

Association of Liver Biopsy Pathology on Outcome of Patients Undergoing Heart Transplantation

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BACKGROUND

- Patients with advanced heart failure needing heart transplant commonly have some degree of liver dysfunction, ranging from mild liver fibrosis to cirrhosis.
- Liver biopsies are the gold-standard for evaluating the severity of liver disease and are commonly obtained as part of the work up prior to listing a patient for heart transplant, particularly in patients with abnormal liver function tests, long-standing right ventricular failure or image-based studies suggestive of liver cirrhosis.
- There is limited data on the impact of liver fibrosis on outcomes for HT candidates.

OBJECTIVES

- **To determine the relationship between liver fibrosis severity and mortality rates for patients on the heart transplant waitlist and post-heart transplant.**

METHODS

- **Study Design:** Retrospective cohort study
- **Study Population:** Adults age > 18 who are listed for heart transplant and underwent liver biopsy before transplant at Tufts Medical Center.
- **Study Definitions:** Inclusion criteria were adults listed for HT who underwent a liver biopsy for evaluation of liver fibrosis. Degree of fibrosis was categorized as either no/early or advanced:
 - Patients with only fibrosis expansion of portal areas with or without short fibrous septa or no fibrosis were categorized as no/early fibrosis
 - Patients with any evidence of portal-to-portal bridging or cirrhosis were categorized as advanced fibrosis
- **Data Collection and Study Period:** Clinical, laboratory and mortality data were obtained from the Tufts transplant center registry from 08/12/2004-02/16/2022.
- **Analysis:** Trend analysis was performed using Cox proportional hazard model with transplantation as a time varying covariate (RStudio, R Foundation, Austria). MELD-XI was controlled for in the model.

RESULTS I

- Fourteen of 42 patients (33%) had advanced fibrosis and 28 (67%) had no/early fibrosis (Figure 1). Two (5%) patients had cirrhosis.
- Ten (24%) patients with no/early liver fibrosis died and six (14%) patients with advanced fibrosis died.
- Fifteen (36%) waitlisted patients did not eventually receive transplants; 9 of these 15 patients died on the waitlist.
- Twenty-seven (64%) patients did eventually receive transplants
- Average time from liver biopsy to listing was 124 days (median = 8 days, SD = 749 days; Figure 2).
- For both transplanted and non-transplanted patients, the predicted five-year survival is 68.2% for those with no/early liver fibrosis and 59.2% for those with advanced liver fibrosis (Table 1, Figure 3).
- For all patients from time of listing, there was no significant difference in the survival of patients with advanced fibrosis compared to no/early fibrosis (HR 0.73, CI 0.25-2.11, p = 0.56).

Figure 1. Number of no/early and advanced liver fibrosis patients who did and did not receive transplants

