Predictors and Clinical Outcomes of Lymphoproliferative Disorders in Heart Transplant Recipients

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Background

- **Post-transplant malignancy can be a major risk during long term management of heart transplantation (HT).**
- **More than 10% of adult HT recipients develop de novo malignancy between years 1 and 5 after transplantation, and this was associated with increased mortality.**
- **The cumulative incidence of de novo solid malignancy increased from 2000-2005 to 2006-2011 (10.0% vs. 12.4%, $p < 0.0001$) with the largest increase in skin cancer.**

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Background

- **From the previous study, the incidence of post-transplant lymphoproliferative disorder (PTLD) was approximately 1%, and it is lower than the compared to what has previously been reported, from 3% to 9%**

- **The incidence of PTLD including the earlier period after HT and the mortality of the patients were not well evaluated.**

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Purpose

- **Evaluate temporal trends, clinical characteristics, predictors, and clinical outcomes in patients with post-transplant lymphoproliferative disorder (PTLD).**
- **Analyze the prevalence, types, and time interval of de novo PTLD in heart transplant recipients.**
- **Analyze the predictors and clinical outcomes of de novo PTLD in heart transplant recipients.**

Study Population

- **Retrospective cohort study using data routinely collected in the ISHLT Thoracic Organ Transplant Registry. Information provided in this report is based on data reported to the ISHLT Registry as of April 19, 2019**

- **This analysis cohort started with 68,212 recipients who underwent heart transplantation between January 1, 2000 and June 30, 2015. Of these, 40,076 were excluded and finally 28,136 patients were analyzed.**

