

Unmet Needs in Residual Congestion : how biomarker may help ?

Dian Yaniarti Hasanah

Working Group of Heart Failure and Cardiometabolic
Indonesian Heart Failure

Introduction

- Congestion has been one of the **most common sign** in HF
- 3 major causes directly affect the rehospitalization in HF :
 - Congestion ✓
 - Comorbidities
 - Target Organ Lesion

iHEFCARD 2023

We think we are good at decongesting patients but...

In multiple studies, patients admitted with acute heart failure were discharged when still congested

The extent of **residual congestion** was associated with the **risk of death and heart failure readmissions**

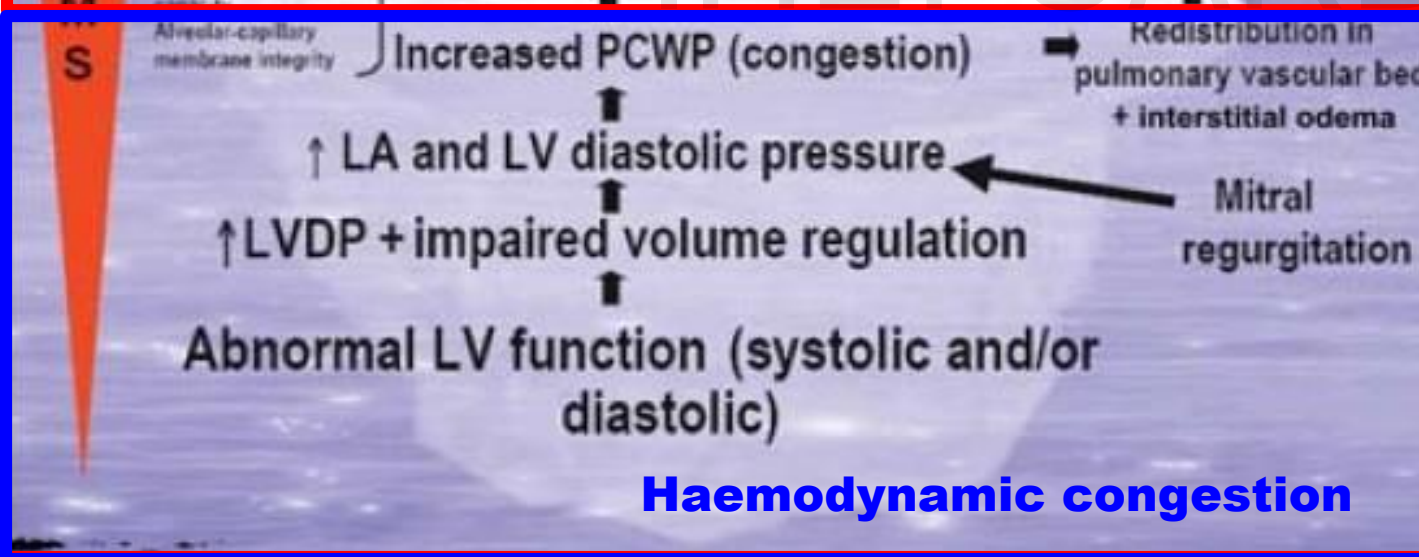
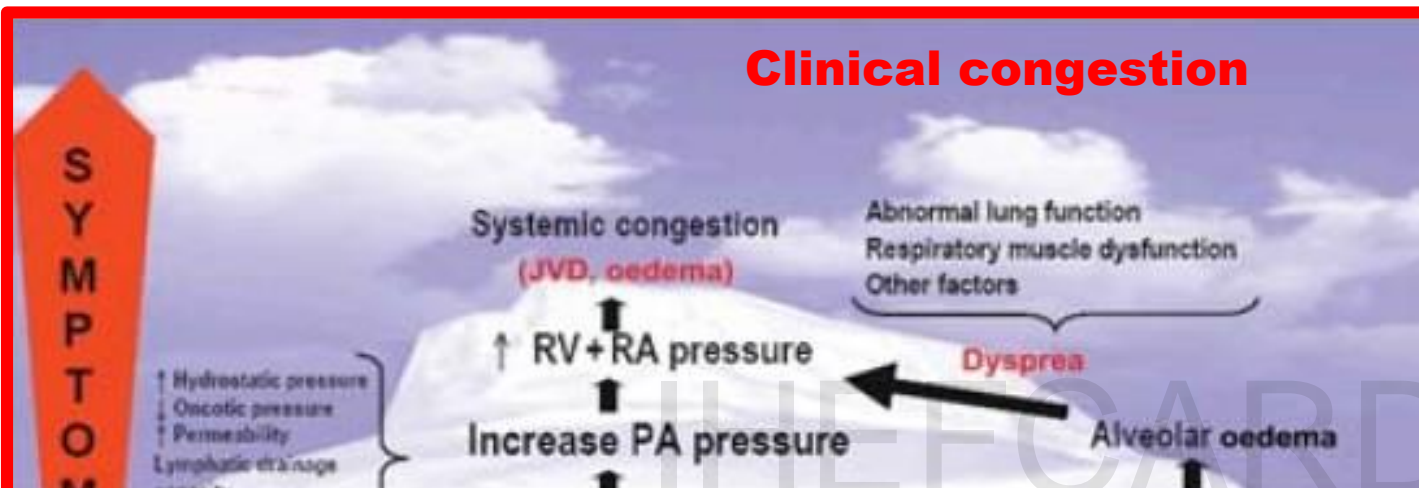
Tsutsui, H et al. *Journal of Cardiac Failure*. 2023



The perils of congestion.....

