GALECTIN 3: DẤU ẤN MỚI TRONG TIÊN LƯỢNG BỆNH NHÂN SUY TIM

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Tổng thư ký Hội Tim mạch can thiệp Việt nam
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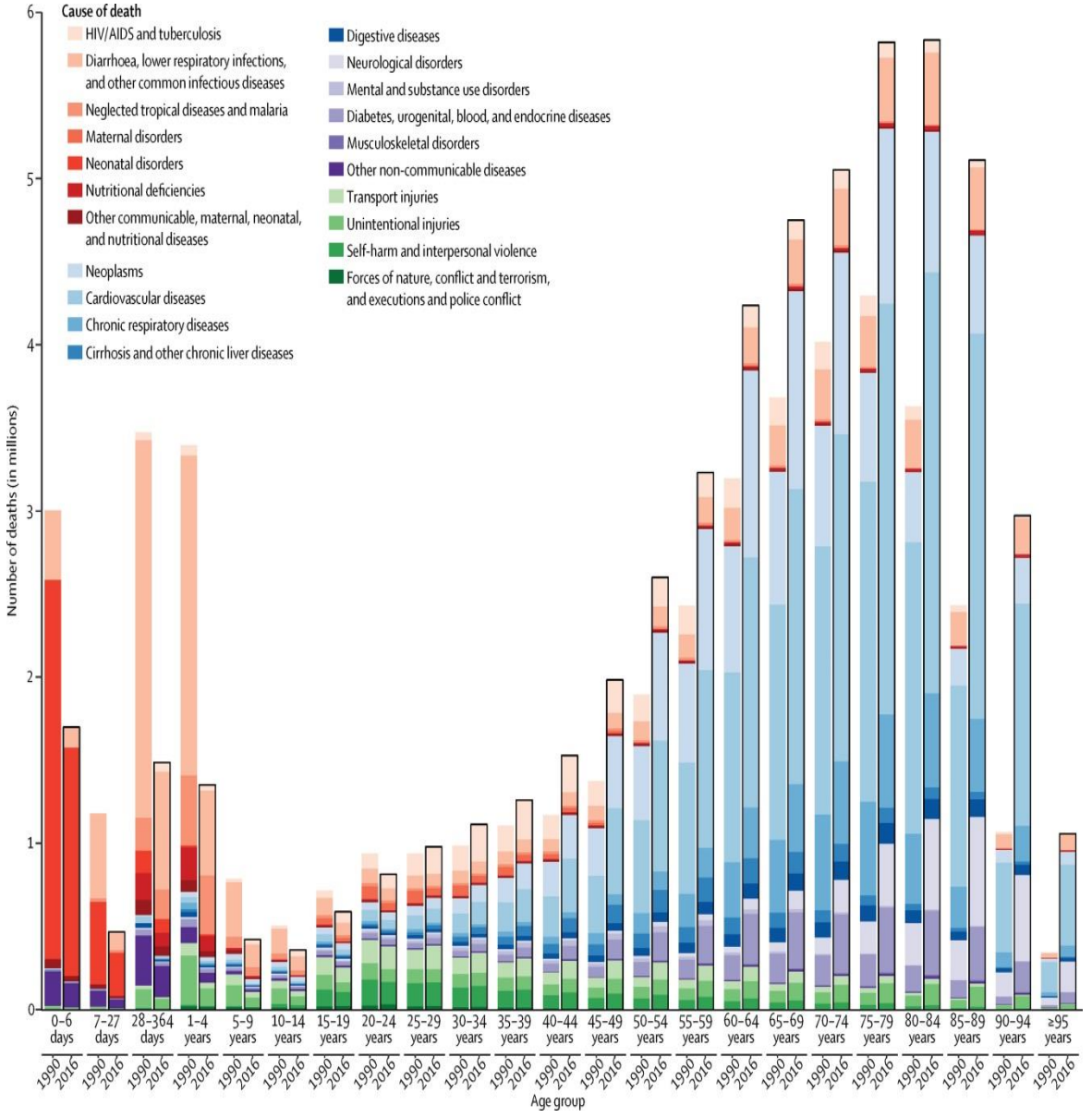
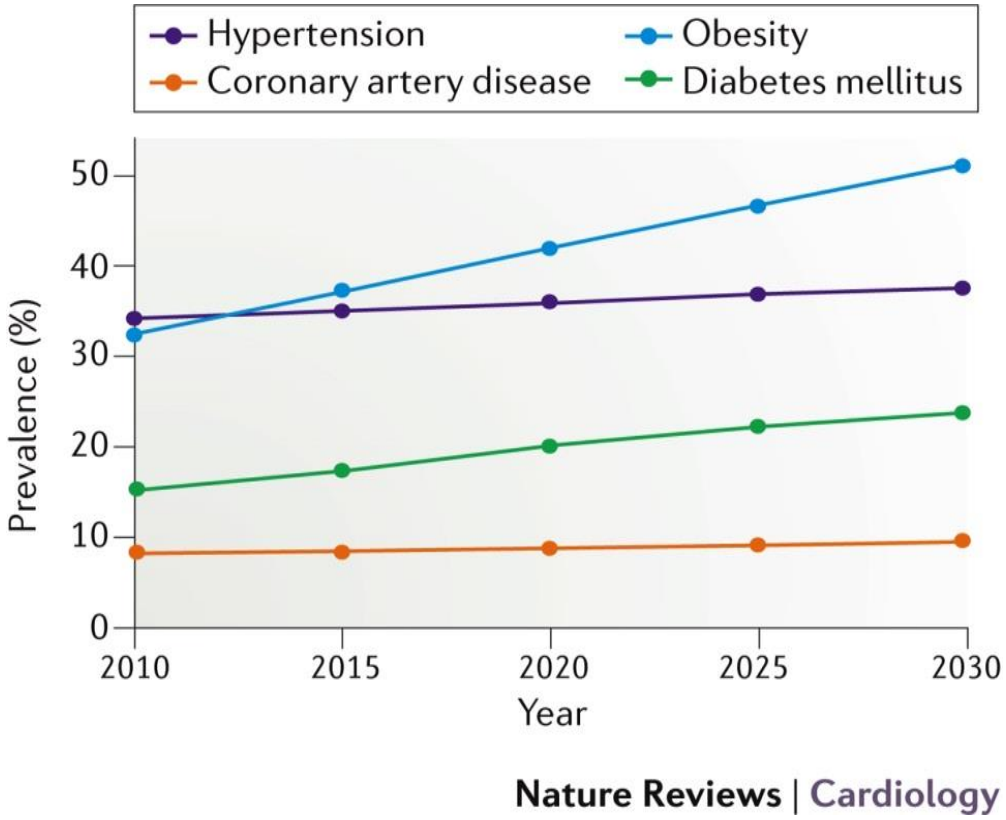
Nguyên nhân tử vong toàn cầu 1990 - 2016



Lancet 2017, 390;10110: pg1151-1210

Bùng phát một số yếu tố nguy cơ suy tim tại Mỹ



Dunlay, S. M. *et al.* (2017) *Nat. Rev. Cardiol.* doi:10.1038/nrcardio.2017.65

High hospital readmission rates

Study	Country/region	Rehospitalization rate (%)	
Medicare[49]	USA	30-day	24.8
Medicare[51]	USA	30-day	26.9
VA health care system[52]	USA	30-day	22.5
ADHERE[8]	USA	30-day 1-year	22.1 65.8
Medicare[50]	USA	30-day 1-year	22.7 67.0
Medicare[38]	USA	6–9-month	60
EHFS I[10]	Europe	12-week	24.2
ESC-HF Pilot[4]	Europe	1-year[a]	43.9
EAHFE[48]	Spain	1-year	27.2
CCU[47]	Italy	6-month	38.1
IN-HF Outcome[46]	Italy	1-year	30.7

www.escardio.org/communities/HFA/Pages/global-heart-failure-awareness-programme.aspx

