The 3rd Indonesian Symposium on Heart Failure and Cardiometabolic Disease 2023

Management of Congestion in Acute Heart Failure

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Disclosure

This symposium session is supported by Otsuka

Profile and in-hospital outcomes of Acute HF in various clinical studies

Table 7 Acute heart failure registries

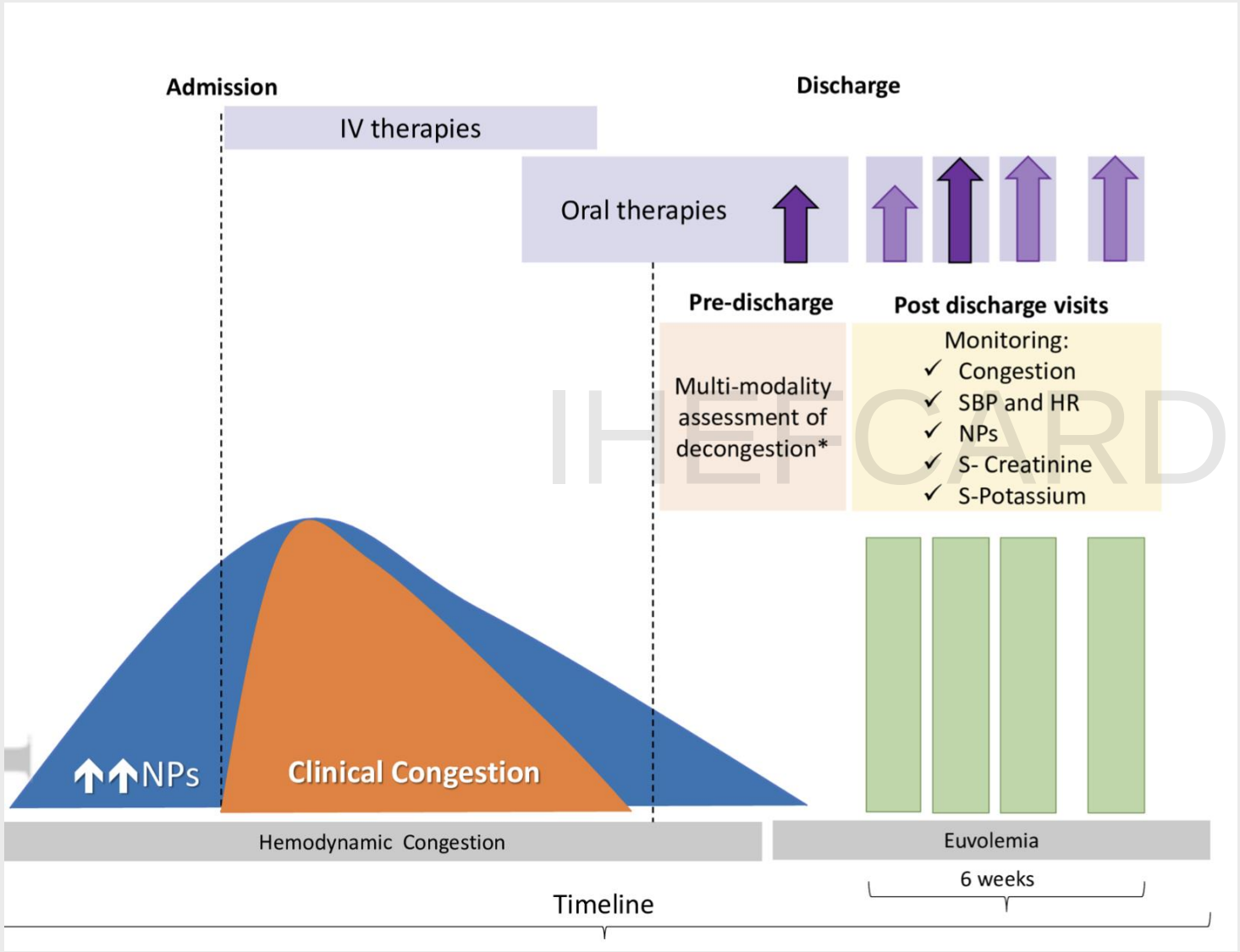
	Dokoupil et al.	ADHERE	OPTIMISE-HF	EHFS I	EHFS II	ESC-HF Long-term	ATTEND	ALARM-HF	IN-HF	AHEAD	FINN-AKVA	KorAHF	KCHF
Time period	2017	2001–2004	2003–2004	2000–2001	2004–2005	2011–2013	2007–2011	2006–2007	2007–2009	2006–2009	2004	2011–2014	2014–2016
number of patients	385	105 388	48 612	11 327	3580	5039	4842	4953	1855	4153	620	5625	4056
Age (mean, SD)	74 (median)	72 (14)	73.2 (14)	71	69.9 (12.5)	71 (median)	73 (13.8)	66–70 (median)	72 (12)	71.5 (12.4)	75.1 (10.4)	68.5 (14.5)	80 (median)
Female (%)	34	52	52	47	39	37.3	42	38	39.8	42.4	49.6	46.8	45
Arterial hypertension (%)	77.7	73	71	53	62.5	64.5	69.4	70.2	57.8	73.1	54.7	62.2	72
Diabetes mellitus (%)	47	44	42	27	32.8	38.9	33.8	45.3	40.4	42.6	32.3	40	37
Coronary artery disease (%)	63.1	57	50	68	53.6	54	31.1	70.2	—	64.9	55.2	42.9	33
Atrial fibrillation (%)	54.6	31	31	43	38.7	44	39.6	24.4	37.7	26.5	27	28.5	41
Chronic kidney disease (%)	57.1	30	30	17	16.8	26.4	—	21.4	32.5	—	9.4	14.3	45
COPD (%)	16.1	31	28		19.3	20.2	9.5	24.8	30.1	16.2	12.6	11.3	8.2
History of heart failure (%)	57.7	75	87	65	63	54.5	36.2	64	57	41.7	51	47.8	36
Cardiogenic shock (%)	7.3	2	—	<1	3.9	—	—	11.7	2.3	14.7	2.3	—	—
ICU/CCU care (%)	47.5	19	—	7	51	—	—	75	51.9	—	11.9/39.5	—	—
Length of hospital stay (median)	10	4	4	11	9	—	21	6	10	7.1	7	9	16
In-hospital mortality (%)	12.7	4	3.8	6.9	6.7	4.9	6.4	11	6.4	12.7	7.1	4.8	6.7

COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; CCU, cardiac care unit.

Burden of Acute HF:

Frequent re-hospitalization; Prolonged length of stay, increased in-hospital mortality and poor quality of life after discharge

Dokoupil J, et.al. ESC Heart Failure 2022; 9: 2249–2258



Management of HF patients according to hospitalization phase

Main problem at initial phase is congestion; thus, early decongestion is important, followed by carefully monitoring of response to treatment and pre-discharge assessment.

Metra M, et.al. Eur J Heart Failure 2023
doi: 10.1002/ejhf.2888

Predictor of 30-days re-admission in ADHF with DMT2

Variabel	*p*	OR	Interval Kepercayaan 95%	
			Minimum	Maksimum
EKG Fibrilasi Atrium	0,000	2.616	1.604	4.267
Denyut jantung saat pulang	0.010	1.022	1.005	1.039
GDPP < 140 mg/dL	0.003	0.528	0.348	0.802

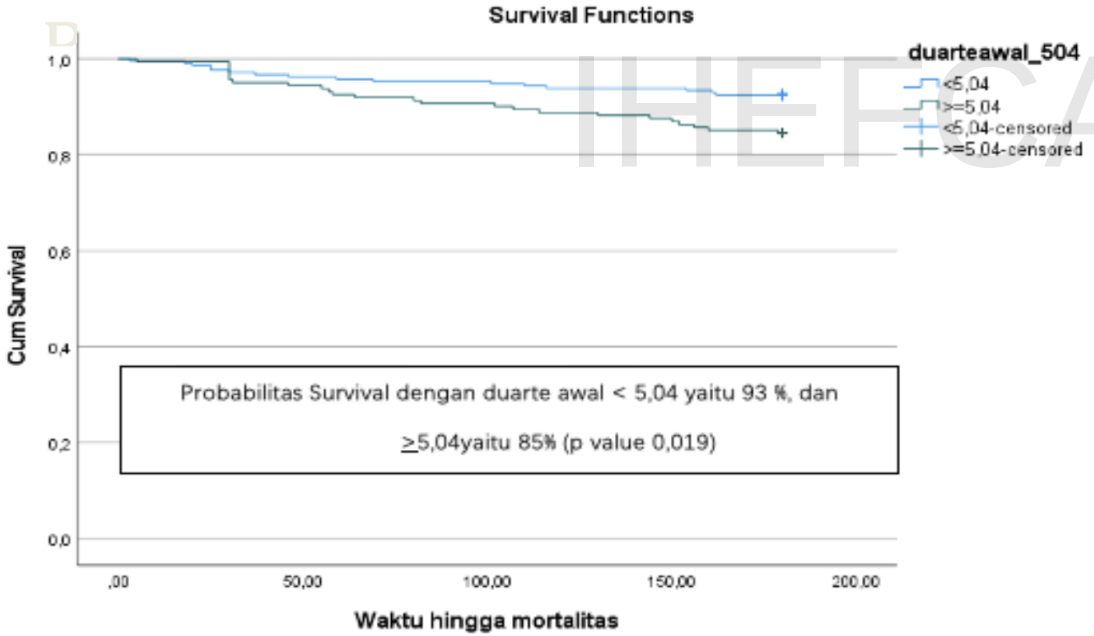
Retrospective Cohort Studies
N=747 patients with ADHF and DMT2 [LVEF < 40%]
30-days re-admission rate was 27.3%

Predictors of re-admission:
Atrial Fibrillation, Pre-discharge HR > 80 bpm. GDPP < 140 mg/dL was protective to re-admission.

