The 4th Indonesian Symposium on Heart Failure and Cardiometabolic Disease

MASTERING ACUTE HF

Prime Time for Diuretic Combination

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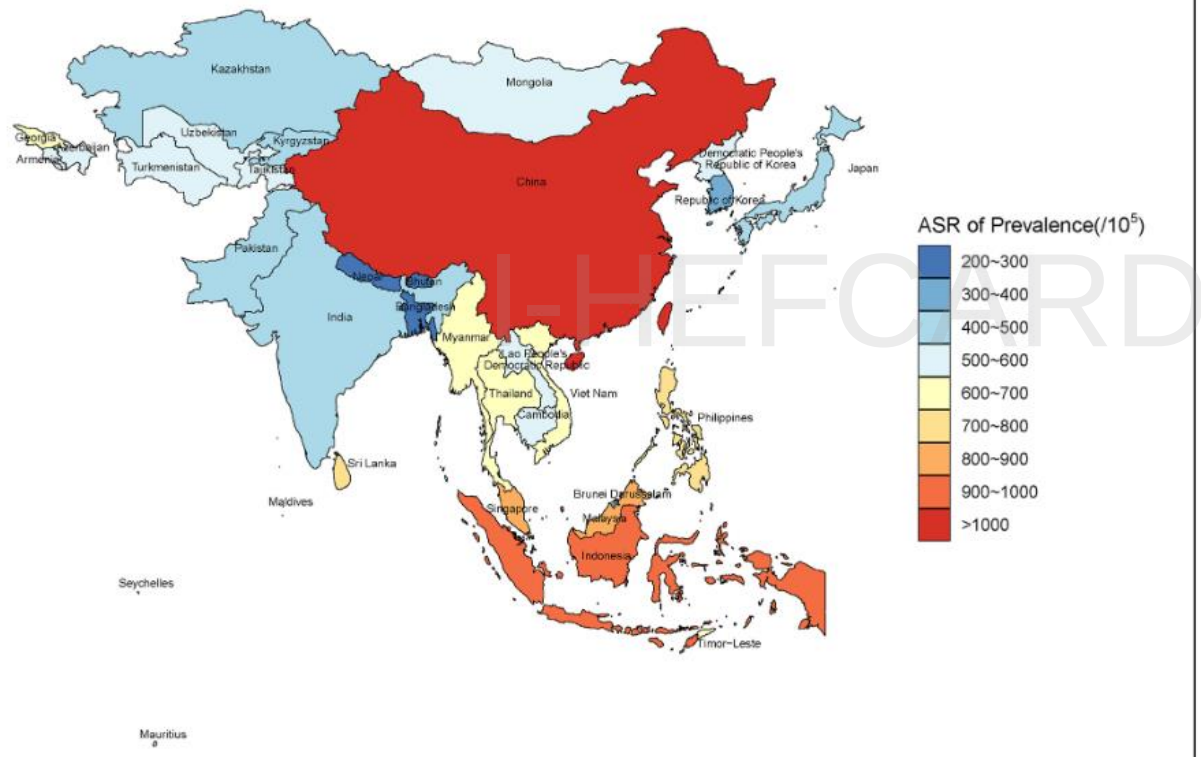
Disclosure

- **This is a session by PT OTSUKA Indonesia**
- Scientific speaker for :

  Servier, Novartis, Dexa Medica, Boehringer Ingelheim (ZPT), Bayer, Astra Zeneca, Otsuka, Menarini, Medtronic, Merck, Abbott

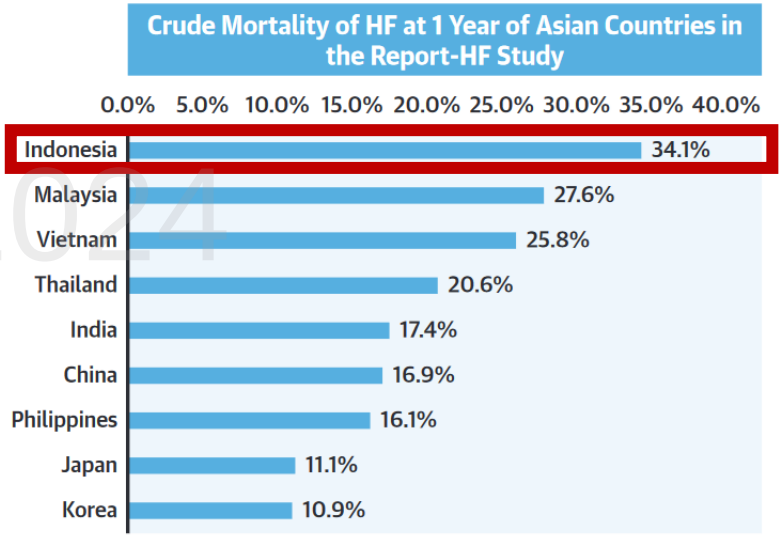
The Facts

FIGURE 1 **Age-Standardized Prevalence Rate of Heart Failure in Asia From GBD 2019**



From the GBD (Global Burden of Disease) data, the national and territorial age-standardized rate (ASR) of heart failure prevalence ranged from 211.86 to 1,032.84 cases per 100,000 population in Asia. China (1,032.84), Indonesia (900.90), and Malaysia (809.47) are the 3 highest nations in terms of ASR for prevalence of HF in 2019. Conversely, Nepal (211.86), Bhutan (255.54), and Bangladesh (275.00) reported the lowest rates.

The 1-Year Mortality of Asian HF Patients Is Still High, Especially in Southeast and South Asia: CV Death is the Primary Cause of Death for HF



Feng J, et al. JACC: Asia. 2024;4(4):249–264.

	Total (N=18 102)	Central and South America (n=2525)	Eastern Europe (n=2761)	Eastern Mediterranean region and Africa (n=2172)	North America (n=1565)	Southeast Asia (n=2292)	Western Europe (n=3489)	Western Pacific (n=3298)	p value*
(Continued from previous page)									
Medication at 6-month follow-up									
ACEi or ARB†	9189 (59%)	1272 (61%)	1704 (69%)	1140 (63%)	712 (53%)	876 (44%)	1923 (64%)	1562 (55%)	<0·0001
β blocker†	10 437 (67%)	1400 (67%)	1883 (76%)	1222 (68%)	1057 (78%)	925 (47%)	2330 (78%)	1620 (57%)	<0·0001
Diuretics†	11 176 (67%)	1345 (65%)	1923 (78%)	1376 (63%)	1078 (80%)	1326 (67%)	2516 (84%)	1614 (57%)	<0·0001
MRA†	6608 (43%)	9539 (45%)	1289 (52%)	573 (32%)	469 (35%)	528 (27%)	1411 (47%)	1399 (50%)	<0·0001
Length of stay, days†	8 (5–12)	8 (5–14)	9 (6–13)	6 (4–10)	6 (4–10)	6 (4–8)	9 (6–13)	9 (7–14)	<0·0001
1-year mortality	3461 (20%)	547 (23%)	439 (16%)	472 (22%)	324 (21%)	470 (21%)	668 (20%)	541 (17%)	<0·0001
Hospitalisation									
Hospitalised for any cause	6674 (38%)	799 (33%)	1062 (39%)	773 (36%)	955 (62%)	428 (19%)	1583 (47%)	1074 (34%)	<0·0001
Hospitalised for heart failure	3940 (22%)	482 (20%)	654 (24%)	478 (23%)	626 (41%)	240 (11%)	826 (24%)	634 (20%)	<0·0001
Death or heart failure hospitalisation	6928 (39%)	972 (40%)	1038 (38%)	913 (43%)	830 (54%)	673 (30%)	1395 (41%)	1107 (35%)	<0·0001

Data are n (%), unless otherwise stated. BMI=body-mass index. DCHF=decompensated chronic heart failure. NYHA=New York Heart Association. LVEF=left ventricular ejection fraction. JVP=jugular venous pressure. ACEi=angiotensin-converting enzyme inhibitor. ARB=angiotensin receptor blocker. MRA=mineralocorticoid receptor antagonist. *All comparisons p<0·001. †No data missing.

Table 1: **Differences between patients according to region**

Tromp J, et al. Lancet Glob Health 2020; 8: e411–22

RUMAH SAKIT UNS

Klinik Gagal Jantung Sebelas Maret

CORE - HF

2023 Interim Analysis

Drug Regiments

According to :

- 2021 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure
- 2021 CCS/CHFS Heart Failure Guidelines Update
- 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure

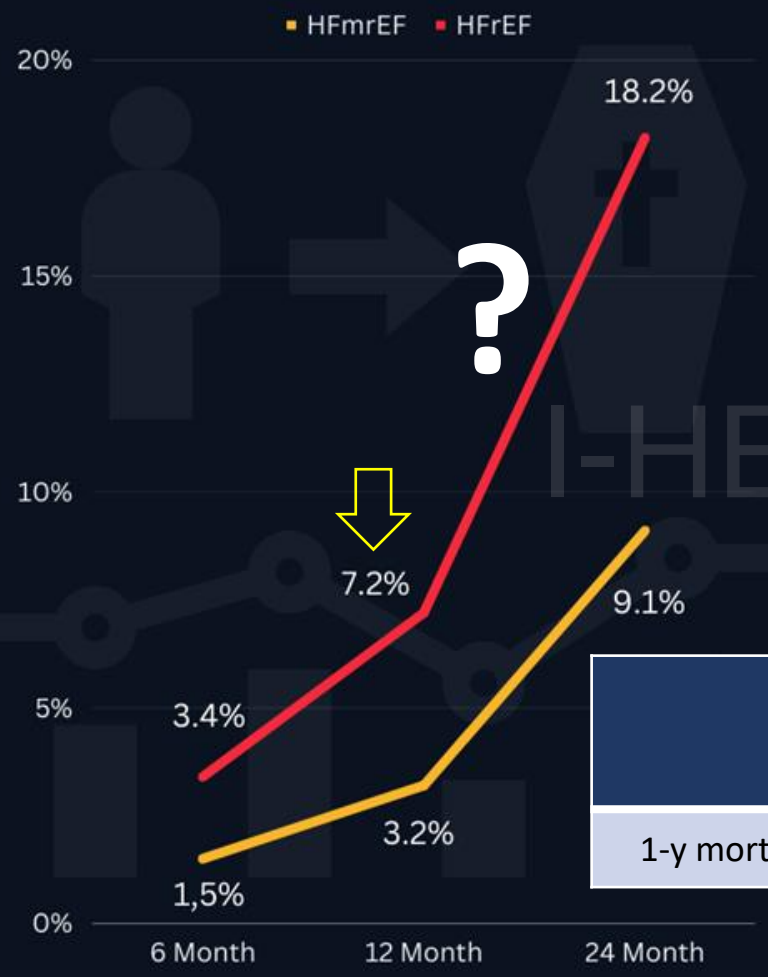
DRUG CLASS	HFmrEF			HFrEF		
	Initial	3 Mo (Opt.)*	12 Mo (Opt.)**	Initial	3 Mo (Opt.)^	12 Mo (Opt.)^^
ACE-Inhibitor				86.7%	82.6% (98.8%)	76.0% (98.4%)
ARB				8.9%	11.0% (83.7%)	17.6% (95.5%)
ARNI				4.4%	6.1% (54.2%)	6.0% (93.3%)
Beta-Rec. Blocker				98.5%	99.5% (84.6%)	99.6% (92.8%)
MRA	23.5%	34.5% (26.3%)	39.7% (41.9%)	48.7%	65.0% (51.6%)	70.4% (59.7%)

