

# Incidence, Risk Factors, and Outcomes among Patients with Venous Thromboembolic Events in the Early Post-transplant Period

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## Introduction

- Although risk factors for venous thromboembolism (VTE) in the general population are well-defined, limited data exist regarding risk factors for early VTE (during the first 30 days) among lung transplantation (LT) patients.
- With the introduction of the lung allocation score (LAS), progressively sicker patients are undergoing LT, which has the potential to increase the risk for VTE during the post-transplant period.
- This study was conducted to determine the incidence and risk factors for early VTE and its association with 2 year survival.

## Methods

- All adult patients with single, double, or heart LT at UTSW between 2012-2014 were included in the study.
- Various demographic, clinical, and laboratory values before and after LT were recorded.
- Development of any VTE during the first 30 days after LT was the primary outcome variable.
- Variables were compared among patients with and without VTE to identify risk factors for VTE.
- Associations were initially evaluated in a univariate fashion by chi-square and independent t-test as appropriate.
- Multivariate logistic regression modeling was done to identify the independent predictors of development of VTE.
- Kaplan-Meier curves were constructed to compare survival at 1 and 2 years among patients with and without VTE.

## Results

- Overall incidence of VTE during the first 30 days after LT was 28.5% (n=55).
- Various types of VTE events are presented in Figure 1.
- Pulmonary embolism was uncommon (n=3).
- Majority of events (78%) were diagnosed within the first 15 days after LT.
- Comparative profile of patients with and without VTE are presented in Figure 2
- Pre-transplant history of hyperlipidemia and use of anticoagulation (AC) for at least 72 hours were independently associated with a reduced risk of VTE.
- Development of primary graft dysfunction at 72 hours and use of >3 central catheters during the post-transplant period were independently associated with increased risk of VTE.
- Development of VTE was associated with increased risk of mortality at 2 yrs (log rank comparison)
- Kaplan Meier curves showed progressive separation beyond 3 months after LT (Figure 3)