Sain A, Soerarso R, Widyantoro B, et.al.
Manuscript in submission 2022

Estimated Plasma Volume Predicts 30-day-Readmission in Acute Decompensated Heart Failure with Type-2 Diabetes Mellitus

Ghina Shabirina K. Bambang Widyantoro*. Hary S. Muliawan. Vidya G. Rejeki, Dian Y. Hasanah, Dafsah A. Juzar.



Retrospective Cohort Study
N=373 patients first hospitalized with ADHF and DMT2 [LVEF < 40%]

30-days re-admission rate was 27.1%;
180-days mortality rate was 11%

Initial ePV 35,04 ml/g is associated with 180-day mortality (HR 2,12; 95%CI 1,13-3,98; p = 0,019).

Pre-discharge ePV is also associated with 30-day readmission
(HR 1,23; IK95 1,05 – 1,46; p = 0,025).

Shabirina G, Widyantoro B et.al. Submitted manuscript 2023

Burden of Acute HF:

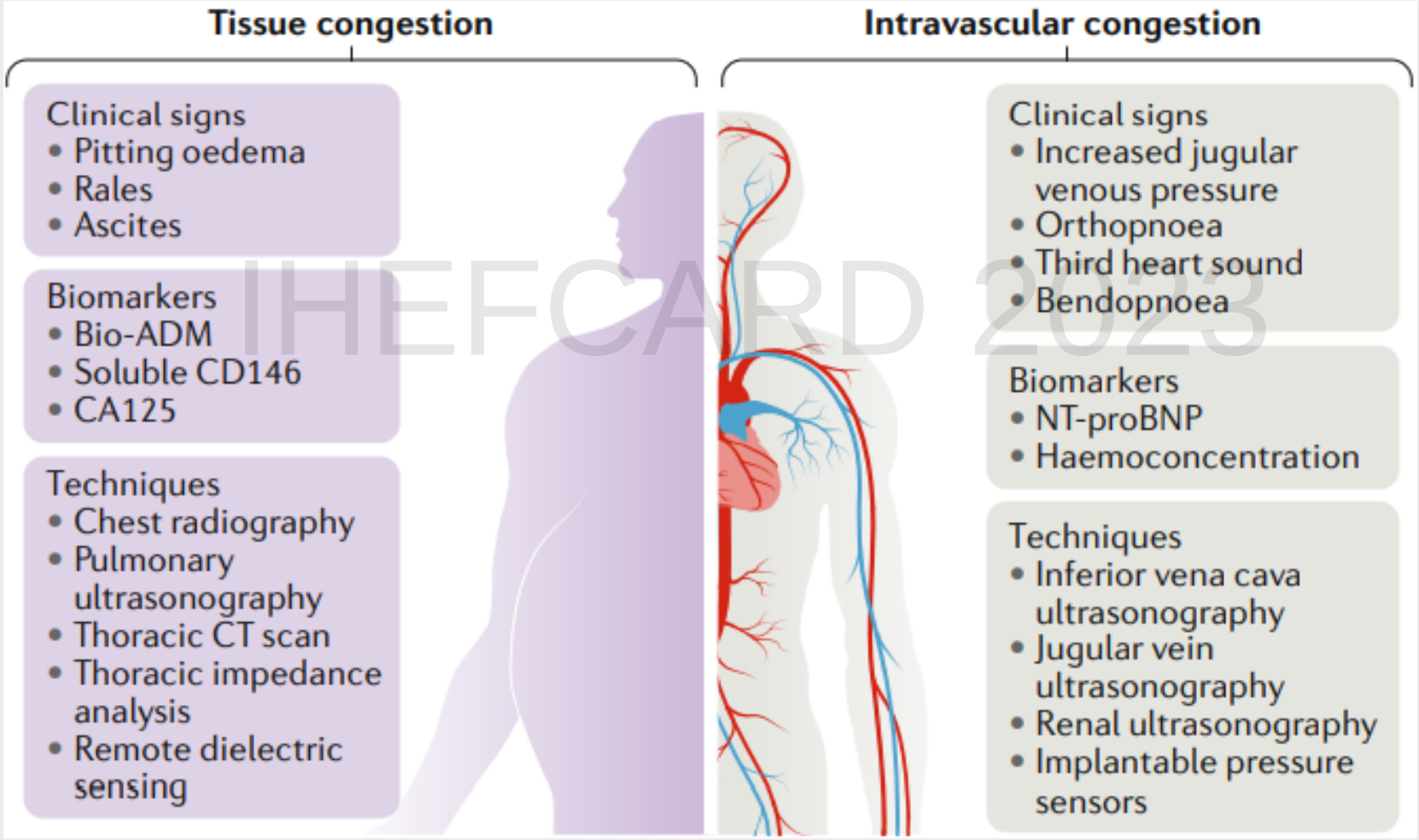
Frequent re-hospitalization; Prolonged length of stay, increased in-hospital mortality and poor quality of life after discharge

Challenges in Management of Acute HF:

Assessment of congestion, initial diuretics treatment,
Close monitoring of therapeutic response at initial phase and decision to aggressive de-congestion.

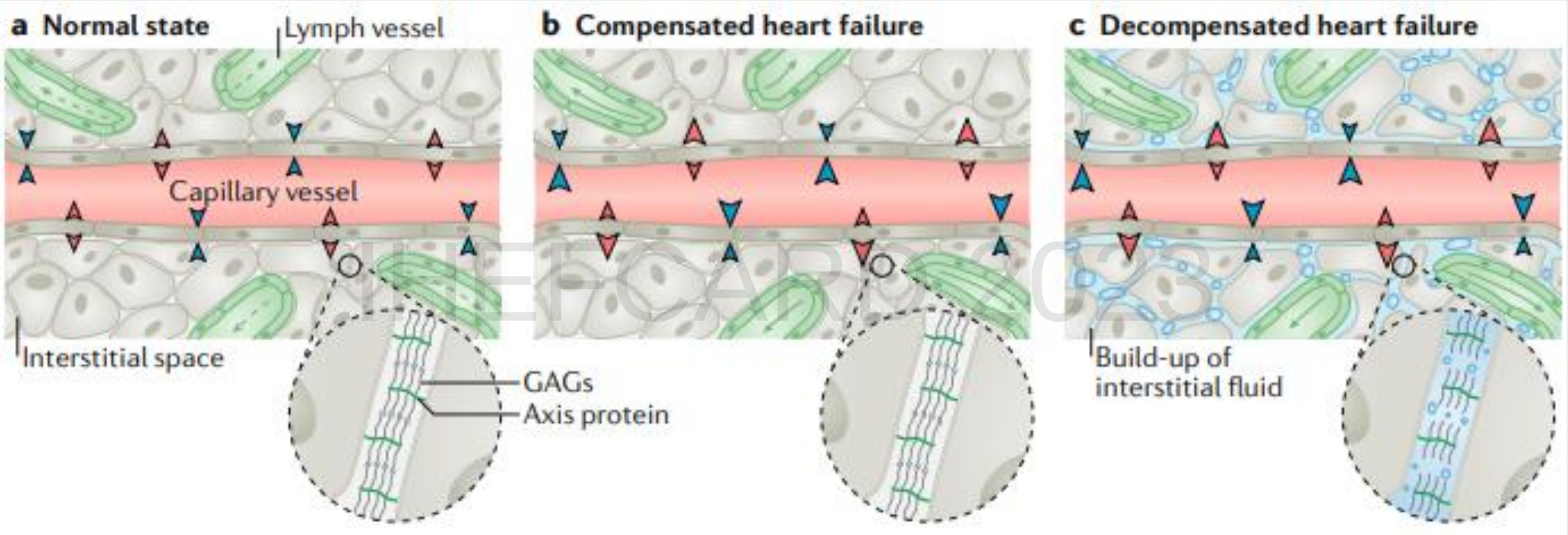
Q1. When should we consider escalation or combination or de-congestion treatment modalities?

HYPOTHESIZED DIFFERENCES BETWEEN TISSUE CONGESTION AND INTRAVASCULAR CONGESTION



Boorsma. Nat Rev Cardiol. 2020 Oct;17(10):641-655

PATHOPHYSIOLOGY OF TISSUE CONGESTION



Congestion can be present predominantly in the vascular system (intravascular congestion) or in the interstitium (tissue congestion), although the majority of patients have a combination of both intravascular and tissue congestion.

