

Significance Of Phenotype Change Post CLAD-onset On Allograft Survival

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Purpose

Previous studies suggest Chronic Lung Allograft Dysfunction (CLAD) subtypes with RAS-like opacities (RLO) (i.e. persistent parenchymal or pleural fibrosis) at CLAD onset to have worse survival. However, the significance of transitions between CLAD subtypes remains obscure.

Methods

This was a single center, retrospective cohort study of consecutive adult, first bilateral lung transplants from 2010-2015. Patients with CLAD were classified into ISHLT phenotypes BOS, RAS, Mixed, undefined and some remained unclassified. We defined phenotype transition as a change of at least one of three determinants: obstruction, restriction or RLO. Association of phenotype transition with time to death or retransplant starting at CLAD onset or transition date was assessed using Cox PH models. Multivariable models included age and CMV mismatch.

Results

Of 173 patients with CLAD, 108 patients with no RLO and 28 with RLO at CLAD onset did not change phenotype. 37 patients (21.3%) had a phenotype transition at a median time of 329 days (IQR 166-591) post CLAD onset. 15 patients without RLO (12 BOS, 2 undefined, 1 unclassified) developed RLO and changed phenotype to RAS (1), mixed (7), or undefined (7). 22 patients had a phenotype transition owing to a change in the ventilatory defect pattern (10 with RLO and 12 without RLO). Patients who developed RLO after CLAD onset had a non-significant trend towards worse survival from CLAD onset (HR=1.29, p=0.7) and also from transition date (HR=3.45, p=0.1) compared to patients who transitioned to a phenotype without RLO (Fig 1A), probably due to small number of patients. Survival after RLO emergence did not differ between patients with RLO at CLAD onset and patients who developed RLO post CLAD onset (HR=1.69, p=0.17 (Fig 1B).

The authors do not have any conflicts of interest to disclose.

