

**NHS BLOOD AND TRANSPLANT
CARDIOTHORACIC ADVISORY GROUP
CLINICAL AUDIT GROUP: CHAIRMAN'S REPORT MARCH 2019**

SUMMARY

- 1 This paper provides an overview of the work of the CTAG Clinical Audit Group (CTCAG) since the last CTAG meeting in October 2018, and my second report as the Chair of CTAG Clinical Audit Group. I am grateful to the Audit Group members together with Sally Rushton and her colleagues in NHSBT Statistics and Clinical Studies for their work and to Lucy Newman for administrative support.

INTRODUCTION

- 2 The Group welcomed its first new member this year, Dr Mo Al-Aloul who joined us for his first meeting in February having been elected as Lung Transplantation Representative following the end of tenure for Dr Richard Thompson in December. On behalf of members, I would like to thank Dr Thompson for his involvement and commitment to the Clinical Audit Group, and to welcome Dr Al-Aloul to the Audit Group. Membership and attendance at CTCAG are listed in **Appendix A**

Katie Morley was appointed to the role of Allied Health Professional within the Clinical Audit Group in March 2018, however she has recently relinquished her role. Katie has accepted a secondment opportunity, covering Laura Stamp as Lead Nurse Recipient Co-ordinator whilst Laura is on Maternity Leave. The position of Allied Health Professional will be open for election following the CTAGH Hearts and CTAGL Lungs meetings in March 2019.

- 3 The Clinical Audit Group holds four meetings each year. This year we will hold one further telecon and two face to face meetings. Dates will be advised to members in due course. Additional telecons will be arranged when necessary. Membership and attendance at CTCAG will be reported annually at CTAGH and CTAGL.

CLINICAL AUDIT FELLOWS

- 4 The two Audit Fellows, Aravinda Page and Sanjeet Singh reached the end of their terms last year. During the Expressions of Interest phase of the appointment process for the new Clinical fellow, CTAG/CTCAG received Project Applications from five centres; Freeman, Golden Jubilee, Great Ormond Street, Papworth and Wythenshawe. Following a robust election process, the Project from Freeman which will focus on Lung Donor Scoring Systems and Cardiac Donor Studies with additional studies in alignment with Theme 1 of BTRU. (**Appendix B**)
- 5 John Dark, Karen Booth, Sally Rushton and I interviewed two candidates for the Clinical Audit Fellow post on January 24th. Gill Hardman (ST6 Cardiothoracic Surgical Trainee) was the successful applicant appointed into the role. Gill has previous transplant experience from Papworth and Wythenshawe and will start working with us in August. Tanveer Butt will train and facilitate Gill's experience in transplant retrieval over the coming months. We welcome Gill to the group and look forward to working closely with her, which will further improve the cohesivity between CTAG, the Clinical Audit Group and the wider Cardiothoracic Community.
- 6
- 7 Gill Hardman attended a meeting with JD and others at the Freeman Hospital on 20/02/19 – her work will predominantly focus on Lung Donor Scoring and Lung Utilisation and will involve lab work using newly established QUOD Samples to assess a link between biomarkers and the lung donor score.

DATA APPLICATIONS

- 6 There have been two new external applications for data.

Callan – Pre-emptive therapy for managing Cytomegalovirus following Heart Transplantation

This data application matched the criteria required for SR to release the standard cardiothoracic dataset, and the application is included on the agenda for information only.

Pufulete - LVAD as a Destination Therapy for advanced heart failure NIHR HTA.