corehfrsuns@gmail.com

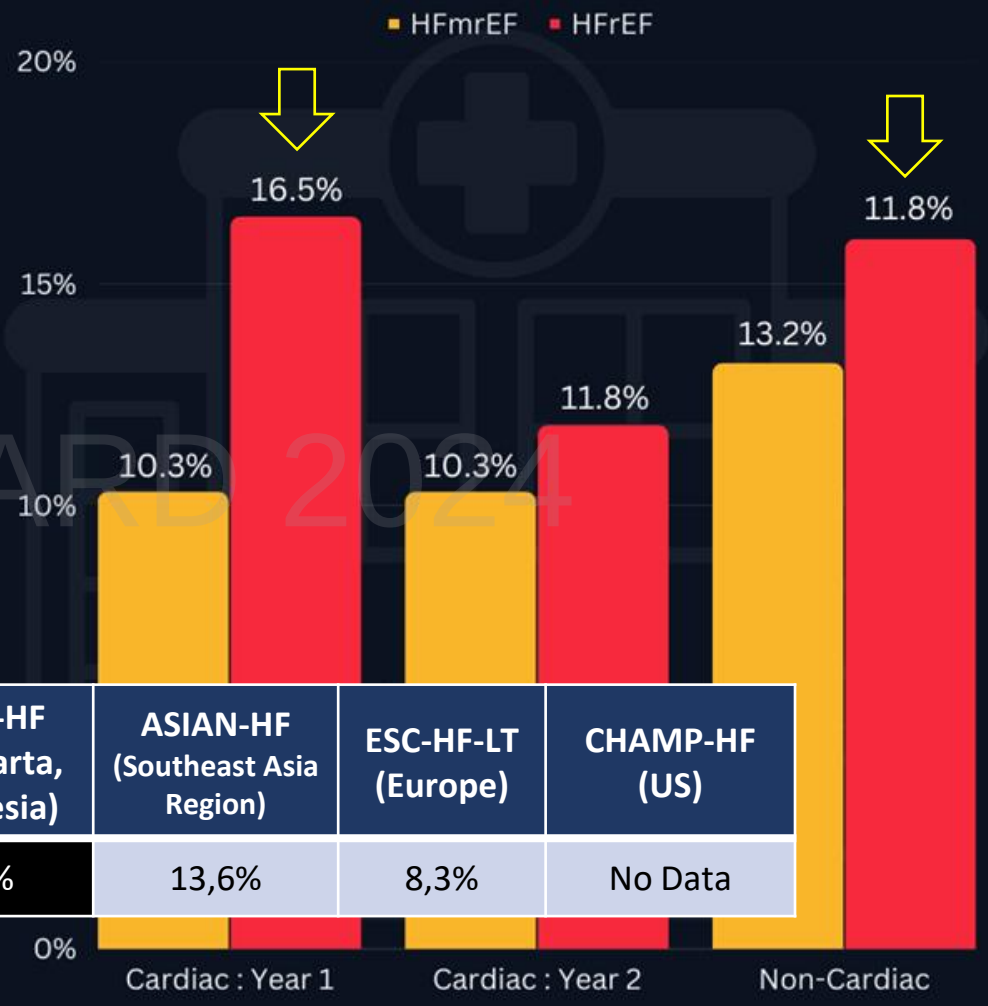
*110 Subjects ; **78 Subjects ; ^391 Subjects ; ^^250 Subjects

Outcome

2023 Interim Analysis



Cummulative All-Cause Mortality



Rehospitalization

	CORE-HF (Surakarta, Indonesia)	ASIAN-HF (Southeast Asia Region)	ESC-HF-LT (Europe)	CHAMP-HF (US)
1-y mortality	7,2%	13,6%	8,3%	No Data

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VERY IMPORTANT

3 major causes directly affect the rehospitalization in HF :

- Congestion
- Comorbidities
- Target Organ Damage

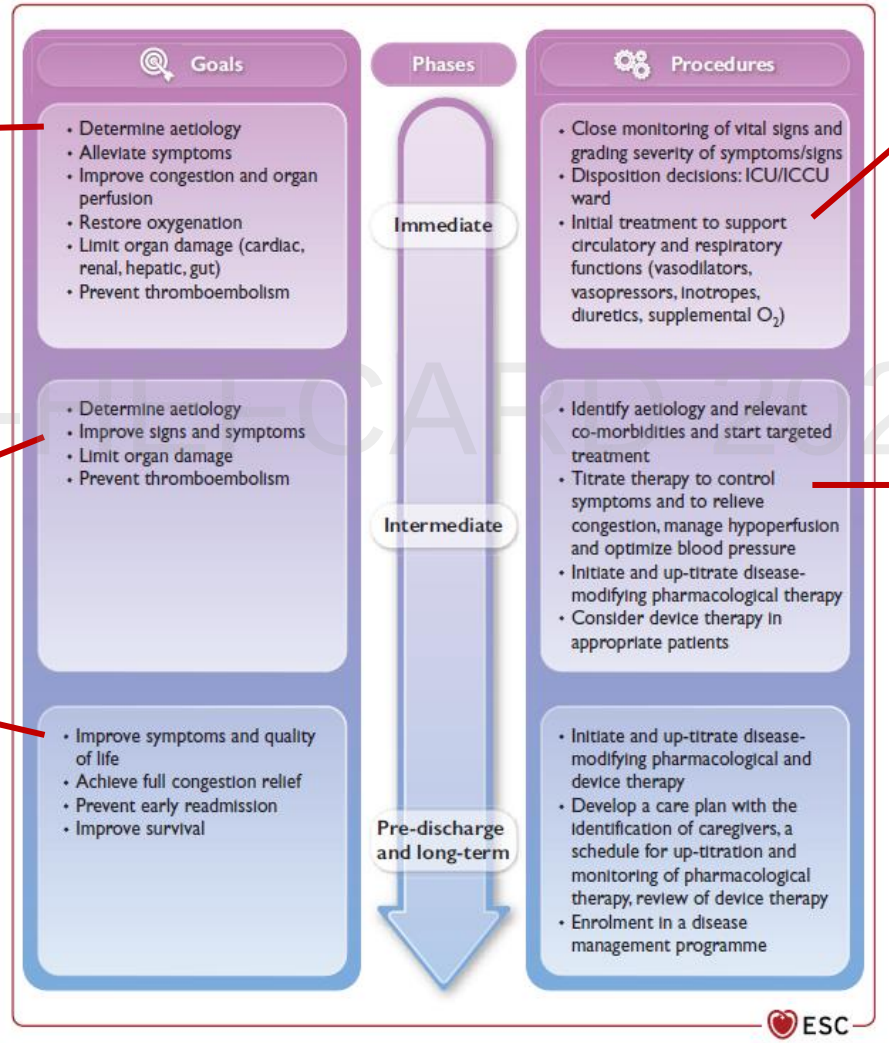
Mesquita, et al. Int J Cardiovasc Sci.2017;30(1):81-90

Acute HF: Decongestion Plays Essential Part!

- Alleviate symptoms
- Improve congestion and organ perfusion
- Restore oxygenation
- Limit organ damage (cardiac, renal, hepatic, gut)

- Improve signs and symptoms
- Limit organ damage

- Improve symptoms and quality of life
- Achieve full congestion relief



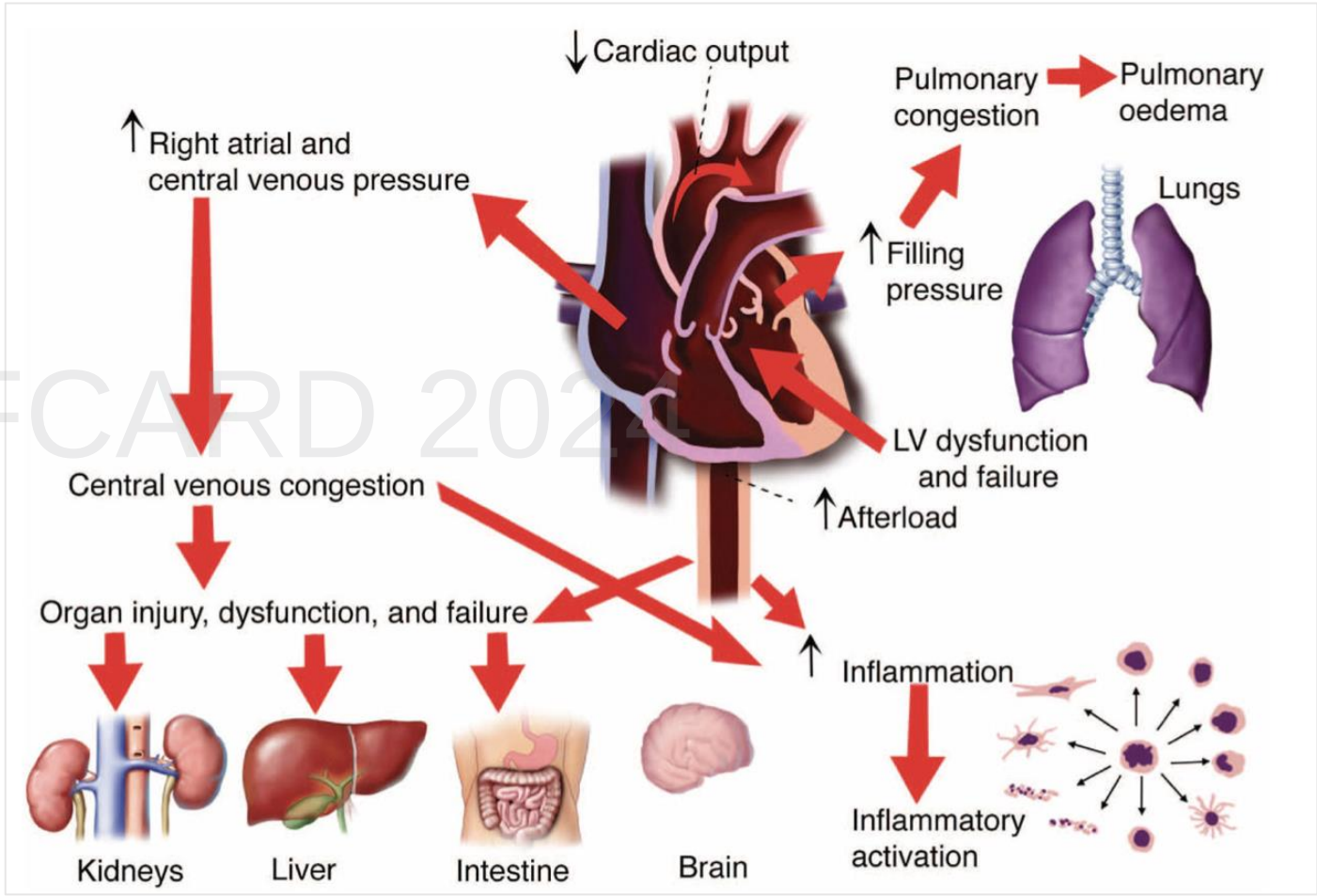
- Initial treatment to support circulatory and respiratory functions (vasodilators, vasopressors, inotropes, diuretics, supplemental O_2)

