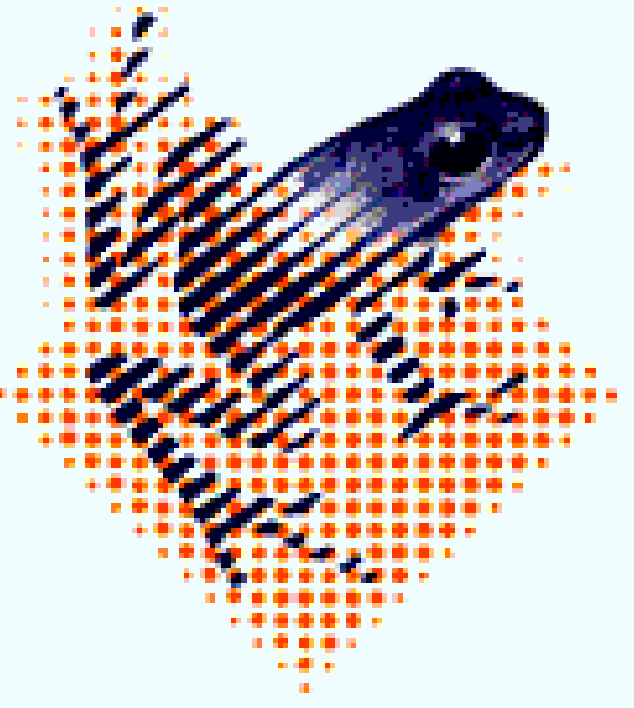




Plasma Galectin-3 is Associated with Near-Term Rehospitalization in Heart Failure

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Introduction and Aim

Among heart failure (HF) patients in the US, the rate of unplanned hospital readmission approaches 20% within 30 days of discharge, and 50% within 180 days. This high prevalence of rehospitalizations adversely affects health care costs, resource utilization and quality of care, and is likely unsustainable. Patient stratification tools that predict risk of near-term readmission would allow the clinician to better direct more resource-intensive HF disease management efforts to patients at higher risk. Such tools would preferably be unaffected by level of decompensation and be usable either upon admission, during stay, or at discharge, with a simple interpretation such as a single threshold value. We studied whether high levels of circulating galectin-3, a biomarker of myocardial fibrosis, inflammation and consequent myocardial remodeling, evaluated by a simple blood test upon admission or discharge and using a previously established threshold value of 17.8 ng/mL, identified HF patients at higher risk of unplanned hospital readmission.

Methods

Galectin-3 was measured in a total of 892 patients diagnosed with HF across 3 studies that had follow-up data on HF-related rehospitalizations. The studies considered were the Coordinating Study Evaluating Outcomes of Advising and Counseling in Heart Failure (COACH; n=582, sample taken at discharge), the Pro-BNP Investigation of Dyspnea in the Emergency Department study (PRIDE; n=181, sample taken at admission), and the University of Maryland Pro-BNP for Diagnosis and Prognosis in Patients Presenting with Dyspnea study (UMD H-23258; n=129, sample taken at admission). Galectin-3 was measured in plasma specimens using a galectin-3 test recently cleared by the FDA, and the cutoff value of 17.8 ng/mL— indicated by the FDA-approved package insert to identify high-risk patients— was used to categorize patients. Meta-analysis risk ratios were calculated for HF-related rehospitalization at 30, 60, 90 and 120 days after enrollment using a fixed effects Mantel-Haenszel model and a random effects DerSimonian-Laird model.

Results

Compared to HF patients with galectin-3 levels below 17.8 ng/mL, those with levels exceeding 17.8 ng/mL were significantly more likely to be rehospitalized for HF after initial discharge, being 2 to 3 times more likely to be readmitted to hospital in the near-term (odds ratio (OR) for 30 days: 2.80 (95% CI: 1.41-5.57); OR for 90 days: 3.01 (1.79-5.05); p<0.01 for all (Figure 1 and Table 2)). Baseline galectin-3 remained a significant predictor of hospital readmission even upon adjustment for age, gender, renal function (eGFR), NYHA class, LVEF and NT-proBNP levels (Table 3).