Hoạt động thần kinh hóc môn trong bệnh nhân suy tim

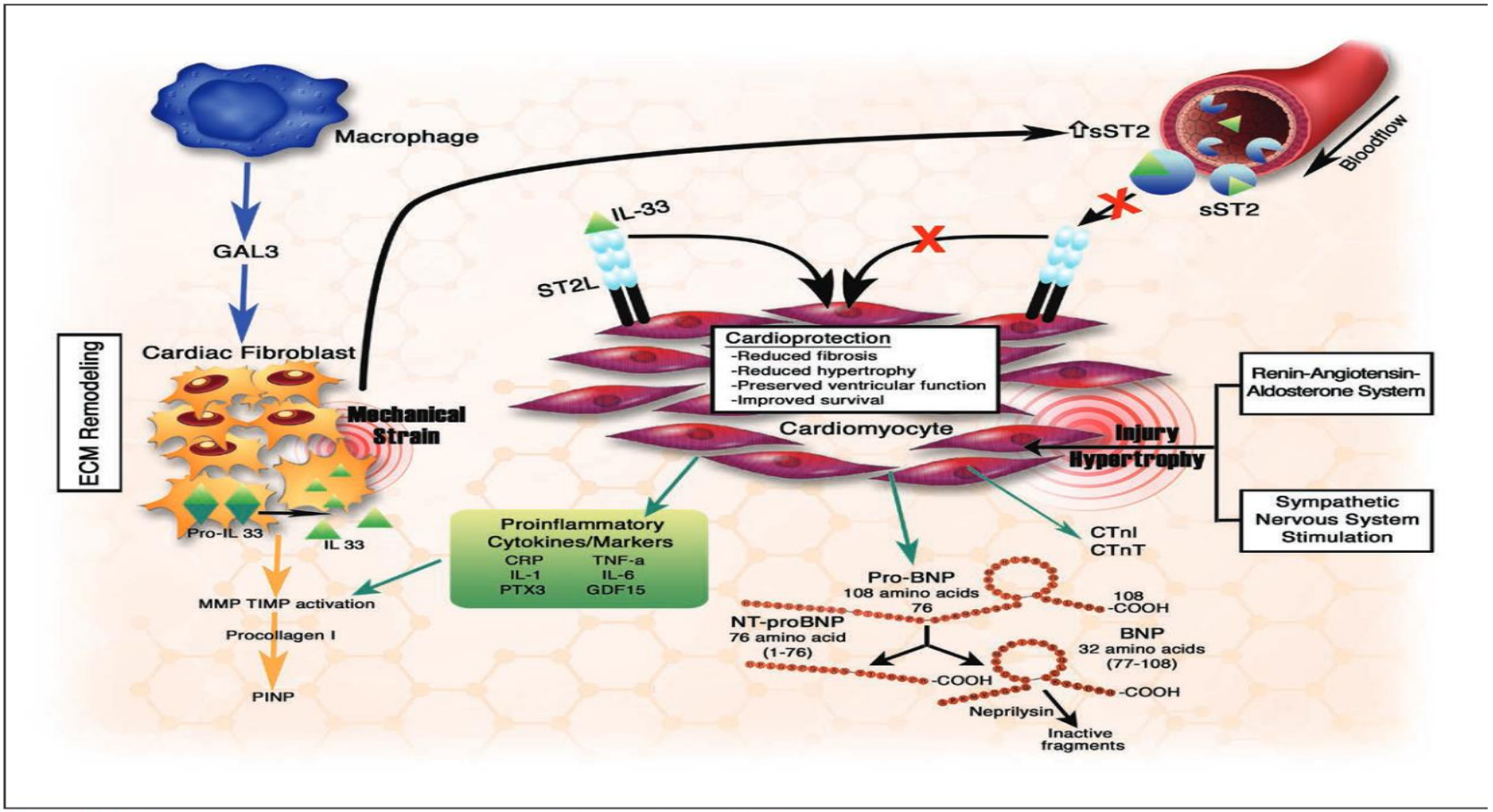


Figure 1. Mechanisms and responses to injury in heart failure.

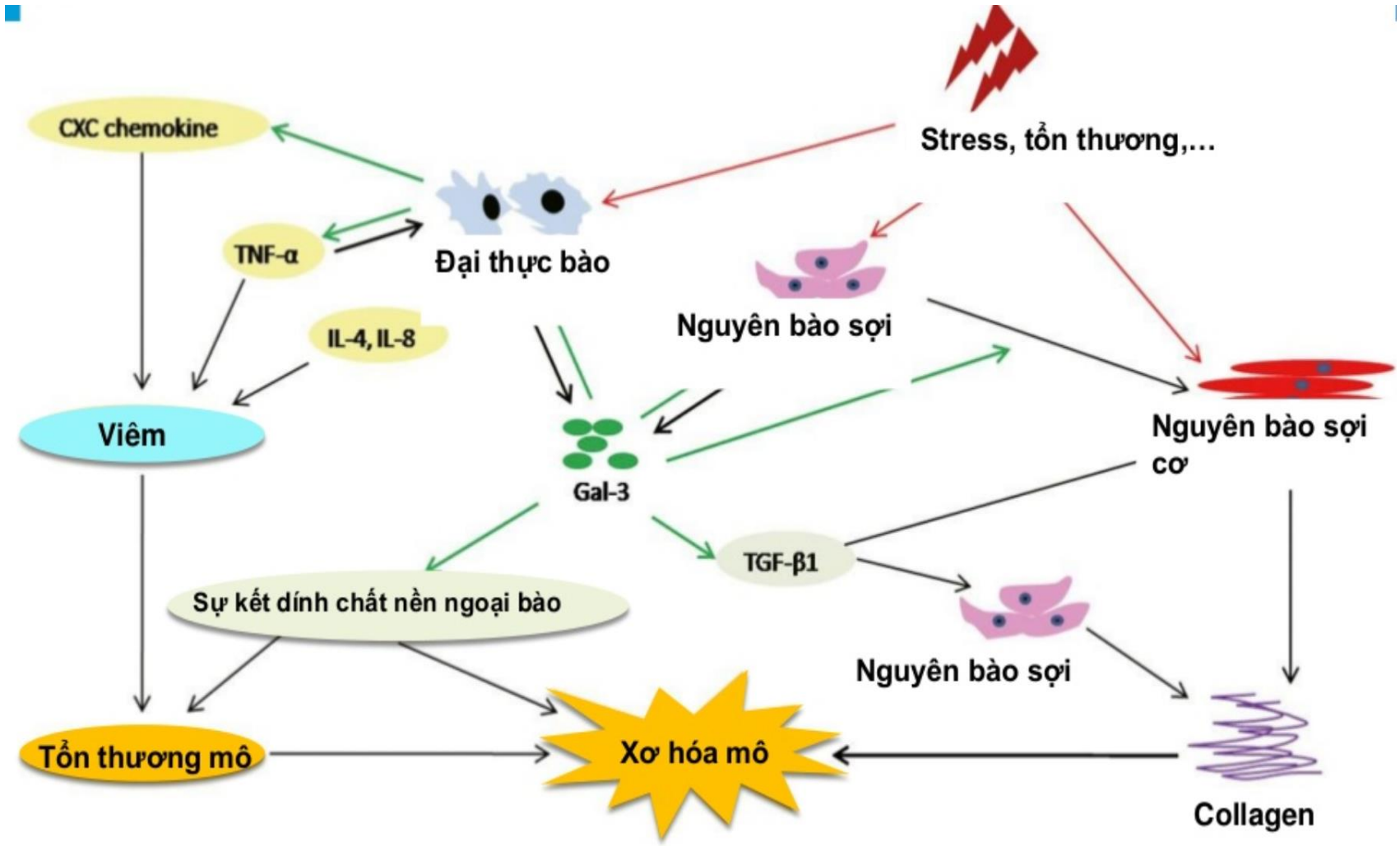
Circulation. 2017;135:e1054–e1091.

Galectin 3

- Galectin 3 là một protein trong họ lectin. Galactin được tạo ra bởi gen LGAS 3 trên nhiễm sắc thể 14 tại vị trí q 21-22.
- Galectin3 gắn với Ƀ lactoside tan trong nước và được tiết bởi sự hoạt hóa các đại thực bào.
- Galectin 3 được thấy trong các mô và chủ yếu trong bào tương. Vị trí chính xác của Galactin 3 ở cơ tim chưa được xác định

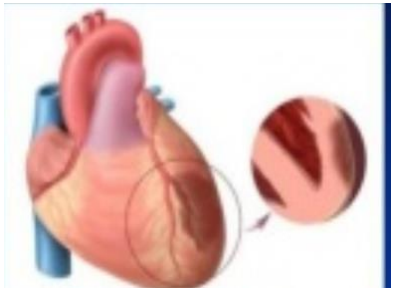
JACC 2006; 48: 1217-24

Galectin 3 và vai trò xơ hóa mô

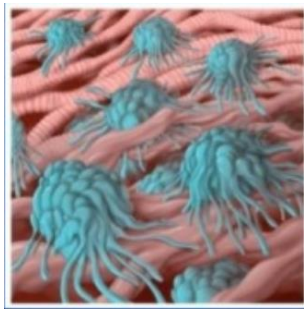


Liu-cheng Li et all. J Pharmacol Exp Ther 351:336–343, November 2014

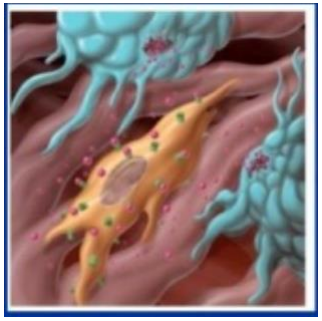
Galectin 3



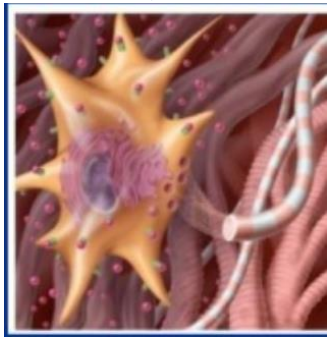
Tổn thương cơ tim



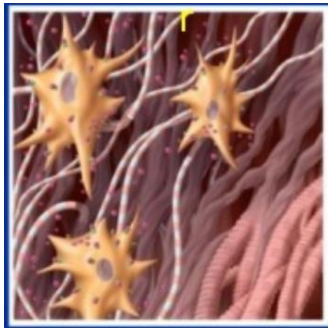
Đại thực bào mang galactin 3



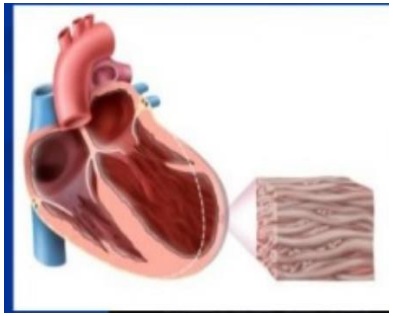
Phóng thích galactin 3



Galactin 3 gắn kết và hoạt hóa xơ



Tích tụ collagen tạo sẹo



Tái cấu trúc cơ tim và giãn cơ tim

European Journal of Heart Failure (2009)11, 811–817

Giá trị chẩn đoán của Galectin 3

Table 2
Diagnostic information for a proposed biochemical diagnosis of HF.