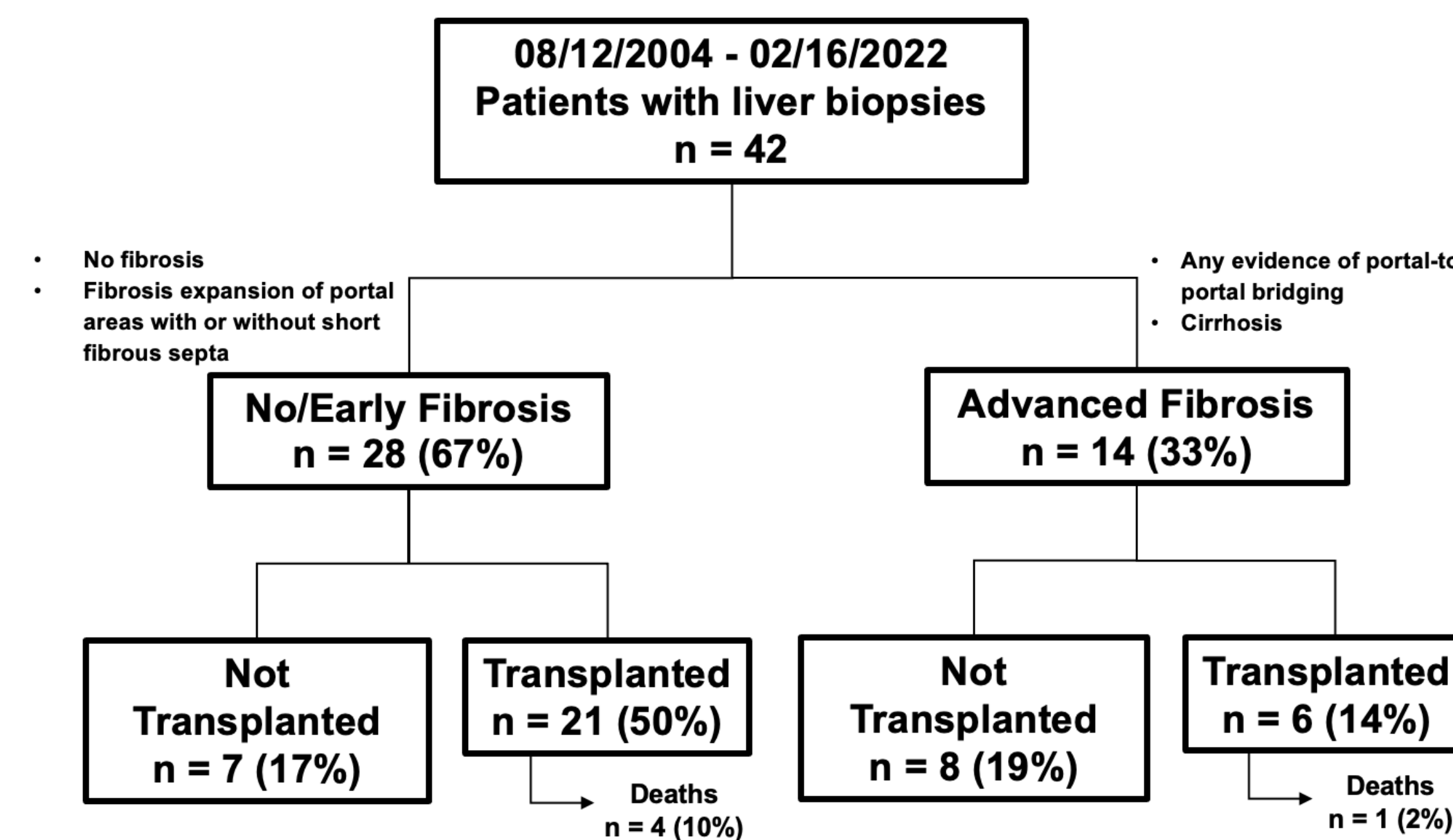
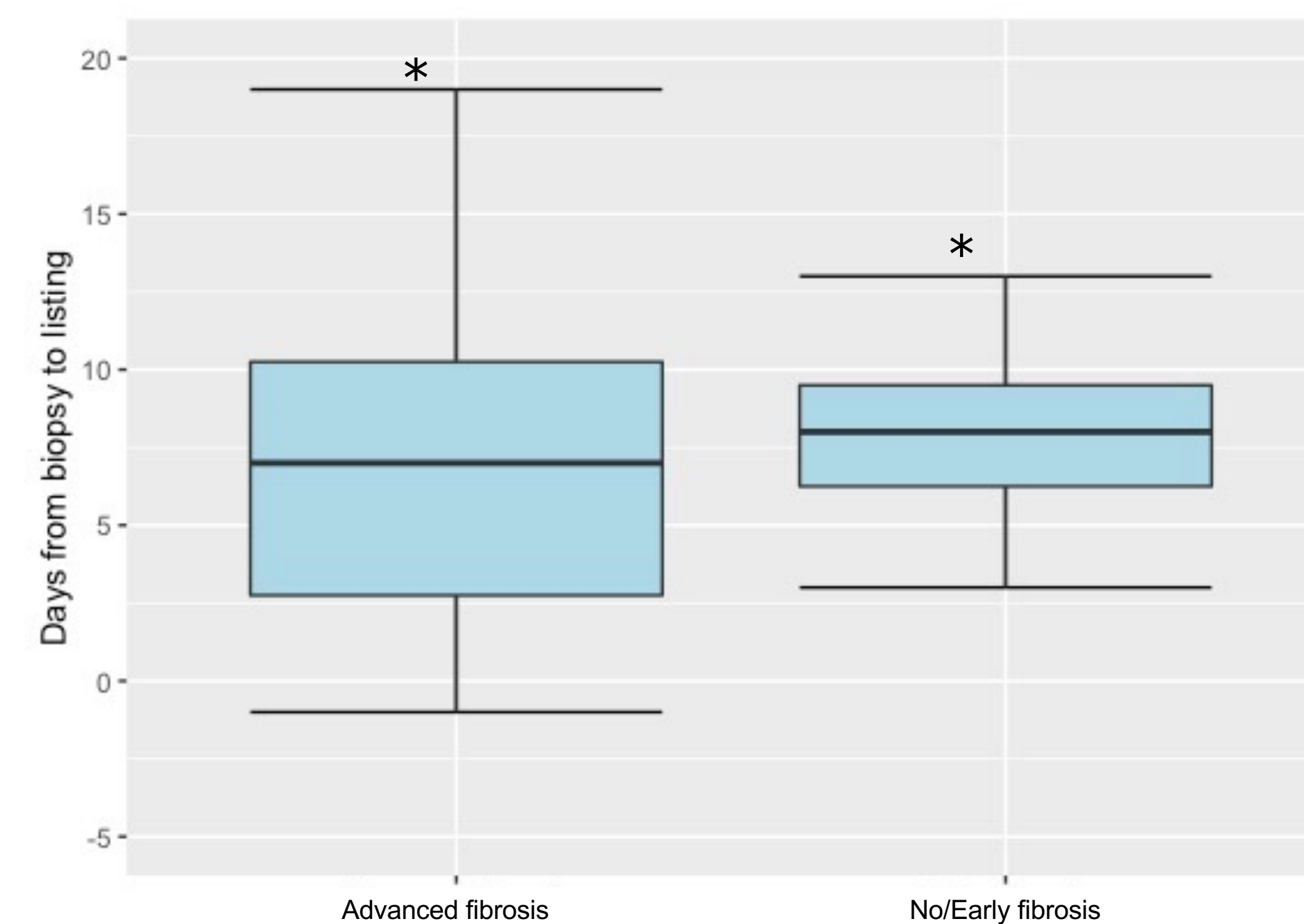