- Titrate therapy to control symptoms and to relieve congestion, manage hypoperfusion and optimize blood pressure

ESC HF guidelines, 2021

How Crucial is Congestion?

causes **Multi Organ Dysfunction**

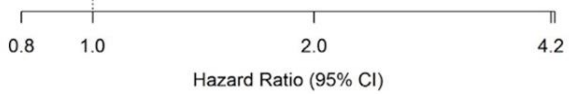


European Journal of Heart Failure (2017) 19, 821–836

One-Year Mortality After Intensification of Outpatient Diuretic Therapy

Christian Madelaire, MD; Finn Gustafsson, MD, PhD, DMSc; Lynne Warner Stevenson, MD; Søren Lund Kristensen, MD, PhD; Lars Køber, MD, DMSc; Julie Andersen, MScPH; Maria D'Souza, MD, PhD; Tor Biering-Sørensen, MD, PhD; Charlotte Andersson, MD, PhD; Christian Torp-Pedersen, MD, DMSc; Gunnar Gislason, MD, PhD; Morten Schou, MD, PhD

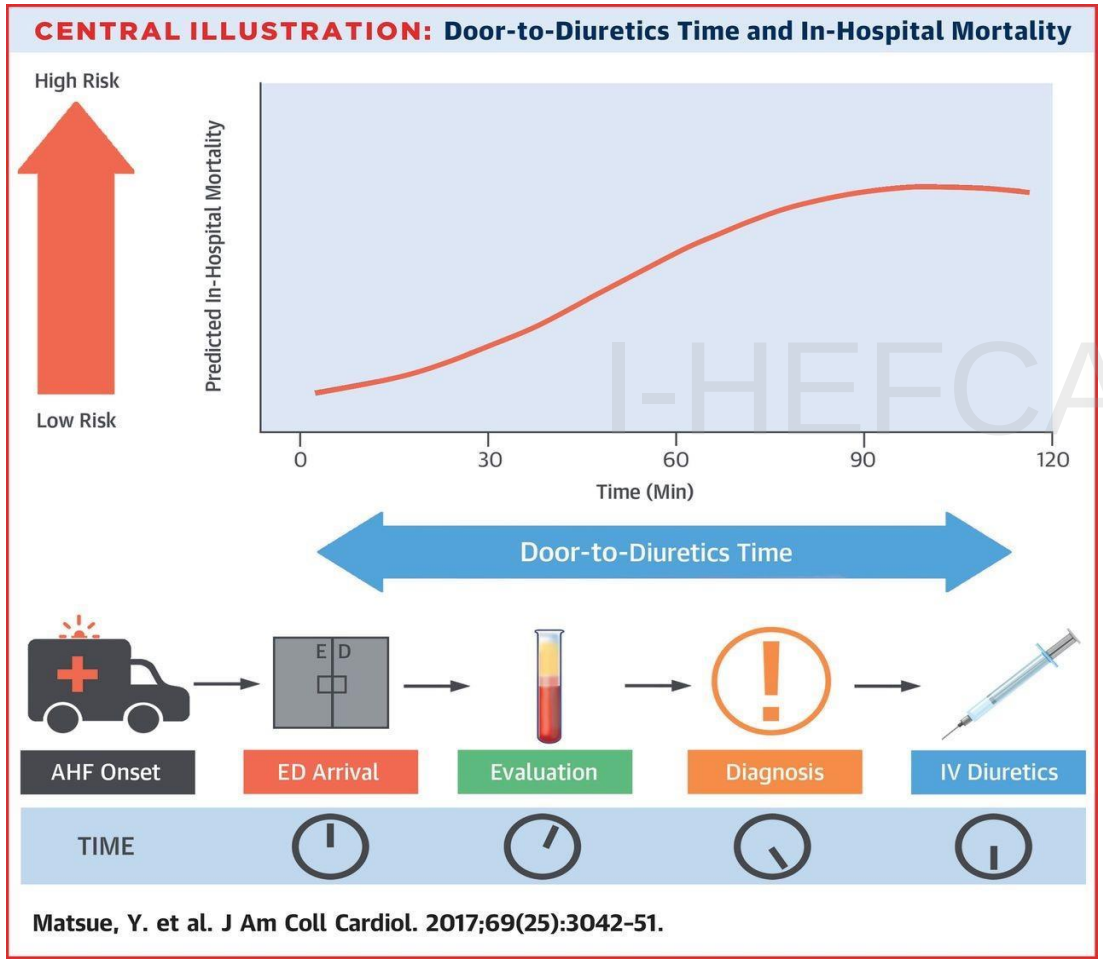
Time since HF diagnosis	Event	$N_{patients}$	N_{deaths} (%)	Hazard ratio (95%-CI)	P-value
Year 1	No worsening	53,794	3,944 (7.3)	1	
	HF hospitalization	3,160	420 (13.3)	1.88(1.70-2.08)	<0.001
	Diuretic intensification	4,517	567 (12.6)	1.49(1.36-1.62)	<0.001
	Both events	942	176 (18.7)	2.31(1.99-2.69)	<0.001
Year 2	No worsening	41,557	2,897 (7.0)	1	
	HF hospitalization	1,122	195 (17.4)	2.39(2.07-2.77)	<0.001
	Diuretic intensification	2,575	357 (13.9)	1.67(1.50-1.87)	<0.001
	Both events	426	83 (19.5)	2.33(1.87-2.90)	<0.001
Year 3	No worsening	32,393	2,340 (7.2)	1	
	HF hospitalization	719	120 (16.7)	2.06(1.71-2.47)	<0.001
	Diuretic intensification	1,800	233 (13.0)	1.48(1.29-1.69)	<0.001
	Both events	285	68 (23.9)	2.95(2.31-3.75)	<0.001
Year 4	No worsening	24,956	1,679 (6.7)	1	
	HF hospitalization	525	90 (17.1)	2.23(1.80-2.76)	<0.001
	Diuretic intensification	1,244	171 (13.8)	1.68(1.44-1.97)	<0.001
	Both events	225	55 (24.4)	3.24(2.48-4.25)	<0.001
Year 5	No worsening	19,185	1,323 (6.9)	1	
	HF hospitalization	348	61 (17.5)	2.19(1.69-2.84)	<0.001
	Diuretic intensification	931	155 (16.7)	1.99(1.68-2.36)	<0.001
	Both events	155	30 (19.4)	2.15(1.49-3.09)	<0.001



CONCLUSIONS: In a nationwide cohort of patients with HF, outpatient intensification events were associated with almost 2-fold risk of mortality during the next year. Although HF hospitalization was associated with a higher risk, the need to intensify diuretics in the outpatient setting is a signal to review and intensify efforts to improve HF outcomes.

J Am Heart Assoc. 2020 Jul 21;9(14):e016010.

How Fast should we respond?



Matsue, Y. et al. J Am Coll Cardiol. 2017;69(25):3042-51.