Analyte	Cut off value	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Diagnostic accuracy
BNP [ng/L]	100[a]	96%	61%	75%	93%	80%
	118	95%[c]	64%	76%	91%	81%
	160	90%[c]	73%	80%	87%	83%
	295[b]	80%	86%	87%	78%	83%
Galectin-3 [ng/mL]	11.5	95%[c]	8%	55%	56%	55%
	13.4[b]	90%[c]	17%	56%	58%	57%
	17.8[a]	70%	39%	58%	52%	56%
	25.9[a]	41%	75%	66%	51%	56%
sST2 [ng/mL]	14.5	95%[c]	4%	54%	42%	54%
	18.8	90%[c]	21%	58%	63%	59%
	26.5[b]	76%	49%	64%	63%	64%
	35.0[a]	60%	61%	65%	56%	60%

Clinica Chimica Acta 463 (2016) 158–164

Giá trị tầm soát suy tim của Galectin 3

Table 1 Comparison of echocardiographic changes after intrapericardial infusion of placebo or galectin-3.

LVEF (%)	Placebo	Galectin-3
Baseline	67.3 ± 2.5	66.1 ± 1.6
Post-infusion (4 weeks)	66.0 ± 0.4	51.8 ± 3.1

LVEF: left ventricular ejection fraction. Adapted with permission from[23].

Sharma UC et al. Circulation. 2004 Nov 9;110(19):3121-8

Nồng độ Galectin-3 trong tầm soát suy tim

Study or Author Name, Date	Sample Size (N)	Assay	Median Gal-3 Levels (ng/mL)	Follow-up Period (y)	End Points	Main Findings/ Results
Framingham Offspring Cohort,[29] 2012	3353	BGM	Women, 14.3 Men, 13.1	8.1	Several sequences of events	Galectin-3 significantly predicted new-onset HF after adjustment for BNP and several other clinical variables in general population
FINRISK cohort,[31] 2015	8444	ARCHITECT Galectin-3	Women, 12.0 Men, 11.5	15	All-cause mortality Cardiac death MI Ischemic stroke HF	Predictor for incident HF and death after correction for NT-proBNP in general population
PREVEND study,[78] 2016	5958	BGM	Baseline, 10.7; after ~9 y, 11.5	Median 9.3	New-onset HF CV death All-cause mortality New-onset atrial fibrillation CV event	Increases in galectin-3 associated with increased blood pressure and urinary albumin >30 mg/24 h

Heart failure clinics 2018DOI:10.1016/j.hfc.2017.08.009

Biomarkers

Biomarkers for Prognosis or Added Risk Stratification

COR	LOE	Recommendations	Comment/ Rationale
IIa	B-NR	During a hospitalization for HF, a predischarge natriuretic peptide level can be useful to establish a postdischarge prognosis.	NEW: Current recommendation reflects new observational studies.
IIb	B-NR	In patients with chronic HF, measurement of other clinically available tests, such as biomarkers of myocardial injury or fibrosis, may be considered for additive risk stratification.	MODIFIED: 2013 recommendations have been combined into prognosis section, resulting in LOE change from A to B-NR.

Thử nghiệm COACH

Annals of Medicine, 2011; 43: 60–68

informa
healthcare

ORIGINAL ARTICLE

Predictive value of plasma galectin-3 levels in heart failure with reduced and preserved ejection fraction

RUDOLF A. DE BOER[1], DIRK J. A. LOK[2], TINY JAARSMA[1], PETER VAN DER MEER[1], ADRIAAN A. VOORS[1], HANS L. HILLEGE[1] & DIRK J. VAN VELDHUISEN[1]

[1]*Department of Cardiology, University Medical Centre Groningen, University of Groningen, PO Box 30 001, Hanzeplein 1, 9700 RB, Groningen, The Netherlands, and* [2]*Department of Cardiology, Deventer Hospital, Deventer, The Netherlands*

Ann Med2011;43:60 – 68

Thử nghiệm COACH

Table I. Base-line parameters according to the plasma galectin-3 levels.

Variables	Quartiles of galectin-3 (ng/mL) Quartile 1 (5.0–15.2)	Quartile 2 (15.2–20.0)	Quartile 3 (20.0–25.9)	Quartile 4 (25.9–66.6)	*P*-value
n	148	148	148	148	
Age (years)	66 ± 11	70 ± 11	72 ± 11	76 ± 9	<0.001
Gender (% male)	69	64	62	52	0.023
NYHA (%, II / III / IV)	61/38/1	51/48/1	45/51/4	30/63/8	<0.001
BMI (kg/m^2)	27 ± 5	28 ± 5	27 ± 5	28 ± 7	0.56
LVEF (%)	30 ± 13	34 ± 16	32 ± 15	34 ± 13	0.093
% patients LVEF ≥ 40%	18	28	23	26	0.26
eGFR (mL/min/1.73 m^2)	67 ± 17	61 ± 18	50 ± 16	37 ± 15	<0.001
Hb (g/dL)	14.0 ± 1.9	13.3 ± 1.9	13.0 ± 2.0	12.5 ± 2.0	0.001
BNP (pg/mL) (median; IQR)	339 (173–780)	457 (190–781)	488 (244–1120)	518 (229–1240)	0.001
NT-proBNP (pg/mL) (median; IQR)	1767 (1048–3464)	2386 (1283–4666)	3051 (1480–6652)	4302 (1664–11640)	<0.001
Medical history (%)					
Hypertension	39	41	45	49	0.33
Myocardial infarction	38	39	42	43	0.74
Diabetes	19	29	37	35	0.004
Atrial fibrillation	35	41	49	57	0.001
COPD	22	28	26	36	0.048
CVA	7	12	9	13	0.35
Medication (%)					
ACE inhibitors	79	72	78	61	0.002
ARB	9	16	12	7	0.10
Beta-blocker	72	69	66	62	0.28
Diuretics	95	95	97	97	0.55

Ann Med2011;43:60 – 68

Thử nghiệm COACH

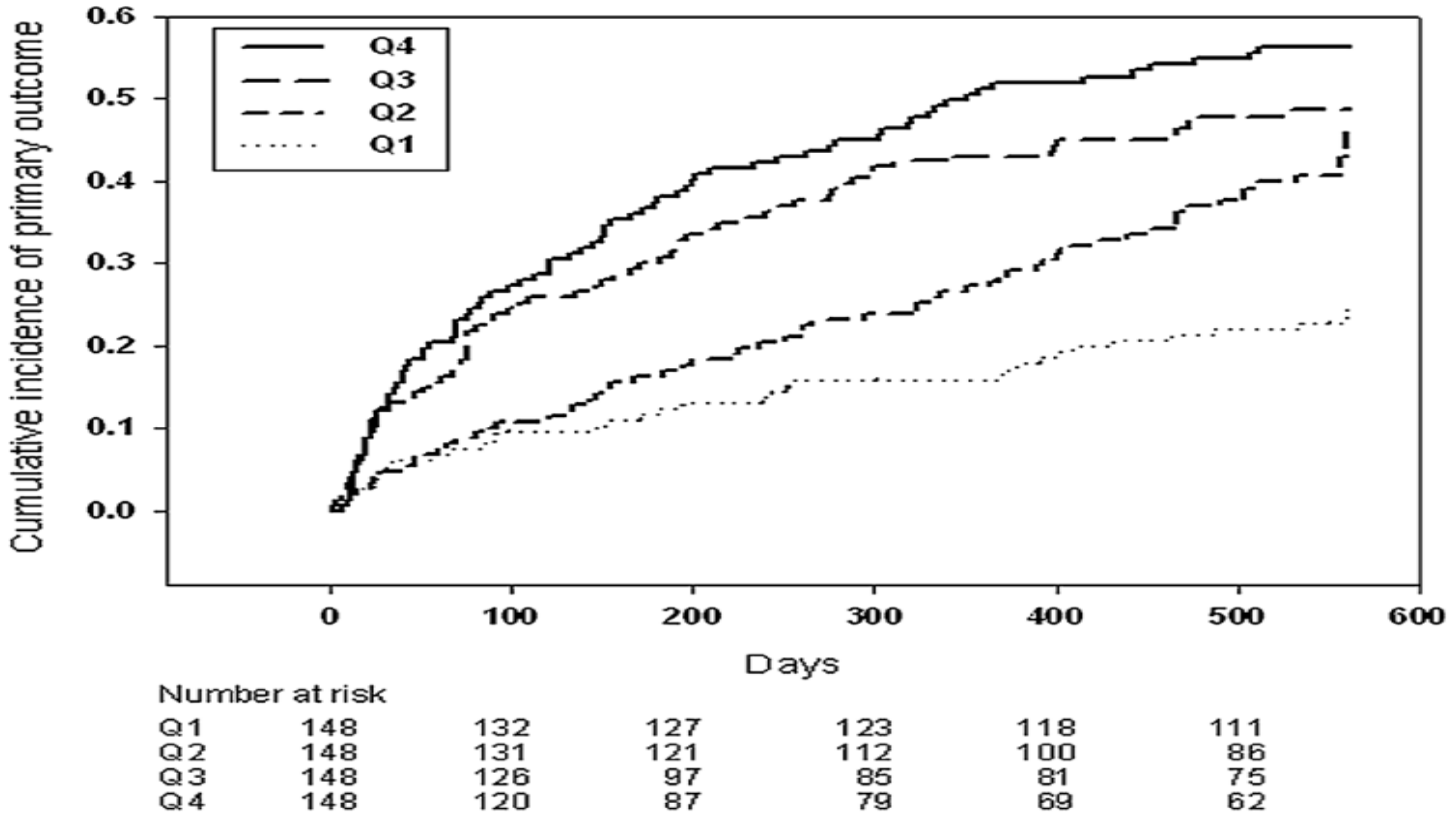


Figure 1. Adjusted Cox regression curves for quartiles of plasma galectin-3 showing the cumulative risk for the combined end-point all-cause mortality and hospitalization for HF.