Figure 2. Box plot of number of days from time of liver biopsy to time of listing



*Outliers are not included in graph

Table 1. Predicted survival percentages for transplanted patients, non-transplanted patients, and both groups combined from time of listing

	Transplanted Patients n = 27	Non-transplanted Patients n = 15	Transplanted & Non-transplanted Patients [†] n = 42
No/Early Liver Fibrosis (% CI)			
30 Days	100 (0-100)	84.6 (66.0-100)	97.9 (93.8-100)
1 Year	96.2 (88.8-100)	53.5 (29.2-97.9)	86.8 (76.4-98.6)
5 Years	88.1 (74.6-100)	17.3 (3.6-84.0)	68.2 (52.4-88.8)
Advanced Liver Fibrosis (% CI)			
30 Days	100 (0-100)	89.7 (75.7-100)	97.1 (91.5-100)
1 Year	96.2 (86.6-100)	66.6 (42.4-100)	82.4 (67.3-100)
5 Years	88.2 (67.4-100)	32.1 (9.8-100)	59.2 (37.5-93.3)

* CI = confidence interval . [†] analyzed with transplant as a time varying covariate

Figure 3: Predicted survival curve from time of listing for waitlisted patients, including those who do and do not receive transplants (model p = 0.8)

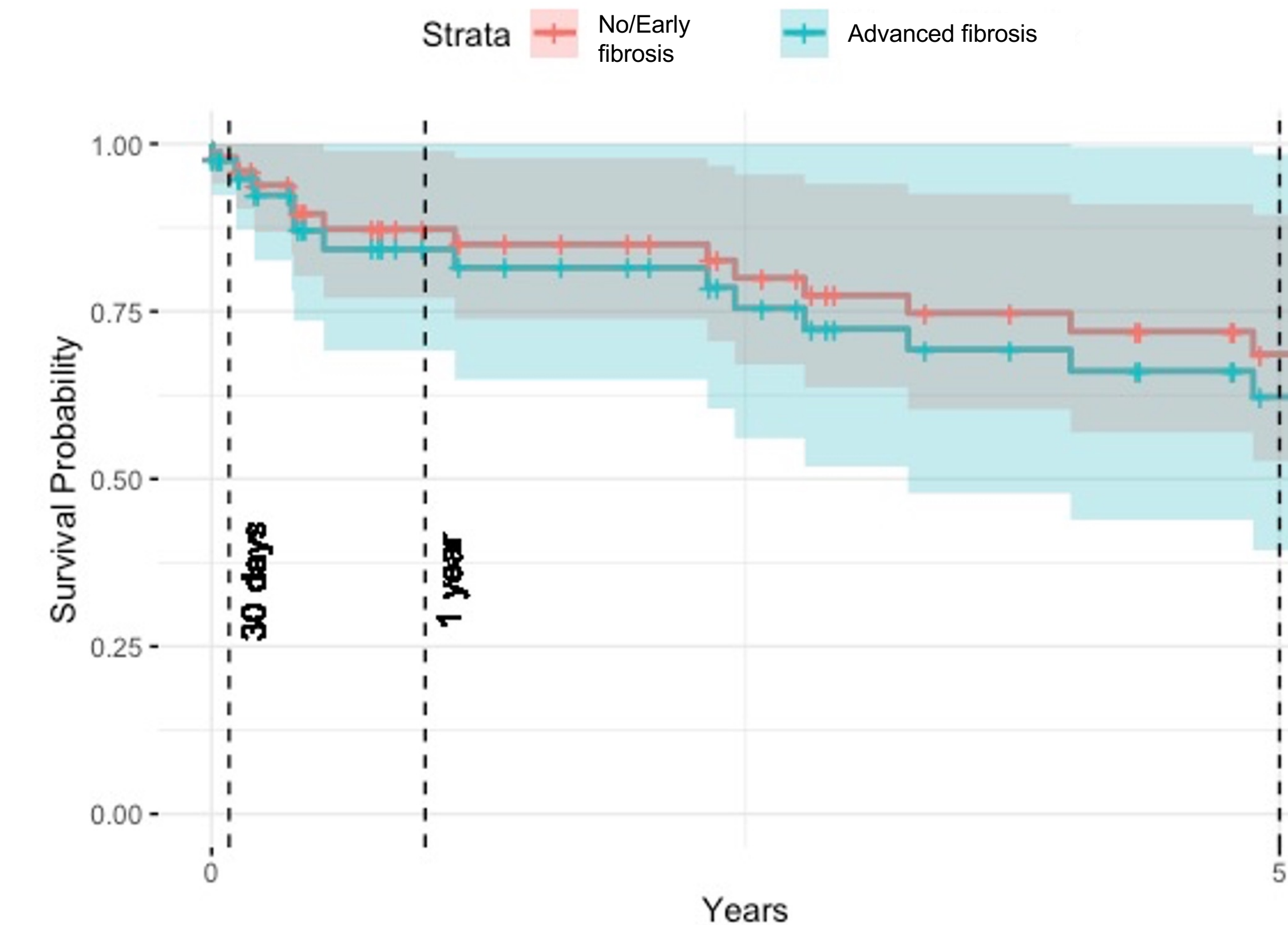
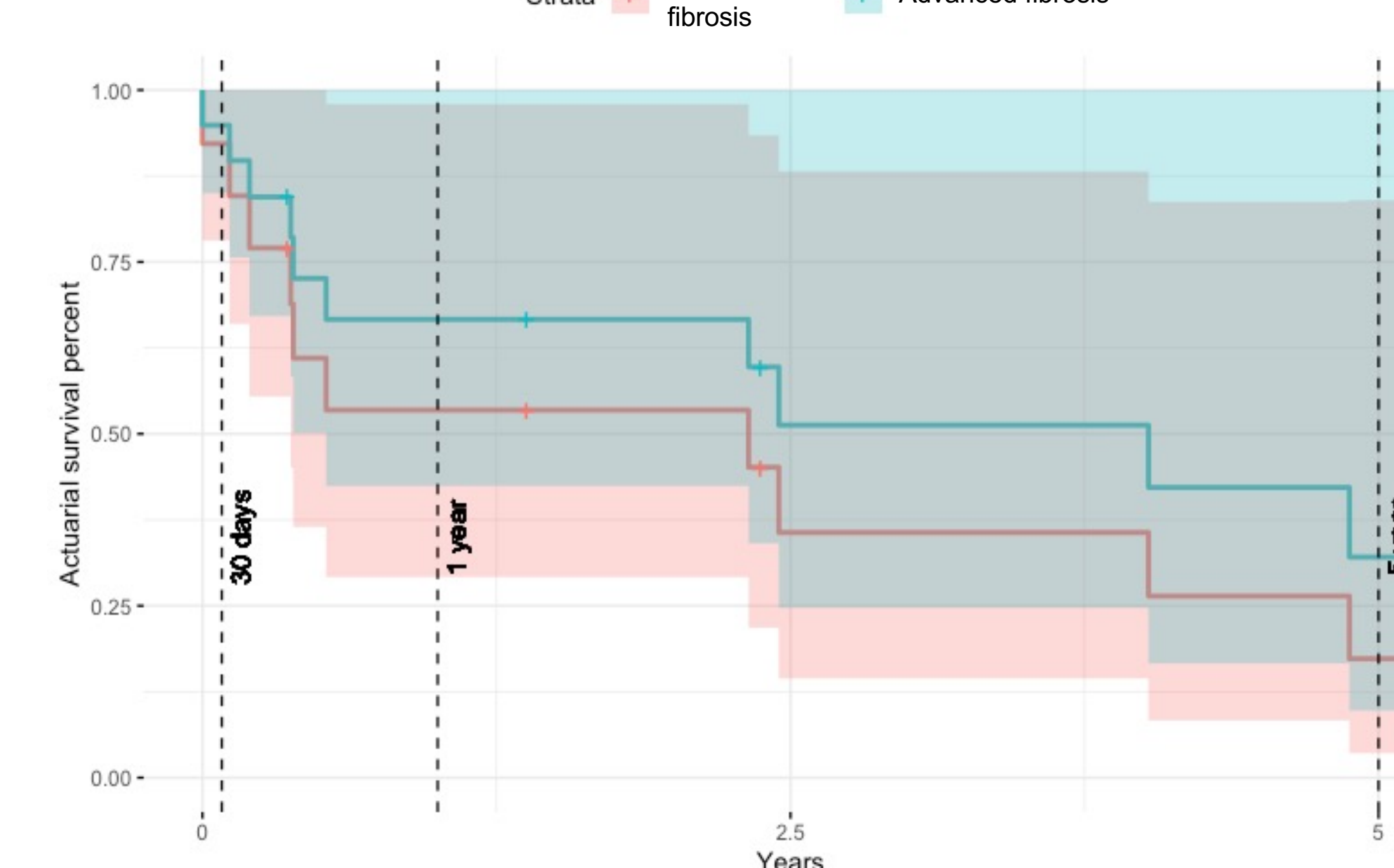