Congestion

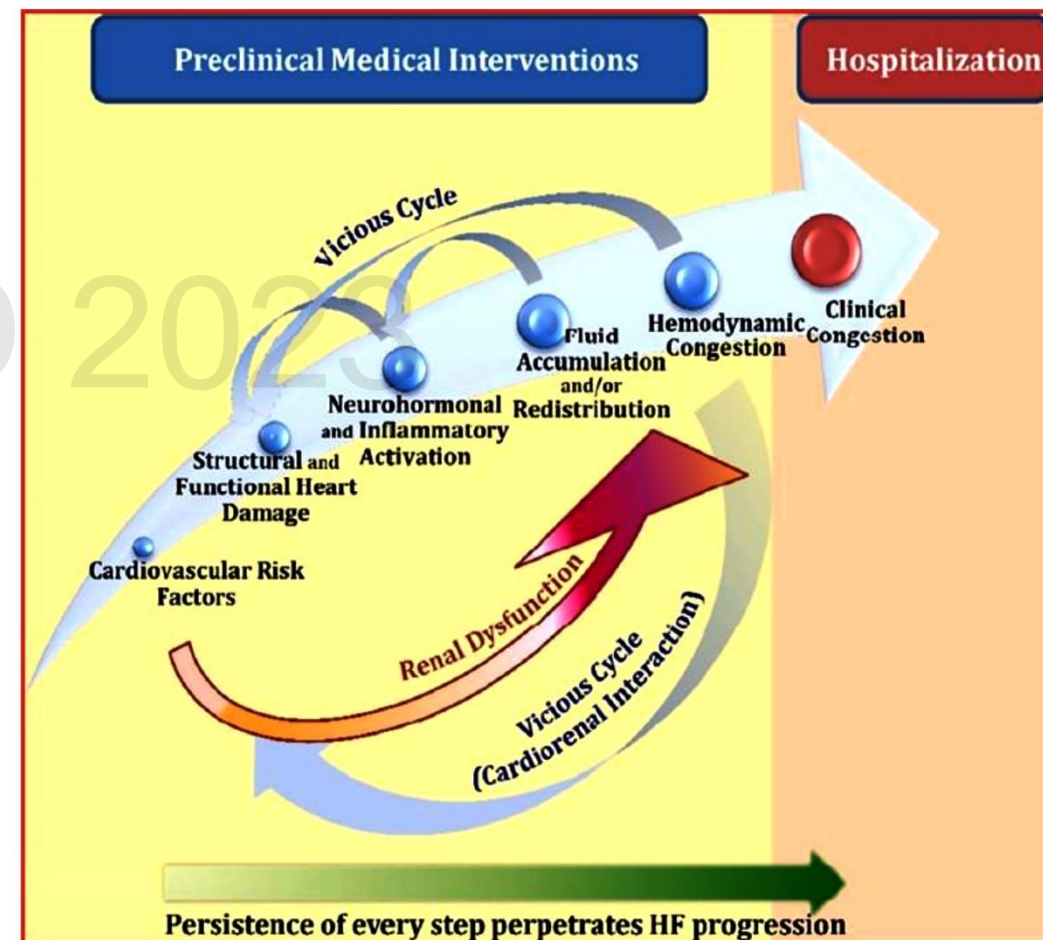
Clinical congestion



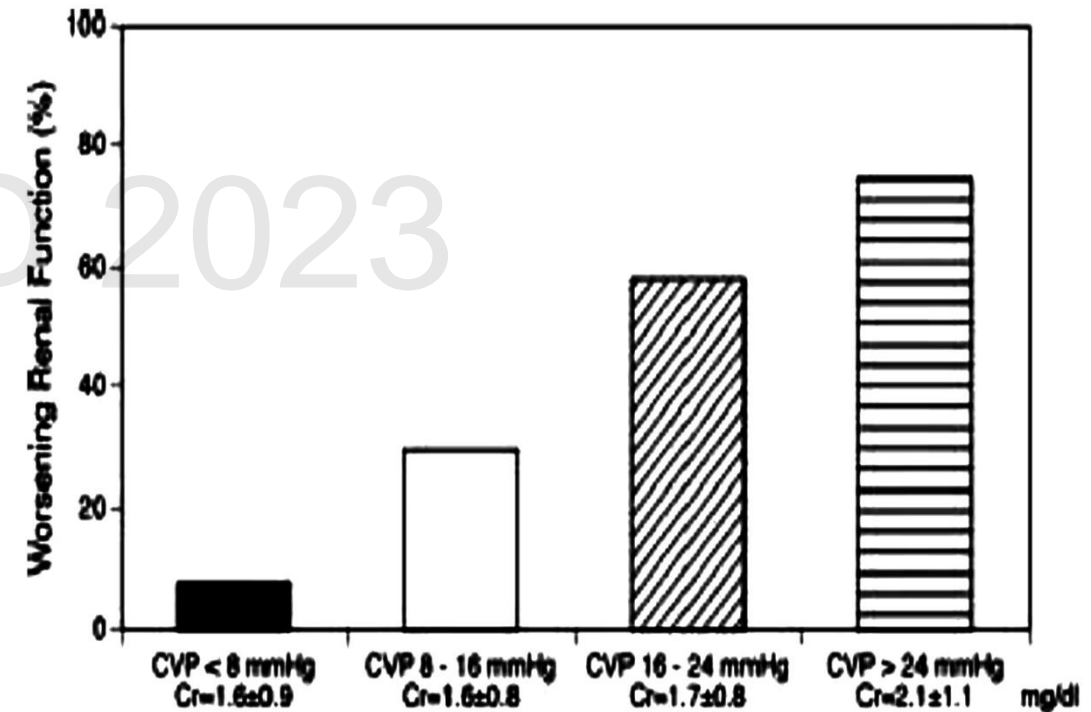
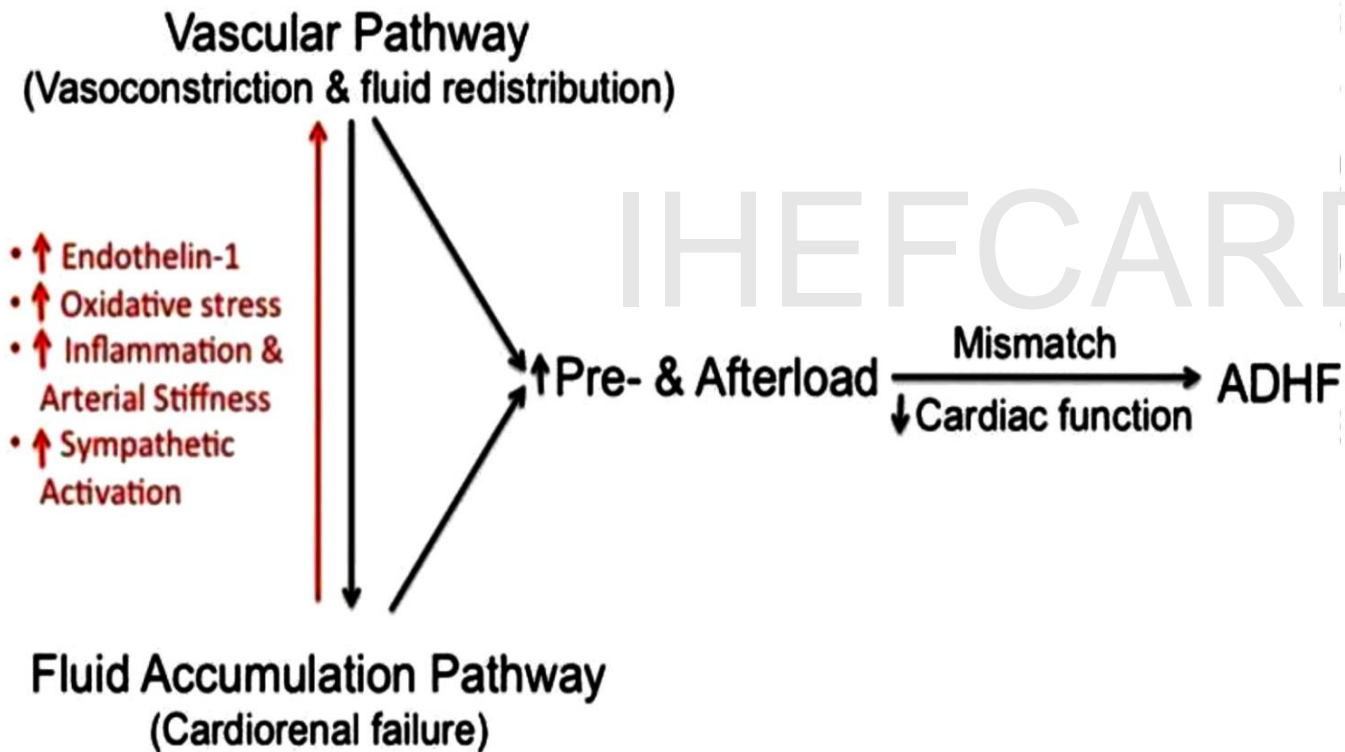
Water and Sodium in Heart Failure: A Spotlight on Congestion