Outcomes

- **Primary outcome**

  - PTLD within 3 years of heart transplant

- **Secondary outcome**

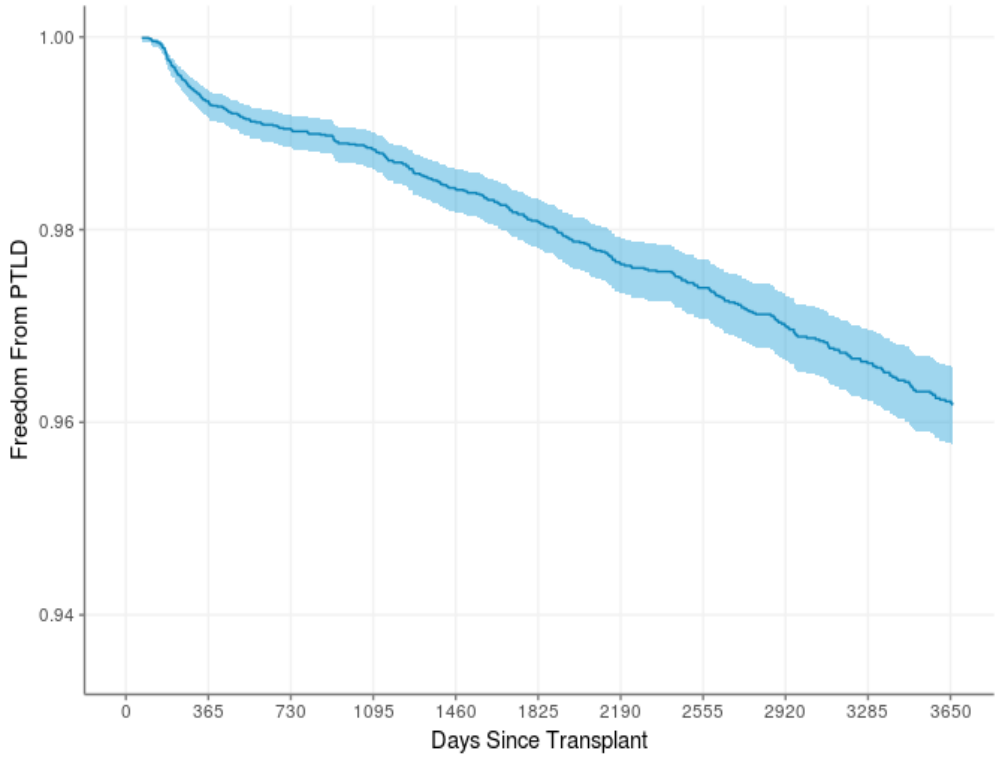
  - Mortality after PTLD development

  - Causes of death for recipients who developed PTLD and subsequently died

Result 1

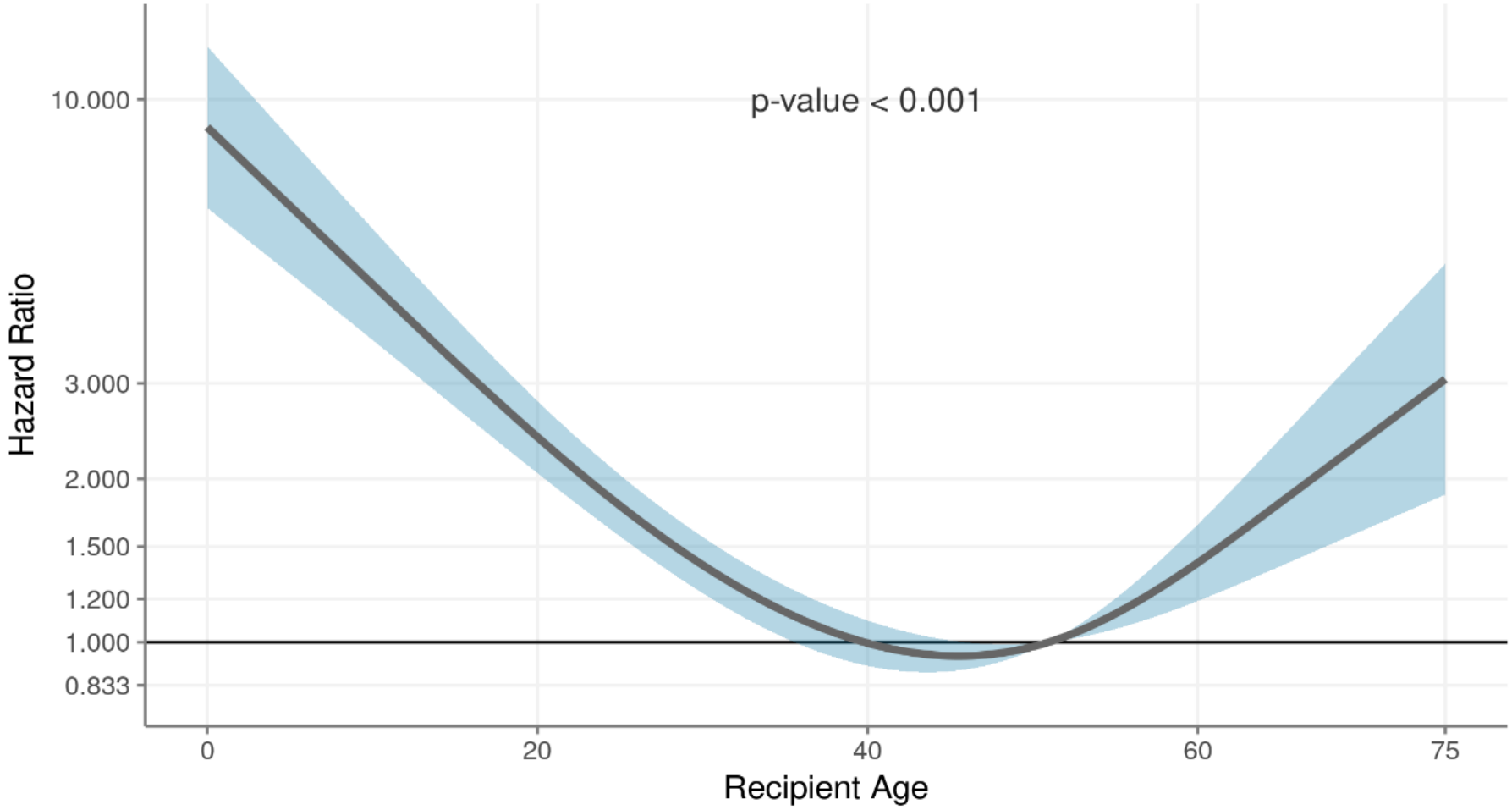
- **Overall incidence of PTLD is 0.7% in 1 year, 1.0% in 2 years, 1.2% in 3 years, 1.9% in 5 years, 3.8% in 10 years after HTx**