Boorsma. Nat Rev Cardiol. 2020 Oct;17(10):641-655

Diuresis and Aquaresis Defined

Diuresis

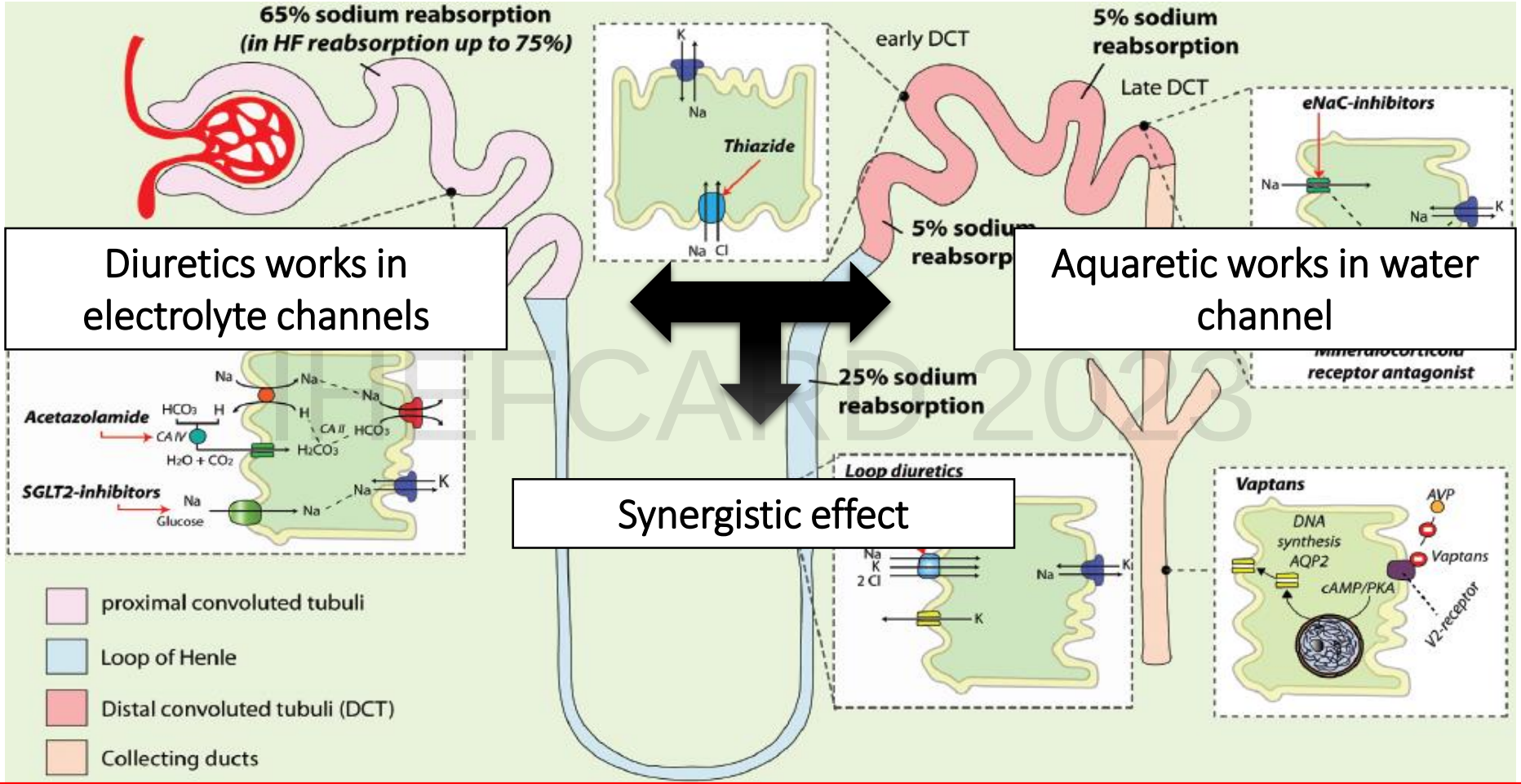
- Increased excretion of urine by the kidney; includes water and typically increased solute excretion as well

Aquaresis

- Increases excretion of water by the kidney without increased excretion of solute, i.e., electrolyte-sparing excretion of free water by the kidney

Q2. Should we combine diuretic with aquaretic for decongestion??

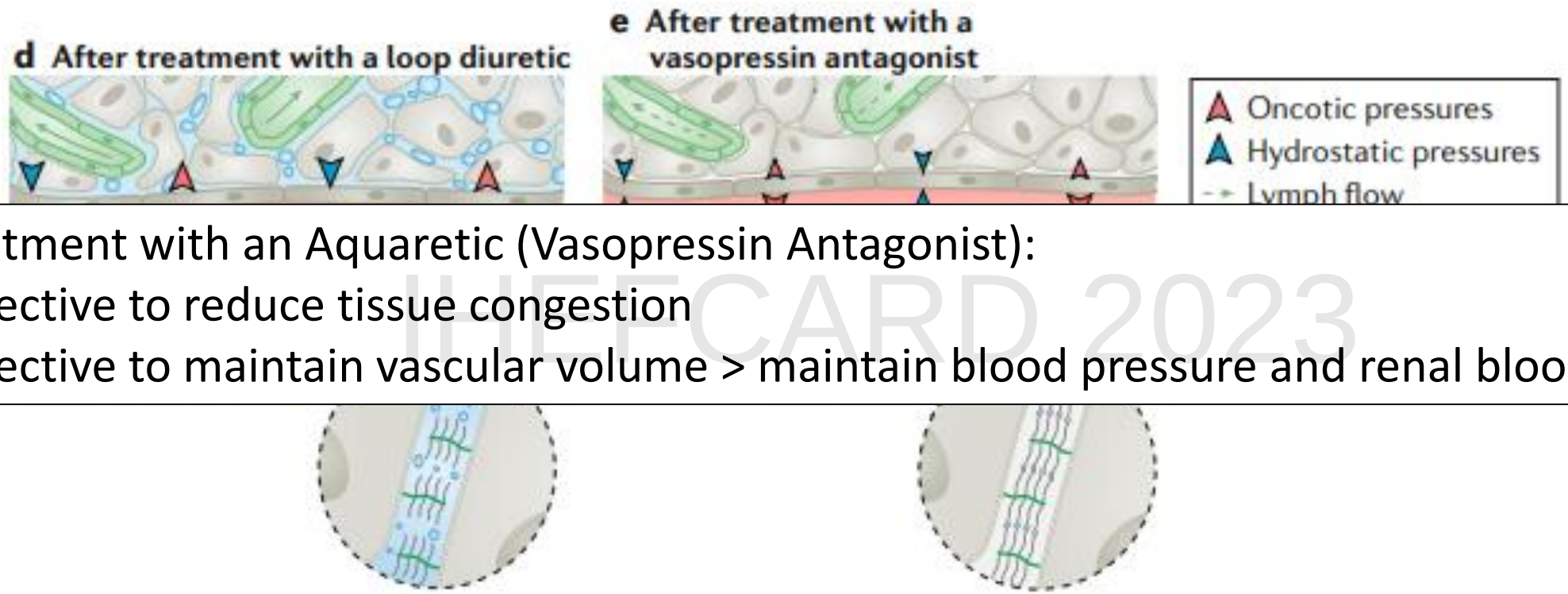
Different Routes of Diuretics and Aquaretic (Vasopressin Antagonist)



Diuretics works in electrolytes channel	Vasopressin Antagonist (Vaptans) works in water channel

Mullens, D, et al. 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) 21, 137–155

Different Effect on Tissue Congestion Between Loop Diuretic and Aquaretic (Vasopressin Antagonist)



Treatment with an Aquaretic (Vasopressin Antagonist):
- Effective to reduce tissue congestion
- Effective to maintain vascular volume > maintain blood pressure and renal blood flow

Loop diuretic therapy reduces circulating blood volume, thereby improving intravascular congestion; however, these therapies do not increase plasma osmolality, which might impede translocation of fluid from the tissues to the circulation.

Aquaretic drugs, such as vasopressin antagonists, reduce plasma volume and increase plasma osmolality, which might stimulate translocation of fluid from the tissues to the circulation.

Boorsma. Nat Rev Cardiol. 2020 Oct;17(10):641-655

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

- Hypokalemia is often induced by **loop** and **thiazide diuretic** administration. It may cause lethal ventricular arrhythmias and increase CV mortality.

- **Tolvaptan**, an orally active selective arginine vasopressin V2 receptor antagonist, can be considered to increase serum sodium and diuresis in patients with persistent hyponatremia and congestion.