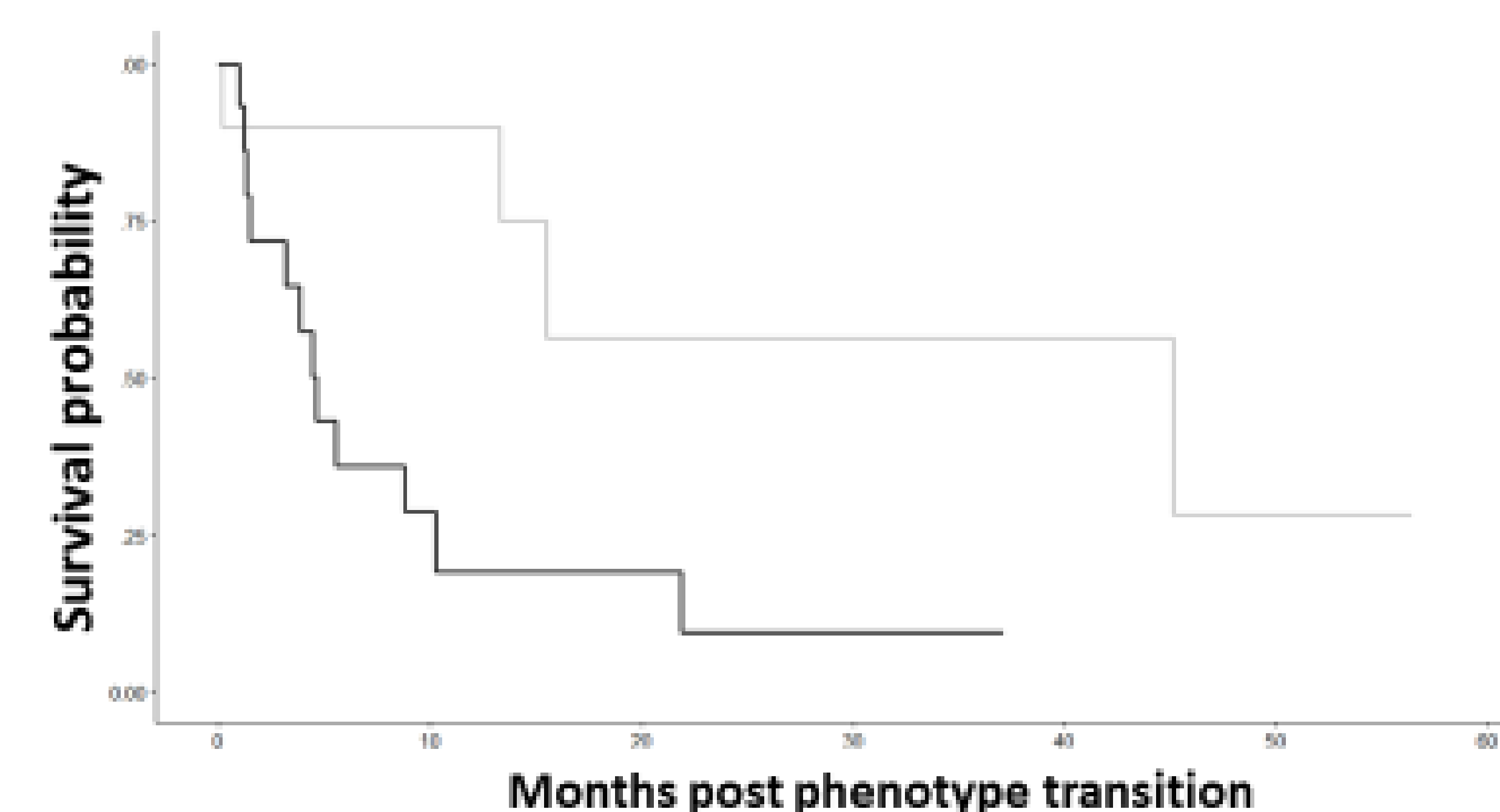


Figure 1A: Survival curves post phenotype transition by transition type

— Transition to Non RAS-like opacities phenotype
— Transition to RAS-like opacities phenotype

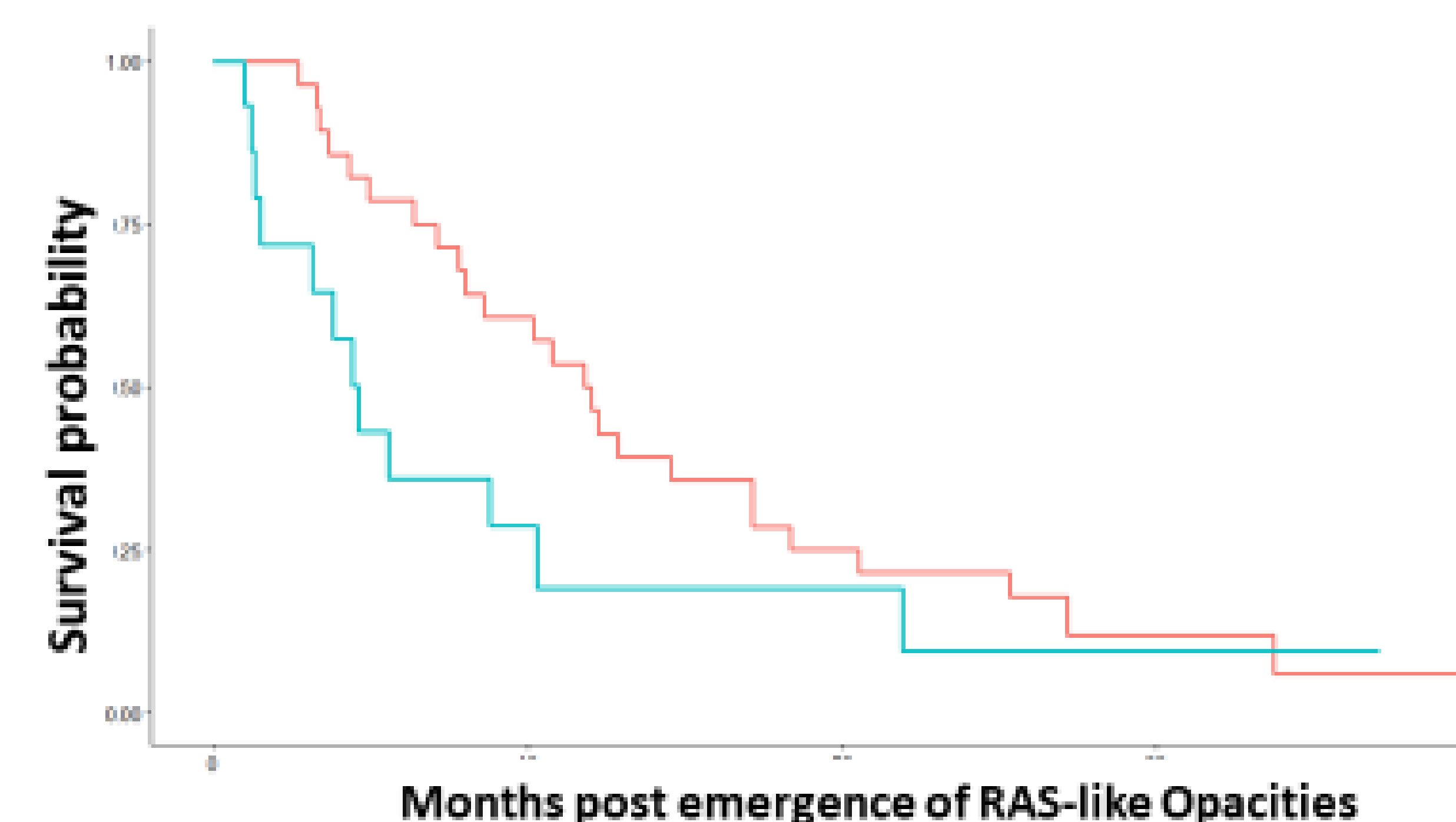


Figure 1B: Survival curves after emergence of RAS-like opacities

— Survival since the transition to RAS-like opacities phenotype (for transition group)
— Survival since CLAD onset for RAS-like opacities phenotype (without transition)

Conclusion

Our study shows that phenotype transition is a relatively common phenomenon, although a transition to RAS-like opacities occurred in only 9% of CLAD patients. The poor survival from emergence of RAS-like opacities appears to be similar regardless of timing relative to CLAD onset.