Year	N at Risk	Rate (95% CI)
1	12,637	99.3% (99.2% - 99.5%)
2	11,529	99.0% (98.9% - 99.2%)
3	10,629	98.8% (98.6% - 99.0%)
4	9,716	98.4% (98.2% - 98.6%)
5	8,843	98.1% (97.8% - 98.3%)
6	8,044	97.6% (97.3% - 97.9%)
7	7,356	97.4% (97.1% - 97.7%)
8	6,692	97.0% (96.6% - 97.3%)
9	6,095	96.6% (96.2% - 97.0%)
10	5,530	96.2% (95.8% - 96.6%)



Result 2

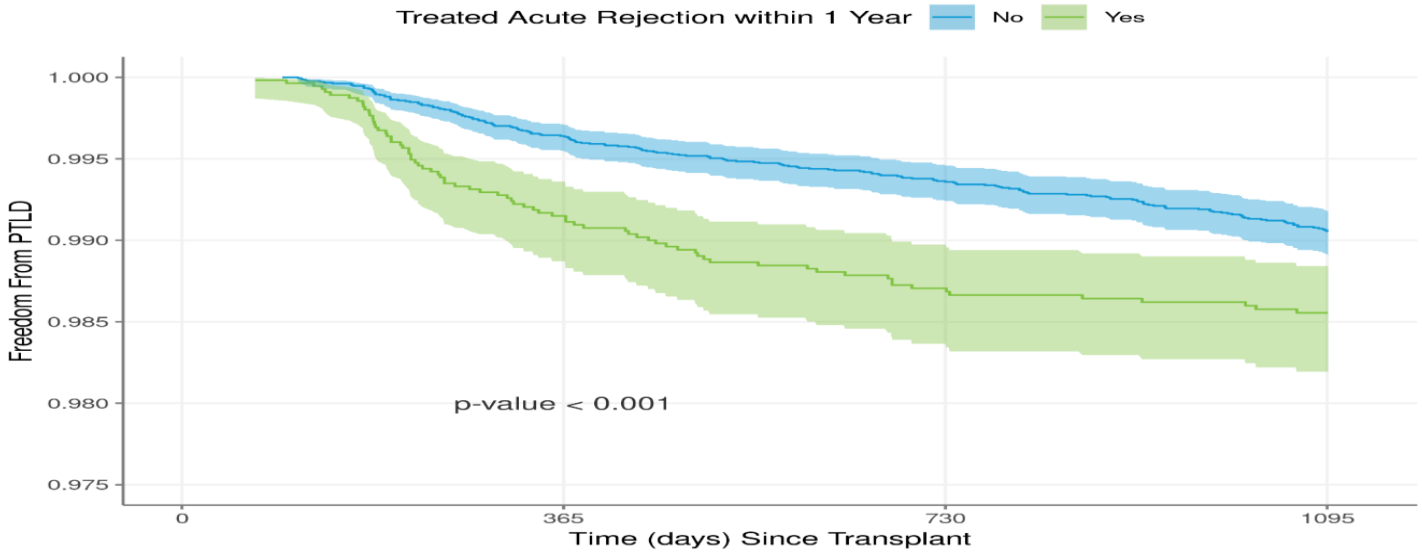
- **The incidence of PTLD was highest in young age, and increased in older age – bimodal peak (U shape)**



Result 3

- **AR within 1 year is significantly related with increased risk of PTLD 1.4% vs. 0.9% (p<0.001)**

Treatment for Acute Rejection within 1 Year				
	No		Yes	
Time (days)	N at Risk	Freedom from PTLD (95% CI)	N at Risk	Freedom from PTLD (95% CI)
365	20,798	99.6% (99.5% - 99.7%)	5,421	99.1% (98.9% - 99.4%)
730	19,470	99.4% (99.2% - 99.5%)	4,814	98.7% (98.4% - 99.0%)
1,095	17,953	99.1% (98.9% - 99.2%)	4,354	98.6% (98.2% - 98.8%)