Heart Fail Rev (2015) 20:13-24

Gaspare Parrinello · Stephen J. Greene · Daniele Torres · Michael Alderman · Joseph Vincent Bonventre · Pietro Di Pasquale · Luna Gargani · Anju Nohria · Gregg C. Fonarow · Muthiah Vaduganathan · Javed Butler · Salvatore Paterna · Lynne Warner Stevenson · Mihai Gheorghiade



CONGESTION CAUSES MULTIORGAN DYSFUNCTION

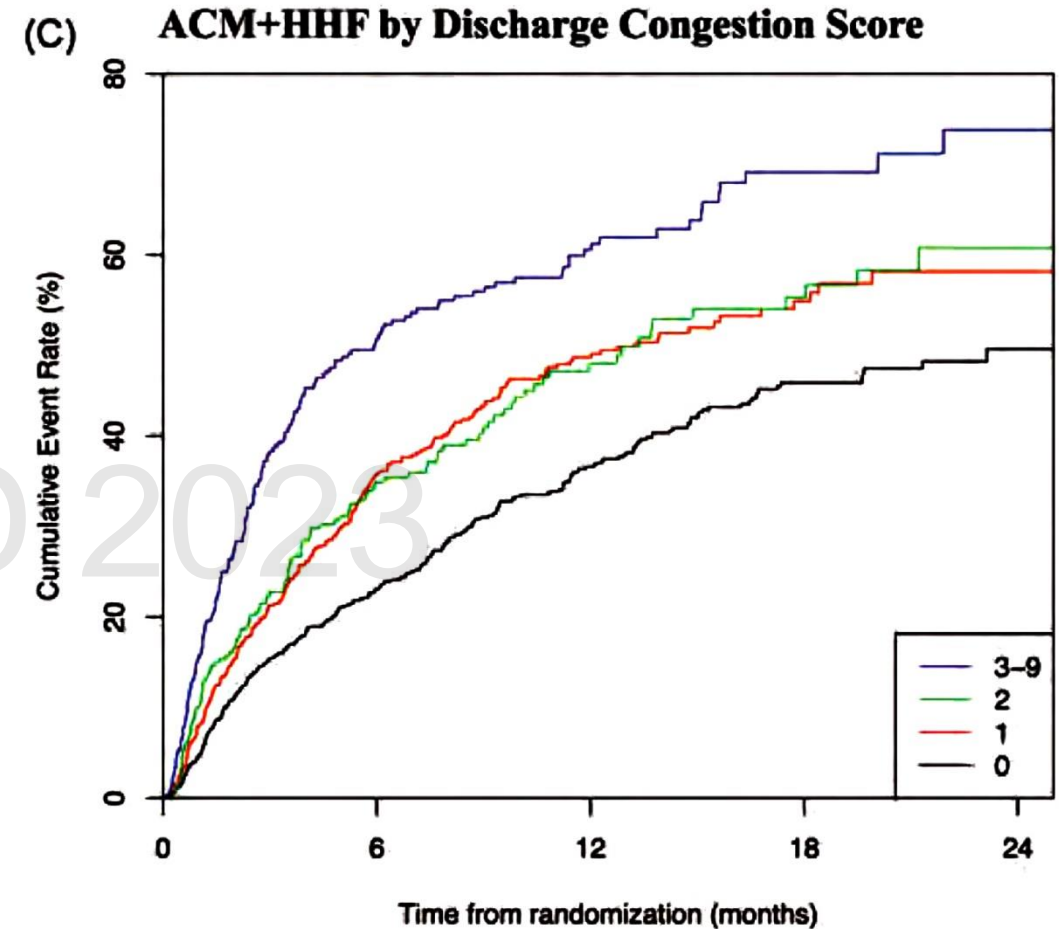


Colombo Curr HF Rep (2015) 12(3):215-
Mullens JACC 53(7):589-596

Clinical course and predictive value of congestion during hospitalization in patients admitted for worsening signs and symptoms of heart failure with reduced ejection fraction: findings from the EVEREST trial[†]

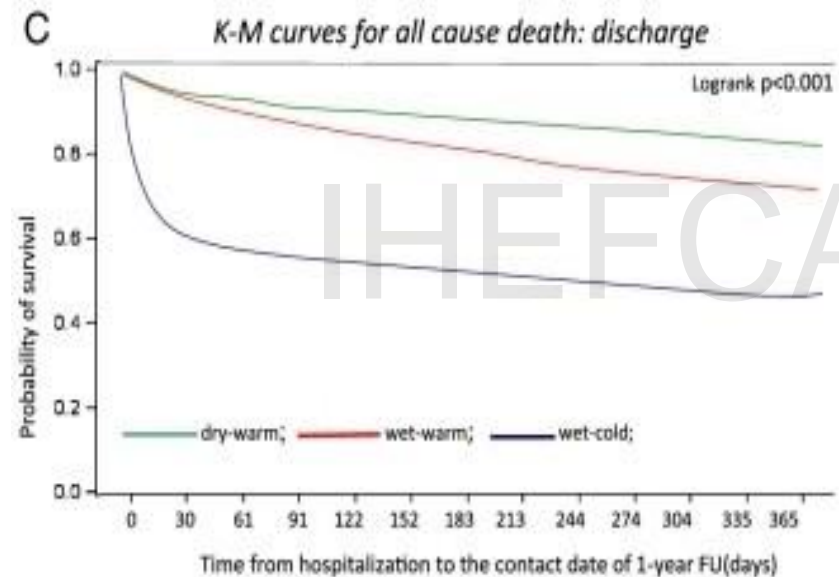
Andrew P. Ambrosy¹, Peter S. Pang^{2,3}, Sadiya Khan⁴, Marvin A. Konstam⁵, Gregg C. Fonarow⁶, Brian Traver⁷, Aldo P. Maggioni⁸, Thomas Cook⁷, Karl Swedberg⁹, John C. Burnett Jr¹⁰, Liliana Grinfeld¹¹, James E. Udelson⁵, Faiez Zannad¹², and Mihai Gheorghiade^{3*}, on behalf of the EVEREST trial investigators