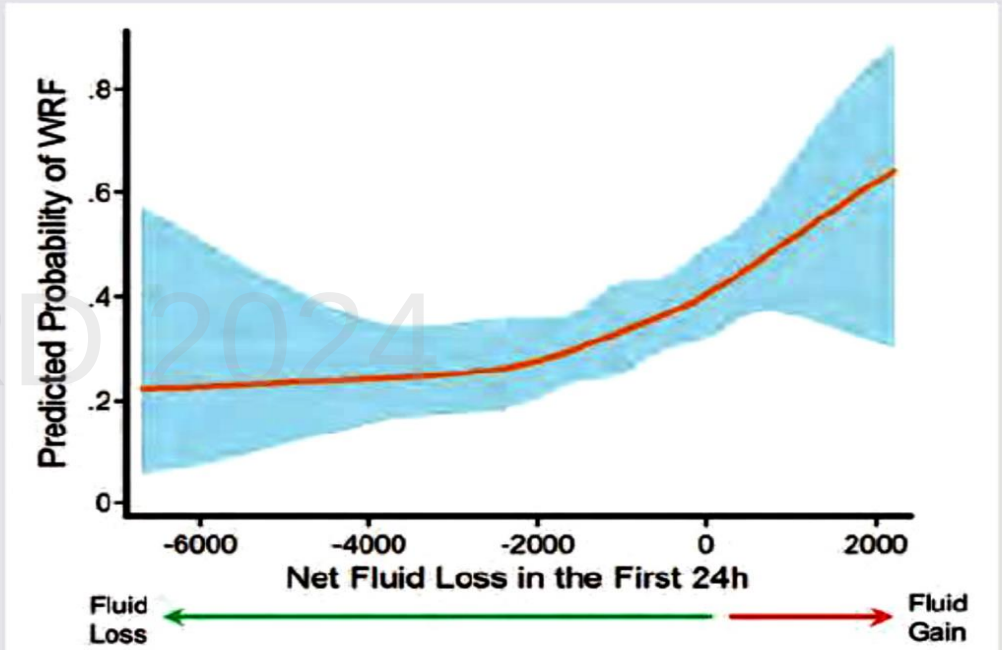


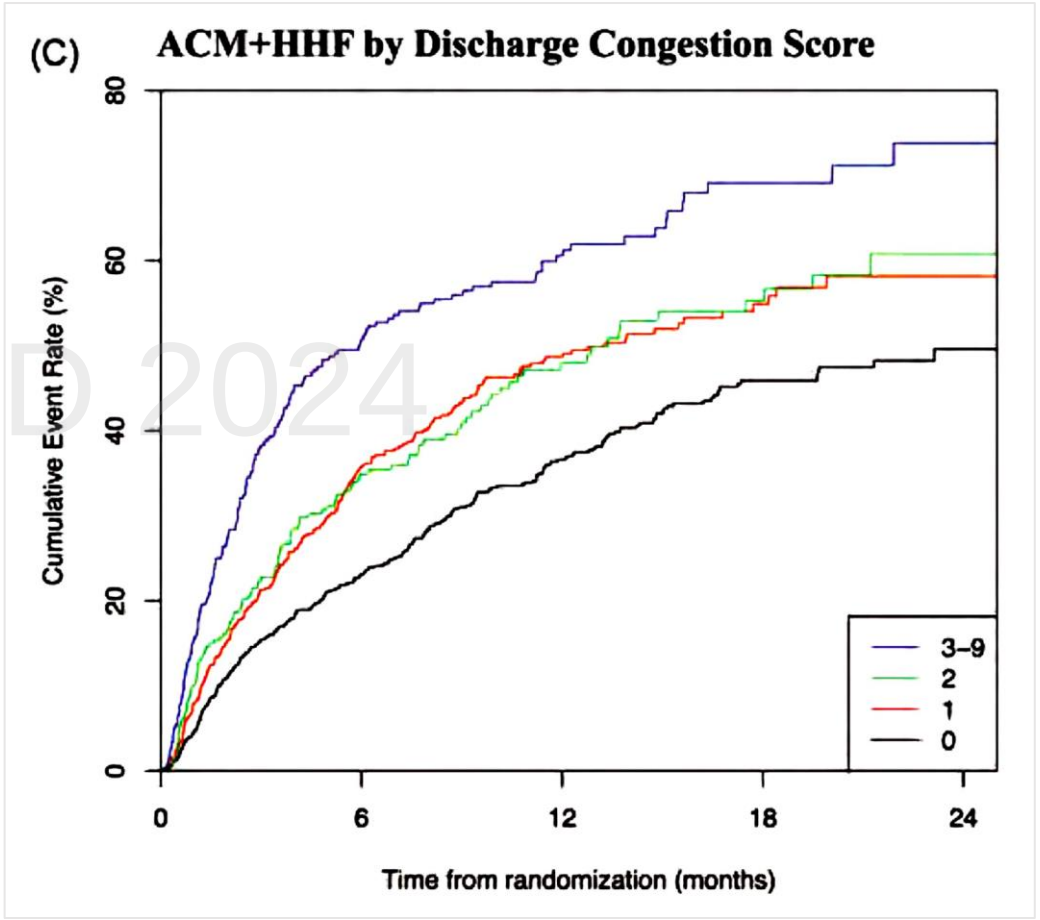
Figure 1 Cubic spline analysis of the probability of worsening renal function (WRF) and net fluid loss. The blue area represents the pointwise 95% confidence interval. Negative numbers on the *x*-axis indicate net fluid loss.

Eur J Heart Fail 2013; 15: 637-43

How Clean should we made?

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†

Cumulative incidence of all-cause mortality + hospitalization for heart failure by composite congestion score at discharge/day 7.



Eur Heart J. 2013 Mar;34(11):835-43. doi: 10.1093/eurheartj/ehs444. Epub 2013 Jan 4

Congestion Evaluation

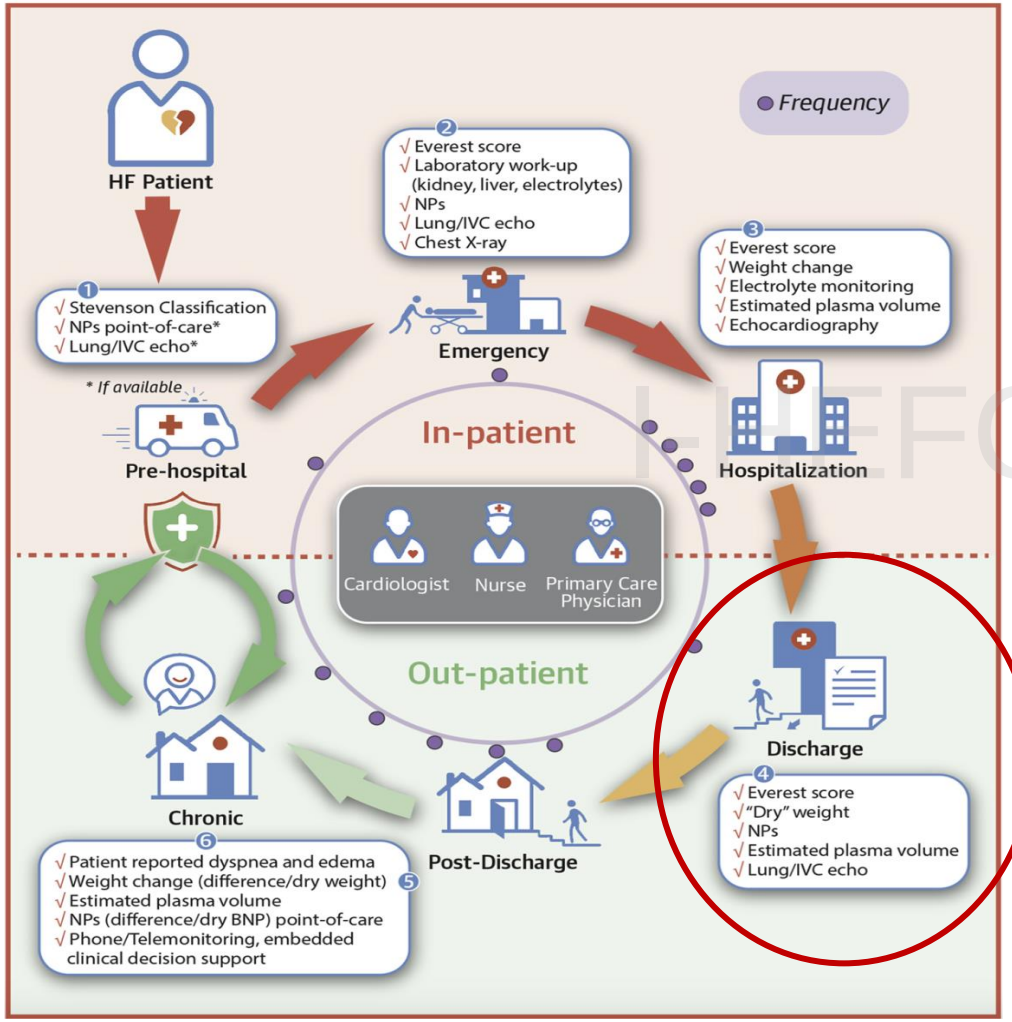


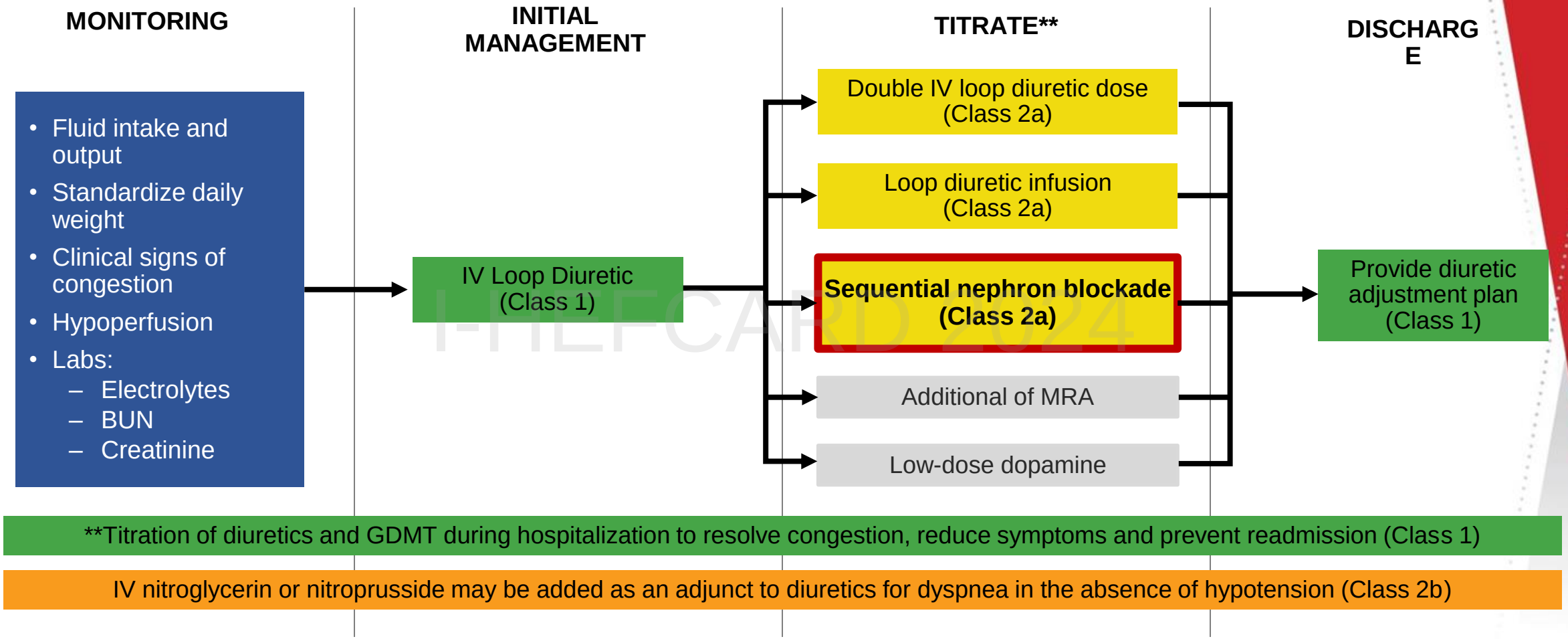
TABLE 2 Selected Set of Decongestion Targets at Discharge From Hospitalization for Worsening Heart Failure

Congestion Parameter	Target at Discharge	Reference
Clinical tools		
EVEREST score	≤2	Ambrosy et al. (2).
NYHA functional class	≤2	Salah et al. The ELAN-HF study. Heart 2014;100:115-25
Biomarkers		
NT-proBNP	>30% drop during hospitalization Discharge value <1,500 pg/ml	McQuade et al. (28). Salah et al. The ELAN-HF study. Heart 2014;100:115-25 and Kociol et al. The DOSE-AHF trial. Circ Heart Fail 2013;6:240-5
BNP	Discharge value <250 pg/ml	McQuade et al. (28)
Hemoglobin	>10 g/l increase during hospitalization	Van der Meer et al. The PROTECT trial. J Am Coll Cardiol 2013;61:1973-81
Imaging tools		
IVC imaging	Maximum diameter <2.1 cm IVC collapsibility index >50%	Goonewardena et al. J Am Coll Cardiol Img 2008;1:595-601
Lung ultrasound	<30 us-B lines	Coiro et al. (3) and Gargani. Cardiovasc Ultrasound 2015;13:40

IVC = inferior vena cava; NYHA = New York Heart Association; us = ultrasound.