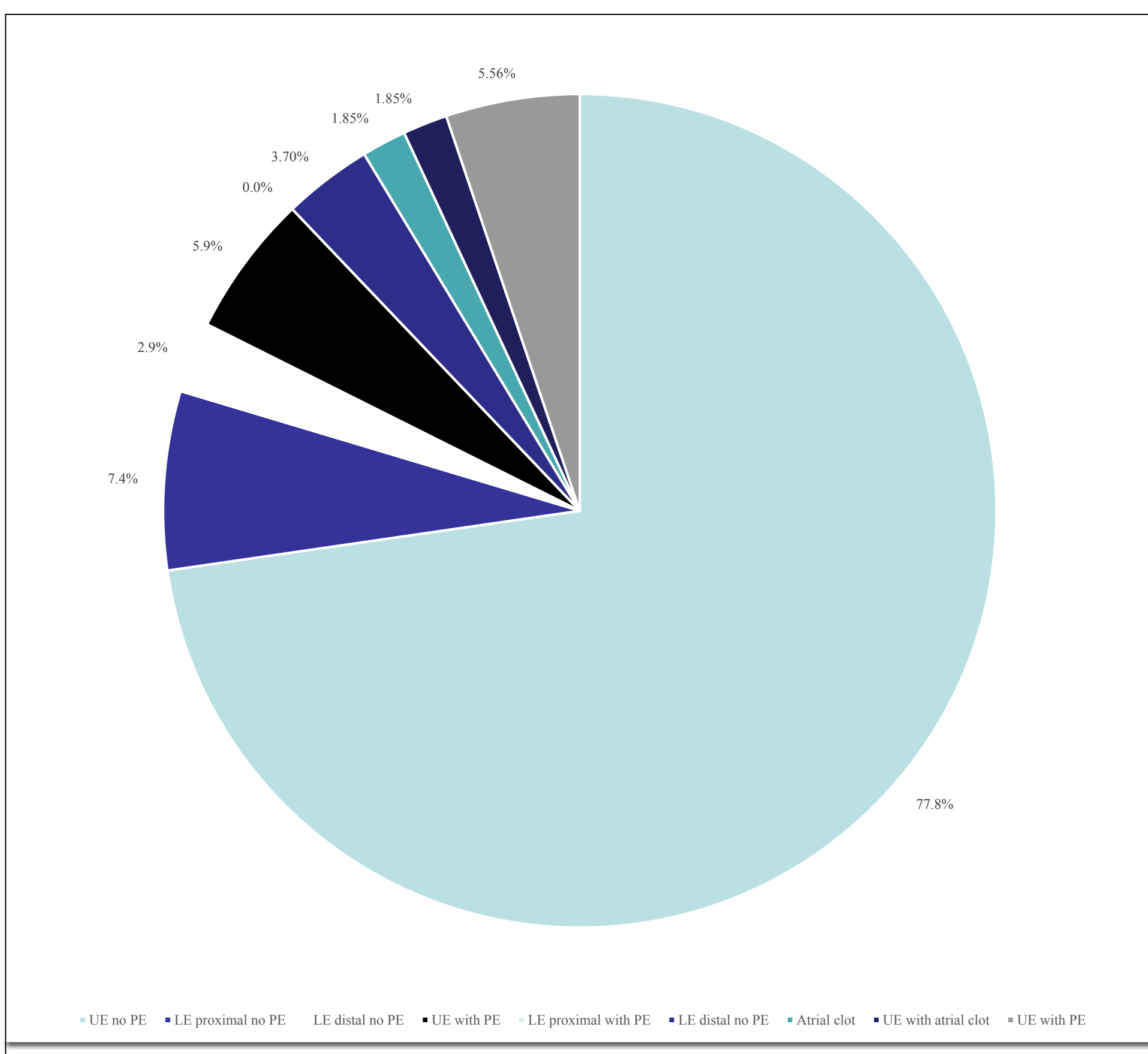


Figure 1: Spectrum of VTE events in the first 30 days after lung transplantation

| Variable                                              | VTE<br>Median with range or<br>proportion<br>(Number of patients) |                     | Odds ratio<br>(95% CI) | p value | Adjusted<br>Odds ratio<br>(95% CI) | p value |
|-------------------------------------------------------|-------------------------------------------------------------------|---------------------|------------------------|---------|------------------------------------|---------|
|                                                       | Yes (n=55)                                                        | No<br>(n=138 )      |                        |         |                                    |         |
| Age at transplant (years)                             | 54.1<br>(52.0-56.2)                                               | 56.6<br>(55.5-57.7) |                        | 0.283   |                                    |         |
| Body mass index at<br>transplant (Kg/m <sup>2</sup> ) | 24.4<br>(23.7-25.07)                                              | 24.7<br>(24.4-25.1) |                        | 0.669   |                                    |         |
| Male gender                                           | 49%                                                               | 62%                 | 0.58<br>(0.31-1.1)     | 0.092   |                                    |         |
| Ethnicity                                             |                                                                   |                     |                        |         |                                    |         |
| Caucasian                                             | 71%                                                               | 73%                 |                        |         |                                    |         |
| African-American                                      | 18%                                                               | 12%                 |                        | 0.31    |                                    |         |
| Hispanic                                              | 7%                                                                | 12%                 |                        |         |                                    |         |
| Others                                                | 4%                                                                | 3%                  |                        |         |                                    |         |
| Underlying diagnosis group                            |                                                                   |                     |                        |         |                                    |         |
| Restrictive                                           |                                                                   |                     |                        |         |                                    |         |
| Obstructive                                           | 62%                                                               | 59%                 |                        |         |                                    |         |
| Vascular                                              | 20%                                                               | 25%                 |                        | 0.66    |                                    |         |
| Suppurative                                           | 9%                                                                | 10%                 |                        |         |                                    |         |
| Type of transplant                                    |                                                                   |                     |                        |         |                                    |         |
| Left single                                           | 5.4%                                                              | 6.5%                |                        |         |                                    |         |
| Right single                                          | 5.4%                                                              | 5.8%                |                        | 0.956   |                                    |         |
| Bilateral                                             | 89%                                                               | 87.7%               |                        |         |                                    |         |
| History of diabetes                                   | 22%                                                               | 24%                 |                        | 0.76    |                                    |         |
| History of hyperlipidemia                             | 27%                                                               | 41%                 | 0.55<br>(.28-1.09)     | 0.084   | 2.83<br>(1.11-7.25)                | 0.03    |
| LAS at listing                                        | 53.7<br>(50.7-56.7)                                               | 44.3<br>(43.2-45.4) |                        | <0.001  |                                    |         |
| LAS at match                                          | 59.6<br>(56.6-62.6)                                               | 50.3<br>(48.8-51.8) |                        | 0.002   |                                    |         |
| Use of cardiopulmonary<br>bypass                      | 62%                                                               | 44%                 | 2.04<br>(1.08-3.87)    | 0.027   |                                    |         |
| Use of anticoagulation for 72<br>hours                | 25%                                                               | 47%                 | 0.38<br>(0.19-0.77)    | 0.006   | 4.13<br>(1.80-9.50)                | 0.001   |
| >3 central catheters                                  | 90%                                                               | 24.7%               | 3.64<br>(2.62-5.05)    | <0.001  | 25.94<br>(1.97-342.13)             | 0.013   |
| Use of Steroid Pulse 1 <sup>st</sup> 2<br>weeks       | 27%                                                               | 10%                 | 3.32<br>(1.48-7.47)    | 0.003   |                                    |         |
| PGD score at 72hrs                                    |                                                                   |                     |                        |         |                                    |         |
| 0                                                     | 43%                                                               | 56%                 |                        |         | 1.64<br>(1.13-2.36)                | 0.009   |
| 1                                                     | 18%                                                               | 28%                 |                        | 0.003   |                                    |         |
| 2                                                     | 18%                                                               | 11%                 |                        |         |                                    |         |
| 3                                                     | 20%                                                               | 5%                  |                        |         |                                    |         |
| Duration of intubation<br>(days )                     | 8.2<br>(5.6-10.7)                                                 | 3.4<br>(3.2-3.7)    |                        | 0.004   |                                    |         |
| Duration of ICU stay (days)                           | 14.3<br>(12.5-16.1)                                               | 8.1<br>(6.9-9.3)    |                        | 0.006   |                                    |         |
| Duration of hospital stay<br>(days)                   | 24.6<br>(22.4-26.8)                                               | 16.8<br>(15.4-18.2) |                        | 0.003   |                                    |         |
| Hospital survival                                     | 93%                                                               | 96%                 |                        | 0.278   |                                    |         |
| One year survival                                     | 80%                                                               | 89%                 | 0.49<br>(0.21-1.14)    | 0.094   |                                    |         |
| Two year survival                                     | 65.5%                                                             | 79%                 | 0.83<br>(0.67-1.02)    | 0.05    |                                    |         |

