DCD) Donor Hearts. *Current Transplantation Reports*, 3(3), 199–206. <http://doi.org/10.1007/s40472-016-0106-9>

Courses and Conferences

- During the last 12 months I have attended the EACTS courses on heart and lung failure as well as the NHSBT Retrieval Masterclass.
- I have had the privilege to attend the 16th International Victor Chang Symposium in Sydney, Australia and had the opportunity to deliver a presentation on DCD heart transplantation which was well received.
- I have also attended the Transplant Academy Event hosted by Novartis Pharmaceuticals UK and Sandoz Limited.
- I attended the ISHLT Annual Meeting in Washington, this was part funded by a travel grant from TransMedics.
- I am due to present at the EACTS Annual Meeting in Barcelona in October on the topic of DCD heart transplantation. The travel expenses for this are kindly being sponsored by an educational grant from TransMedics.

Future Work

1. Scout project – The paper for the Scout pilot is currently being reviewed by my supervisor and we intend to publish this to include the 1 year survival data from the pilot project kindly provided by NHSBT.
2. Following the external peer review of phase 2 of the scout project, we intend to write this up to share our experience of using early donor management in the form of 'scouting' to improve donor organ utilization
3. Evaluation of the trends in cardiac donor organ utilization in the UK over the past 20 years from the available NHSBT registry data
4. Experimental work – we will shortly be commencing our experimental work at the Royal Vet College. This will form the basis of my PhD which is to be registered at the University of Cambridge under the additional supervision of Prof C Watson.
5. I have been actively involved in the organization of a symposium focusing on DCD heart transplantation which is due to be held in Cambridge on the 26th and 27th of September – www.dcdheart.com

Sanjeet Singh – NHS Scotland Clinical Fellow (Supervisor N Al-Attar)

Primary Graft Dysfunction National Audit

I have completed data collection of all 450 adult heart transplants across the UK from October 2012-September 2015. I am currently analysing the data alongside attempting modelling with help from Sally Rushton and colleagues during Dr Mehew's maternity leave.

The descriptive statistics of the incidence of Primary Graft Dysfunction will be ready soon and we aim to submit this to SCTS and ISHLT as planned.

Glasgow Transplant Score

We took a revised version of the Glasgow Transplant Score to the CTAG Clinical Trials meeting in July this year with favourable responses from the other members. We are currently piloting its use with our pre-operative patients.

We also intend to compare the GTS to other published scoring systems (Sequential Organ Failure Assessment (SOFA) and the Cardiac Intensive Care Score (CASUS) with Primary Graft Dysfunction, Length of Stay and Mortality as endpoints.

I am also writing up preliminary data on the GTS post-operative score that has been presented at ACTA in Belfast (June 2016) and will be presented at the Scottish Cardiac Society Meeting (September 30, 2016).

Appendix B

PROGRESS REPORTS FROM PROJECT LEADS

1. Long-term VAD outcomes – Jayan Parameshwar

The VAD outcomes project group last discussed the study in a teleconference in April 2016. While considerable progress had been made, it was felt that some additional analysis was required and that the data needed to be presented differently. These analyses were not discussed at the previous teleconference of the Project group. It was also considered reasonable to start writing the paper while the additional analyses were carried out.

Both NHSBT statisticians associated with the project are now on maternity leave. They were unable to devote enough time to this project before going on maternity leave owing to other work commitments. The statisticians now associated with the project are not familiar with what needs to be done (this became apparent during a teleconference on the 29th September 2016). Dr Parameshwar will therefore schedule a teleconference with the statisticians (in the next few weeks) to discuss the additional analyses required. In the interim he has started writing the paper so that it can be completed swiftly once the additional data is available.

2. Outcomes from listing for lung transplantation - Jas Parmar/Richard Thompson

Outcomes from Listing; a large amount of data has been generated by the NHSBT statistical team. The group, which has representation from all 5 centres, have had a number of teleconferences to help refine the data and consider its interpretation. Data issues and then technical problems meant that the last 2 were not as productive as had been hoped. The group intend to meet again face to face on the day of the next CTAG meeting; hopefully an agreed view will be available shortly after this next meeting.

Specific points:

- 1) There are 2 centres that have a significantly higher proportion of CF patients (H & N). I think this relates to referral practice.
- 2) We are all doing lots of COPD transplants which have very low waiting list mortality, there are likely to be multiple reasons of which TLC may be predominant, but certainly something that merits more detailed examination.
- 3) H and P have the lowest number of IPF patients. For us there has been an error in the way the patients have been registered with NHSBT and looking at our true data I think we are around 35% not 18%
- 4) H are doing smallest proportion of IPF patients but with low WLM
- 5) Early waiting list mortality (6 months) is highest in IPF and CF, yet the largest number of transplants in this same period is COPD
- 6) Blood group A have a very short waiting time with more A transplants being done than O's at 6 months? Are some being transplanted with O lungs? This is a concern given the very high mortality in O IPF patients
- 7) B/AB waiting times are broadly comparable to O
- 8) Height surprised me a bit as I would have thought below 160 the WLM would go up across the group but it is broadly comparable to the other height categories.

What is clear that the interaction with disease and height is significant with CF and IPF fairing very poorly.

9) Time to transplant does not seem to be different across the centres. Apart from IPF at H (but there was some debate about this)

10) The effect of SLT vs. BLT is pretty self-explanatory, there were sadly not enough numbers to examine in detail the question of SLT vs. BLT in COPD.