Ann Med2011;43:60 – 68

Thử nghiệm COACH

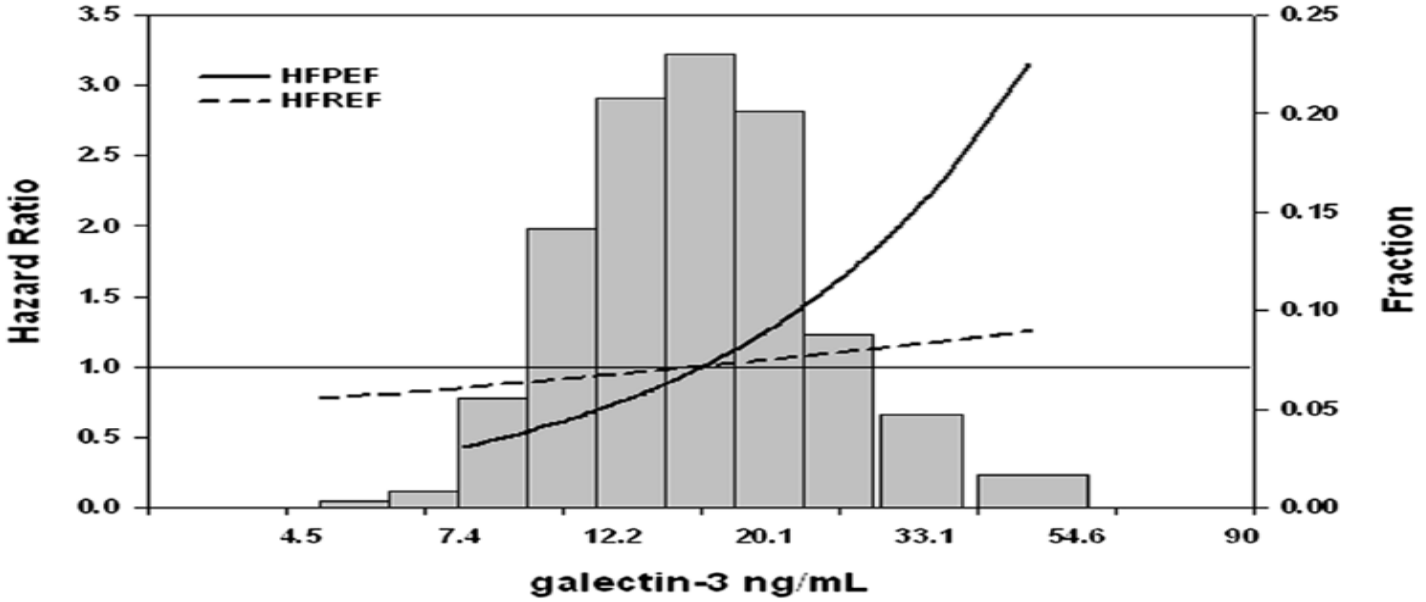
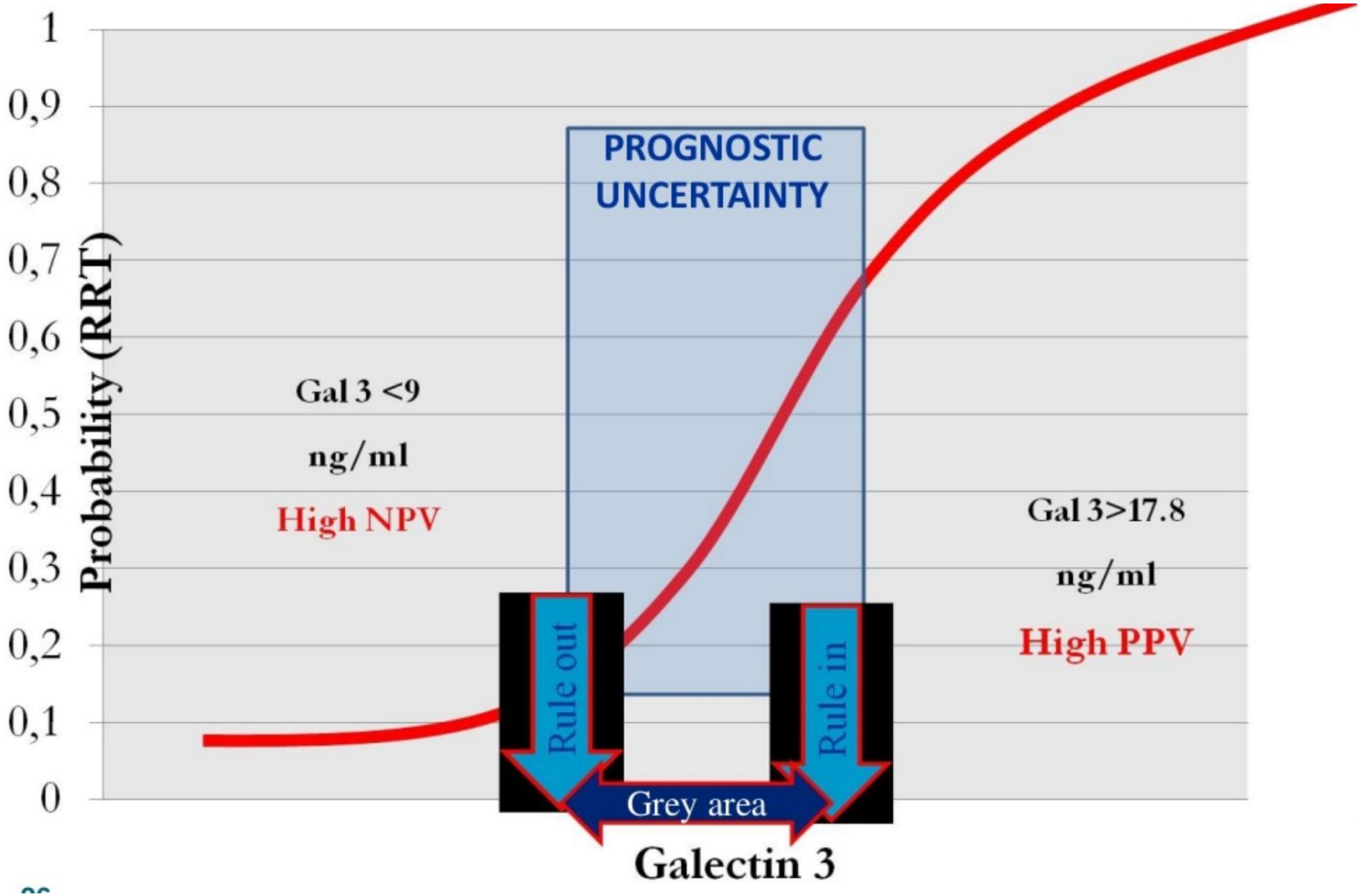


Figure 2. Graphical depiction of the risk estimates for experiencing the primary outcome in patients with HFPEF and HFREF with increasing levels of plasma galectin-3. The distribution of (log-transformed) galectin-3 is depicted in the background in brown bars. A similar increase in galectin-3 causes a much more pronounced increase in risk in patients with HFPEF compared to patients with HFREF.