McDonagh TA, et al. Eur Heart J.2021

AHA/ACC/HFSA CLINICAL PRACTICE GUIDELINE

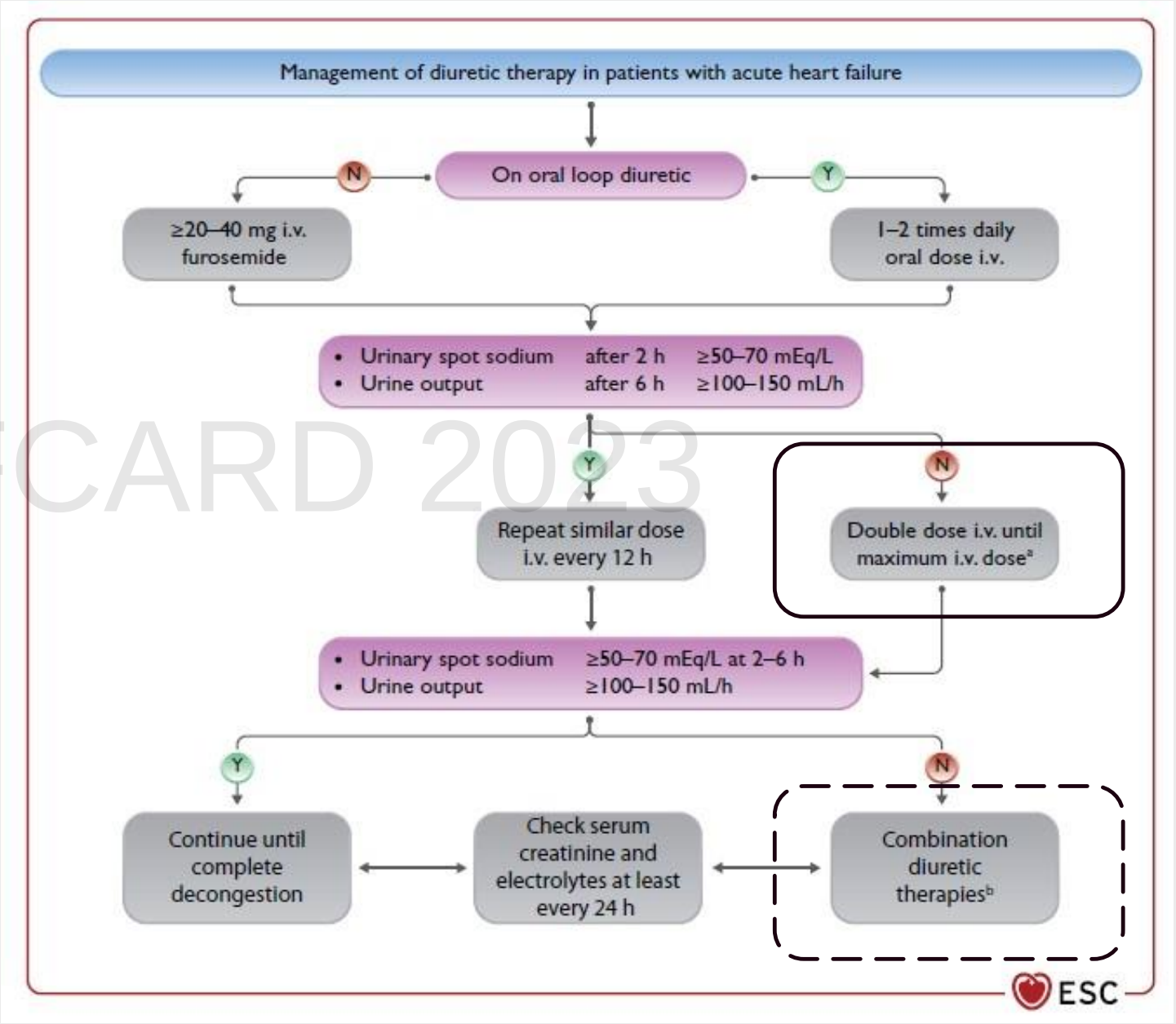
2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

- **Vasopressin antagonists** may be helpful in the acute management of volume overload to decrease congestion while maintaining serum sodium.

- However, in a propensity-score matched analysis in patients with hospitalized HF, **the addition of metolazone to loop diuretics** was found to increase the risk for hypokalemia, hyponatremia, worsening renal function, and mortality, whereas use of higher doses of loop diuretics was not found to adversely affect survival

Diuretic Therapy in Acute Heart Failure

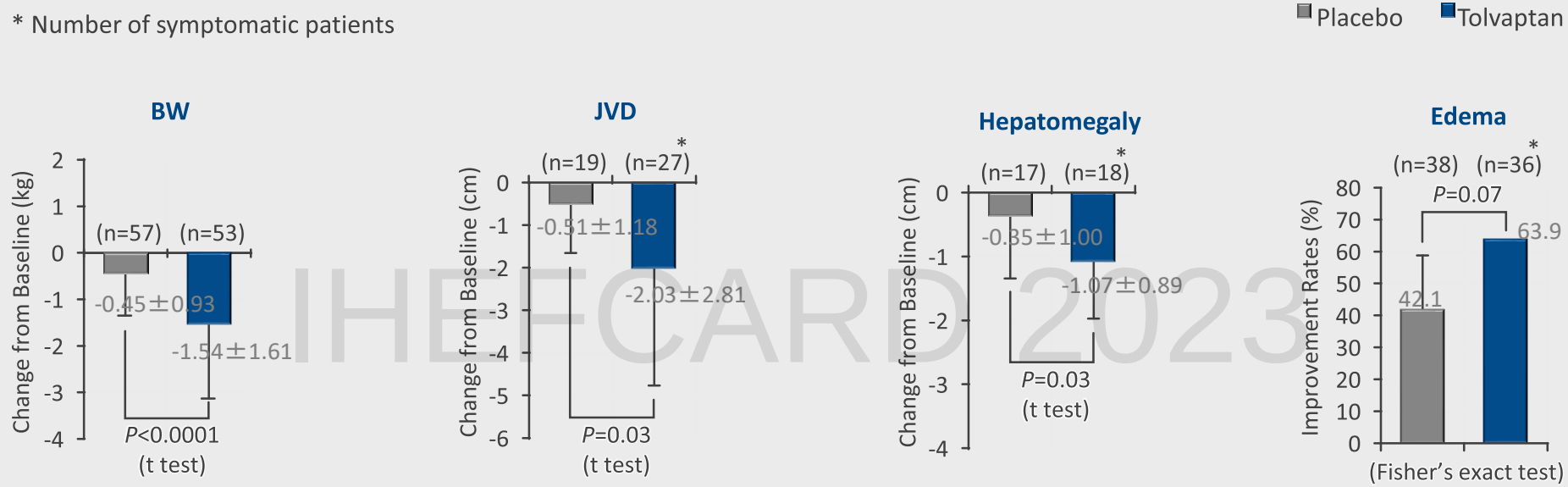
2021 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure



McDonagh TA, et al. Eur Heart J. 2021

TOLVAPTAN **REDUCES BODY WEIGHT** AND **RELIEVES CONGESTIVE SYMPTOMS**

* Number of symptomatic patients



At the End of Treatment (LOCF) Mean±S.D.

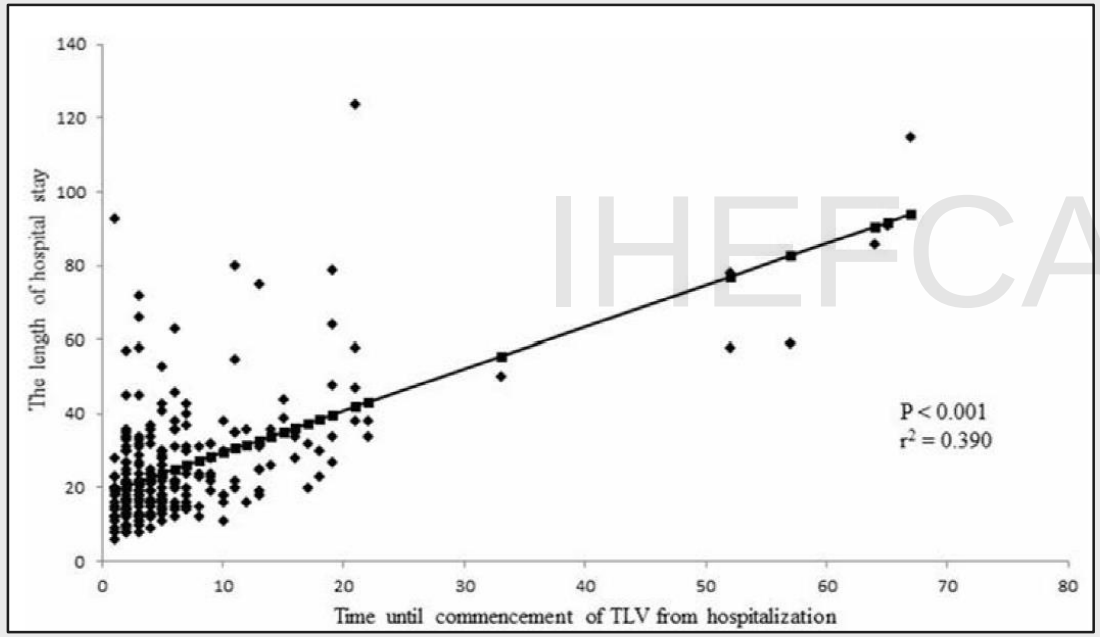
- At the end of treatment, a significant greater reduction in body weight was observed in the tolvaptan group (−1.54±1.61 kg) than in the placebo group (−0.45±0.93 kg), and difference between two groups and its 95% confidence interval was −1.09 kg and from −1.58 to −0.60 kg respectively (p<0.0001).
- In the tolvaptan group, a statistically significant improvement was observed venous distension and hepatomegaly (p=0.03, 0.03 respectively), whereas improvements in other parameters were not significant although all improin jugular ved more in the tolvaptan group than in the placebo group.

QUEST study

Mastsuzaki M, et al. Cardiovasc Drugs Ther 2011;25:S33-45.