	COACH	PRIDE	UMD H23258
Subjects, N	582	181	129
Age, Mean (SD), (years)	70.8 (11.2)	72.9 (13.2)	61.6 (13.4)
Female, N (%)	227 (38.3%)	84 (46.4%)	36 (27.9%)
NYHA I/II, N (%)	275 (46.8%)	25 (13.9%)	37 (28.7%)
NYHA III, N (%)	293 (49.8%)	60 (33.3%)	65 (50.4%)
NYHA IV, N (%)	20 (3.4%)	95 (52.8%)	27 (20.9%)
RACE = Caucasian, N (%)	-	164 (90.6%)	51 (39.5%)
LVEF, Mean (SD) (%)	33.2 (14.2)	48.2 (18.3)	37.2 (14.8)
BMI, Mean (SD), (kg/m ²)	27.1 (5.5)	27.9 (6.3)	31.0 (9.0)
Hypertension, N (%)	256 (43.2%)	113 (62.4%)	101 (78.3%)
Diabetes, N (%)	176 (29.7%)	72 (39.8%)	58 (45.0%)
Smoker, N (%)	101 (17.4%)	23 (12.7%)	40 (31.3%)

Table 1: Baseline characteristics of HF patients by study.

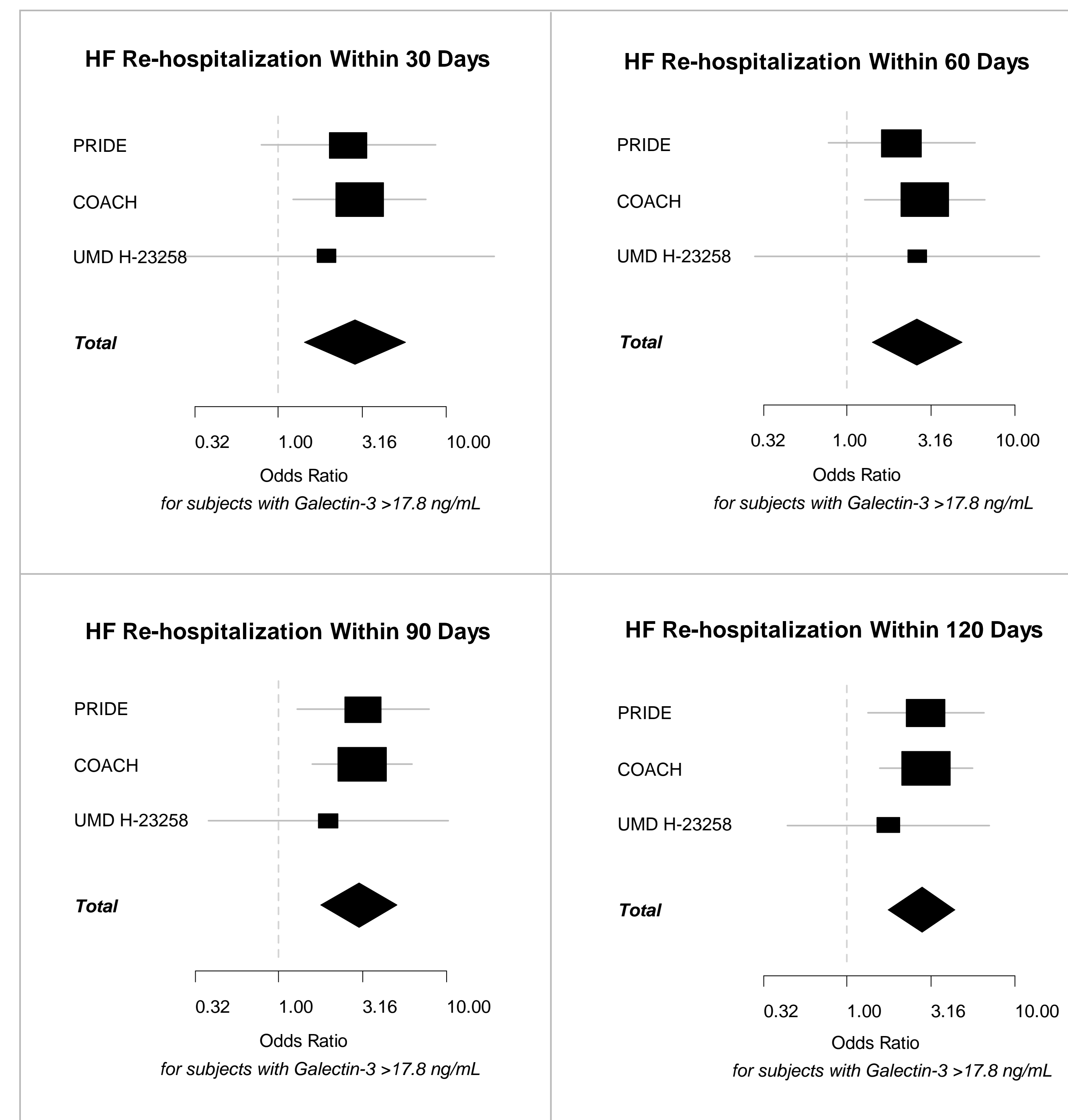


Figure 1. Meta-analysis of the relative risk (odds ratio) of hospital readmission by discharge level of plasma galectin-3, at 30, 60, 90 and 120 days after initial discharge. Test for overall effect: P=0.0034 at 30 days, P=0.0012 at 60 days, P<0.0001 for 90 days and 120 days. Tests for heterogeneity were non-significant at P=0.92, 0.89, 0.87 and 0.79 at 30, 60, 90 and 120 days respectively.

Results (continued)

Table 2: Results of meta-analyses for unplanned hospital re-admission.

	Meta-analysis OR (95% CI)	Meta-analysis OR (95% CI)	p-value (Fixed effects)	Percentage of Patients Re-hospitalized for HF (across all studies)	
	Fixed effects (Mantel-Haenszel)	Random effects (DerSimonian-Laird)		≤17.8 ng/mL	>17.8 ng/mL
30 days	2.80 (1.41-5.57)	2.78 (1.40-5.52)	0.003	3.0%	7.3%
60 days	2.61 (1.46-4.65)	2.57 (1.44-4.59)	0.001	4.5%	10.0%
90 days	3.01 (1.79-5.05)	3.01 (1.80-5.04)	<0.001	5.5%	13.6%
120 days	2.79 (1.75-4.45)	2.79 (1.75-4.44)	<0.001	7.3%	15.8%

Figure 2: Kaplan-Meier plots for re-hospitalization, by galectin-3 category.