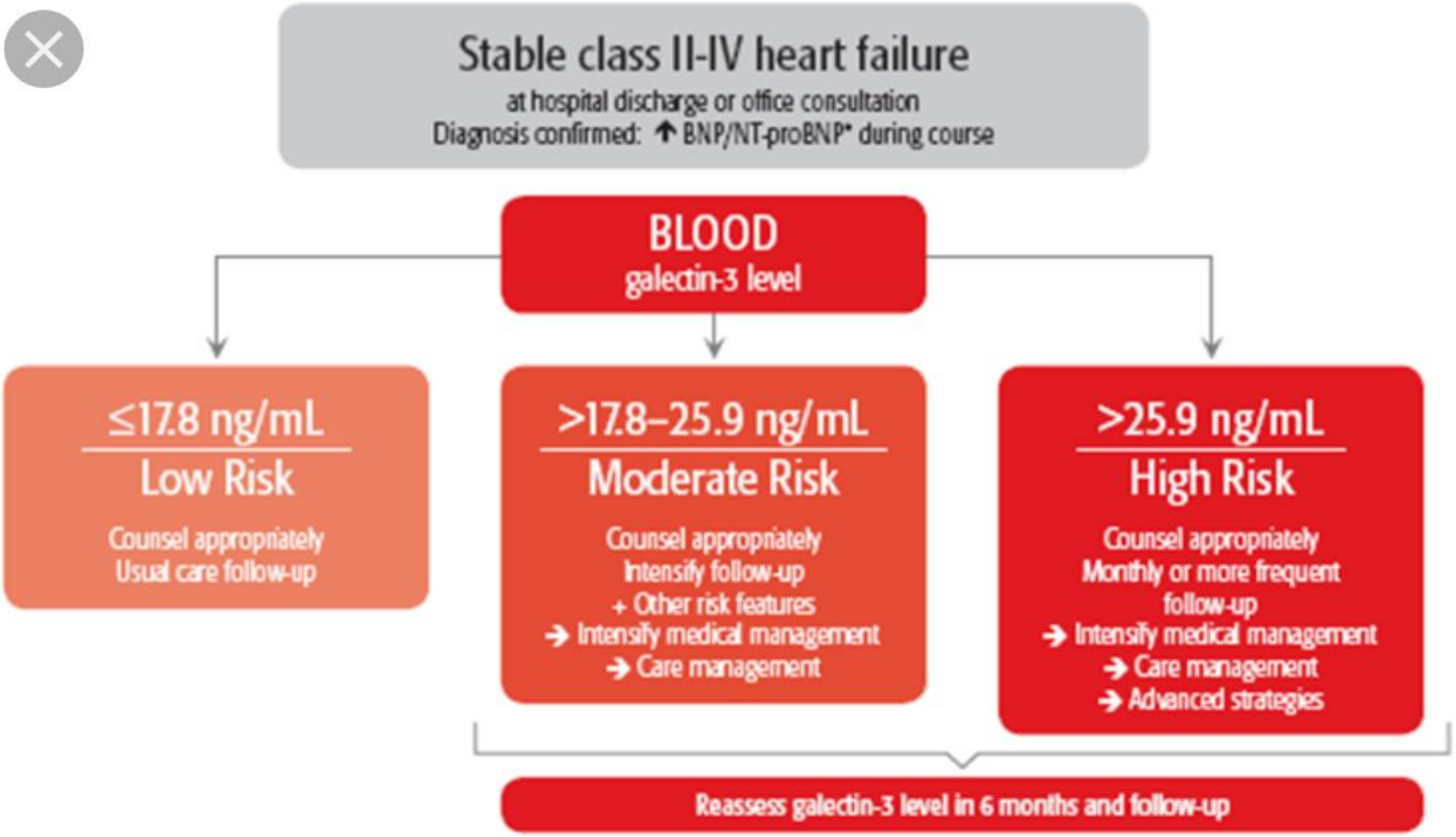
Ann Med2011;43:60 – 68

Giá trị Galectin 3



JACC 2006; 48: 1217-24

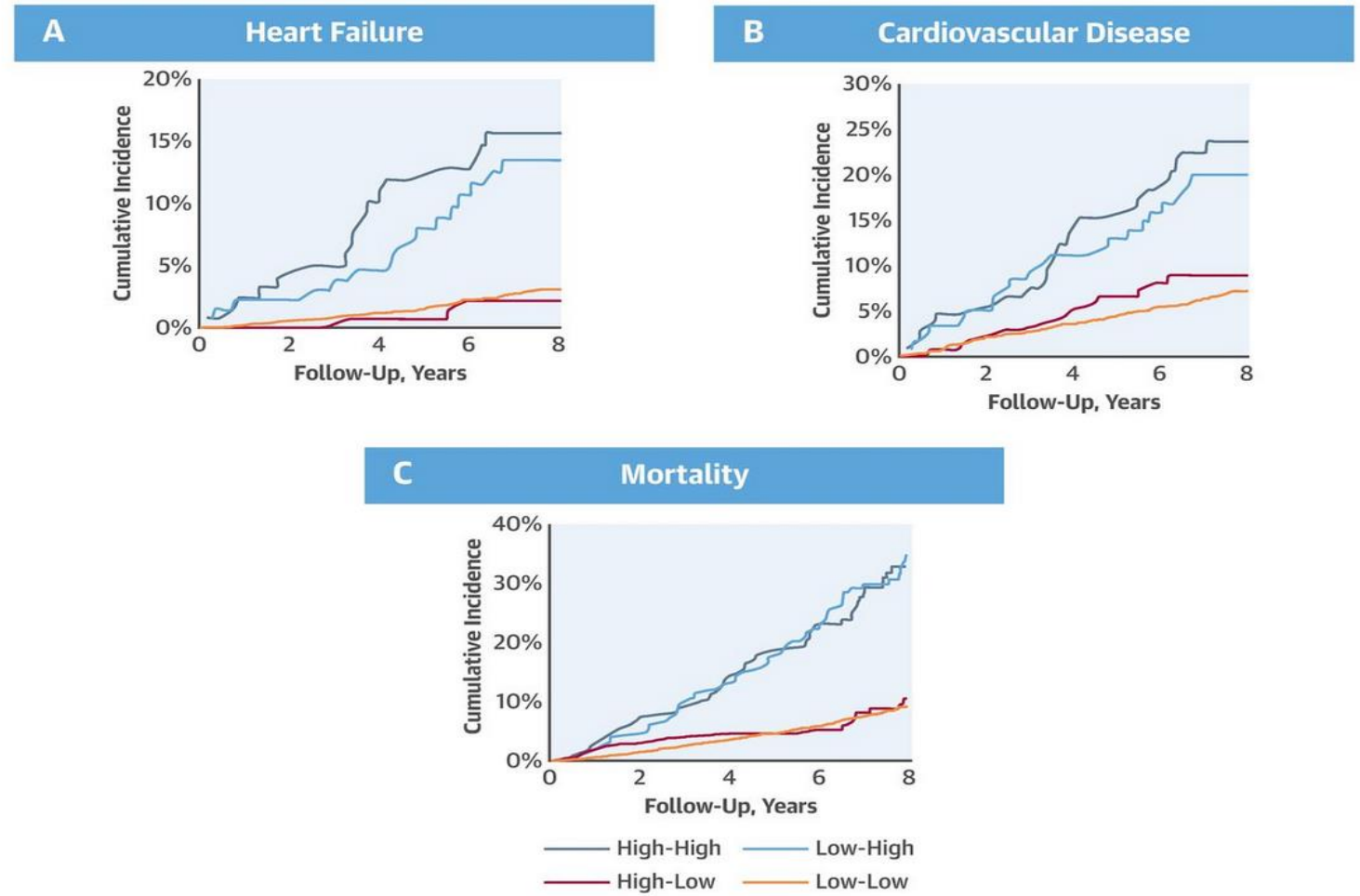
Giá trị Galectin 3



JACC 2006; 48: 1217-24

Giá trị Galectin 3 và EF

CENTRAL ILLUSTRATION: Cumulative Incidence of Heart Failure, Cardiovascular Disease, and Mortality by Classes of Longitudinal Change in Galectin-3



Ghorbani, A. et al. J Am Coll Cardiol. 2018;72(25):3246–54.

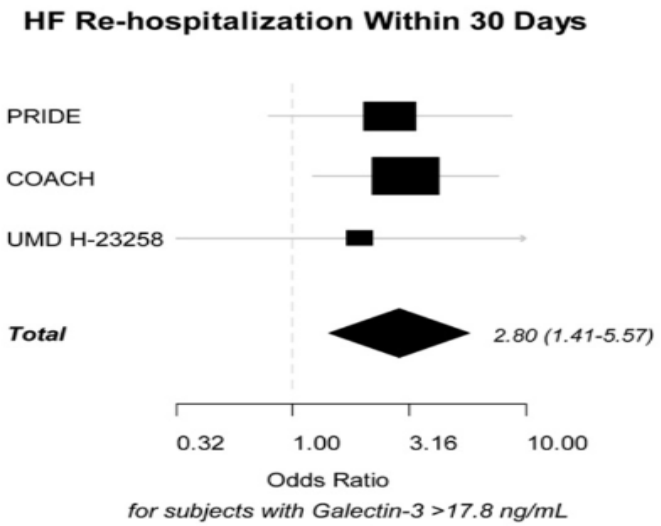
Galectin 3 trong tiên lương bệnh nhân suy tim:
Dự báo tái nhập viện

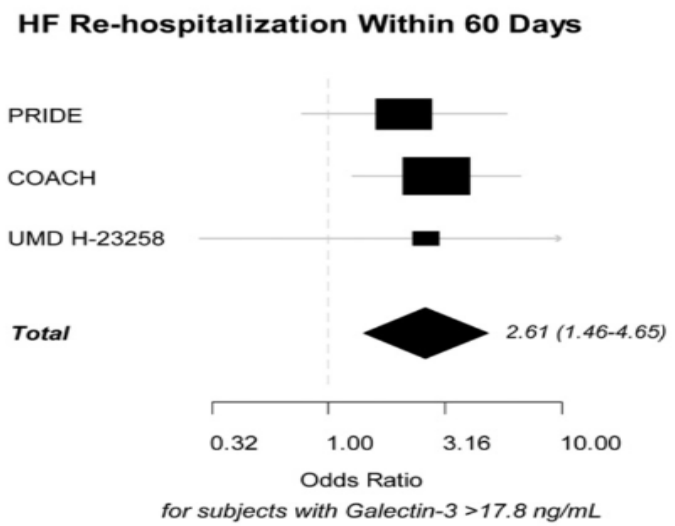
Table 2 Risk for rehospitalization in patients with heart failure and elevated or low galectin-3 levels.