Girerd N, et al.J Am Coll Cardiol.2018

Decongestion **Strategy**



Abbreviations: BUN indicates blood urea nitrogen; GDMT, guideline-directed medical therapy IV, intravenous; and MRA; mineralocorticoid.

American Heart Association.

Diuretic in Acute HF

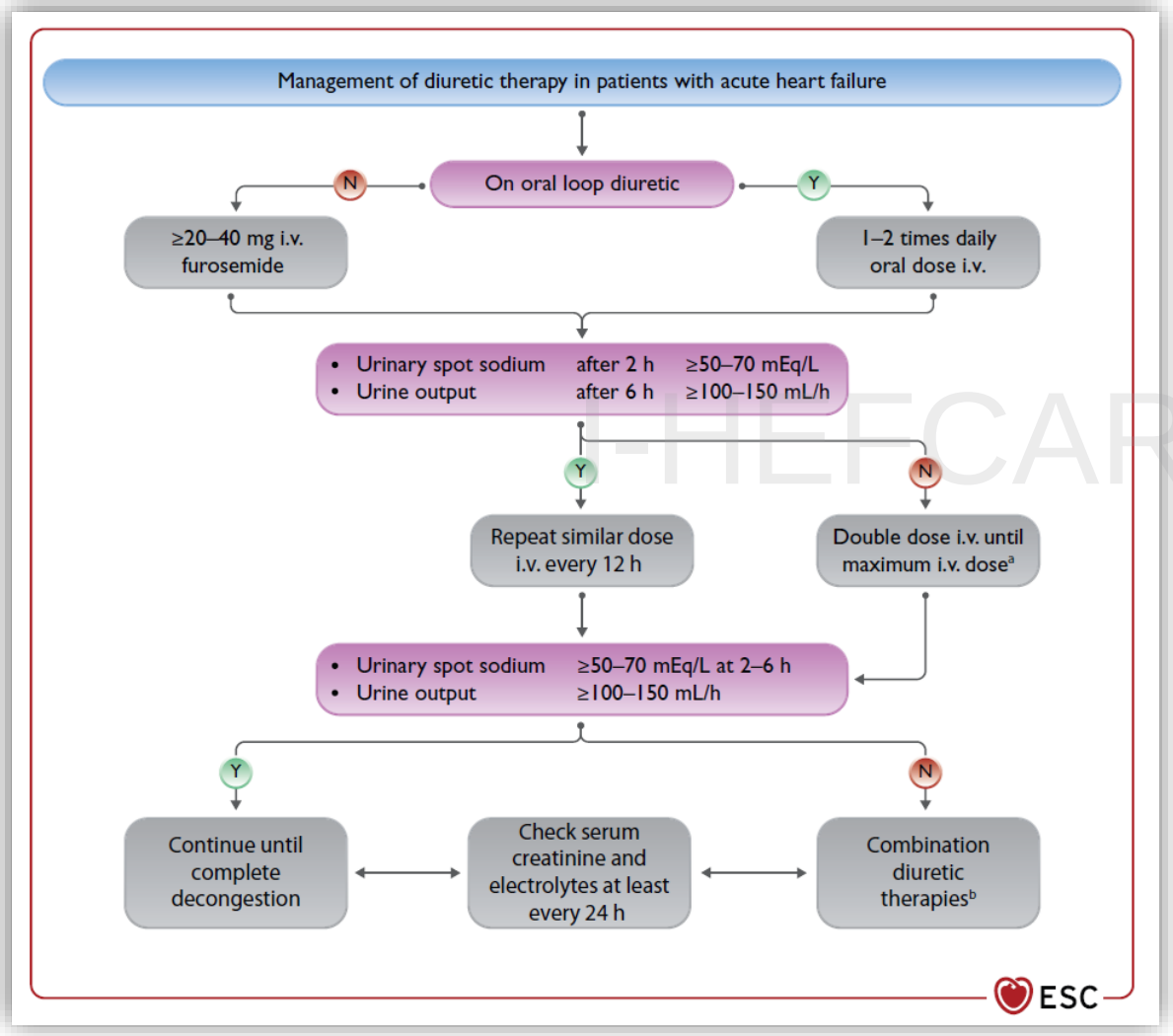


TABLE 1 Pharmacokinetic and Pharmacodynamic Properties of Common Loop Diuretics

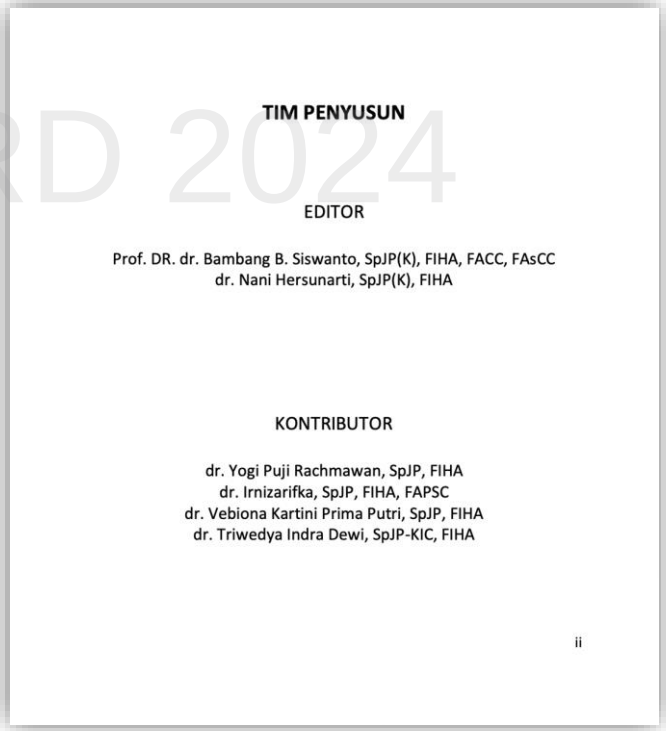
	Furosemide	Bumetanide	Torsemide
Relative IV potency, mg	40	1	20
PO to IV conversion, approximate	2:1	1:1	1:1
Bioavailability, %	10–100 (average = 50)	80–100	80–100
Initial outpatient PO dose, mg	20–40	0.5–1	5–10
Maintenance outpatient PO dose, mg	40–240	1–5	10–20
Maximum daily IV dose, mg*	600	10	200
Onset, min			
Oral	30–60	30–60	30–60
IV	5	2–3	10
Peak serum concentration after PO administration, h	1	0.5–2	0.5–2
Affected by food	Yes	Yes	No
Metabolism	50% renal conjugation	50% hepatic	80% hepatic
Half-life, h			
Normal	1.5–2	1	3–4
Renal dysfunction	2.8	1.6	4–5
Hepatic dysfunction	2.5	2.3	8
HF	2.7	1.3	6
Average duration of effect, h	6–8	4–6	6–8

A] The maximal daily dose for i.v. loop diuretics is generally considered furosemide 400-600 mg, though up to 1000 mg may be considered in patients with severely impaired kidney function.

B] Combination therapy is the addition to the loop diuretic of a diuretic with a different site of action, e.g. thiazides or metolazone or acetazolamide.

European Heart Journal, Volume 42, Issue 36, 2021, Pages 3599–3726.

Available at https://inahfcarmet.org



TIM PENYUSUN

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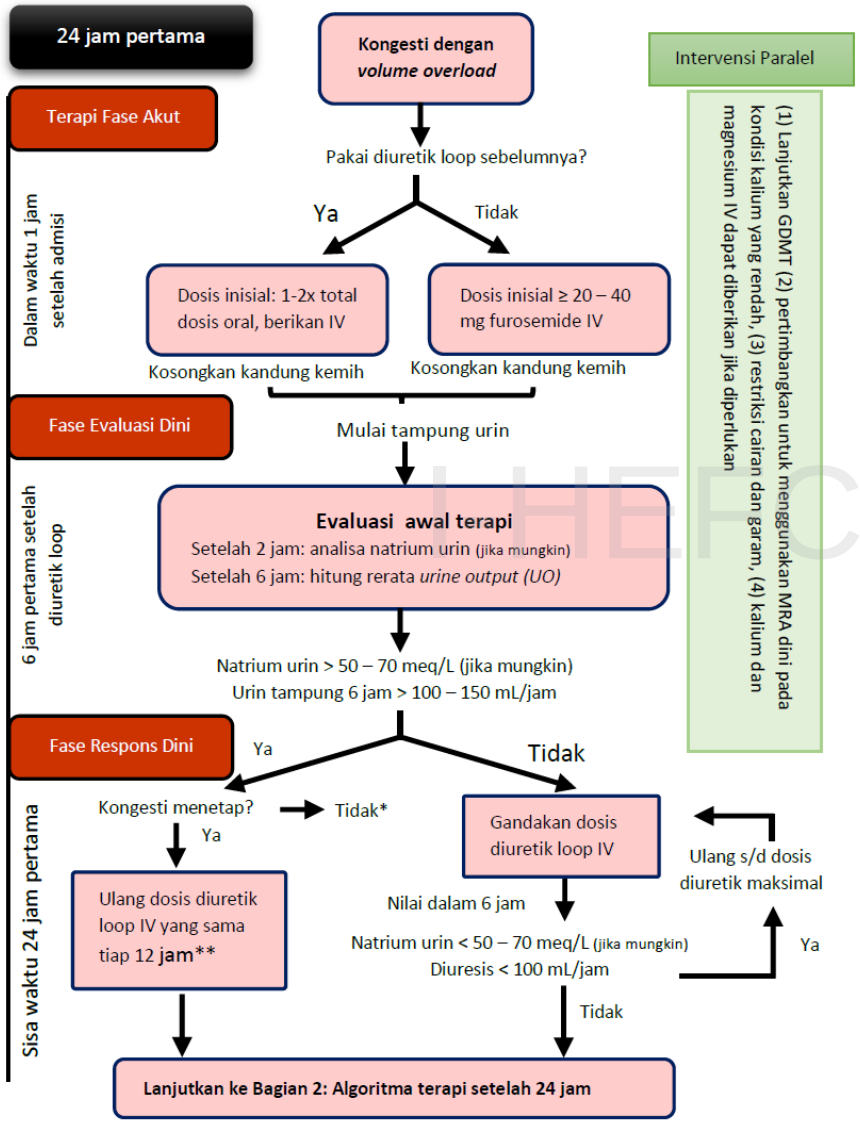


Is Furosemide enough?