RESIDUAL CONGESTION

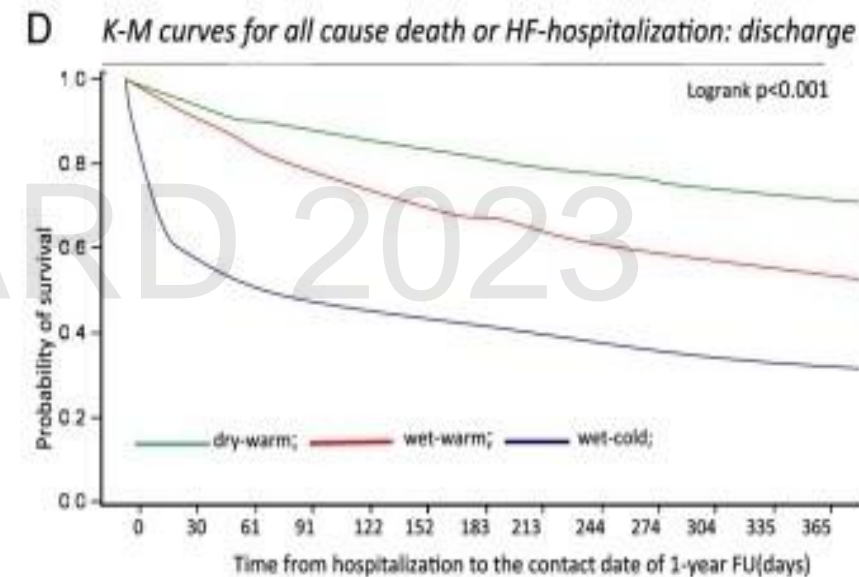


...
endpoint

Patients free of congestion at discharge have a significantly lower 1-year mortality compared to patients with residual congestion



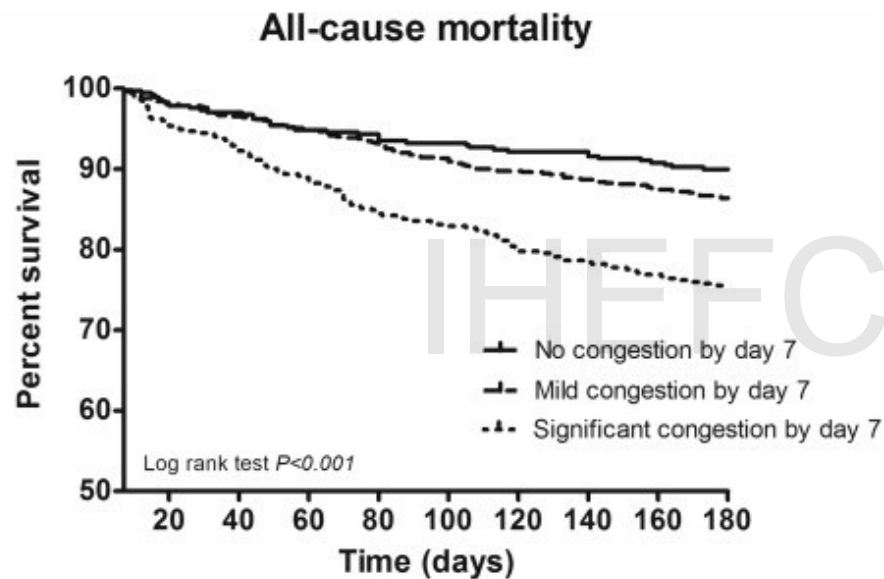
wet-cold	465	271	251	242	234	227	217	210	206	203	202	190	166
wet-warm	2559	2230	2134	2062	1991	1935	1884	1815	1773	1729	1664	1603	1438
dry-warm	4422	3839	3758	3694	3645	3591	3526	3469	3388	3325	3245	3150	2900



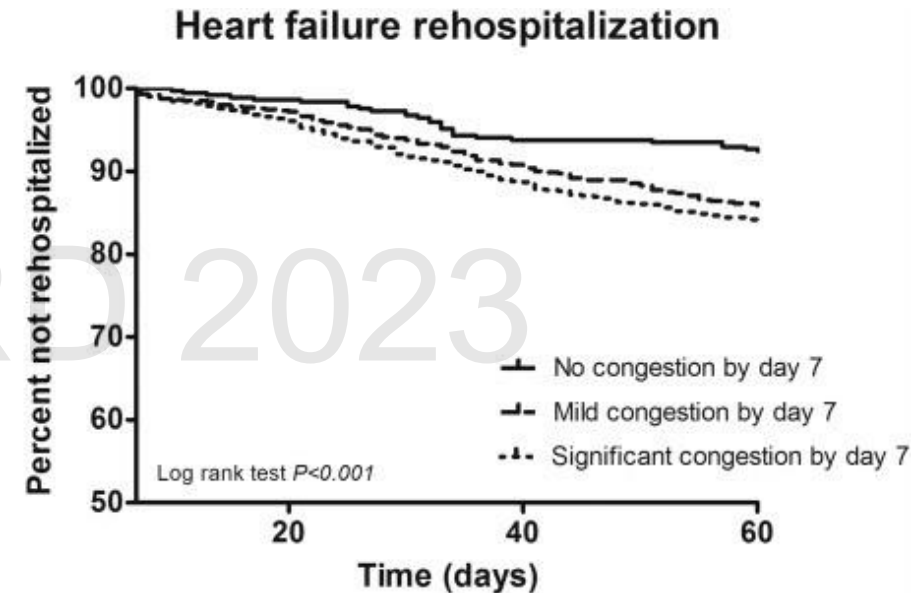
wet-cold	464	262	234	224	210	202	191	180	174	167	163	152	134
wet-warm	2499	2106	1936	1814	1687	1608	1541	1457	1398	1338	1288	1207	1081
dry-warm	4390	3753	3600	3486	3396	3306	3208	3119	3026	2940	2850	2751	2525