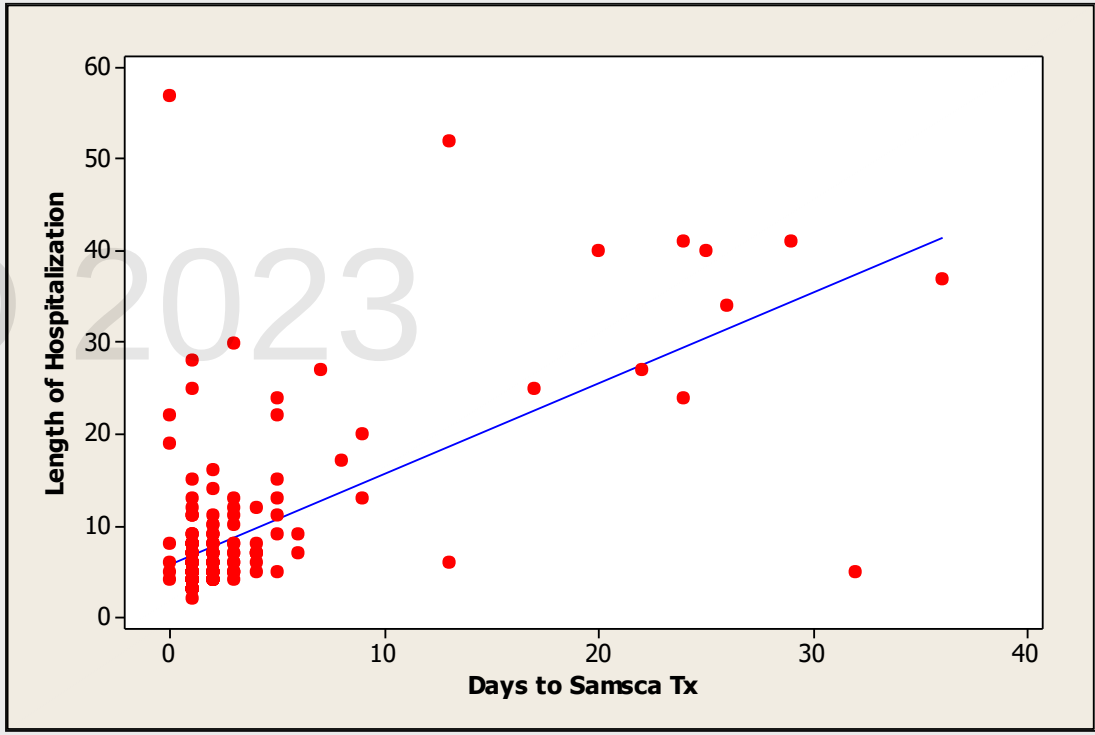
EARLY INITIATION OF TOLVAPTAN SHORTENS LENGTH OF HOSPITAL STAY

- The relationship between the time until commencement of tolvaptan and the length of hospital stay in heart failure patients[1]



Regression curve of the relationship between time and commencement of TVT from hospitalization and the length of hospital stay. Time until commencement of TVT from hospitalization were strongly correlated with the length of hospital stay: P <0.001, r^2 = 0.0390.

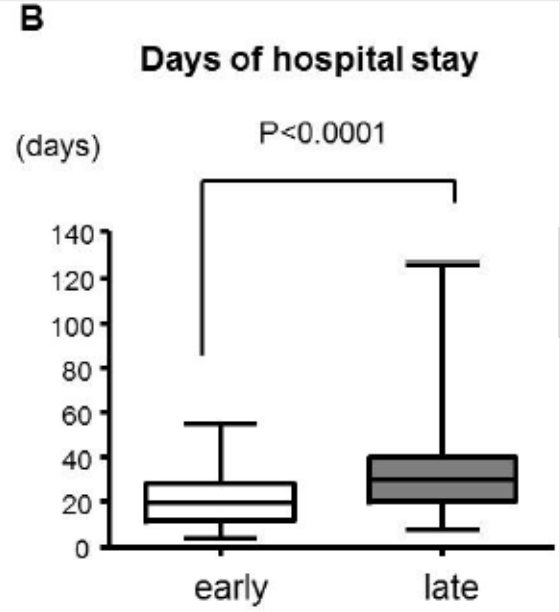
- The Philippine Tolvaptan Experience[2]

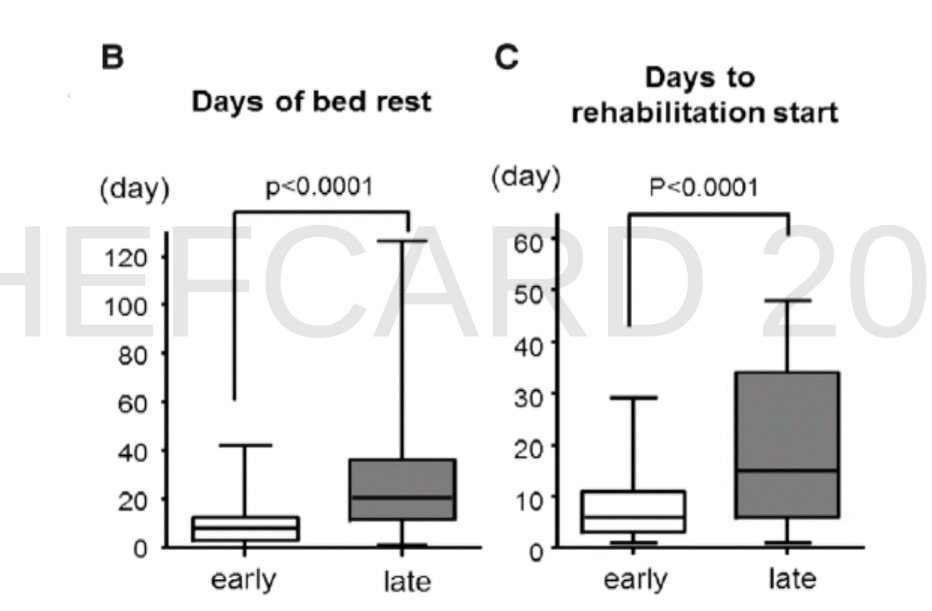


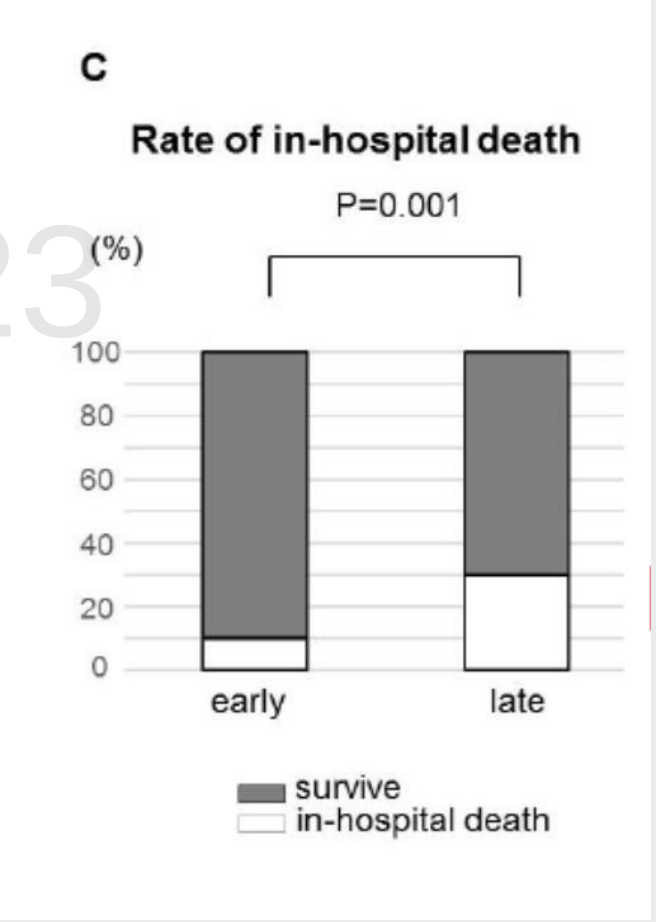
Scatterplot Showing Relationship between Days to oral Tolvaptan tablets and Length of Hospitalization. Correlation Coefficient: 0.6350; p value: <0.0001.

1. Kiuchi, S. et al. The relationship between the time until commencement of tolvaptan and the length of hospital stay in heart failure patients. Heart Vessels. 2018 Apr;33(4):367-373. 2. Data on file. Based on the result of the Tolvaptan Philippine Early Experience

THE EARLY USE OF TOLVAPTAN IS SIGNIFICANTLY ASSOCIATED WITH SHORTER HOSPITAL STAY AND EARLY INITIATION OF CARDIAC REHABILITATION





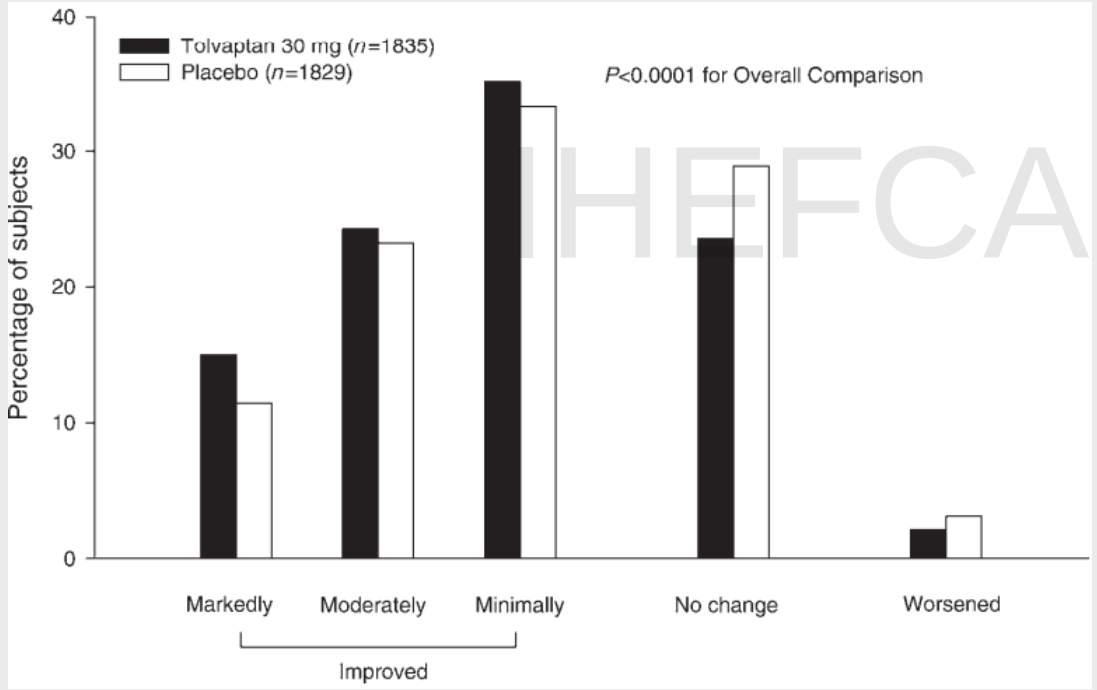


Retrospective Study, single center, 102 consecutive patients with decompensated heart failure treated with tolvaptan