This application requires group approval

- 7 The NHSBT Annual Cardiothoracic Organ Specific Report 2017/2018 can be found on the ODT Clinical Website: [Cardiothoracic Annual Activity Report 2017/2018. The interim Report on Cardiothoracic Transplantation will be published by CTAG in March 2019](#)
- 8 The NHSBT Annual VAD Report, now called the 2017/2018 Annual Report on Mechanical Circulatory Support related to Heart Transplantation, has been delayed due to reworking of the analysis as well as a large number of queries from centres about the data. the report should be published prior to CTAG in March 2019: [MCS Annual Report 2018](#)

CHAIRMAN'S PERSPECTIVE

- 9 The Clinical Audit Group is moving into its 7th year in its present format and I have almost come to the end of my first year as its Chairperson. The group includes representatives from all clinical areas of cardiothoracic transplantation and will continue in to maintain its dynamism when opportunities for elections arise, along with a natural turn-over of representatives. New members have helped generate new ideas and project proposals. Regular reports to CTAG have increased the transparency of the CAG's activities and we have new projects in development.

We are an advisory group with no staff or budget, and our work depends on the goodwill of the group's members and colleagues. We are grateful for the expertise and support of the NHSBT statistics team. Clinical Audit Group members and the statistics team have many other demands on their time; which sometimes means that worthwhile projects take longer than we would like to reach a conclusion. Several of our ongoing projects have now reached completion and work is progressing well on other projects.

One continuing frustration has been the ongoing difficulty in modifying and updating the databases on which our Audit and Research work depends. An annual VAD meeting has been set up between the Chair of CTCAG, NHS England (NHSE) and NHSBT to discuss Audit priorities and plan for the years Annual Reports; NHSE agree that they have an important role in ensuring that adequate resources are made available to maintain and update the Transplant Databases, managing the process through their contract with NHSBT. The Chair of CTAG will liaise with Sarah Watson to move the plans forward.

A further issue is the need to revise the Mechanical Circulatory Support database to improve its user-friendliness and adapt it in a period of rapid technological change and changes in clinical practice. I am pleased to report that NHS England have agreed to support this process and manage the stewardship of the MCS database through its relationship with NHSBT.

Overall the CAG is in good health, with a dynamic membership together with a continuing flow of new ideas and projects. It continues to adapt to our changing clinical, technological and organisational environment.

UPDATING THE MECHANICAL CIRCULATORY SUPPORT (LVAD) DATABASE

- 10 An annual VAD meeting has been set up between the Chair of CTCAG, NHSE and NHSBT to discuss Audit priorities for the years Annual Reports.

UPDATE ON AUDIT PROJECTS

- 11 Progress reports from project leaders and project proposals from members are detailed in **Appendix C**.



Prof. Nawwar Al-Attar
CTAG Clinical Audit Group Chair

APPENDIX A
CLINICAL AUDIT GROUP – MEMBERSHIP AND ATTENDANCE

CTCAG Attendance	Tenure Dates	Position in CTCAG	Centre	TELECON: 29/03/18	TELECON: 26/07/18	FACE TO FACE: 21/09/18	TELECON: 21/02/19	Attendance at last 4 CTCAG Meetings
Prof. Nawwar Al-Attar	May 2018 - May 2021	CTAG Clinical Audit Group Chair	Golden Jubilee National Hospital, Glasgow	Yes	Yes	Yes		3
Mr Marius Berman	Nov 2017 - Nov 2020	Donor Management and Organ Retrieval Representative	Royal Papworth Hospital, Cambridge	Yes	No	Yes		2
<i>Prof. Mike Burch</i>	<i>Honorary Member</i>	<i>Honorary Member</i>	<i>Great Ormond Street Hospital, London</i>	<i>No</i>	<i>No</i>	<i>No</i>		0
Mrs Margaret Harrison	Jan 2017 - Jan 2020	CTAG Lay Member Representative	CTAG Lay Member	Yes	Yes	No		2
Sr Katie Morley	Mar 2018 - Mar 2021	Allied Health Professional	Royal Papworth Hospital, Cambridge	Yes	No	Yes		2
<i>Dr Jayan Parameshwar</i>	<i>Honorary Member</i>	<i>Honorary Member</i>	<i>Royal Papworth Hospital, Cambridge</i>	<i>Yes</i>	<i>No</i>	<i>No</i>		1
Dr Stephen Pettit	Jul 2018 - Jul 2021	Heart Transplantation Representative	Royal Papworth Hospital, Cambridge	N/A	No	Yes		1
Dr Zdenka Reinhardt	Dec 2016 - Dec 2019	Paediatrics Representative	Freeman Hospital, Newcastle	No	No	Yes		1
Miss Sally Rushton	N/A	Senior Statistician	NHSBT	Yes	Yes	Yes		3
Dr Steven Shaw	Dec 2016 - Dec 2019	Mechanical Circulatory Systems Representative	Wythenshawe Hospital, Manchester	Yes	Yes	No		2
Dr Mo Al- Aloul	Feb 2019 - Feb 2022	Lung Transplantation Representative	Wythenshawe Hospital, Manchester	N/A	N/A	N/A		0
Miss Lucy Newman	N/A	Secretary	NHSBT	Yes	Yes	Yes		3
Attendees per meeting				8	5	7	0	

