NHS BLOOD AND TRANSPLANT

CARDIOTHORACIC ADVISORY GROUP

ASSOCIATION BETWEEN LUNG ISCHAEMIA TIME AND PATIENT SURVIVAL FOLLOWING LUNG TRANSPLANTATION

DATA

1 We analysed 1,662 first adult lung-only transplants in the UK between 1 January 2003 and 31 December 2014 where EVLP was not used.

METHODS

2 The relationship between ischaemia time, defined as the time between cross-clamp and reperfusion in the recipient, and different periods (30 day, 90 day, 1 year and 5 year) of survival was investigated using Cox proportional hazards regression. The unadjusted effect was analysed as was the risk adjusted effect using the likelihood ratio test. The factors adjusted for were those used in the post-transplant survival analyses presented in the NHSBT Annual Report on Cardiothoracic Transplantation (Table A3.2 http://www.odt.nhs.uk/pdf/organ_specific_report_cardiothoracic_2016.pdf).

3 Ischaemia time was primarily tested as a linear effect to assess whether there was an effect on survival that was uniform as the duration increased. Ischaemia time was then split into quartiles to test for the presence of non-linearity. If the non-linear term was more appropriate, the inclusion of the quartiles term would be significant over and above the linear term.

4 Missing values amongst the standard list of risk-factors (ranging from <1% to 5.8%) were imputed using multiple imputation. Missing data for ischemia time (7%) were imputed using the median ischemia time observed from complete data for that transplant unit, and according to whether the organ came from a hospital within the unit's allocation zone or elsewhere.

5 Investigating any temporal trend in ischaemia time was assessed by calculating the median and interquartile range for each calendar year and then using linear regression to examine if there was a significant change over the time period.

RESULTS

Temporal Trend in Ischaemia Time

6 Considering ischaemia time over the time period, the median length of time has increased from 4.95 hours in 2003 to 6.1 hours, with the spread shown in **Figure 1**. This increase over time was found to be significant ($p<0.0001$) and could be due to a variety of reasons.

Effect of Ischaemia Time on Survival

7 When looking at the unadjusted association of ischaemia time on post-transplant survival, there was no significant effect at the 5% level: 30 days p=0.8, 90 days p=0.2, 1 year p=0.08, 5 years p=0.1. The Kaplan-Meier plot for 5 year survival by ischaemia time quartile is shown in **Figure 2**.

8 In the risk-adjusted model, the linear effect of ischaemia time on survival was not significant at 30 days and 90 days (p-values 0.4 and 0.08 respectively). However, it was found to have a significant effect at 1 year and 5 years post-transplant (p=0.04 and p=0.01 respectively). There was no evidence of non-linearity of ischaemia time in any of these models (p-values: 30 days p=0.9, 90 days p=0.8, 1 year p=0.8, 5 years p=0.8).

9 However, when conducting a sensitivity analysis using the complete case dataset (N=1,281), ischaemia time was not found to be significant (p-values: 30 days p=0.7, 90 days p=0.2, 1 year p=0.1, 5 years p=0.06). This casts doubt over the significance found in the analysis which used multiple imputation. There is also limited clinical evidence to support a long-term effect of ischaemia time but not a short-term effect.

FURTHER WORK

- Investigate the effect of ischaemia time on time to ITU/hospital discharge where death is considered a competing risk.

Figure 1 Temporal trends in ischaemia time by calendar year

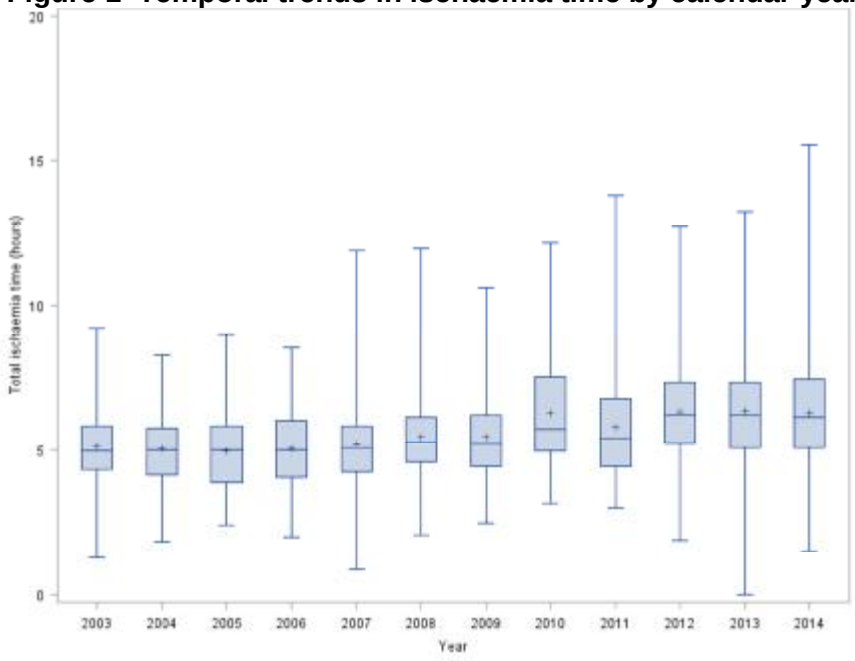
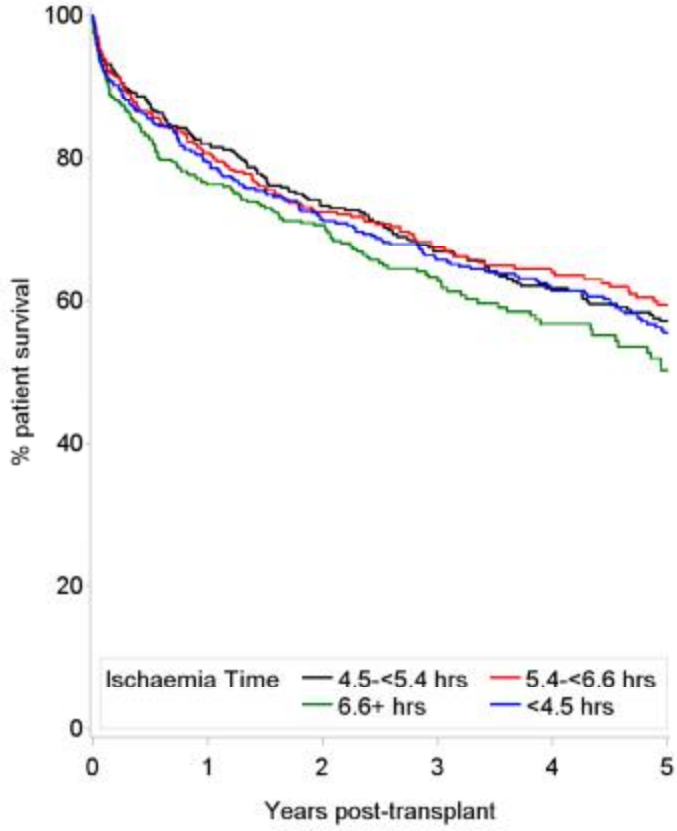


Figure 2 5 year unadjusted survival by ischaemia time quartile



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