Chioncel, O et al. *European Journal of Heart Failure*. 2019

Residual congestion at 7 days after admission is associated with a greater risk of death and heart failure readmission



No	370	359	348	341	336	265
Mild	751	725	699	674	654	564
Significant	451	417	381	360	346	284
	Numbers at risk					



No	370	366	348	344
Mild	751	731	682	648
Significant	912	879	810	768
	Numbers at risk			

Rubio-Garcia, J et al. *International Journal of Cardiology*. 2018

MODEST ACCURACY OF CLINICAL EVALUATION

Table 1 Diagnostic value of clinical markers of congestion

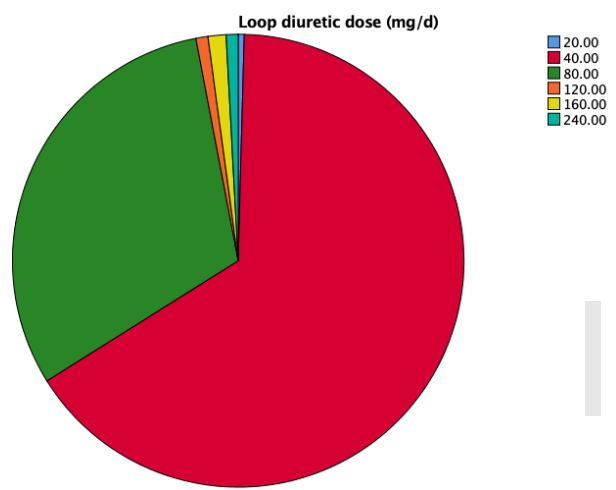
Sign or symptom	Sensitivity	Specificity	PPV	NPV
Dyspnoea on exertion	66	52	45	27
Orthopnoea	66	47	61	37
Oedema	46	73	79	46
Resting JVD	70	79	85	62
S3	73	42	66	44
Chest X-ray				
Cardiomegaly	97	10	61	—
Redistribution	60	68	75	52
Interstitial oedema	60	73	78	53
Pleural effusion	43	79	76	47

Table 2 Accuracy for Examination and Noninvasive Tests for Detecting Normal vs Abnormal Right and Left Heart Filling Pressures

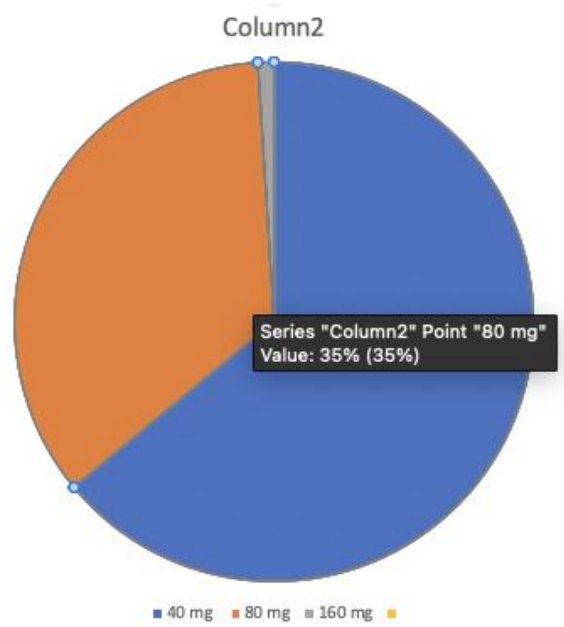
	Accuracy for RFP (%)	Accuracy for LFP (%)
Examination alone	<u>153/215 (71)</u>	<u>128/215 (60)</u>
NT-pro-BNP	—	73/109 (67)
Echo E/e' ratio	—	101/169 (60)
Echo inferior vena cava	142/190 (75)	—

BNP = B-natriuretic peptide; LFP = left heart filling pressure; RFP = right heart filling pressure.
All $P < .001$ compared with chance alone (Fisher's exact test). $P = \text{NS}$ for all noninvasive tests compared with examination alone (McNemar Test).

Gheorghiade Eu J HF (2010) 12, 423–4
Form AJM (2011) 124(11):1051-7



	JUMLAH KORESPONDEN	PERSENTASE
40 mg loop diuretic	36	64 %
80 mg loop diuretic	20	35 %
160 mg diuretic	1	1 %
Total populasi	56	100 %



Dari 56 pasien yang rehospitalisasi dalam waktu 1 bulan terdapat 64% responden mendapatkan 40 mg loop diuretic, 35% responden dengan 80 mg loop diuretic dan 1% dengan 160 mg loop diuretic

Wetscore registry, PJNHK

Predictors of Residual Congestion

- Higher BMI
- Lower blood pressure
- Diabetes
- Higher BUN levels
- Poor diuretic response
- Lower proportion of Acei/ARB
- Lower total cholesterol

Rubio-Gracia J, et al. Prevalence, predictors and clinical outcome of residual congestion in acute decompensated heart failure. International journal of cardiology. 2018 May 1;258:185-91.

The ‘Peptide for Life’ Initiative: a call for action to provide equal access to the use of natriuretic peptides in the diagnosis of acute heart failure across Europe

Antoni Bayes-Genis^{1,2*}, James L. Januzzi^{3,4,5}, A. Mark Richards^{6,7}, Henrike Arfsten Rudolf A. de Boer⁹, Michele Emdin^{10,11}, Arantxa González^{2,12}, Tiny Jaarsma¹³, Pardeep S. Jhund¹⁴, Christian Mueller¹⁵, Julio Núñez^{2,16}, Patrick Rossignol¹⁷, Ivan Milinkovic¹⁸, Giuseppe M.C. Rosano¹⁹, Andrew Coats^{20,21}, and Petar Seferovic^{18,22}



Figure 3 The ‘Peptide for Life’ Initiative logo.