APPENDIX B CLINICAL AUDIT GROUP – AUDIT FELLOW PROPOSALS

CTAG Clinical Audit Fellow Proposal – Freeman Hospital

Suggested workplan

Principal Project – Lung Donor Scoring Systems

1. Development of a UK donor risk score for lung donors. This would be analogous to the work done on a liver score [1], and earlier work done on a kidney score[2]. However, there is a range of evidence suggesting that *recipient* factors play a major role in predicting outcomes after lung transplant[3]. Because of this, we will need to include a recipient element. This has been done separately from the donor for liver transplants[4], and there is an existing risk factor stratification for lung transplants in the UK. There would be a high degree of analytical sophistication in the linking of both donor factors and recipient elements, but all the data is already collected. This is a scientifically challenging, but potentially hugely beneficial project. As we move towards recipient specific offering, the opportunity exists for providing the decision-making clinician with a realistic risk calculation including both donor and recipient variables
 - a. A corollary of the above piece of work is that it lends itself both to local audit of organ offers, and development of broader lung utilisation indices
 - b. With appropriate collaborations, there is the opportunity to develop machine-learning approaches to organ offering, streamlining the whole process
2. Testing existing donor risk scores. The Oto Score was described some time ago, from Melbourne[5], and has been updated[6]. There is a scoring system from Minnesota[7] and a similar system has been examined within EuroTransplant[8]. We would propose, in parallel with the initial work, to test these scores in the UK context, using UK data. This would enable us to assess the utility of a system which incorporates purely donor variables

Cardiac Donor Studies

3. As an adjunct, if it has not already been done by the previous Fellow, we would repeat the process for *heart* donor calculators, particularly the most recent EuroTransplant model[9]
4. Donor age for heart transplantation is gradually increasing, raising questions about which older hearts are potentially suitable for transplantation. From work done previously in Newcastle (Dr Guy MacGowan and colleagues) we know that as the heart ages there are changes in left ventricular diastolic function, cardiac energetics and regional strains[10, 11]. If conditions such as diabetes and hypertension are present this can add to these effects, and cause additional issues such as left ventricular hypertrophy[12]. In the potential donor situation, additional factors such as cause of death, ischaemic time, and cardiac support may further compound effects on left ventricular function.

Large numbers have donors with echo data, which, with training, can be analysed. To study these issues we propose collecting echo-derived measurements of left systolic function (ejection fraction), diastolic function (E/E' ratio and left atrial size) from used and un-used donor hearts, linking medical history (age, smoking, diabetes, hypertension, cause of death), current cardiac treatments (inotropes, blood pressure medications), ischaemic time, and haemodynamics, and stratifying patients by age and co-morbidities to look at measures of systolic and diastolic function. In those hearts that are used there will be correlation with outcomes and post-operative haemodynamics. This will help to determine, in a novel manner, which older heart donors are safe to use for heart transplantation.

Collaboration with Dale Gardner

1. Audit of lung protective ventilation in lung donors. Protective ventilation has been proven to be of benefit in lung donors, in Italian[13] and Spanish[14] multicenter studies. It is a part of the Donor Care Bundle, but there is anecdotal evidence that application is variable. A French study, presented at the ISHLT similarly realised patchy application, but demonstrated, in a real world setting an improved lung utilization when fully applied. Dr Gardner has offered to facilitate establishing an audit of current UK practice, working with NHSBT Regional Managers and Regional CLODS. Other aspects of utilization of the Donor Care Bundle could be incorporated in this audit.