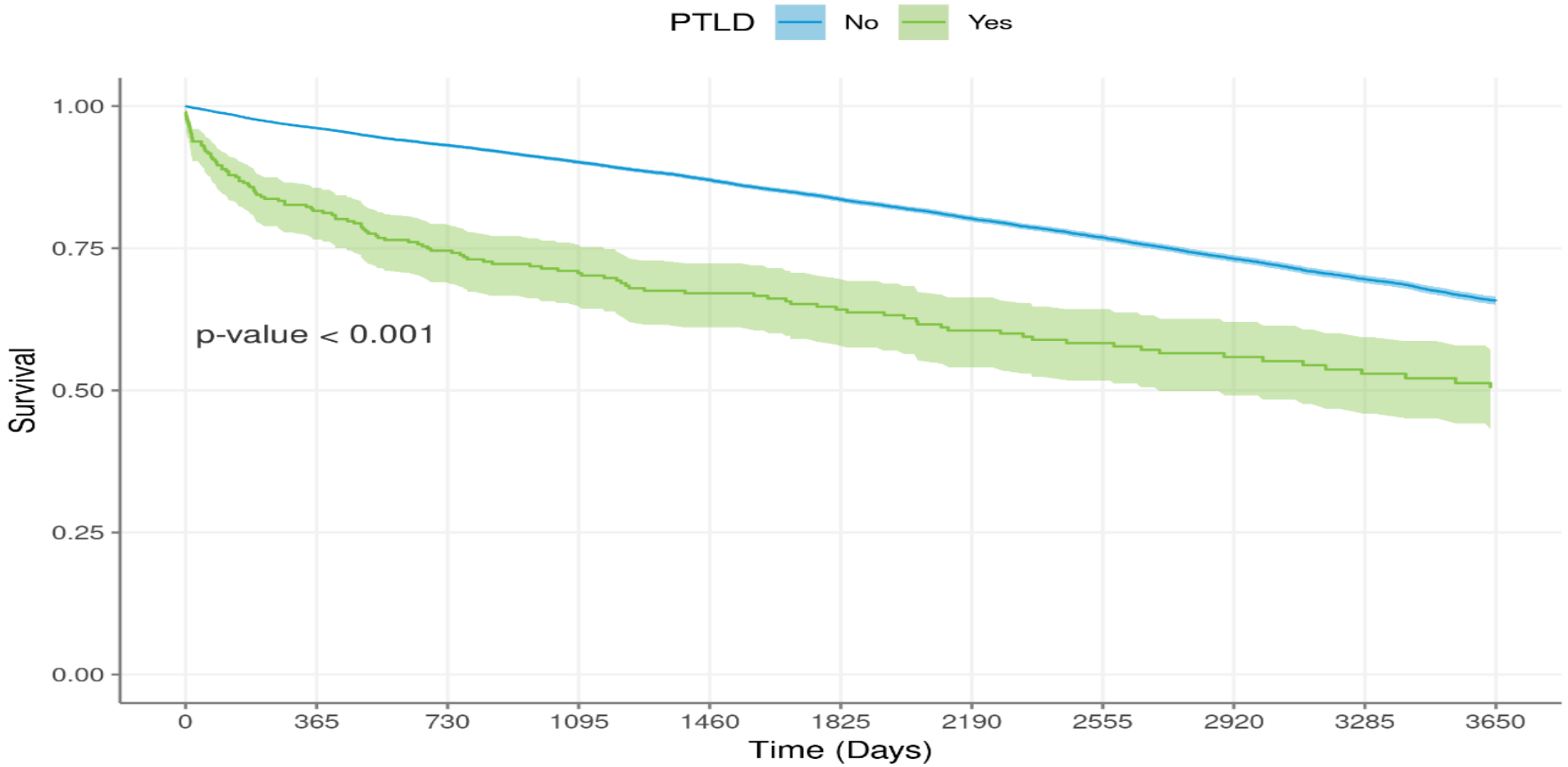
Result 4

- **AR within 1 year is significantly related with increased risk of PTLD 1.4% vs. 0.9% (p<0.001)**

	No PTLD		PTLD Within 3 Years	
Time (days)	**N at Risk**	**Survival Estimate (95% CI)**	**N at Risk**	**Survival Estimate (95% CI)**
365	25,505	96.1% (95.9% - 96.4%)	231	81.6% (76.6% - 85.6%)
730	24,194	93.1% (92.8% - 93.4%)	197	74.6% (69.1% - 79.2%)
1,095	21,891	90.1% (89.8% - 90.5%)	170	70.6% (64.9% - 75.6%)
1,460	19,108	87.0% (86.6% - 87.4%)	149	67.1% (61.1% - 72.4%)
1,825	16,546	83.6% (83.1% - 84.1%)	132	64.2% (58.0% - 69.7%)
2,190	14,239	80.2% (79.7% - 80.7%)	113	60.5% (54.1% - 66.3%)
2,555	12,086	76.9% (76.3% - 77.4%)	103	58.3% (51.8% - 64.3%)
2,920	10,080	73.2% (72.5% - 73.8%)	84	55.9% (49.2% - 62.0%)
3,285	8,347	69.5% (68.9% - 70.2%)	69	52.9% (46.0% - 59.4%)
3,650	6,800	65.8% (65.0% - 66.5%)	57	50.4% (43.2% - 57.1%)