Effect of ischemia time upon post lung transplant survival – John Dark

The original project group was;

N Yonan, S Clark, J Mascaro, P Catarino, A Simon, J H Dark, Jenny Lannon Rachel Hogg. We also had Alex Ball and BC Ramesh working with us.

An Introduction was written by Ramesh and Alex Ball, but requires updating to take into account of recent papers.

The cohort being studied was first lung-only UK adult transplants between 1 January 2005 and 31 December 2014 where EVLP was not used. We initially presented this at ISHLT last year, but that was data up to 2012. It initially showed a difference in survival after about 6.5 hours, but with the addition of two more years, that difference disappeared

The current data with risk adjustment according to the standard model developed for reporting outcomes shows no effect of ischaemic time on ITU stay, hospital stay or 30 day survival. There is an effect on 1 and 5 year survival, which is entirely linear Jenny Mehew wrote a paper containing the methods and the results. As with similar papers using the risk-correction methods, it is statistically very complex (see appended draft paper). In Jenny's absence I think Sally Rushton is now the relevant person for taking this forwards

The next step is to re-draft the methods section and put the results into a format understandable by clinicians. I will then write the discussion and we will circulate around the project group. We anticipate submission to either AJT or JHLT by the end of the year

Congenital Heart Disease project – Mike Burch

The first results of the project were presented at ISHLT in April. Amy Taylor performed the initial analysis but has now returned to her clinical studies. I am working on this but need some additional data from the Freeman and I have been in touch about this. Once this is available, I will ask Sally Rushton, Esther Wong and colleagues to review the statistical analysis before drafting the manuscripts.

Interval between Brain Stem Death to organ retrieval - R 'Venkat' Venkateswaran (Heart), John Dark (Lung)

Heart:

Brain stem death impacts severe catecholamine storm which impacts on heart and lung function of the donor. The audit was conducted to assess the duration from actual brain death and the chance of heart being retrieved for transplantation. We hypothesised that a longer interval between BSD and assessment may be associated with a higher heart transplantation rate due to improved function. We analysed the data from the NHSBT dataset and found that:

- After risk-adjustment, there was evidence to suggest that the duration between BSD and retrieval had a non-linear effect upon heart donation ($p=0.047$).
- Longer durations up to approx. 36 hours were associated with a higher probability of donation, after which time, the probability of donation remained relatively constant for all durations.
- Analysis of a subset of donors attended by a cardiothoracic retrieval team showed a similar pattern

Abstract was submitted to ISHLT-2016 and was presented in Washington meeting. We are currently preparing a manuscript for submission towards publication. We hope to send the first draft of the paper to the relevant authors by second week of October.

Lung:

This work was started back in 2014, and an abstract presented by Esther Wong at a statistical meeting in that year. The time from brain death had no impact on the rate of lung retrieval in all brain dead organ donors in the 2008-2012 era. We presumed that the recovery from the effects of brain death, which we see in animals, is offset by increasing ventilator-associated pneumonia.

The work to be done includes bringing the cohort up to date, then looking at the effect on survival post-transplant, something we have not yet done. The standard risk-adjustment model will be used in examining outcome data. Esther Wong is the statistician for this project. The project group is the same as for the heart-BSD work lead by Venkat, but I take the senior position.

The timetable has to be agreed with the Stats department, but I would hope for a draft paper by the end of the year

Cardiac PGD Study - Nick Banner/Sally Rushton

The aim of this project is to model the incidence and assess predictors of PGD post heart-transplantation with a particular focus of ischaemia time which has become a potentially modifiable risk factor. This work began in 2014 but progress had stalled because Professor Chris Rogers had been unable to devote sufficient time to the project following the transfer of all audit work from the RCS to NHSBT. In August of this year Professor Rogers formally handed the project and the existing data analysis to Jenny Mehew at NHSBT. We now have an opportunity to update the data set and potentially include data from Birmingham who were unable to provide data for the first analysis, making it a truly national study. Jenny Rushton and her colleagues will prioritise the further analysis as some of the current audit projects draw to a close. We hope to hold a teleconference with the original project group in November. The initial work of Chris Rogers will be acknowledged in the final manuscript.

Appendix C – Clinical Audit Group meeting/telecon attendance

	21 August 2014 meeting	30 October 2014 telecon	4 February 2015 meeting	4 June 2015 telecon	19 August 2015 meeting	6 January 2016 telecon	10 March 2016 telecon	11 August 2016 telecon	29 September 2016 telecon	Total N=9
Dr Nicholas Banner	Y	Y	Y	Y	Y	Y	Y	Y	Y	9/9
Dr Jayan Parameshwar	Y	Y	Y	Y	Y	Y	Y	Y	Y	9/9
Dr Richard Thompson	Y	Y	Y	Y	Y	Y	Y	Y	*	8/8
Mr Rajamiyer Venkateswaran	Y	N	N	N	Y	N	Y	N	N	3/9
Prof Mike Burch	Y	Y	Y	Y	N	Y	Y	Y	N	7/9
Dr Jenny Mehew/Miss Sally Rushton	Y	Y	Y	Y	Y	Y	Y	Y	Y	9/9
Dame Joan McVittie	-	-	-	N	N	Y	Y	Y	N	3/6

* Administrative error