Collaboration with Andrew Broderick

1. Data review of potential and proceeding donors over 55 and over 60 to determine how applicable the heart utilisation factors are in the UK (Smokers, On treatment for HTN, Female, Diabetes, Cause of

Death – CVA, Cause of Death – ICH). This is an extension of work in collaboration with Andrew Broderick, who has already established a process for reviewing factors likely to result in all centres turning down a donor. The aim is to suggest criteria which would exclude offering, and therefore accelerate the whole donation process, as well as reducing workload across both donation and recipient coordinator teams. Criteria may change with time, and as above, a machine-learning process might evolve from initial sets of observations

2. Review how often Troponin is available in potential donors and impact on utilisation

Additional Studies – Alignment with Theme 1 of BTRU

The laboratory facilities for a number of lab-based projects are already in place within the BTRU

1. Testing QUOD derived BAL's for Pepsin. The routine collection of research Bronchiolar-Alveolar Lavages (BALs) is due to start in September. We have previously used a pepsin assay in a study of post-transplant aspiration, relating positive pepsin specimens to early rejection, so the techniques are all in place. "Aspiration" is frequently recorded in donor records, in an unsubstantiated form. A frequent result is that the lung is turned down for transplant. It would be fascinating to correlate a history of aspiration with objective measurement of pepsin – the hypothesis being that a history alone is meaningless.
2. The availability of QUOD BAL's opens up a range of other opportunities to explore some of the newer biomarkers. We have some preliminary data on cytokine expression in DCD lungs, which could be expanded, and linked to early outcomes. We also have an interest in microRNA 21 as a marker of ischaemic injury. It is has been linked to TLR4 expression, which again we showed previously to be important in brain-death associated lung injury.

Future Projects

We would encourage the Fellow, in the latter part of his or her time, to develop prospective, UK-wide studies. Possible options are shown below, but these could be developed with other centres

1. Chest CT scans in donors. In older donors, or with a smoking history, these are routine in Europe and North America. They gives info on lung condition – emphysema in particular – and coronary calcification. We would do a retrospective audit, and propose a prospective study, asking for CT's in a range of donors and expecting better organ utilisation and fewer pointless NORS trips. Assuming we could recruit centres to do CT's, we could compare two large cohorts of donors.
2. Donor Statin Pre-treatment. A study from Finland, presented at the recent TTS meeting, showed a significant advantage in terms of post-transplant cardiac function in donors randomised to receive a statin. We have had very preliminary discussions with Karl Lemstrom, head of cardiac surgery in Helsinki, and the investigator on the Finnish study, concerning a collaboration. The UK is ideally placed to perform such a piece of work.

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APPENDIX C
CLINICAL AUDIT GROUP – PROJECT REPORTS AND PROPOSALS

ACTIVE PROJECTS

- 1 **Time after Brain Stem Death – The Effect on the Lung – John Dark (JD)**
 All the analysis is complete, and I have almost finished the draft of the paper. We have approached two additional centre Reps, for Manchester and Harefield, as they were either not previously represented. This paper shows, in contrast to the heart study, no effect of time from brain death. We plan to submit to JHLT
- 2 **MCS – HM3 (L)VAD Project Proposal Steve Shaw/Rajamiyer ‘Venkat’ Venkateswaran (SSh/RV)**
 A preliminary analysis was performed by the statistics team and sent to me in October. Between the dates of 1 November 2015 and 31 March 2017, 132 patients had LVADs, comprising 58% with HVAD and 42% with Heartmate3. These time dates were chosen to ensure a minimum of 1 years follow up for all patients. At 1 year, there was a large, and statistically significant difference in survival between the two devices (60.2% v 83.6%, p-value=0.0119). There were no significant differences in patient selection parameters known to influence survival including age, sex, Intermacs profile, BMI, eGFR, RVAD use, RA pressure, or concomitant surgery at the time of implant.