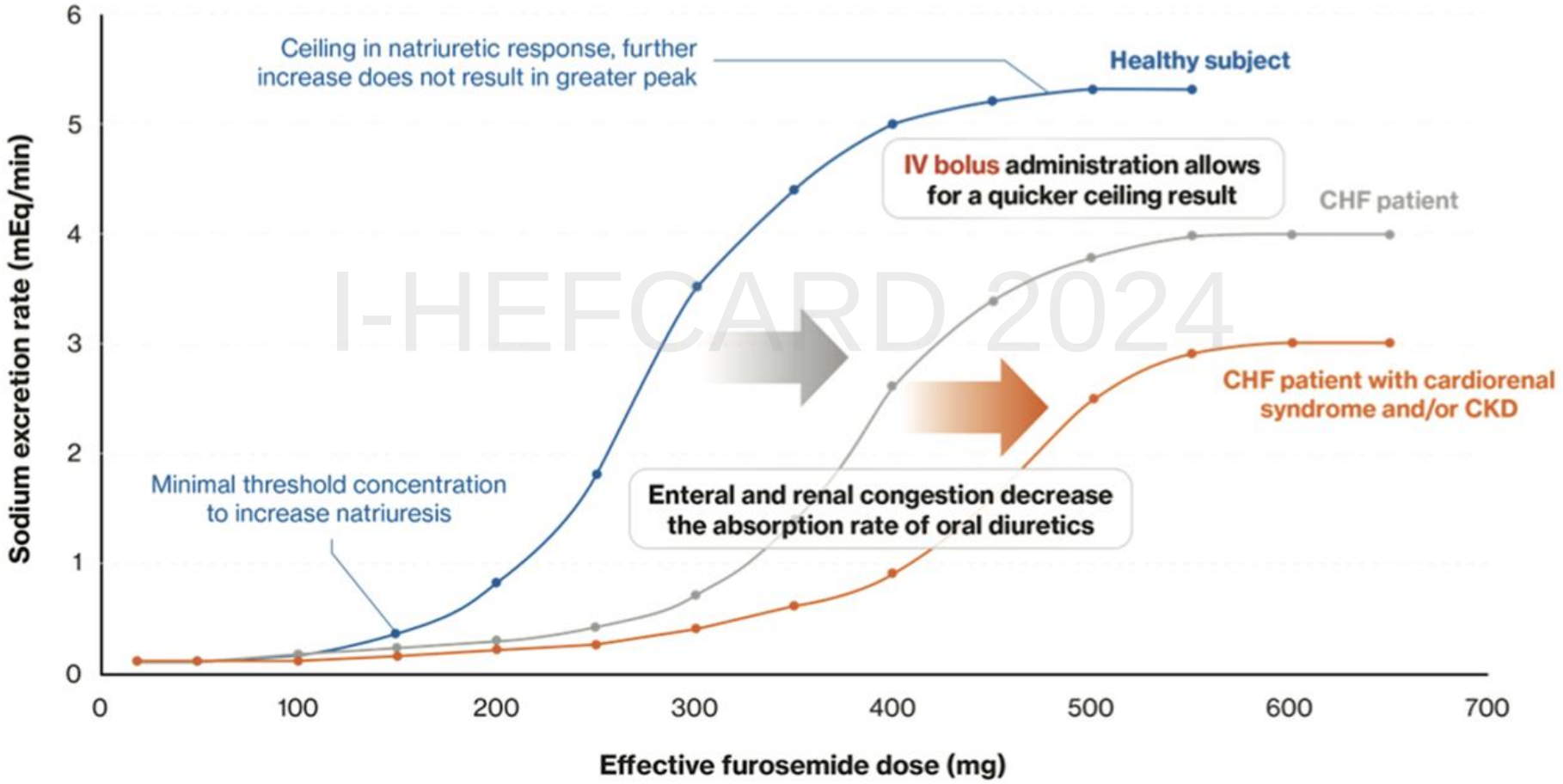
Table 2 Summary of Reviewed Studies in Heart Failure Patients

First Author (Ref. #), Year	Patients	Design	TD Dose	LD Dose	Benefits	Adverse Events
Robson et al. (18), 1964	1 CHF	Observational	HCTZ 100 mg IV	FSM 50–100 mg IV + 1–5 mg/min	None	Not reported
Dettli and Spring (17), 1966	18 mixed edematous	Observational	HCTZ 200 mg	FSM 30–240 mg/day	Improved diuresis, similar to 4× higher FSM dose	Hypochloremic alkalosis + hypokalemia
Olesen et al. (19), 1970	24 CHF	Randomized active-control	QEZ 50–100 mg/day	FSM 40–80 mg/day	Superior diuresis to doubled FSM dose in mild CHF only	Hypokalemia (−0.5 mEq/l) bigeminy
Olesen et al. (20), 1971a	12 CHF	Randomized active-control	QEZ 50 mg/day	FSM 40 mg/day	Doubled UNa, mean weight loss 0.5 kg/day	Not reported
Olesen et al. (21), 1971b	24 CHF	Randomized active-control	QEZ 50 mg/day BDFZ 5 mg/day	FSM 80 mg BID	Doubled UNa, weight loss ~0.7–0.8 kg/day	Hypokalemia (−0.3 mEq/l)
Beck and Asscher (22), 1971	1 CHF	Observational	MTZ 5 mg/day	FSM 80 mg/day	Clearance of edema	Hypokalemia
Gunstone et al. (23), 1971	13 CHF	Observational	MTZ 2.5–10 mg/day	FSM 120–400 mg/day	≥2 kg weight loss over 4 days in >2/3 overall	Azotemia in most patients, hypokalemia
Asscher (24), 1974	4 CHF	Observational	MTZ 5 mg/day	FSM ≥500 mg/day	Mean weight loss 8.1 kg	Hypokalemia
Sigurd et al. (25), 1975	18 CHF	Randomized active-control	BDFZ 5 mg/day	BMT 2 mg BID	Doubled UNa, mean weight loss 0.8 kg/day	Hypokalemia (−0.45 mEq/l)
Epste						
Ram						28%
Sigur						
Furre						
Ghos						
Allen						
Bamf						
Gross						
Gage				15 mg/week		%
Aravot et al. (35), 1989	12 CHF	Observational	MTZ 2.5–5 mg 2×/week	FSM 160 mg/day	Eliminated need for IV diuresis	Not reported
Friendland and Ledingham (36), 1989	1 ADHF	Observational	MTZ 5–10 mg/day	FSM 240 mg/day IV	16 kg weight loss	Not reported
Kiyingi et al. (37), 1990	10 CHF	Observational	BDFZ 10 mg/day	FSM 200–400 mg/day IV	Mean weight loss 7.7 kg	Hypokalemia (<2.9 mEq/l) in 20%
Channer et al. (38), 1990	17 ADHF	Observational	MTZ 1.25–10 mg/day	FSM 250–500 mg/day PO	Responders (71%) had mean 8.3 kg weight loss + d/c home	Hypokalemia, creatinine ↑ 25%
Kröger et al. (39), 1991	10 ADHF	Observational	MTZ 2.5–5 mg/day	FSM 80–500 mg/day	Mean 8.9 kg weight loss	Hyponatremia, hypokalemia
Dormans and Gerlag (40), 1993	8 CHF	Observational	HCTZ 25–100 mg/day	FSM 500– 4000 mg/day	Doubled UNa, mean 1.3 kg/day weight loss	Creatinine ↑ 50%, ClCr ↓ 33%, hypokalemia
Channer et al. (41), 1994	40 ADHF	Randomized active-control	MTZ 10 mg/day BDFZ 10 mg/day	FSM 80 mg IV BID	5–5.6 kg mean weight loss, hospital d/c in 90%	Hypokalemia (<3.5 mEq/l) in 65%
Mouallem et al. (42), 1995	32 ADHF	Observational	CTZ 500 mg/day	FSM 160–320 mg/day	Mean 4.8 kg weight loss, clearance of edema	Hypokalemia (−0.4 mEq/l)
Dormans and Gerlag (43), 1996	20 ADHF	Observational	HCTZ 25–100 mg/day	FSM 250–4000 mg/day	Doubled UNa, mean weight loss 6.7 kg, d/c home in 70%	Hypokalemia (−0.8 mEq/l), persistent dehydration
Vanky et al. (44), 1997	20 post-CABG	Observational	HCTZ 50 mg/day + amiloride 5 mg/day	FSM 80 mg/day	Mean 2.3 kg weight loss after one dose	None
Rosenberg et al. (45), 2005	21 CHF	Observational	MTZ 2.5–5 mg/day	FSM mean 260 mg/day	Mean 2 kg weight loss + 10/8 mm Hg BP reduction	BUN ↑ 58%, hypokalemia (−0.8 mEq/l), creatinine ↑ 27%