Matsukawa, R. et al.: Heart Vessels, 2015 DOI 10.1007/s00380-015-0780-z

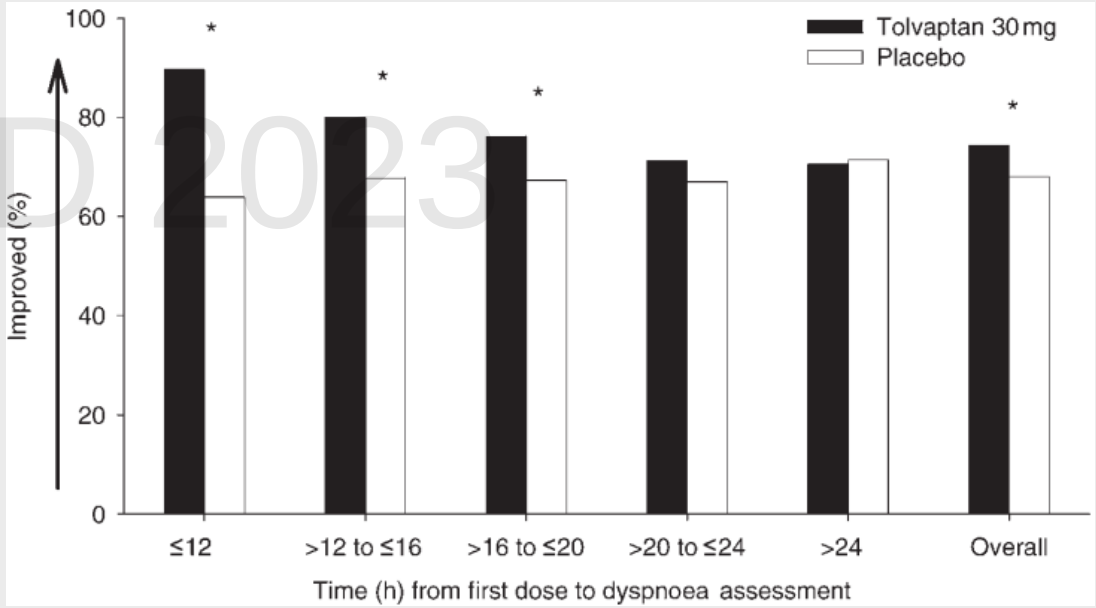
Dyspnea improves within 12 hours after the first dose of tolvaptan and continues to improve for up to 60 hours

- Subjects with frequent or continuous dyspnea as initially determined by the physician, self-reported dyspnea



Patient-assessed dyspnea status at inpatient Day 1 in the combined EVEREST trial population.

- Improvement with tolvaptan in addition to standard medical therapy appears greatest when measured early



Patient-assessed dyspnea as a function of time from first dose of study drug. *P , 0.05 van Elteren test.

JAMA. 2007;297(12):1319-1331.

American Journal of Cardiovascular Drugs (2023) 23:185–196
https://doi.org/10.1007/s40256-023-00571-y

ORIGINAL RESEARCH ARTICLE

Predictors of Poor Very Early Diuretic Response and Effectiveness of Early Tolvaptan in Symptomatic Acute Heart Failure

Hideyuki Takimura[1] · Atsumasa Kurozumi[1] · Rintaro Taniguchi[1] · Ippei Tsuzuki[1] · Emi Tajima[1] · Yukihiro Yamaguchi[1] · Mami Kawano[1] · Yukako Takimura[1] · Satoru Nishio[1] · Masatsugu Nakano[1] · Reiko Tsukahara[1]

Accepted: 18 January 2023 / Published online: 4 February 2023

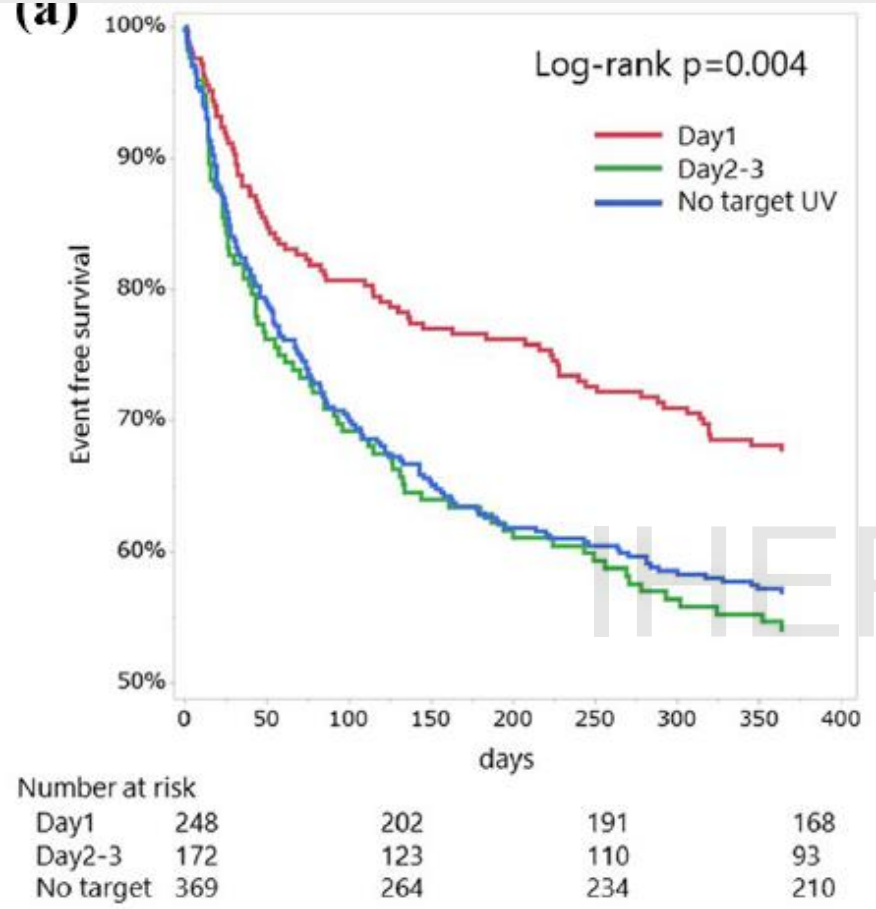
This is multicenter retrospective study included 1670 patients who were admitted for ADHF and received intravenous furosemide within 1 h of presentation.

Table 4 PDR score and risk group

	Points
Risk factor	
Duration since previous heart failure at discharge < 3 months	1
Loop diuretics at admission	1
eGFR <45 mL/min/1.73 m^2	1
Total points	3
Risk group	
Low risk	0
Middle risk	1
High risk	2–3

eGFR estimated glomerular filtration rate, *PDR* Preventing poor DR during the hyperacute phase

Predictors – Multivariate Analysis	Odds Ratio	95% Confidence Interval	P-value
Duration since previous heart failure at discharge <3 months	2.78	1.34–5.83	**0.006**
Loop diuretics at admission	3.05	1.74–5.36	**<0.0001**
Uric acid > 8.0 mg/dL	1.83	0.93–3.62	0.08
Urea nitrogen > 23.0 mg/dL	0.77	0.39–1.49	0.44
eGFR < 45 mL/min/1.73 m^2	2.99	1.58–5.74	**0.0007**
NT-pro BNP > 7000 pg/mL	1.15	0.64–2.05	0.63



One-year composite of death or heart failure hospitalization.
T2TUV – Time to target rate of urine volume: 100 ml/h.

H. Takimura et al. International Journal of Cardiology

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Impact of the time-to-target rate of urine volume concept on the outcome of acute decompensated heart failure

Hideyuki Takimura *, Rintaro Taniguchi, Ippei Tsuzuki, Emi Tajima, Yukihiro Yamaguchi, Mami Kawano, Yukako Takimura, Satoru Nishio, Masatsugu Nakano, Reiko Tsukahara

Department of Cardiology, Tokyo General Hospital, Tokyo, Japan

PATIENTS WITH T2TUV (100 ML/H) OF <24 H HAVE LOWER ALL-CAUSE MORTALITY AND READMISSION RATES AT 1 YEAR AND LOWER WRF AND HOSPITAL LENGTH OF STAY

Clinical outcomes of patients.

	day1 (n = 248)	day 2–3 (n = 172)	No target UV (n = 369)	p value
Worsening of renal function within 48 h	43 (25.6%)	34 (28.1%)	94 (44.1%)	0.0002
Length of hospitalization, days	15.2 ± 8.3	19.2 ± 17.7	19.7 ± 16.2	0.0005

Early administration of tolvaptan is demonstrated to be one of the factors to obtain T2TUV (100 ml/h) in <24 h

Univariable and multivariable predictors of the time to target UV at day1.

	Univariate analysis			Multivariate analysis		
	OR	95%CI	p value	adjusted OR	95%CI	p value
Age (years old)	1.03	1.01–1.04	0.0001	1.02	1.01–1.04	0.007
Previous hospitalized heart failure	1.38	1.01–1.90	0.05	1.47	1.03–2.12	0.03
Chronic kidney disease	1.47	1.05–2.04	0.03			
eGFR (per −10 ml/min/1.73 m2)	1.11	1.04–1.19	0.004			
NT-pro BNP (per 1000 pg/ml)	1.02	1.01–1.04	0.008	1.02	1.01–1.04	0.007
Carperitide	0.73	0.52–1.00	0.05	0.69	0.48–0.99	0.05
Tolvaptan	0.72	0.53–0.98	0.04			
Early administration of Tolvaptan	0.6	0.44–0.82	0.001	0.60	0.42–0.85	0.004

eGFR = estimated glomerular filtration rate; NT-pro BNP = N-terminal pro-brain natriuretic peptide.