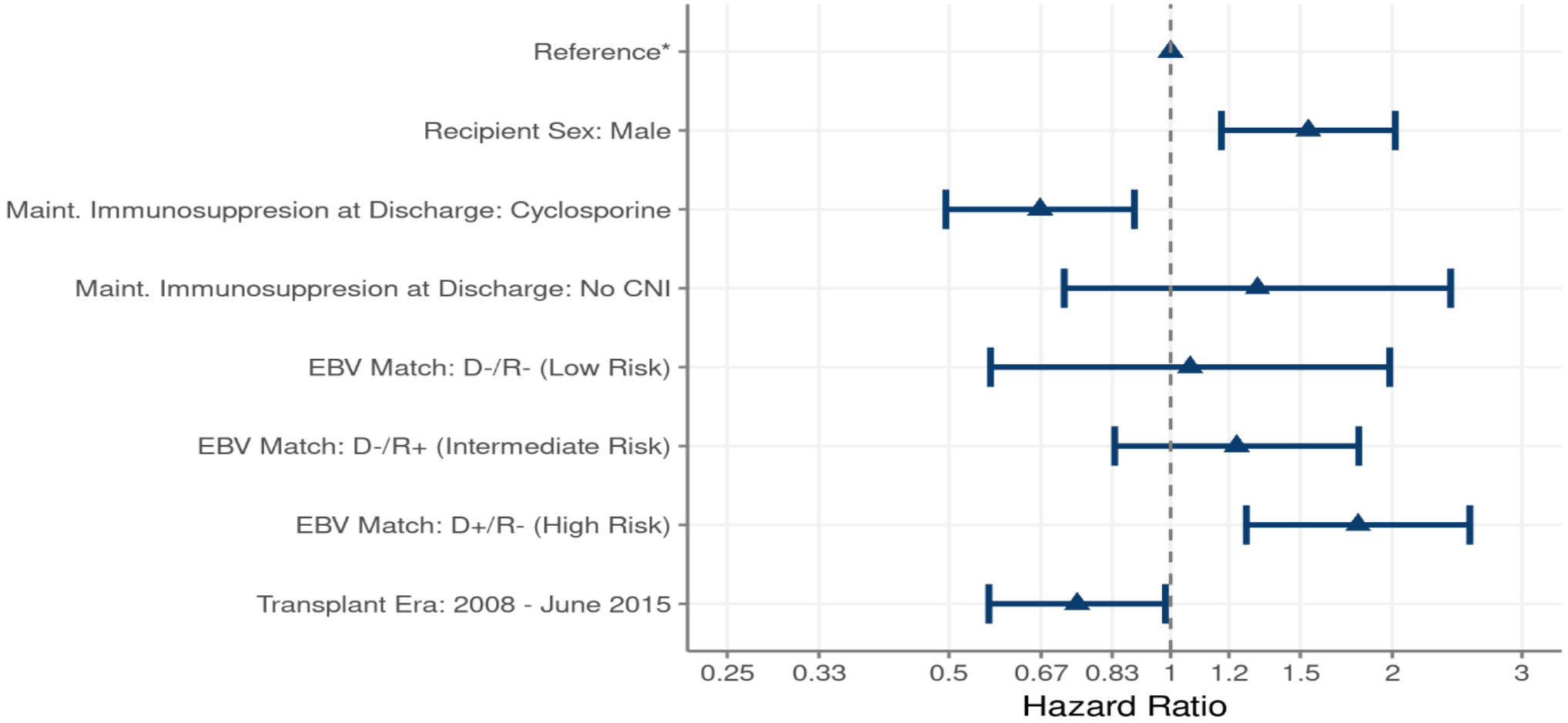
Result 5

- **Significantly lower survival in PTLD (within 3 years) group 65.8% vs. 50.4% (p<0.001)**