Universal Definition

Journal of Cardiac Failure Vol. 27 No. 4 2021

Consensus Statement

Universal Definition and Classification of Heart Failure

A Report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure

Endorsed by Canadian Heart Failure Society, Heart Failure Association of India, the Cardiac Society of Australia and New Zealand, and the Chinese Heart Failure Association

BIYKEM BOZKURT, MD, PhD, Chair, ANDREW JS COATS, DM, DSC, Co-Chair, HIROYUKI TSUTSUMI, MD, Co-Chair, MAGDY ABDELHAMID, MD, STAMATIS ADAMOPOULOS, MD, NANCY ALBERT, PhD, CCNS, CHF, CCRN, NE-BC, STEFAN D. ANKER, MD, PhD, JOHN ATHERTON, MBBS, PhD, MICHAEL BOHM, MD, JAVED BUTLER, MD, MPH, MBA, MARK H. DRAZNER, MD, MSc, G. MICHAEL FELKER, MD, MHS, GERASIMOS FILIPPATOS, MD, GREGG C. FONAROW, MD, MONA FIUZAT, PharmD, JUAN-ESTEBAN GOMEZ-MESA, MD, PAUL HEIDENREICH, MD, TERUHIKO IMAMURA, MD, PhD, JAMES JANUZZI, MD, EWA A. JANKOWSKA, MD, PhD, PRATEETI KHAZANIE, MD, MPH, KOICHIRO KINUGAWA, MD, PhD, CAROLYN S.P. LAM, MBBS, FRCP, PhD, YUYA MATSUE, MD, PhD, MARCO METRA, MD, TOMOHIITO OHTANI, MD, PhD, MASSIMO FRANCESCO PIEPOLI, MD, PhD, PIOTR PONIKOWSKI, MD, PhD, GIUSEPPE M.C. ROSANO, MD, PhD, YASUSHI SAKATA, MD, PhD, PETAR SEPEROVIC, MD, PhD, RANDALL C. STARLING, MD, MPH, JOHN R. TEERLINK, MD, ORLY VARDENY, PharmD, MS, KAZUHIRO YAMAMOTO, MD, PhD, CLYDE YANCY, MD, MSc, JIAN ZHANG, MD, PhD, AND SHELLEY ZIEROTH, MD



European Journal of Heart Failure (2021)
doi:10.1002/ehf.2115

POSITION PAPER

Universal definition and classification of heart failure:

A report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure

Endorsed by Canadian Heart Failure Society, Heart Failure Association of India, the Cardiac Society of Australia and New Zealand, and the Chinese Heart Failure Association.



HEART FAILURE SOCIETY OF AMERICA



HFA
Heart Failure
Association



The Japanese
Heart Failure Society



Canadian Heart Failure Society
Société canadienne d'insuffisance cardiaque



Cardiac Society of Australia and New Zealand



Chinese Heart Failure Association

New Universal Definition of

Symptoms and/or signs
of HF caused by a
structural and/or
functional cardiac
abnormality

and corroborated by *at least one* of the following

Elevated natriuretic
peptide levels

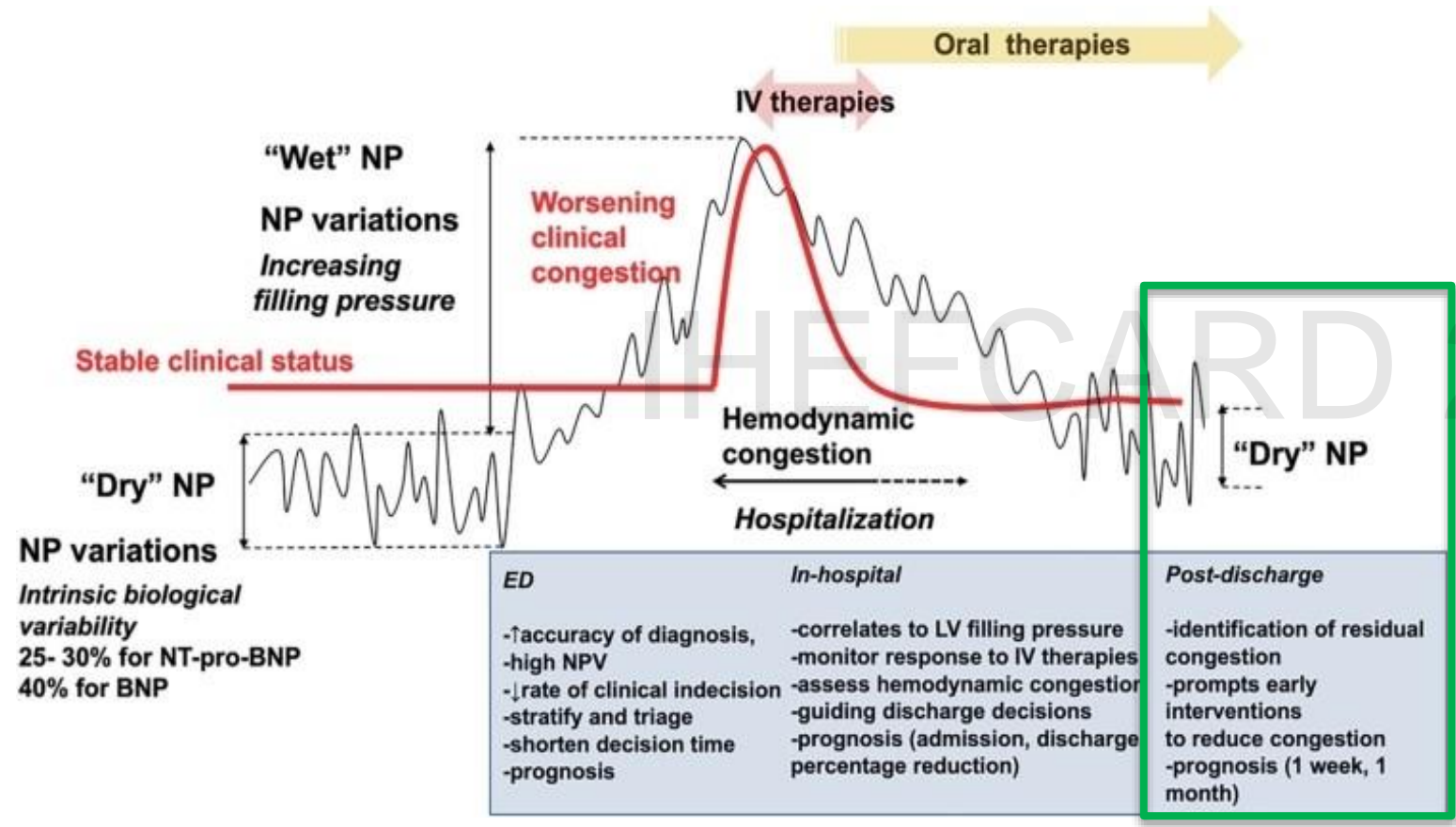
or

Objective evidence of
cardiogenic pulmonary or
systemic congestion

HF is a clinical syndrome with
current or prior

- **Symptoms and or signs caused by a structural and/or functional cardiac abnormality** (as determined by EF<50%, abnormal cardiac chamber enlargement, E/E' >15, moderate/severe ventricular hypertrophy or moderate/severe valvular obstructive or regurgitant lesion)
- **and corroborated by *at least one* of the following:**
 - elevated natriuretic peptide levels
 - objective evidence of cardiogenic pulmonary or systemic congestion by diagnostic modalities such as imaging (e.g. by CXR or elevated filling pressures by echocardiography) or hemodynamic measurement (e.g. right heart catheterization, PA catheter) at rest or with provocation (e.g. exercise)

