Development of the UK Lung Risk Index

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The aim of this paper and CTAG Autumn 2020 discussion is to:

a. Agree the desired outcome measure for the UK Lung Risk Index
b. Agree the candidate variables for inclusion

Proposed outcomes to be predicted by the model and UK lung risk index

1. 1-year mortality and
2. primary Graft Dysfunction (PGD)

Proposed candidate variables for inclusion in model building

Donor characteristics	Age (years) Sex Mode of death Any smoking history Smoking > 20 pack years Lowest PaO2/FiO2 ratio Smoking history Abnormal chest x-ray Secretions Evidence of pulmonary infection Evidence of aspiration Comorbidities Duration of ventilation
Recipient characteristics	Age (years) Sex BMI Primary diagnosis mPAP Diagnosis Recipient status at transplant
Operative variables	Transplant type

Background to project

Organ acceptance, utilisation and allocation in lung transplantation are critical to meet the growing demand of lung transplant candidates, maximising the use of a limited resource, whilst ensuring optimum outcomes for recipients, including low waiting time, improved survival and quality of life. Current decision making is guided by historic criteria with varying degrees of subjectivity. Research focused on recipient outcomes, including mortality and Primary Graft Dysfunction (PGD), has identified multiple donor and recipient variables, accounting for the quality of lungs for transplantation, that are not currently considered in standard acceptance criteria.

Scoring systems and risk indices can be used to capture elements of complex clinical scenarios and aid decision making. Risk scores have previously been developed within lung transplantation (85-87).

While standardised tools for evaluation of donor risk, and organ quality scoring, have been applied in UK renal transplant practice (88), no scoring system is currently in use within UK lung transplantation. Several factors limit the applicability of existing lung donor scores. Firstly, they have not been derived from, or tested within, the UK patient population. Secondly, they have only limited prospective testing of clinical correlation, and thirdly, they include only donor variables in their assessment of acceptability of the organs. The significance of recipient characteristics in the outcomes following lung transplantation has been established.

Applying a numerical value to, or risk stratifying donor organs, according to quality, increases the level of objectivity in the organ acceptance and utilisation process. Inclusion of recipient variables within the risk index will aid in organ allocation and matching of lungs to appropriate recipients, ensuring optimal recipient outcomes. Ultimately, a UK Lung Risk Index is required as the foundation for named-patient organ offering within the UK lung allocation system. We hypothesise that named-patient lung offering will increase organ utilisation in UK lung transplantation. In addition, objective and standardised measures of organ quality facilitate direct comparison of organ acceptance and utilisation practice, aiding further research and providing prompts for audit of acceptance and utilisation practice.

Methods

Patient population

Data prospectively recorded in the UK Transplant Registry (UKTR), hosted by NHSBT, will be used in this study. All consecutive first-time adult lung transplants between 2005 and April 2020 will be included. Recipients aged less that 18 years, recipients with a previous transplant and multi-organ transplant recipients will be excluded from the study. Where data is not available UKTR on patient outcomes, including diagnosis and grading of PGD, retrospective data collection will be performed from UK lung transplant centres. Mechanisms for prospective collection of data identified as significant during this study, will be implemented.

Candidate variables

Donor and recipient candidate variables for inclusion within the model will be defined. Variables deemed to be significant in the early outcomes following lung transplantation, and in defining organ quality, will be identified from review of the literature. Only donor variables that are available at the time of organ offering and recorded recipient variables will be included. The candidate variables must be acceptable to the clinician, considered important in defining donor organ quality and evidenced to

impact early outcomes following lung transplantation. Once identified, the candidate variables will be reviewed by the NHSBT Cardiothoracic Advisory Group (CTAG), to ensure acceptability.

The outcomes to be included in the predictive power of the risk index are 1-year mortality and Primary Graft Dysfunction (PGD). PGD will be diagnosed and graded using the ISHLT 2016 consensus definition (1). These outcomes will be agreed by CTAG to ensure credibility of the Lung Risk Index.

Statistical analysis and model building

The Lung Risk Index will be developed by randomly dividing the transplant dataset into a model derivation cohort, comprising 60% of the dataset, and a validation cohort, comprising 40% of the dataset.

Continuous variables will be described using mean and standard deviation. Categorical variables will be expressed as actual number and proportion. Baseline characteristics of the model derivation and validation cohorts will be compared, to identify significant differences between the distribution of the defined candidate variables, using Student's t test and Mann-Whitney U test as appropriate or Chi square and Fisher's exact test for categorical variables. A P value of <0.05 will be considered statistically significant.

Candidate variables will be tested in the model derivation cohort in unadjusted analysis. Variables with significance will be introduced in a multivariable stepwise logistic regression model for the probability of the defined outcomes measures (1-year mortality and PGD).

Validation cohort and model testing

The ability of the model to predict mortality at 1 year and PGD will be evaluated in the validation cohort using C statistic and the area under a receiver-operating characteristic (AUROC) curve for dichotomous outcomes. Clinical correlation of the score with early and 1-year patient outcomes will be performed.

All statistical analysis will be performed using SAS version 9.4 (SAS Institute; Cary, North Carolina, USA).

References

1. Snell GI, Yusen RD, Weill D, Strueber M, Garrity E, Reed A, et al. Report of the ISHLT Working Group on Primary Lung Graft Dysfunction, part I: Definition and grading-A 2016 Consensus

Group statement of the International Society for Heart and Lung Transplantation. J Heart Lung Transplant. 2017;36(10):1097-103.

2. Diamond JM, Lee JC, Kawut SM, Shah RJ, Localio AR et al. Clinical risk factors for Primary Graft Dysfunction after lung transplantation. American Journal of Respiratory and Critical Care Medicine 2013;187(5):527-534