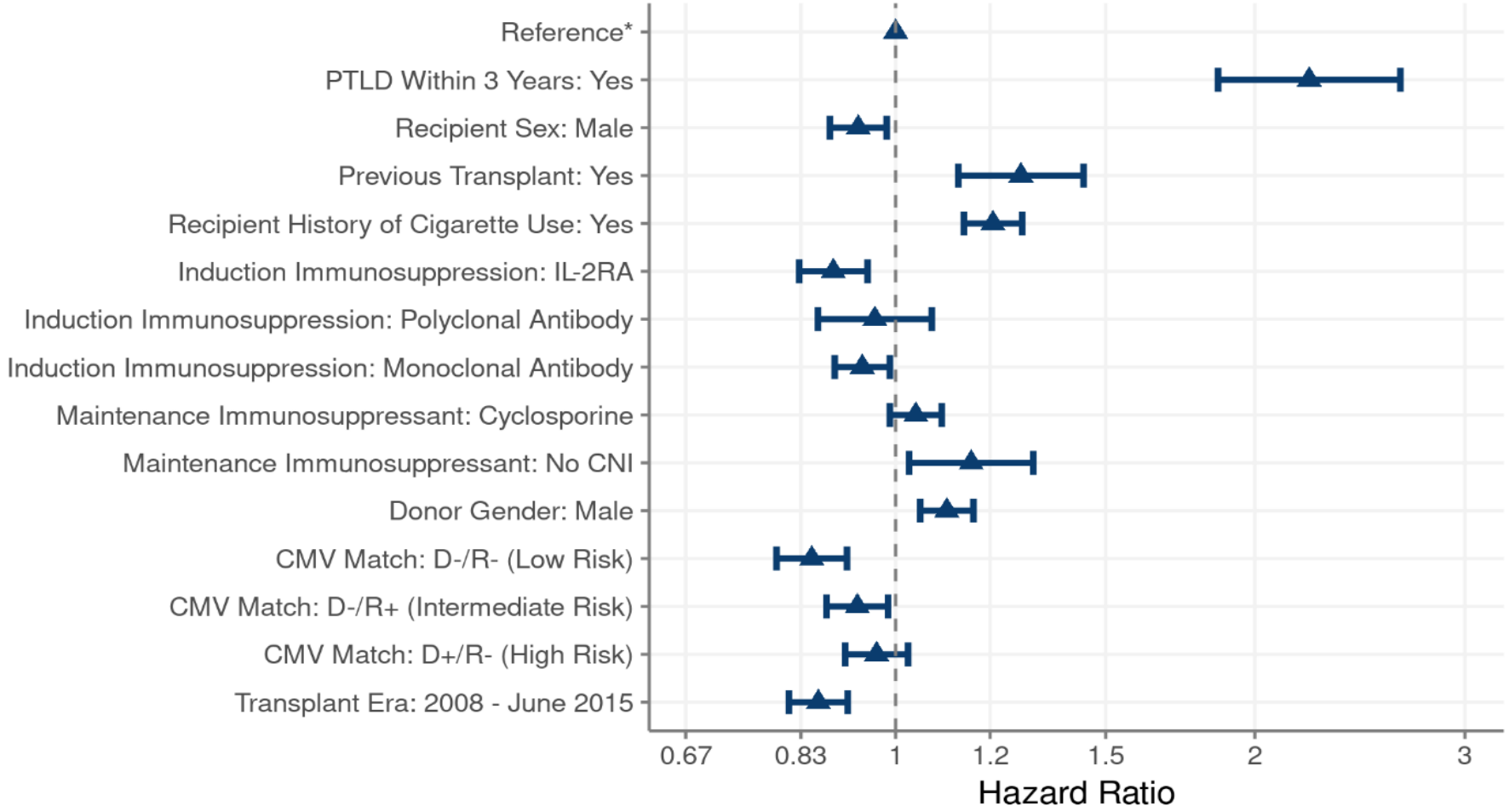
Result 6

- **Incidence of PTLD is higher in male and EBV mismatch. Lower incidence was noted in later period (2008 – 2015).**