Natriuretic peptides' trajectory across the spectrum of acute heart failure care



Congestion Parameter	Target at Discharge
Clinical tools	
EVEREST score	≤2
NYHA functional class	≤2
Biomarkers	
NT-proBNP	>30% drop during hospitalization Discharge value <1,500 pg/ml
BNP	Discharge value <250 pg/ml
Hemoglobin	>10 g/l increase during hospitalization
Imaging tools	
IVC imaging	Maximum diameter <2.1 cm IVC collapsibility index >50%
Lung ultrasound	<30 us-B lines

Tsutsui H, et all. Natriuretic Peptides: Role in the Diagnosis and Management of Heart Failure: A Scientific Statement From the Heart Failure Association of the European Society of Cardiology, Heart Failure Society of America and Japanese Heart Failure Society. Journal of Cardiac Failure. 2023 Apr 17.

Recommendations for management of patients after HF hospitalization	Class
It is recommended that patients hospitalized for HF be carefully evaluated to exclude persistent signs of congestion before discharge and to optimize oral treatment.	I

Exam	Time of measurement	Possible findings	Diagnostic value for AHF	Indication
Natriuretic peptides (BNP, NT-proBNP, MR-proANP)	Admission, pre-discharge	Congestion	High negative predictive value	Recommended

Ila	B-NR	In patients hospitalized for heart failure, a pre-discharge BNP or NT-proBNP level can be useful to inform the trajectory of the patient and establish a post-discharge prognosis
-----	------	---

McDonagh, TA et al. *European Heart Journal*. 2021
 Heidenreich, PA et al. *Circulation*. 2022



Initial & Serial Evaluation: Use of Biomarkers



In patients **with dyspnea**

COR	RECOMMENDATIONS
1	In patients presenting with dyspnea, measurement of BNP or NT-proBNP is useful to support a diagnosis or exclusion of HF.



In patients **at risk for HF**

COR	RECOMMENDATIONS
2a	In patients at risk of developing HF, BNP or NT-proBNP-based screening following team-based care, including a CV specialist, can be useful to prevent the development of LV dysfunction or new onset HF.



In patients **hospitalized for HF**

COR	RECOMMENDATIONS
1	In patients hospitalized for HF, measurements of BNP or NT-proBNP levels at admission is recommended to establish prognosis.
2a	In patients hospitalized for HF, a predischage BNP or NT-proBNP level can be useful to inform the trajectory of the patient and establish a post-discharge prognosis.



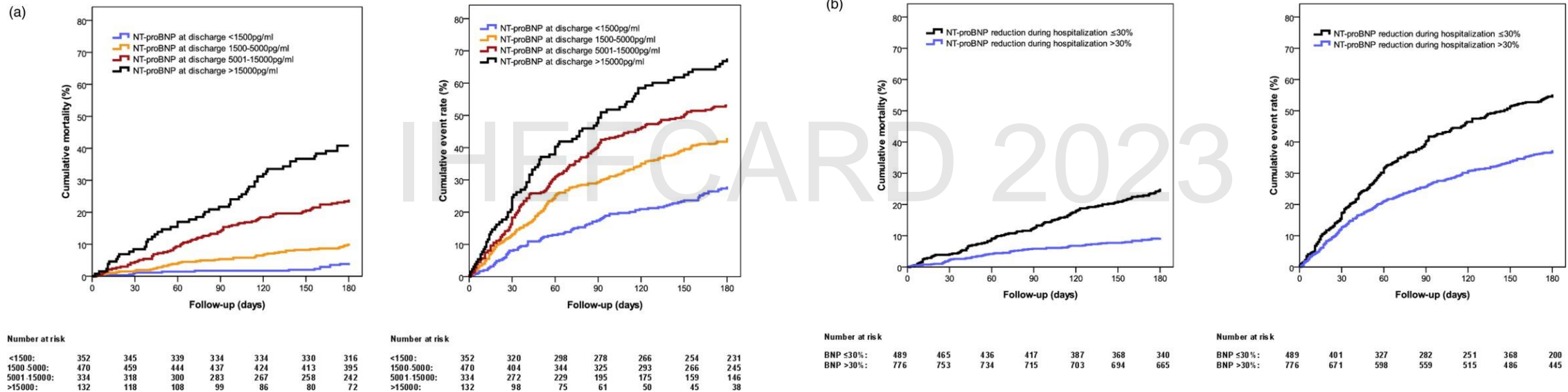
In patients **with chronic HF**

COR	RECOMMENDATIONS
1	In patients with chronic HF, measurements of BNP or NT-proBNP levels are recommended for risk stratification.