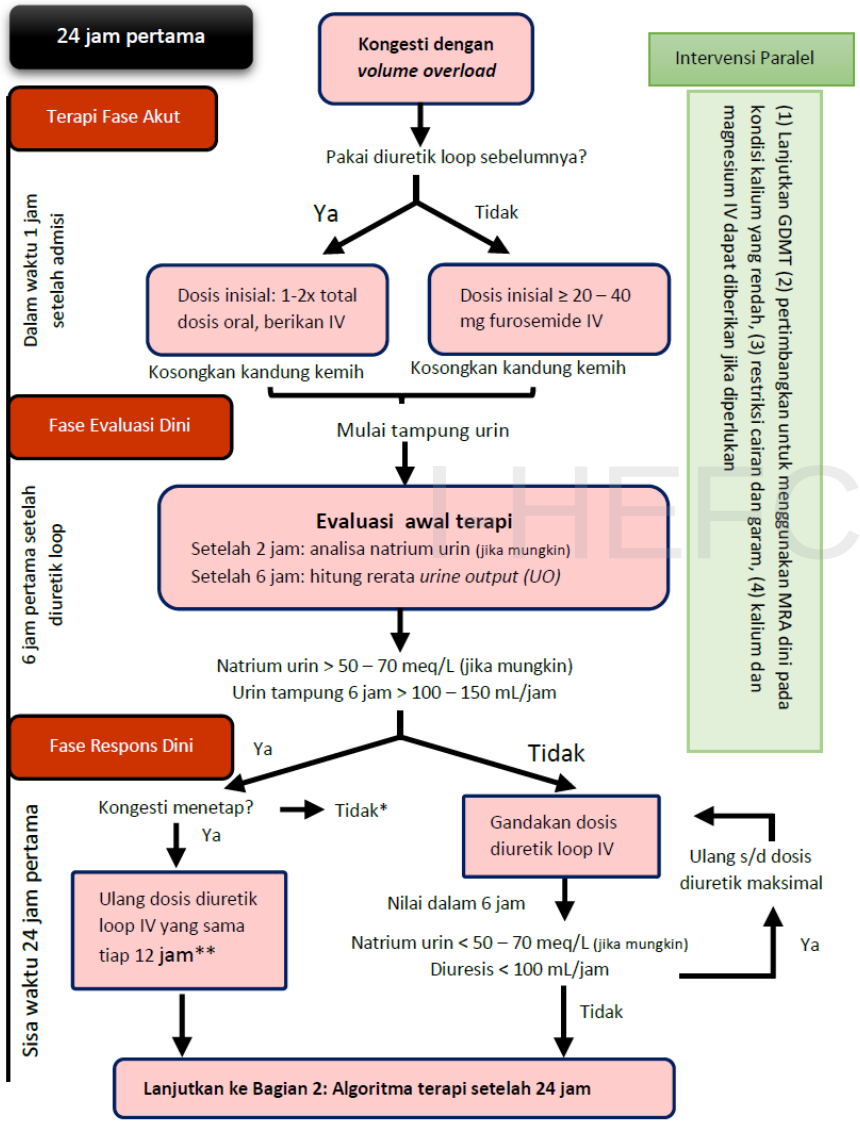
Old publications
Small sample number
Electrolyte imbalance, WRF, and arrhythmia were reported

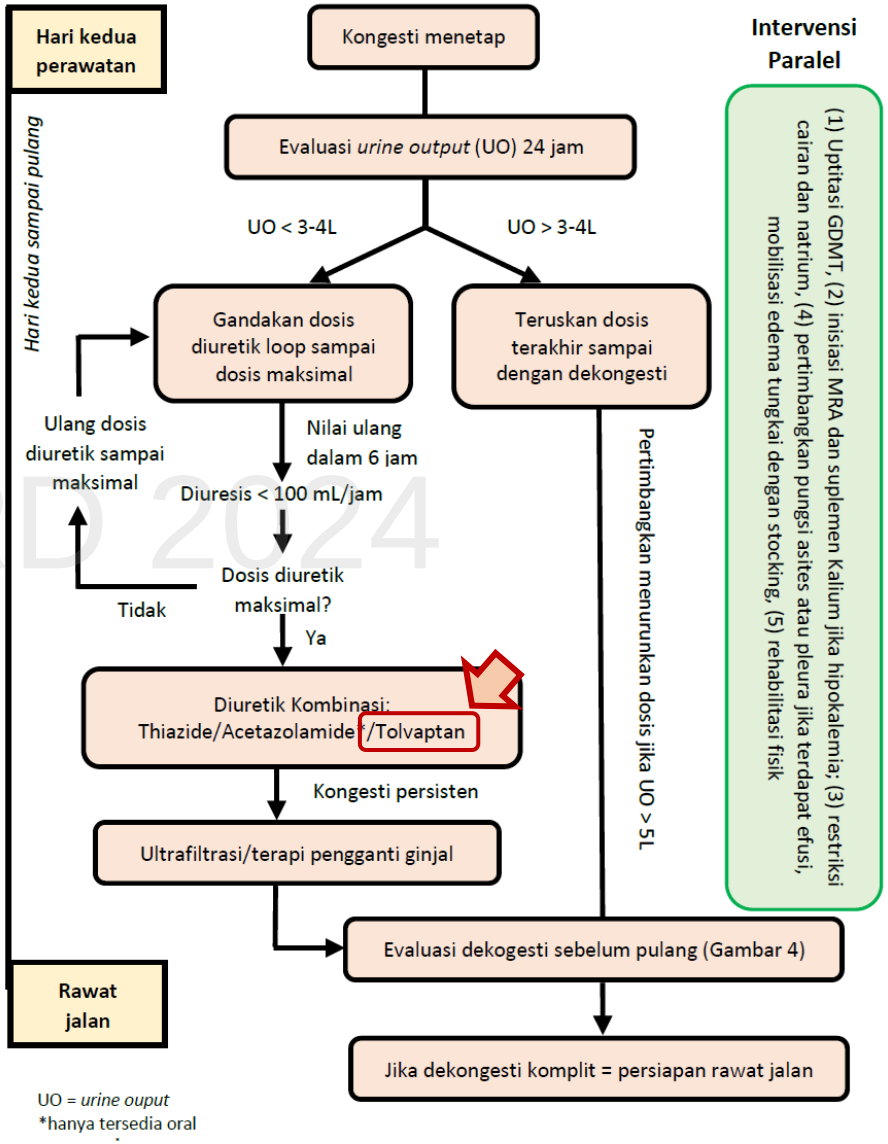
Jentzer JC, et al.J Am Coll Cardiol.2010

Dose-response relation to furosemide



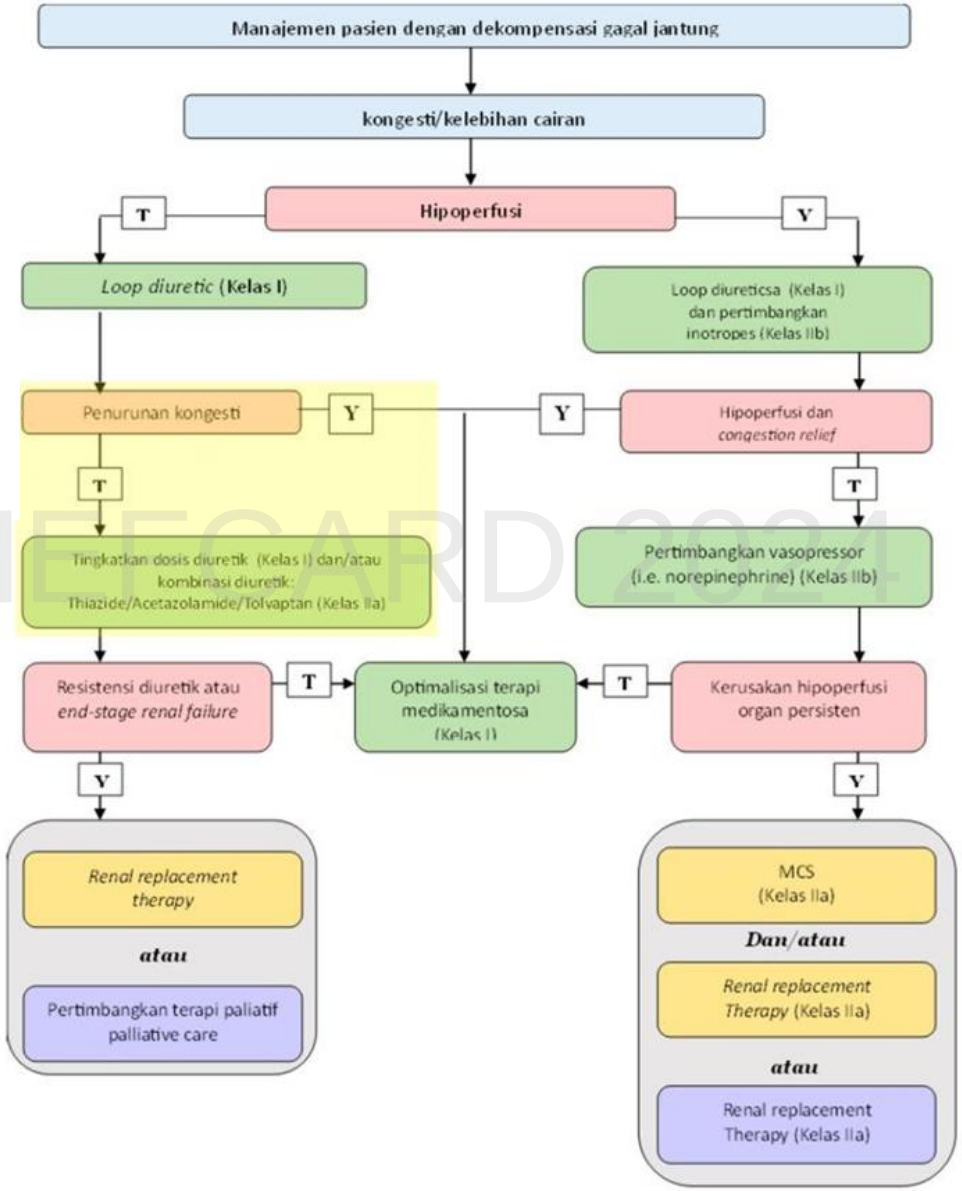
European Heart Journal. 2022. Girerd et al.





UO = *urine ouput*
*hanya tersedia oral

What does the **latest guideline** state?