Figure 4. Predicted survival curve from time of listing for patients who do not receive transplants (model p = 0.8)



RESULTS II

- Of patients who do not receive heart transplants, predicted survival at 5 years from time of listing is 17.3% for patients with no/early liver fibrosis and 32.1% for patients with advanced liver fibrosis (Table 1, Figure 4; HR 0.65, CI = 0.18-2.32, p = 0.51)
- Of patients who receive heart transplants, predicted survival at 5 years from time of listing for patients with no/early and advanced fibrosis is 88.1% and 88.2%, respectively (Table 1; HR 1.00, CI 0.09-11.43, p = 1.00).
- Of patients who receive transplants, the predicted survival at 5 years from time of transplant for patients with no/early liver fibrosis and advanced liver fibrosis is 89.5% and 87.8%, respectively (Table 2; HR 1.16, CI = 0.10-13.55, p = 0.90)

Table 2. Predicted survival percentages for transplanted patients from time of transplant (model p = 1.00)

Time from transplant	No/Early Liver Fibrosis (% CI) n = 21	Advanced Liver Fibrosis (% CI) n = 6
30 Days	96.6 (89.9-100)	96.0 (86.2-100)
1 Year	89.5 (77.0-100)	87.8 (66.8-100)
5 Years	89.5 (77.0-100)	87.8 (66.8-100)

CONCLUSIONS

- Patients with advanced liver fibrosis were less frequently transplanted compared to those with only early stages of fibrosis.
- There was no significant difference in the survival rates between heart transplant candidates with and without advanced fibrosis on the waitlist and post-heart transplant, suggesting that patients on the transplant waitlist may not need liver biopsy for heart transplant workup.
- Because our sample population was derived from patients who were already on the transplant waitlist, our results cannot be extrapolated to the general advanced heart failure population undergoing heart transplant evaluation, many of whom are not waitlisted due to cirrhosis.

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