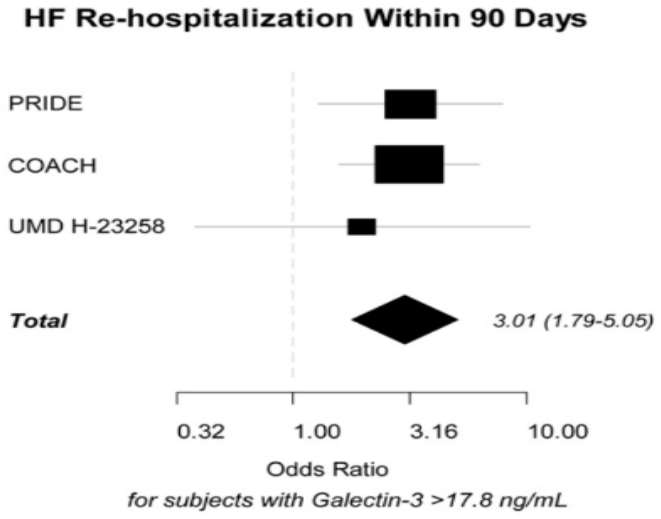
Time after discharge	p	Percentage of patients rehospitalized for HF (galectin-3 ≤17.8 ng/ml)	Percentage of patients rehospitalized for HF (galectin-3 >17.8 ng/ml)
30 days	0.003	3.0%	7.3%
60 days	0.001	4.5%	10.0%
90 days	<0.001	5.5%	13.6%
120 days	<0.001	7.3%	15.8%

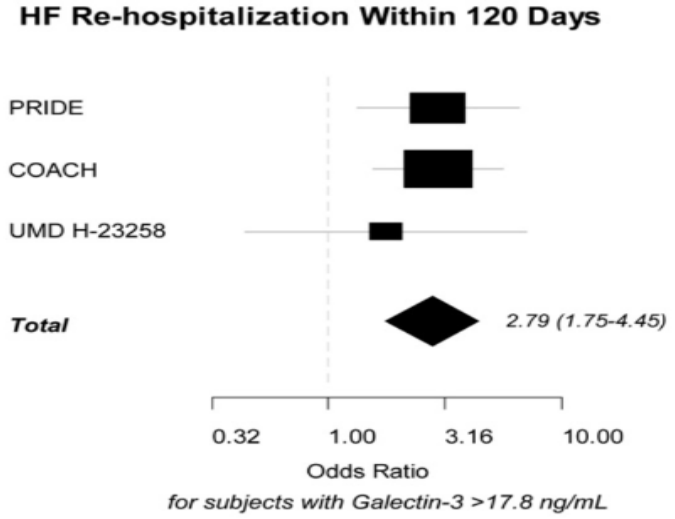
Am Heart J. 2014;167(6), 853---60

Thử nghiệm gộp: dự báo tái nhập viện









Am Heart J 2014;167:853-860.

Galectin 3 trong tiên lương bệnh nhân suy tim: **Dự báo tử vong**

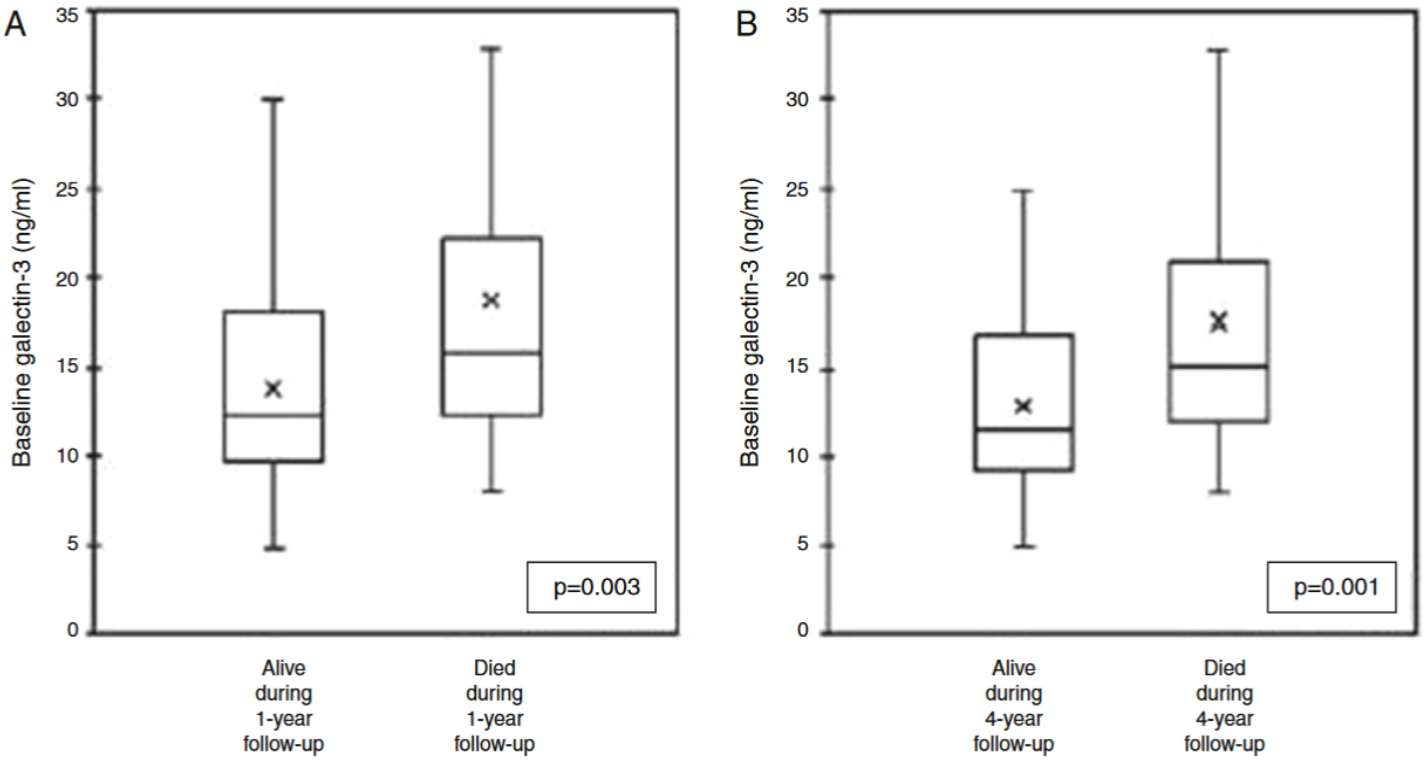


Figure 3 Galectin-3 in patients who died at one year (A) and four years (B) out of all dyspneic patients (n=115). Results from the

Eur J Heart Fail. 2010;12:826-32

Nồng độ Galectin-3 trong suy tim mạn

Study or Author Name, Date	Sample Size (N)	Assay	Median Gal-3 Levels (ng/mL)	Follow-up Period	End Points	Main Findings/Results
Meijers et al,[25] 2017	Healthy controls = 28 CHF = 83	BGM	Controls, 10.7 CHF, 16.1	4 mo and 6 wk Up to 5 y	HF rehospitalization or all-cause mortality	Stable biomarker with very low variability
Substudy of COACH trial,[53] 2011	592	BGM	HFrEF, LVEF $\leq$ 40% = 19.9 HFpEF, LVEF>40% = 20.2	18 mo	Rehospitalization for HF or death	No added value of repeated galectin-3 measurements at baseline and after 6 mo in patients with HF Stronger predictive value in HFpEF Doubling of Gal-3 associated with a hazard ratio of 1.38 for primary end point after correction
Miller et al,[54] 2016	180 (LVEF $\leq$ 40%)	BGM	Baseline, 23.2	2 y	Death/cardiac transplant, HF-related hospitalization	Galectin-3 (>22.1 ng/mL) was predictive of the end points, but only sST2 was an independent predictor
PROTECT trial,[46] 2016	2033	Not standardized	Baseline, 36.3	180 d	30-d all-cause mortality, 30-d death or rehospitalization for renal/CV causes 180-d all-cause mortality	Stable concentration in patients with CHF who were hospitalized for AHF
Valsartan Heart Failure Trial,[49] 2013	1650	BGM	Baseline Average, 16.2 Patients who died, 18.3 Survivors, 15.8	Median, 23 mo	Mortality, first morbid event, hospitalization for HF	Increase in galectin-3 values over time was an independent predictor of worse outcome Valsartan in patients with low galectin-3 level was associated with a reduced rate of hospitalization for HF

Heart failure clinics 2018DOI:10.1016/j.hfc.2017.08.009

Nồng độ Galectin-3 trong suy cấp

Galectin-3 in acute heart failure studies

Study or Author Name, Date	Sample Size (N)	Assay	Median Gal-3 Levels (ng/mL)	Follow-up Period	End Points	Main Findings/Results
Subset of PRIDE study,[34] 2010	56	BGM	15	4 y	Mortality	Increased Gal-3 associated with increase in 4-y mortality, independent of echocardiographic results
Mueller et al,[35] 2016	251	ARCHITECT	22	1 y	All-cause mortality	Predictor of 1-y all-cause mortality Not useful for diagnosis of acute HF in contrast with BNP
Sudharshan et al,[42] 2017	101	BGM/Abbott Gal-3 assay	Not readmitted after 60 d 21.0/24.6 Readmitted 60 d 27.2/32.6	60 d	30-d and 60-d hospital readmission	Predicting 60-d (not 30-d) readmission in patients with HFpEF (significant without BNP)
GALA study,[43] 2017	115	VIDAS Gal-3	Patient who died, 44 Other, 26	1 y	30-d all-cause mortality	Predictor of mortality 1 mo after hospital admission
Pooled analysis of: COACH PRIDE UMD H-23258,[44] 2014	902	BGM	18.2	≥120 d	All-cause mortality and rehospitalization	Predictor for near-term readmission
COACH,[36] 2015	592	BGM	No event, 18.9 Event: 24.5	180 d	All-cause mortality and/or HF rehospitalization	Predictor of absence of events within 180 d at the time of discharge after an episode of acutely decompensated HF
RELAX-AHF trial,[45] 2017	1161	BGM	Baseline, 21.1 At 180 d, 20.6	180 d	Time to CV mortality	Gal-3: stable over time (baseline to day 60) No benefit of repeated measurements could be proved Gal-3 is not independently associated with CV mortality within 180 d
Boulogne et al,[66] 2017	55 acute HFrEF 20 chronic HFrEF	ARCHITECT	Baseline AHF, 22.8 CHF, 13.0 30 d after discharge	1 y	Death Unplanned admission for CV cause	Gal-3 level was significantly higher in AHF compared with CHF Gal-3 values remained stable in both groups over time