Early administration of Tolvaptan is a contributing factors to achieve T2TUV (100 ml/h) in <24 h

+

T2TUV (100 ml/h) is effective in determining the efficacy of diuretic therapy in acute heart failure

=

Early administration of Tolvaptan contributes to efficacy of diuretic therapy in acute heart failure

Early administration of Tolvaptan is defined as administration of TLV within 6 h of treatment initiation.

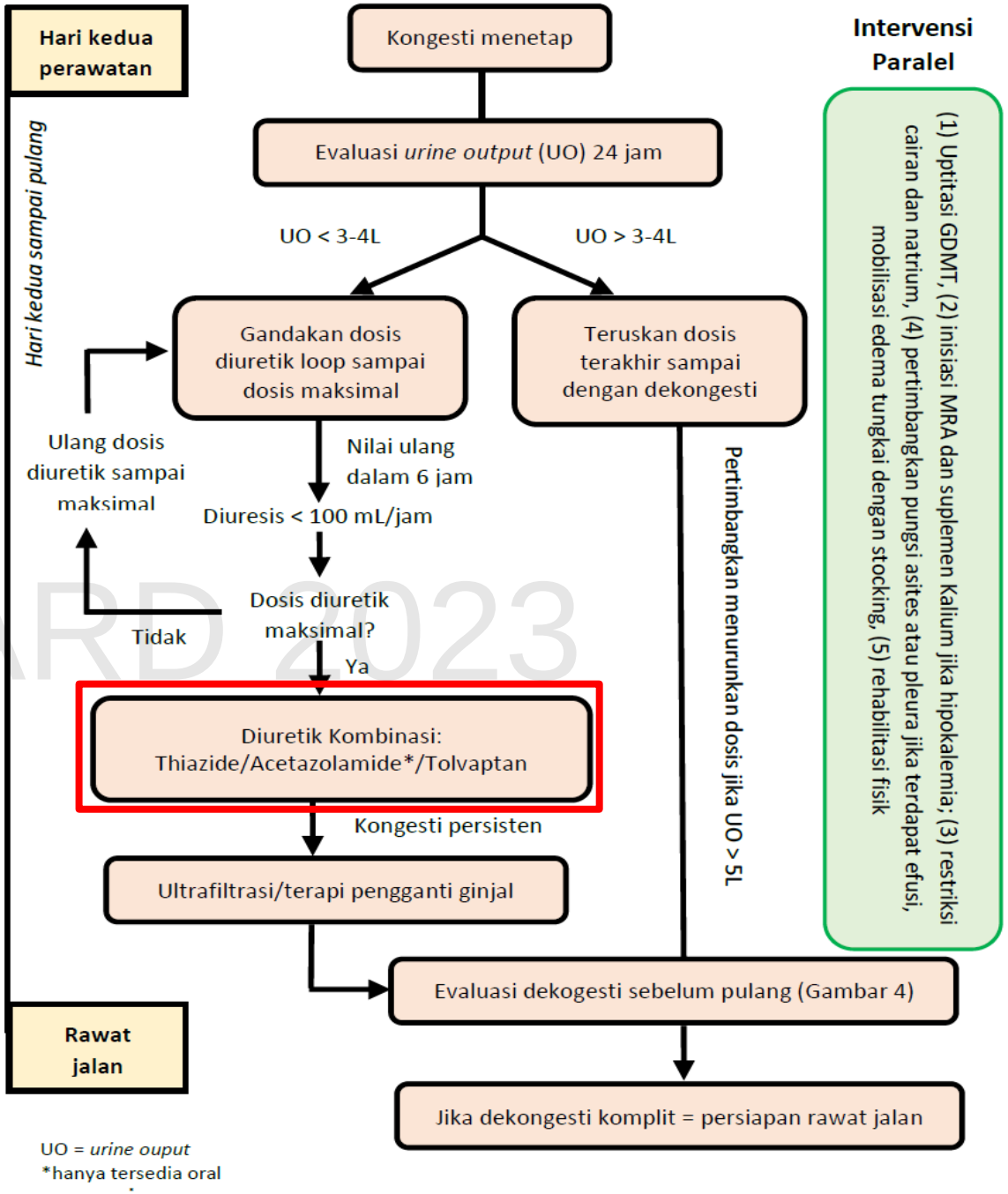
H. Takimura et al. International Journal of Cardiology

KONSENSUS
TATALAKSANA CAIRAN PADA GAGAL JANTUNG

InaHF & Car Met

Disusun oleh:

KELOMPOK KERJA
GAGAL JANTUNG DAN PENYAKIT KARDIOMETABOLIK
PERHIMPUNAN DOKTER SPESIALIS KARDIOVASKULAR INDONESIA
2020



Gambar 6. Algoritma setelah 24 jam

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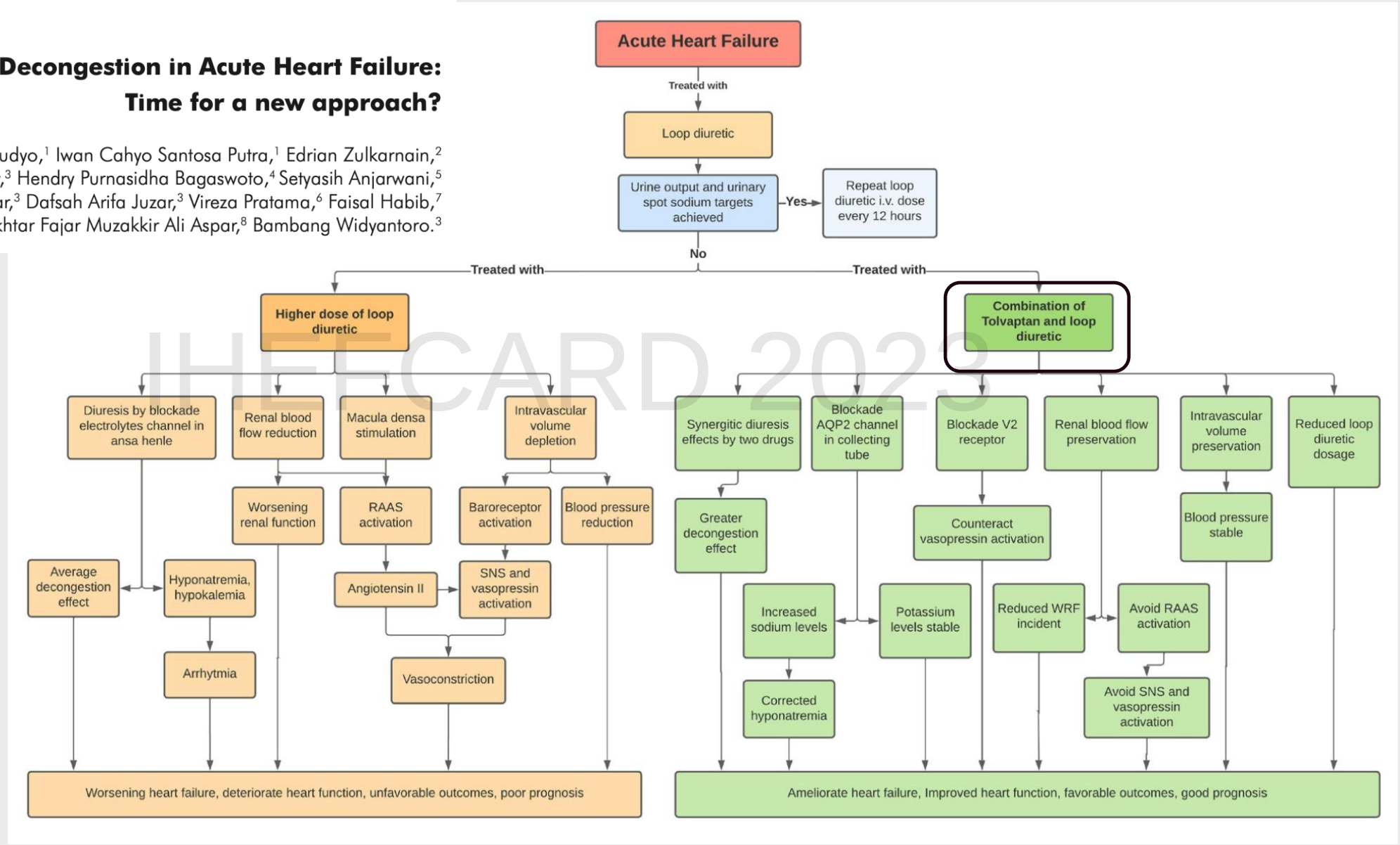
Review

Management of Decongestion in Acute Heart Failure: Time for a new approach?