Figure 2: Characteristics of patients with and without VTE in the first 30 days after lung transplantation.

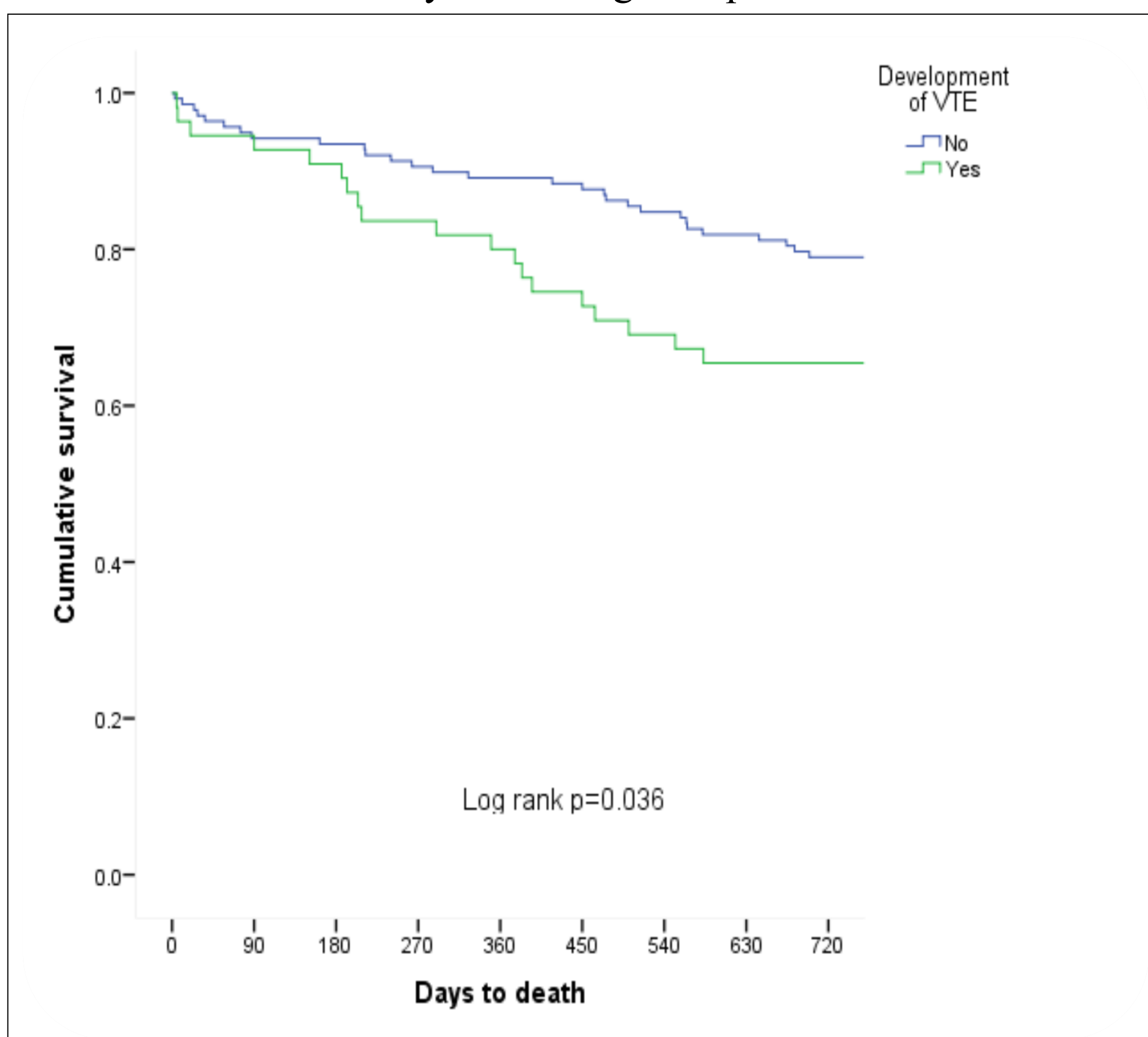


Figure 3: Kaplan Meier survival curves for patients with and without VTE

## Conclusion

- A significant proportion of patients develop VTE early after LT.
- Early development of VTE is associated with worse survival at 2 years post-LT.
- Despite the majority of VTEs being catheter related, the use of anticoagulation appears to be protective.
- The protective effect of hyperlipidemia may be linked to statin use, which needs to be investigated in future studies.

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