I constructed an abstract with the intention of submitting to ISHLT. However, upon circulation amongst the stakeholders, there was a strong objection from Newcastle who stated they were not happy for their data to be included. They cited that the strategy behind the data was not proper science. To avoid any further conflict, I therefore chose not to submit to ISHLT. The future of the study is currently undecided (I have been waiting for a CAG meeting to discuss the situation).

PROJECTS CURRENTLY ON HOLD

- 1 **UK DCD Experience – John Dark (JD)**
 This is a longstanding project, which I would like to complete once I have more time, after my role with NHSBT ends after March. It is slightly less powerful now that both Harefield and Papworth have published institutional papers of their own experience, but we have data on aspects of the agonal phase which they did not include, which I think will make it a valuable paper
- 2 **Perception of Donor Case Practitioners in the Donor Pathway – Katie Morley (KM)**
 Katie Morley has stepped back from her position as Allied health Professional due to a secondment opportunity covering Maternity leave for Laura Stamp (Lead Nurse Recipient Co-Ordinator), this project is currently on hold.

COMPLETED PROJECTS/PROJECTS WHERE NO FURTHER STATISTICAL ANALYSIS IS PLANNED

- 1 **Effect of Ischemia Time on Post Lung Transplant Survival – John Dark (JD)**
 The stats analysis is all finished, thanks to Jenny Mehew and Rachel Hogg, and I have almost finished the draft of the paper. This will then be circulated around the centre reps and then submitted for publication. I think we will be going for Am J Transplant in the first instance, as they give a very quick decision. The conclusion is that there is a measurable, although small, and completely linear effect of ischaemic time on outcome. The data will also be presented at CTAG Lung
- 2 **(Adult) Congenital Heart Disease Project – Mike Burch (MiB)**
 The manuscript has been submitted to *Journal of Heart and Lung Transplantation*. Reviewers comments on the manuscript are expected soon.

PROPOSED PROJECTS

- 1 **HGS Study Proposal – Nawwar AlAttar (NAA)**
 The HGS Study project looks at the **H**and **G**rip **S**trength to assess the frailty of patients/recipients and the subsequent outcomes of heart transplantation in relation to frailty. There are other indicators to frailty and social deprivation, however, hand grip strength is relatively easy to measure with minimal impact and cost to centres. Glasgow, Manchester Harefield and Papworth have identified their local HGS champions, other centres will be asked to do the same. This is the first study of this kind in the field, and its hoped that it will provide some useful insights.

2 Ongoing S/ULAS Audit Work – Richard Thomson/Mo Al-Aloul (RT/MAA)

Richard Thomson kindly provided an interim handover for Mo Al-Aloul who will continue with the S/ULAS Work after his first meeting in February. An initial data gathering exercise has been undertaken, looking at activity and early outcomes, and this will be used to inform discussions of the Lung Allocation working group which has been reconvened to consider efficacy and equity of the current system, and suggest changes if necessary.

3 Paediatric Project Proposal – focus on re-implantation of hearts and lungs in paediatric patients - Zdenka Reinhardt (ZR)

Paediatric heart re-transplantation (re-transplantation) is exceedingly rare, with reports of decreased survival when compared with primary transplantation. The aim of this analysis will be to describe the outcomes of re-tx in paediatric population in the UK and associated morbidities. Methods would utilise data 1998 to 2018 (if possible) to identify all patients whose primary transplant and re-transplantation were performed below age of 18 years. (I will discuss with the group whether to include re-transplantation in >18y). Data would include: causes of re-transplantation, graft survival, clinical status at the time of listing/re-transplantation, (mechanical support), mortality, complications such as acute rejection, RRT for renal failure, neurological event, infection, PTLD, comparison transplantation vs re-transplantation.

4 Retrieval Project Proposal – Marius Berman (MaB)

The research proposal is ready, however at this stage, data is still being analysed. An update is expected at the next CTCAG meeting.