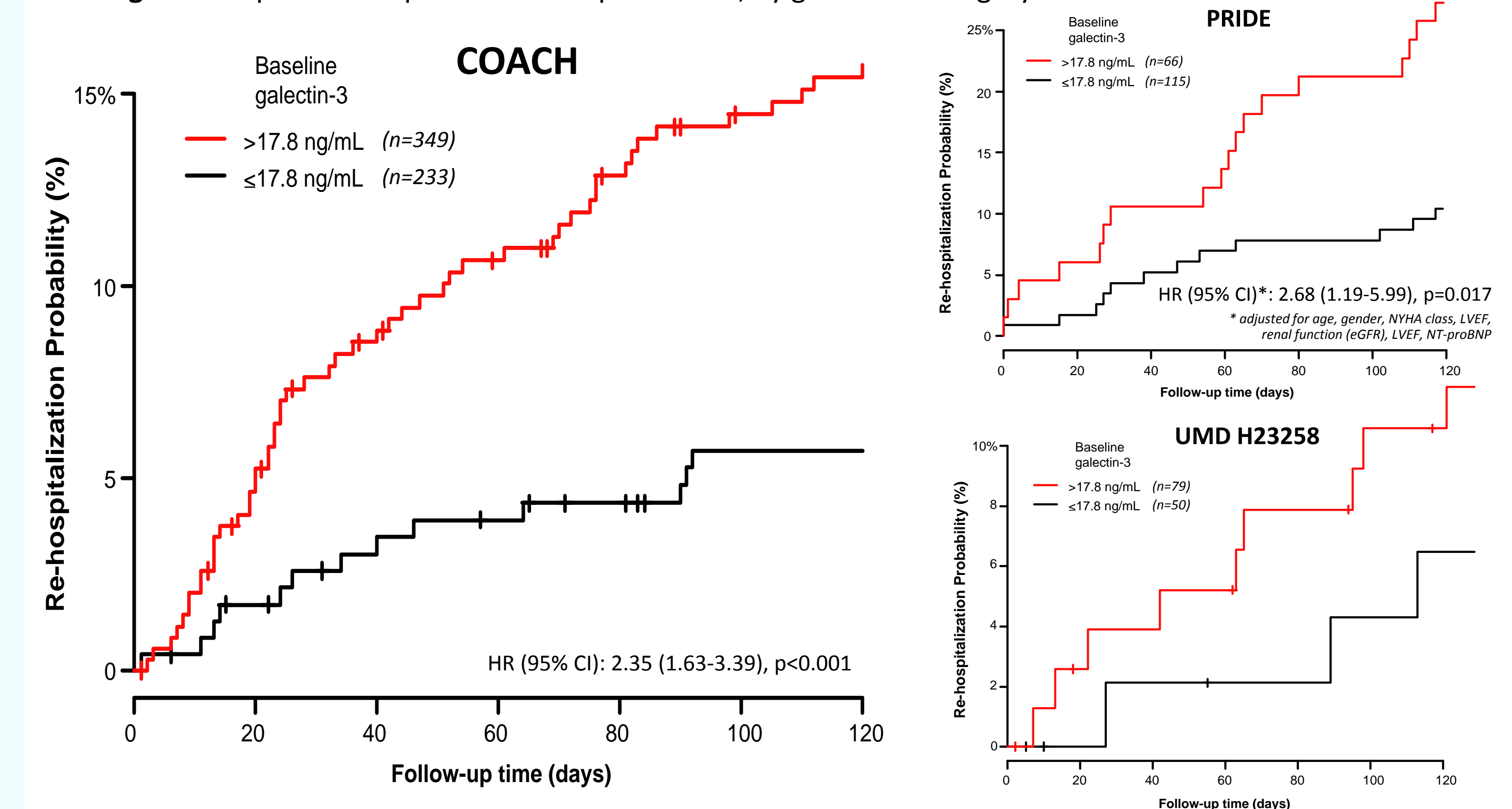


Table 3: Association of galectin-3 and re-hospitalization risk by Cox regression, COACH study.

Model	Hazard Ratio (95% CI)	Chi-square	P-value
Galectin-3 only (>17.8 ng/mL)	2.35 (1.63-3.39)	21.1	<0.001
Age and sex adjusted	2.28 (1.57-3.31)	18.6	<0.001
Multivariable adjusted*	1.62 (1.04-2.52)	4.57	0.033

* Adjusted for baseline age, gender, renal function (eGFR), NYHA class, NT-proBNP, LVEF

Conclusions

An elevated galectin-3 finding, upon discharge from hospitalization for HF or emergency department visit for HF, is associated with higher risk of near-term readmission for HF, independent of patient renal function (eGFR), NYHA class, LVEF, natriuretic peptide, gender and age. Galectin-3 testing may be of benefit in programs aiming to reduce hospital readmission rates for HF.

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