Miftah Pramudyo,[1] Iwan Cahyo Santosa Putra,[1] Edrian Zulkarnain,[2] Siska Suridanda Danny,[3] Hendry Purnasidha Bagaswoto,[4] Setyasih Anjarwani,[5] Irmalita Mazwar,[3] Dafsah Arifa Juzar,[3] Vireza Pratama,[6] Faisal Habib,[7] Akhtar Fajar Muzakkir Ali Aspar,[8] Bambang Widyantoro.[3]



ESC HEART FAILURE
ESC Heart Failure 2021; **8**: 204–221
Published online 9 December 2020 in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/ehf2.13139

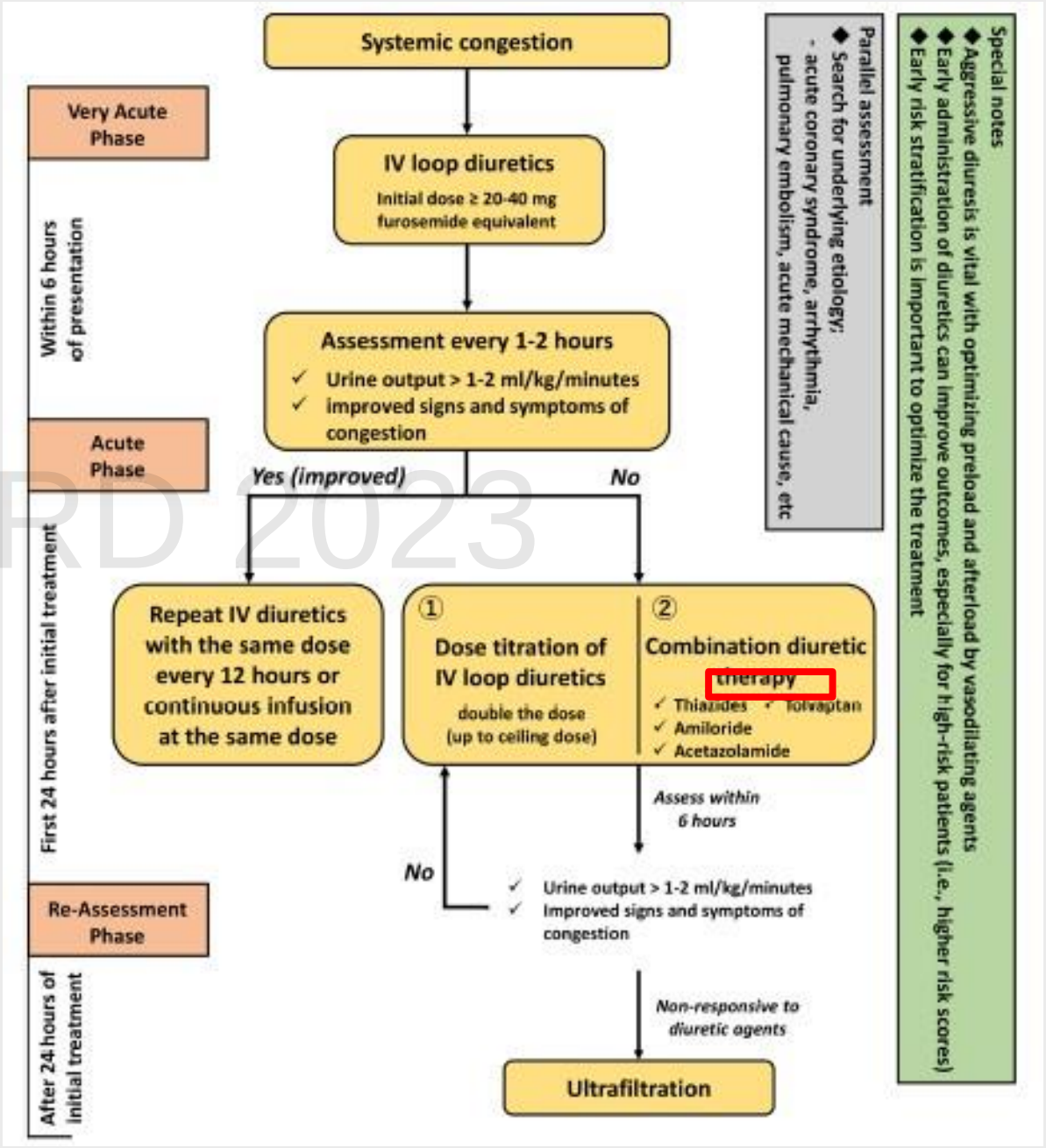
REVIEW

Time-sensitive approach in the management of acute heart failure

Yasuyuki Shiraishi[1], Masataka Kawana[2], Jun Nakata[3], Naoki Sato[4], Keiichi Fukuda[1] and Shun Kohsaka[1]*

[1]*Department of Cardiology, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo, 160-8582, Japan;* [2]*Department of Medicine, Division of Cardiovascular Medicine, Stanford University, Stanford, CA, USA;* [3]*Division of Intensive and Cardiovascular Care Unit, Department of Cardiology, Nippon Medical School Hospital, Tokyo, Japan;* [4]*Department of Cardiovascular Medicine, Kawaguchi Cardiovascular and Respiratory Hospital, Saitama, Japan*

- Proposed timing to initiate aquaretic (tolvaptan) in acute heart failure is **after 6 hours of failure with loop diuretics**



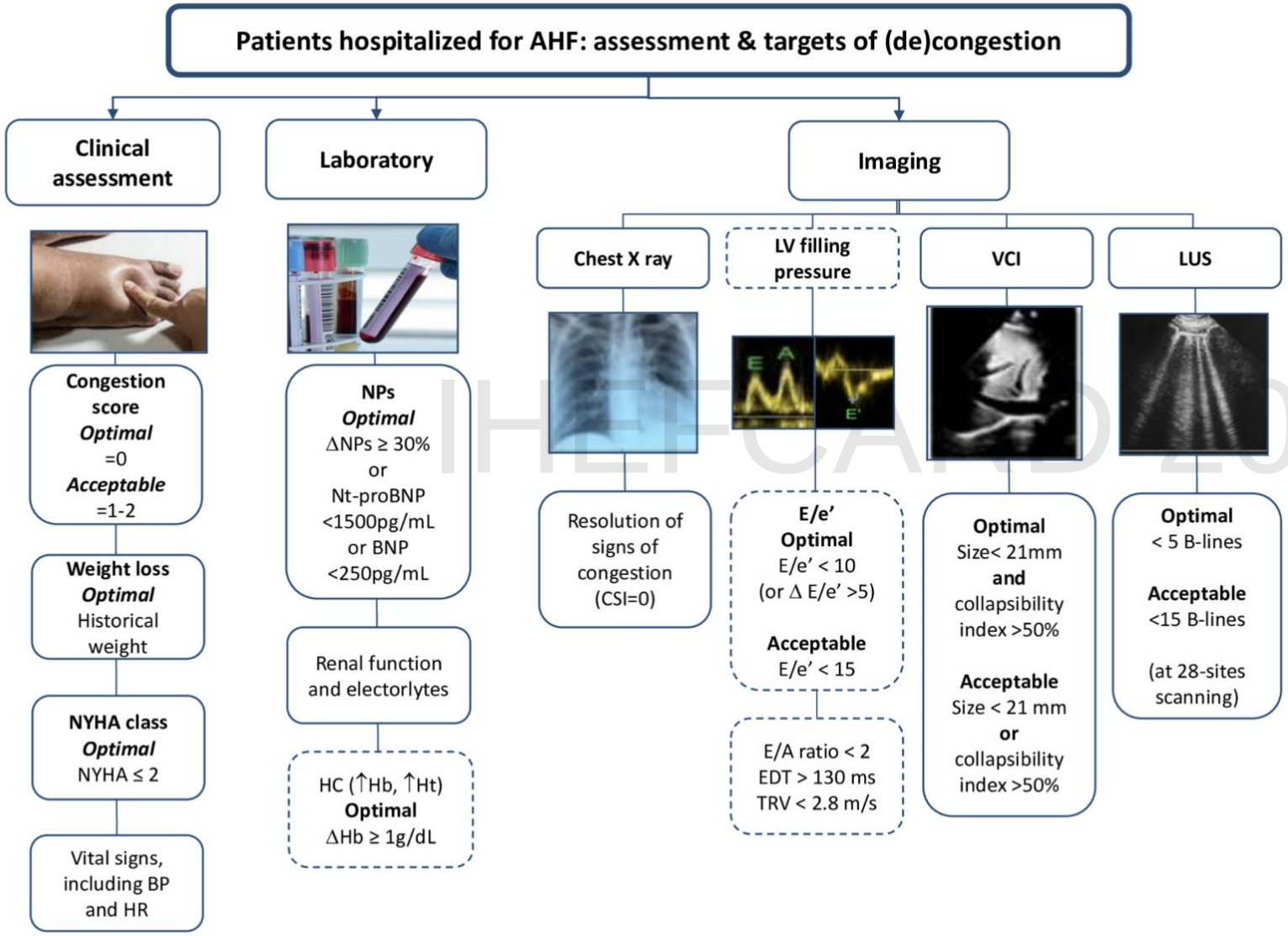
TAKE HOME MESSAGE

- Need deep understanding of tissue and vascular congestion to provide the best treatment for heart failure
- There are some diuretic limitations
- The use of tolvaptan in acute heart failure inpatient cases is proven to be effectively improve congestive symptoms
- Evolving guidelines suggest earlier tolvaptan initiation
- The emergence of validated novel tools and concepts with a more patient-centered approach can improve the efficacy of diuretic therapy in acute heart failure
- Early initiation of tolvaptan has been shown to contribute to the efficacy of diuretic therapy in acute heart failure and overall outcomes (significant diuretic response/greater urine volume and prevent WRF, lower mortality and readmission rates, and lower hospital stay)

IHEFCARD 2023

THANK YOU

BAMBANG.WIDYANTORO@PJNHK.GO.ID



Proposed algorithm for better assessment of congestion status in Acute Heart Failure*

*proposed by authors

Metra M, et.al. Eur J Heart Failure 2023
doi: 10.1002/ejhf.2888