Heart failure clinics 2018DOI:10.1016/j.hfc.2017.08.009

Sự Ổn định của Galectin 3 trong suy tim

	Quartiles (Q) LVEDV (mL) at baseline				Total	*p* value
	Q1 (<229)	Q2 (229–273)	Q3 (273–322)	Q4 (>322)		
Gal-3, baseline	17.7 [13.6–21.3]	18.7 [13.9–22.2]	16.1 [13.1–19.7]	16.4 [13.7–21.4]	17.6 [13.3–21.2]	0.60
Gal-3, 3 months	17.6 [14.6–21.8]	21.8 [14.7–23.2]	17.0 [15.1–21.8]	17.7 [14.2–23.5]	17.9 [14.6–22.8]	0.78
Gal-3, 12 months	17.2 [13.8–20.3]	20.3 [15.0–25.0]	18.4 [14.9–21.4]	18.2 [13.1–24.9]	18.0 [14.2–22.3]	0.61

Baseline quartiles LVEDV and Gal-3 levels

Clin Res Cardiol. 2013;102:103-110

Nồng độ Galectin-3 và Pro BNP

Comparative study of galectin-3 and B-type natriuretic peptide as biomarkers for the diagnosis of heart failure

Qiu-Sheng YIN, Bing SHI, Lan Dong, Lei BI

Department of Geriatric Cardiology, General Hospital of Beijing Command of PLA, Beijing 100700, China

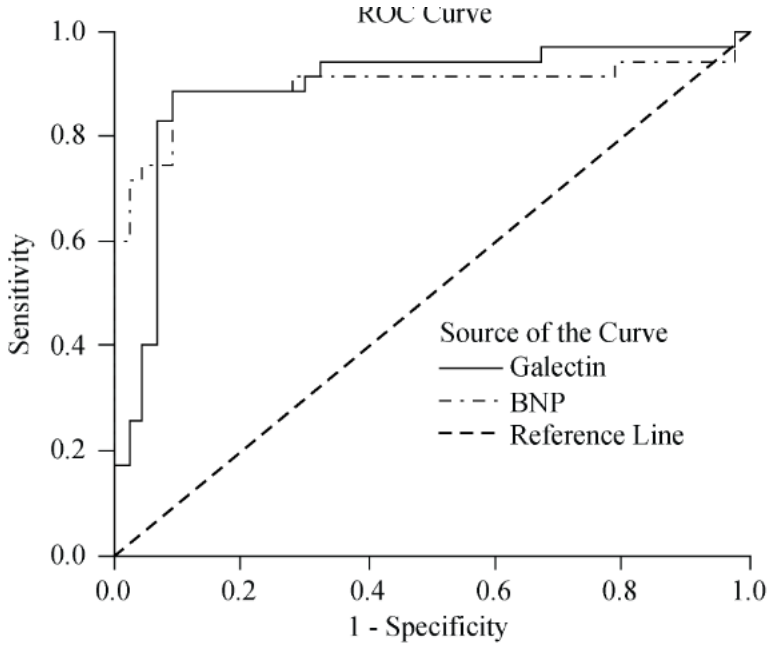


Figure 1. ROC curves of galectin-3 and BNP. BNP: B-type natriuretic peptide; ROC: receiver operating characteristic.

J Geriatr Cardiol 2014; 11: 79−82

Nồng độ Galectin-3 và Pro BNP

Table 3. AUC values of galectin-3 and BNP.

Method	AUC (95% CI)	*P*
Galectin-3	0.891 (0.808–0.974)	0.000
BNP	0.896 (0.809–0.984)	0.000

AUC: area under the receiver operating characteristic curve; BNP: B-type natriuretic peptide.

Table 2. Sensitivity, specificity, and predictive values of galectin-3 and BNP (%).

Method	Sensitivity	Specificity	PPV	NPV	Accuracy
Galectin-3	94.3	65.1	68.8	93.3	78.2
BNP	77.1	90.7	87.1	83.0	84.6
χ^2	4.20	8.174	3.741	1.737	1.059
P	0.04	0.004	0.062	0.187	0.303

BNP: B-type natriuretic peptide; PPV: positive predictive value; NPV: negative predictive value.

J Geriatr Cardiol 2014; 11: 79−82

Phối hợp NT-ProBNP + Galectin 3 trong suy tim cấp

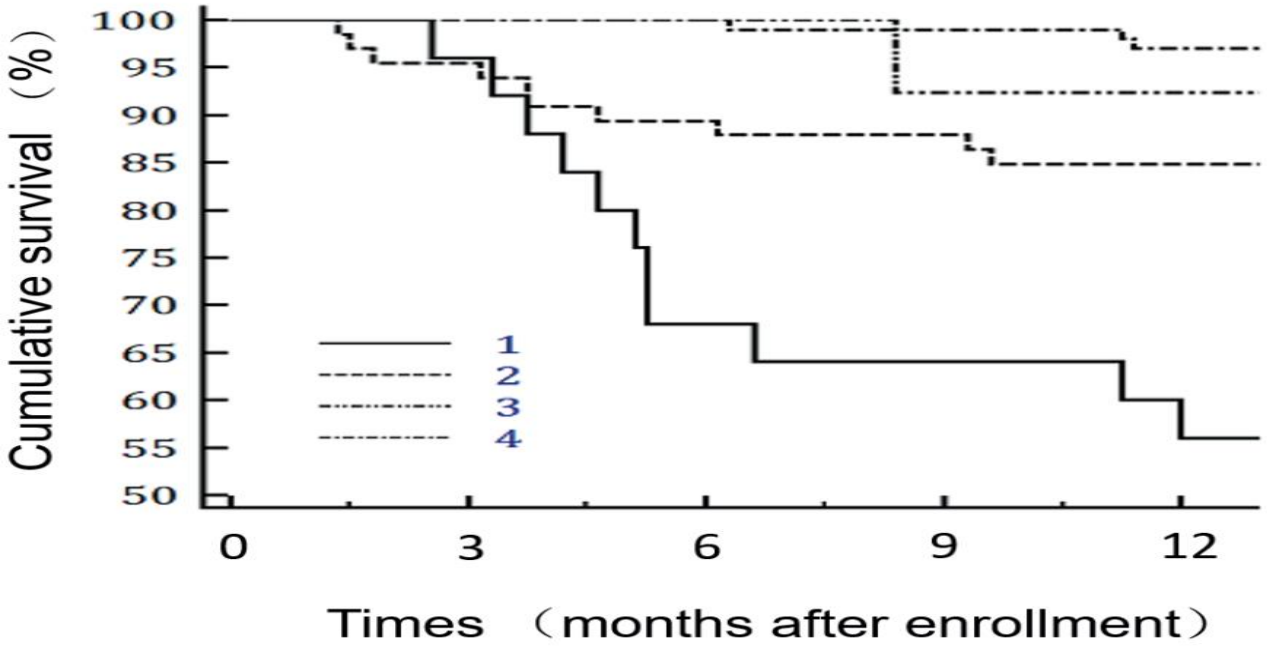
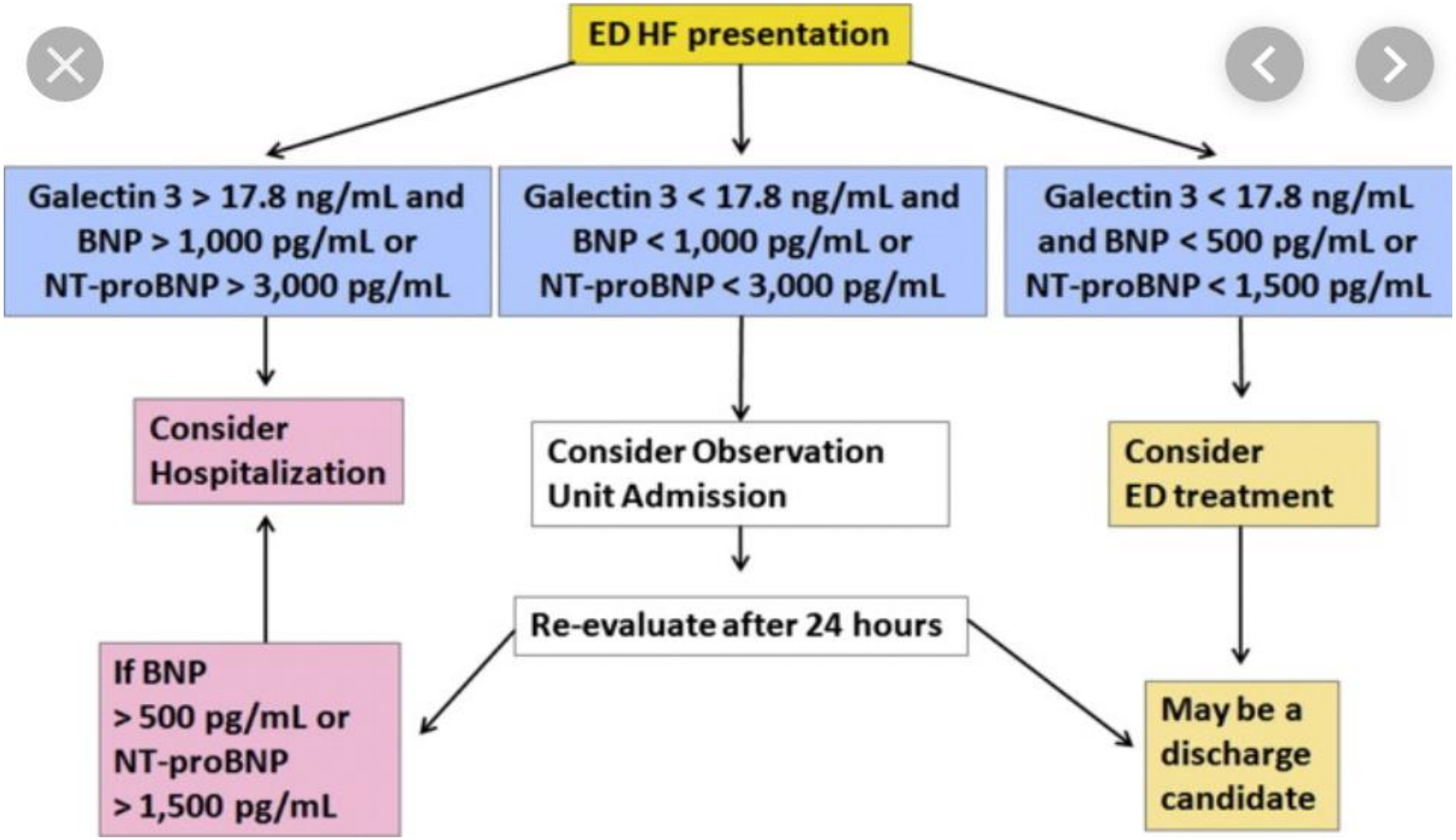