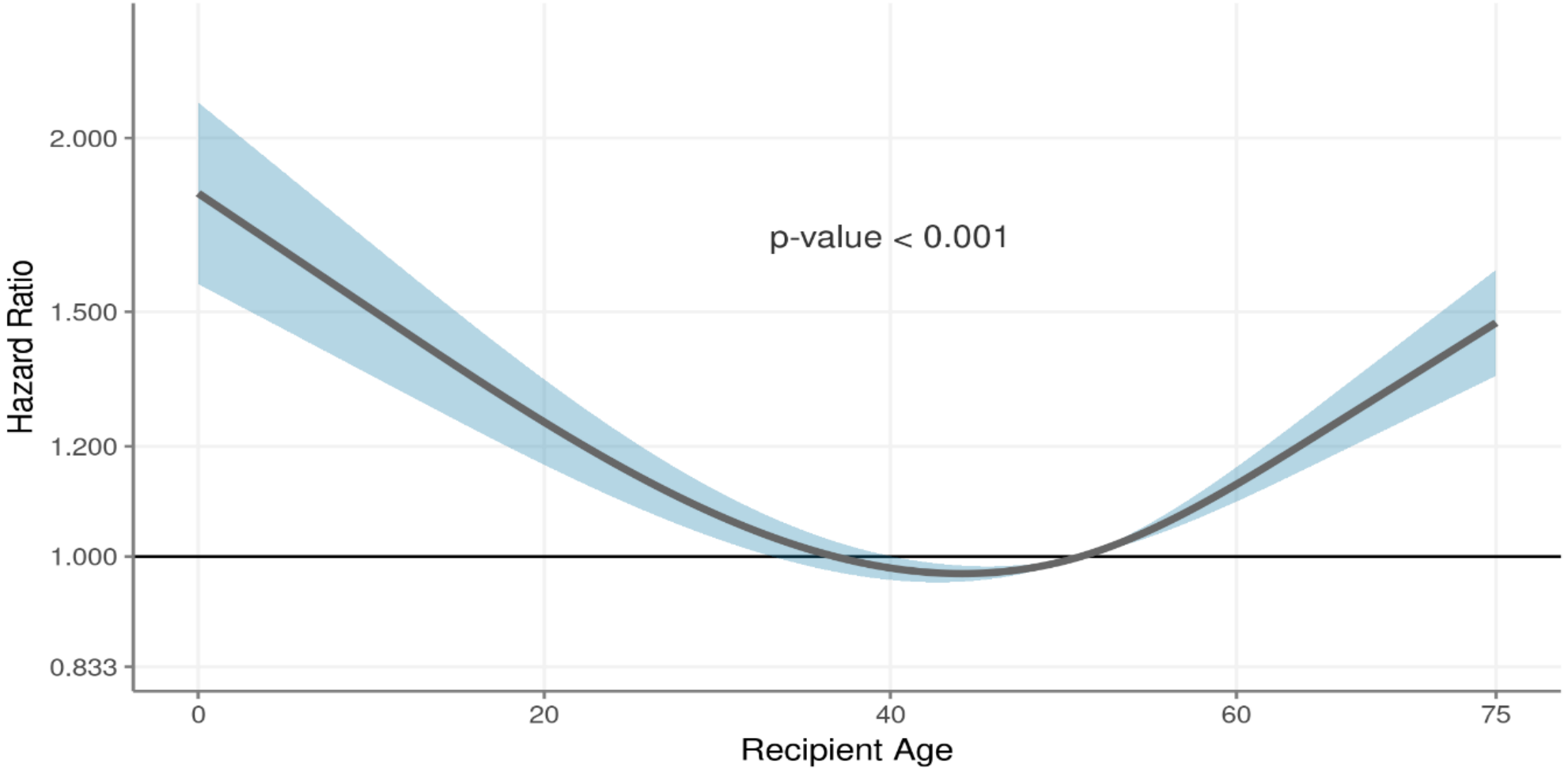
Result 7

- **Higher mortality was noted in the early occurrence, smoker, CNI non-user, and male donor.**
- **Lower mortality was noted in male recipient, induction therapy, donor CMV (-), and later period (2008-2015).**