REMINDER

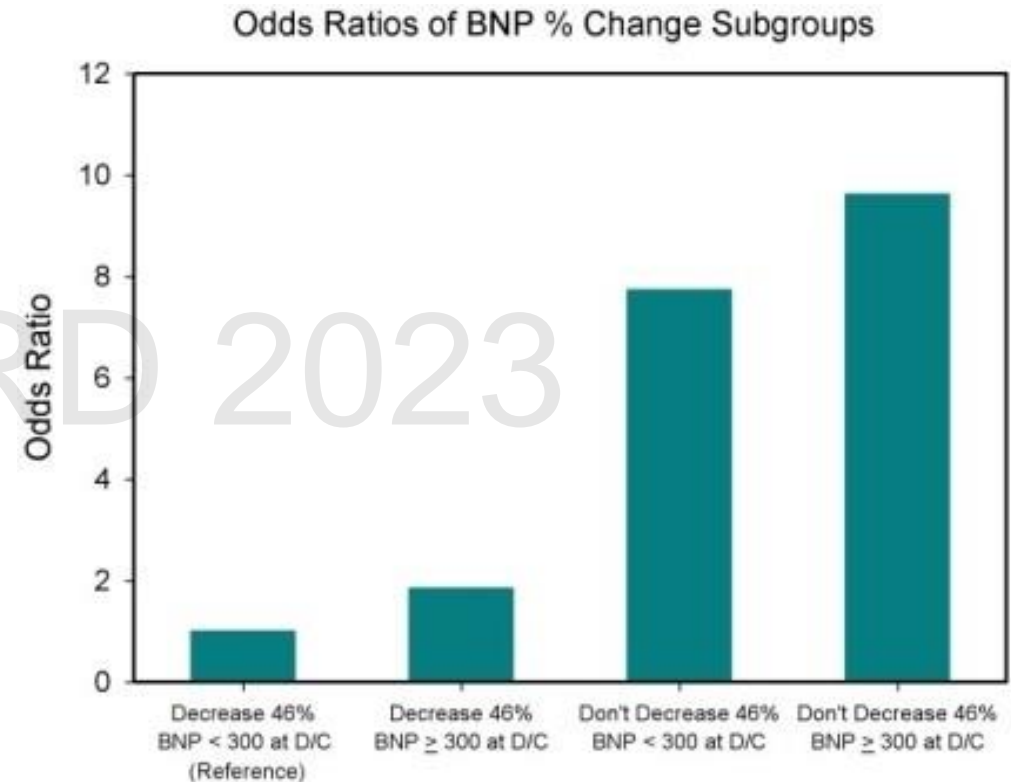
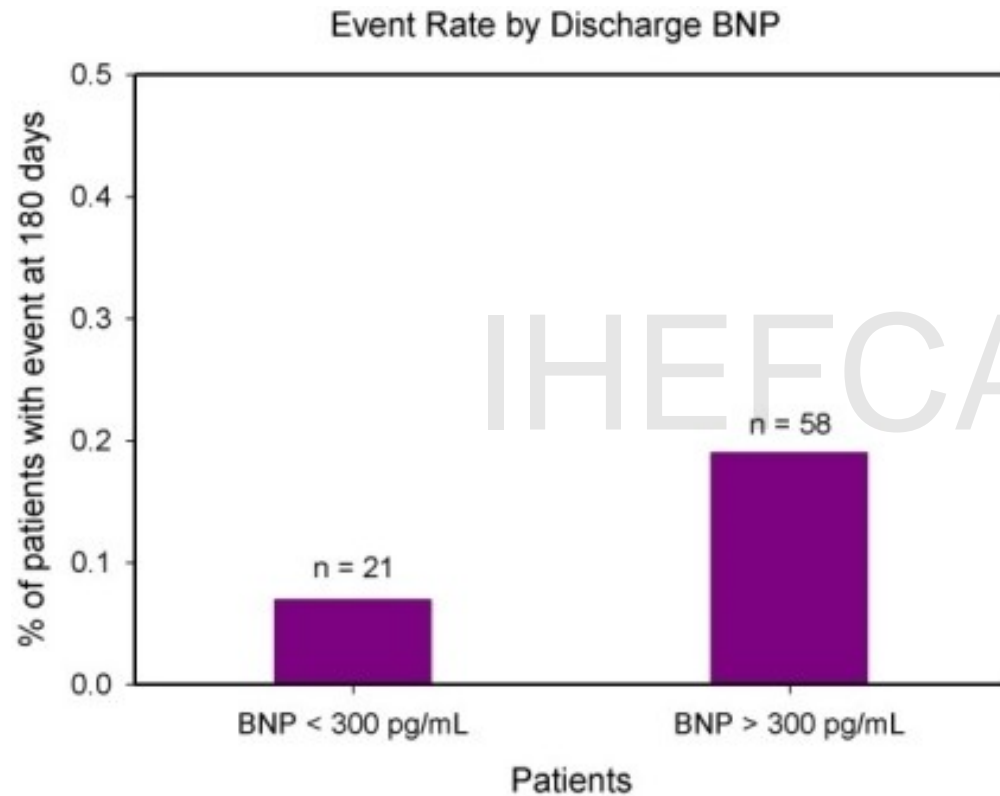
Potential noncardiac causes of elevated natriuretic peptide levels may include advancing age, anemia, renal failure, severe pneumonia, obstructive sleep apnea, pulmonary embolism, pulmonary arterial hypertension, critical illness, bacterial sepsis, and severe burns.

Patients with **higher levels of NT-proBNP at discharge**, or an inadequate decline during hospitalization, have a substantially higher risk of readmission and/or death within 180 days



Salah K, et al. A novel discharge risk model for patients hospitalised for acute decompensated heart failure incorporating N-terminal pro-B-type natriuretic peptide levels: a European coLlaboration on Acute decompensated Heart Failure: ELAN-HF Score. Heart. 2014 Jan 15;100(2):115-25.

In-hospital percentage BNP reduction is highly predictive for adverse events



Di Somma S, et al. In-hospital percentage BNP reduction is highly predictive for adverse events in patients admitted for acute heart failure: the Italian RED Study. Critical care. 2010 Jun;14(3):1-7.

Variable		<div><div></div><div>CONGESTED</div></div> <div><div></div><div>EUVOLEMIA</div></div>				
Clinical congestion	Orthopnea	None		Mild	Moderate	Severe/worst
	JVP (cm)	<8 and no HJR	<8	8-10 or HJR+	11-15	>16
	Hepatomegaly		Absent	Liver edge	Moderate pulsatile enlargement	Massive enlargement and tender
	Edema		None	+1	+2	+3/+4
	6MWT	>400m	300-400m	200-300m	100-200m	<100m
Technical evaluation	NP (one of both): -BNP -NT-proBNP		<100 <400*	100-299 400-1500	300-500 1500-3000	>500 >3000
	Chest X-ray	clear	clear	cardiomegaly	- pulmonary venous congestion* - small pleural effusions*	- Interstitial or alveolar edema
	Vena Cava imaging ⁴⁵	none of two: - Max diameter >2.2 cm - collapsibility <50%		One of two: - Max diameter >2.2 cm - collapsibility <50%		Both: - Max diameter >2.2 cm - collapsibility <50%
	Lung Ultrasound ⁴⁴	<15 B-lines when scanning 28-sites		15-30 B-lines when scanning 28-sites		>30 B-lines when scanning 28-sites

- ▶ The use of a **multi-parameter-based evaluation** of congestion pre-discharge is probably the best contemporary strategy

- ▶ But has never been prospectively evaluated

Mullens W, Damman K, Harjola VP, Mebazaa A, Brunner-La Rocca HP, Martens P, Testani JM, Tang WW, Orso F, Rossignol P, Metra M. The use of diuretics in heart failure with congestion—a position statement from the Heart Failure Association of the European Society of Cardiology. European journal of heart failure. 2019 Feb;21(2):137-55.

Conclusions

- Residual congestion is associated with **death and readmissions**
- **Integral assessment** is needed to evaluate patient before discharge (Residual congestion!), **NOT only one parameter.**
- Pre-discharge BNP and NT-proBNP levels are **strong predictors** of the risk of death or readmission.



Thank you.....