Figure 2. Kaplan-Meier survival curve analysis of CV events within 1 year (p<0.001). Group 1: NT-proBNP>3013.21 pg/mL + galectin-3 >17.15 ng/mL (n=40); Group 2: NT-proBNP>3013.21 pg/mL + galectin-3<17.15 ng/mL (n=121); Group 3: NT-proBNP<3013.21 pg/mL + galectin-3 >17.15 ng/mL (n=31); Group 4: NT-proBNP<3013.21 pg/mL + galectin-3 <17.15 ng/mL (n=124).

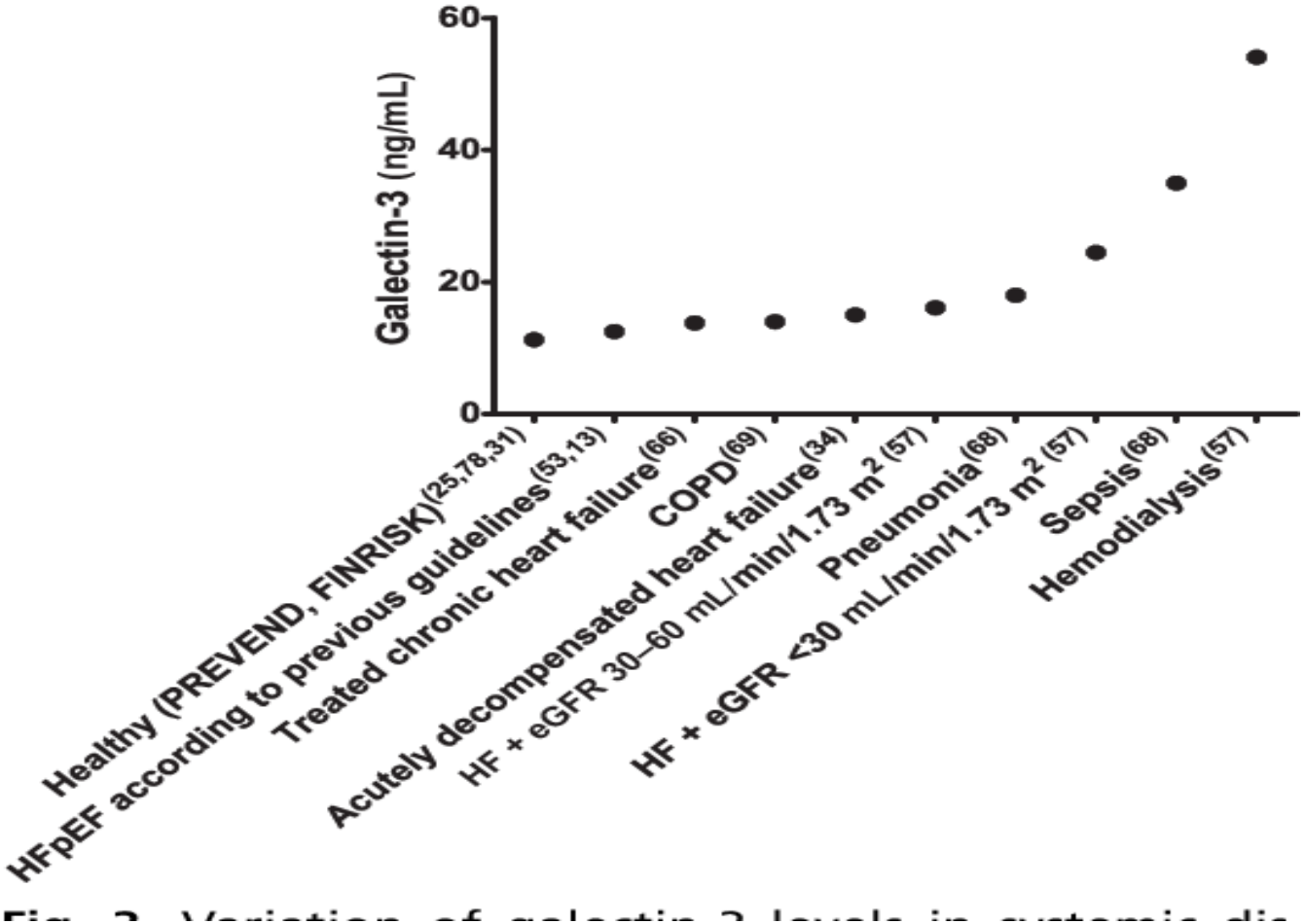
Eur Rev Med Pharmacol Sci 2017; 21: 4406-4410

Phối hợp NT-ProBNP + Galectin 3 trong suy tim



Clinica Chimica Acta 2015; 443: 48-56

Variation of galectin-3 levels in systemic diseases and in the general popular



Heart failure clinics 2018DOI:[10.1016/j.hfc.2017.08.009](10.1016/j.hfc.2017.08.009)

Thực hành lâm sàng hiện nay

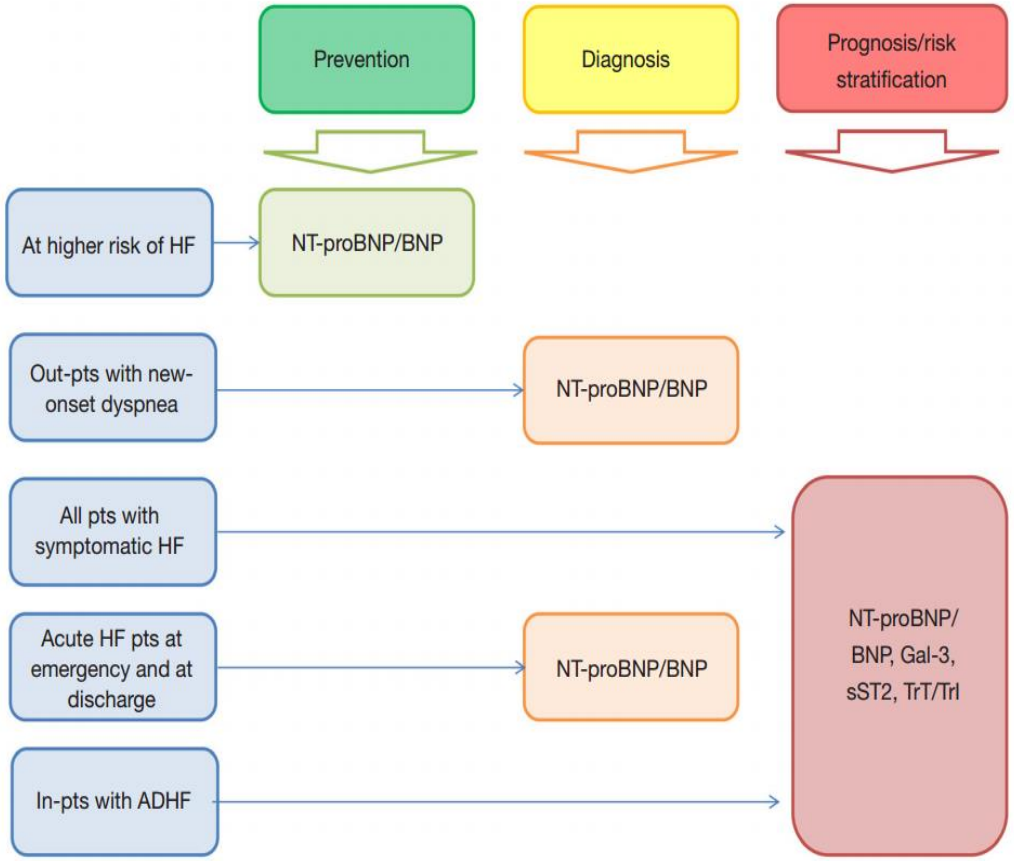


Figure 1 Schema of practical use of various biomarkers along heart failure (HF) development and progression. BNP, brain natriuretic peptide; ADHF, acutely decompensated heart failure.

J Lab Precis Med 2018;3:36- 54

Kết luận

- Galectin 3 được tạo ra bởi đại thực bào có vai trò trong xơ hóa và viêm cơ tim.
- Galectin 3 là maker tiên lượng tốt cho suy tim trên dự báo tử vong tim mạch và tái nhập viện
- Galectin 3 ổn định hơn và dự báo sớm xơ hóa cơ tim và tái cấu trúc cơ tim.
- Kết hợp với NT-pro BNP nó có thể dự báo tốt hơn để phân tầng nguy cơ bệnh nhân suy tim nguy cơ cao.
- Cũng có thể là mục tiêu điều trị trong suy tim

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