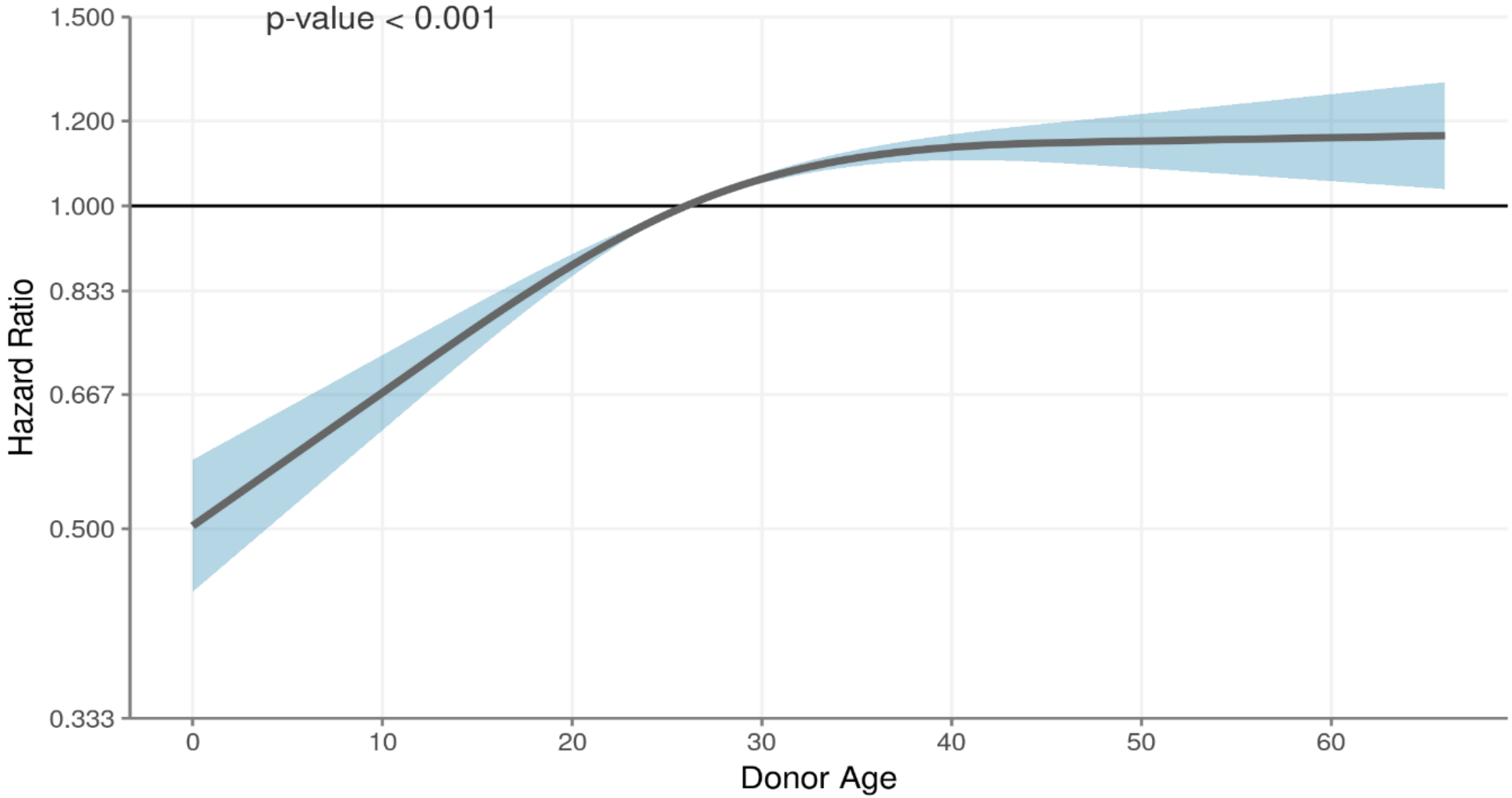
Result 8

- **The mortality was highest in young age, and increased in older age – bimodal peak (U shape)**



Result 8

- **The mortality increased as the donor age increases**



Summary

- **The incidence of PTLD after HTx is 0.7% in 1 year, 1.2% in 3 years, and 3.8% in 10 years.**
- **Patients with acute rejection within 1 year after HTx. showed higher incidence of PTLD**
- **Incidence of PTLD is higher in male and EBV mismatch. Lower incidence was noted in later period (2008 – 2015).**
- **Higher mortality was noted in the early occurrence, smoker, CNI non-user, and male donor and lower mortality was noted in male recipient, induction therapy, donor CMV (-), and later period (2008-2015).**

Conclusion

The incidence as well as mortality of PTLD has decreased in recent years.

Close observation and balanced immunosuppression according to the patient's characteristics such as age, gender, EBV status and rejection history is the key to decrease the burden of PTLD which can be detrimental in the course of heart transplantation.

Thank you for your Attention