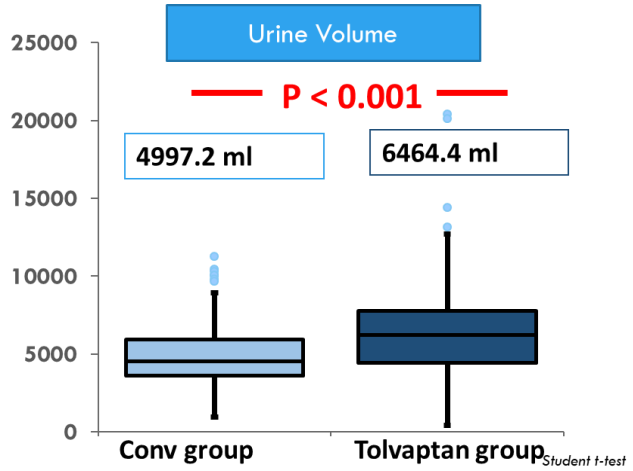


PERKI 2023:

Kombinasi tolvaptan dengan diuretik dapat digunakan untuk tatalaksana gagal jantung kongesti yang **belum optimal dengan diuretik saja**

AQUAMARINE Study

Conventional vs Conventional + Tolvaptan 15 mg/day
1° outcome: 48-hour urine volume
2° outcome: WRF, BW change, dose of furosemide used, relief of symptom (Likert scale), BNP change, Na and K change



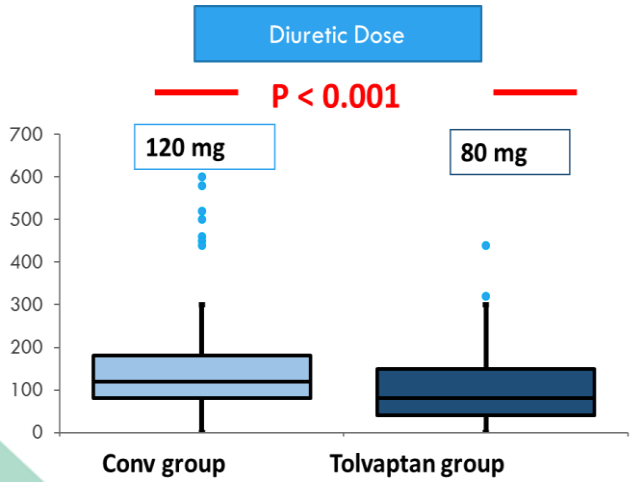


Table 2. Summary of Primary and Secondary End Points

Outcome	Conventional Group (n = 109)	Tolvaptan Group (n = 108)	*P* Value
Primary outcome			
48-hour urine volume (mL)	4997.2 ± 2101.4	6464.4 ± 3173.0	<.001
Secondary outcomes			
Worsening of renal function (%)	30 (27.8)	26 (24.1)	.642
Dose of diuretics use within 48 h (mg)	120 (80–180)	80 (40–150)	<.001
Net fluid loss within 48 h (mL)	3697.9 ± 2112.0	4700.1 ± 2443.3	.004
Change in BNP from baseline to 48 h (pg/mL)	−306.1 (−153.7 to −662.1)	−285.3 (−110.7 to −650.9)	.602
Change in body weight from baseline to 48 h (kg)	−1.99 ± 2.17	−3.16 ± 2.66	<.001
Length of hospital stay (d)	14.6 (10.3–27.2)	14.2 (8.9–20.3)	.36
Adverse events	6 (5.5)	10 (9.3)	.313
In-hospital death	5 (4.6)	4 (3.7)	>.99

Results are presented as mean ± SD, n (%), or median (interquartile range). BNP, B-type natriuretic peptide.

Matsue, Y., et al. J Card Fail. 2016;22(6):423-31

AQUAMARINE Study

Conventional vs Conventional + Tolvaptan 15 mg/day
1° outcome: 48-hour urine volume
2° outcome: WRF, BW change, dose of furosemide used, relief of symptom (Likert scale), BNP change, Na and K change

Tolvaptan therapy significantly higher 48-hour urine output compared to conventional therapy despite significantly lower amounts of loop diuretic use (80 mg vs 120 mg; *P* < .001)

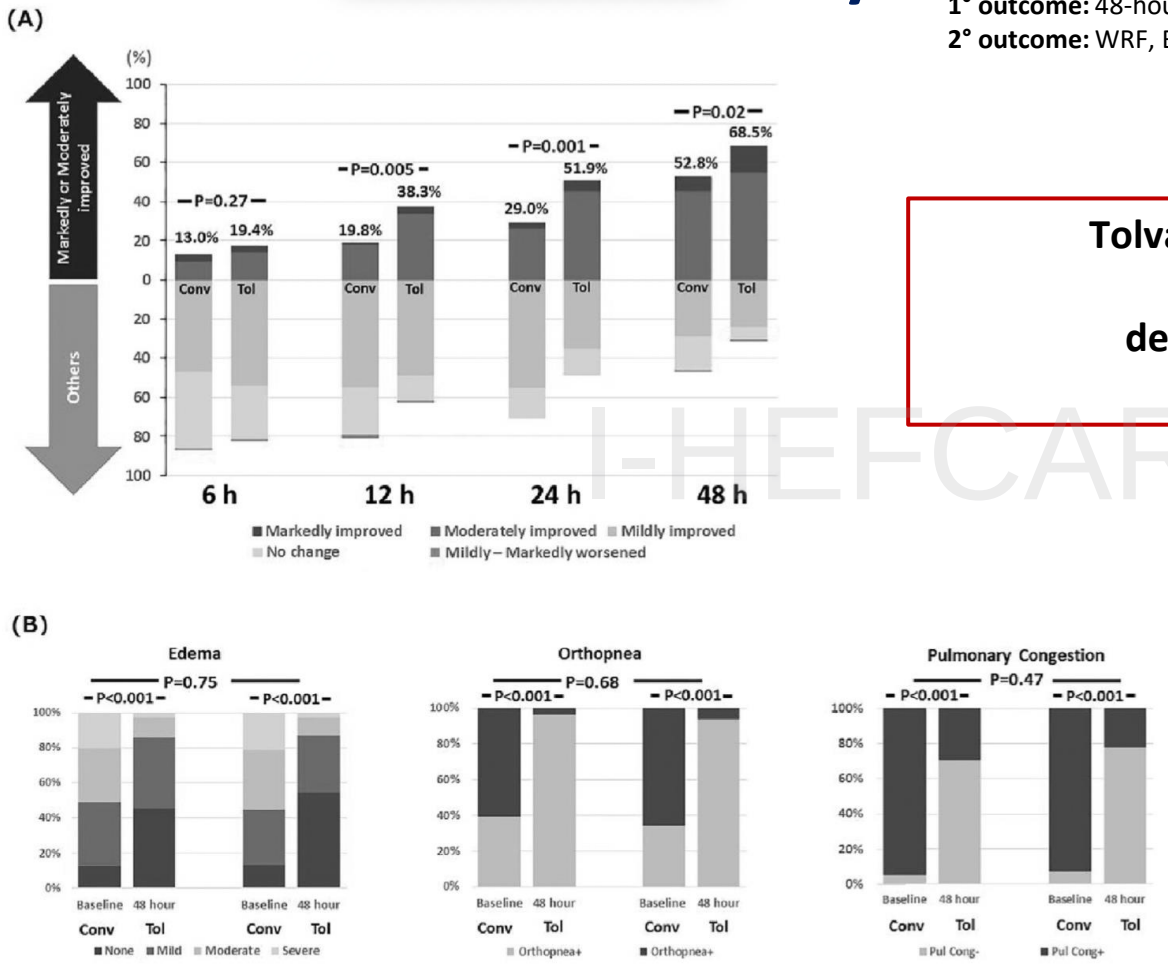


Fig. 3. Changes in dyspnea and edematous symptoms within 48 hours. (A) Patients-reported changes in dyspnea from baseline, as measured on a 7-point Likert scale. (B) Changes in congestive symptoms from baseline to 48 hours. Conv, conventional; Tol, tolvaptan.

Matsue, Y., et al. J Card Fail. 2016;22(6):423-31

Received: 7 May 2020 | Revised: 18 May 2020 | Accepted: 18 May 2020

DOI: 10.1002/prp2.614

ORIGINAL ARTICLE

Tolvaptan add-on therapy in patients with acute heart failure: A systematic review and meta-analysis

Xiandu Luo[1] | Qi Jin[2] | Yanqing Wu[1]

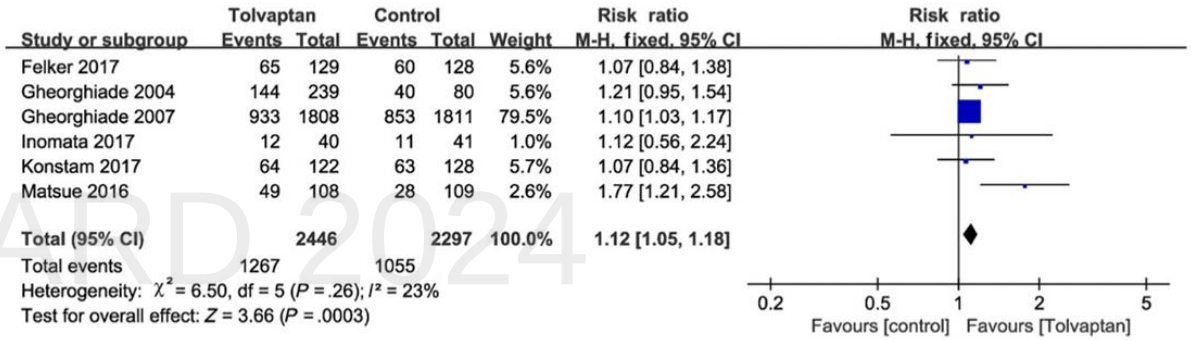


FIGURE 3 Forest plot depicting the effects of tolvaptan on dyspnea: tolvaptan was more effective in relieving dyspnea

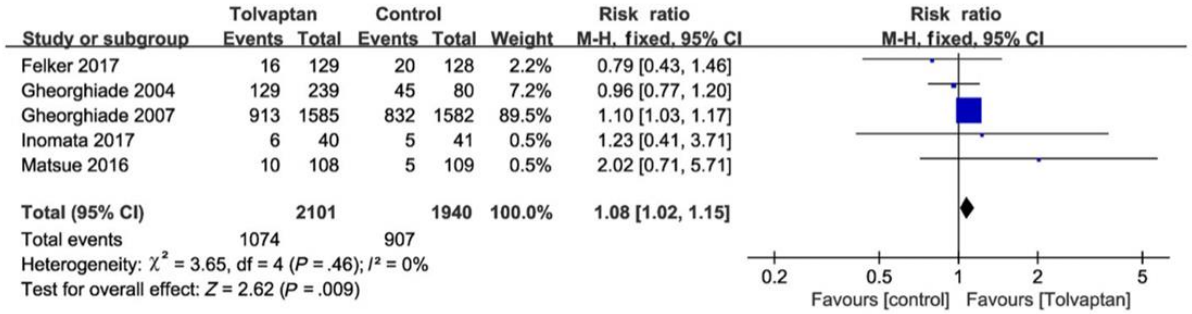


FIGURE 4 Forest plot depicting the effects of tolvaptan on edema: tolvaptan significantly reduced edema

Received: 7 May 2020 | Revised: 18 May 2020 | Accepted: 18 May 2020

DOI: 10.1002/prp2.614

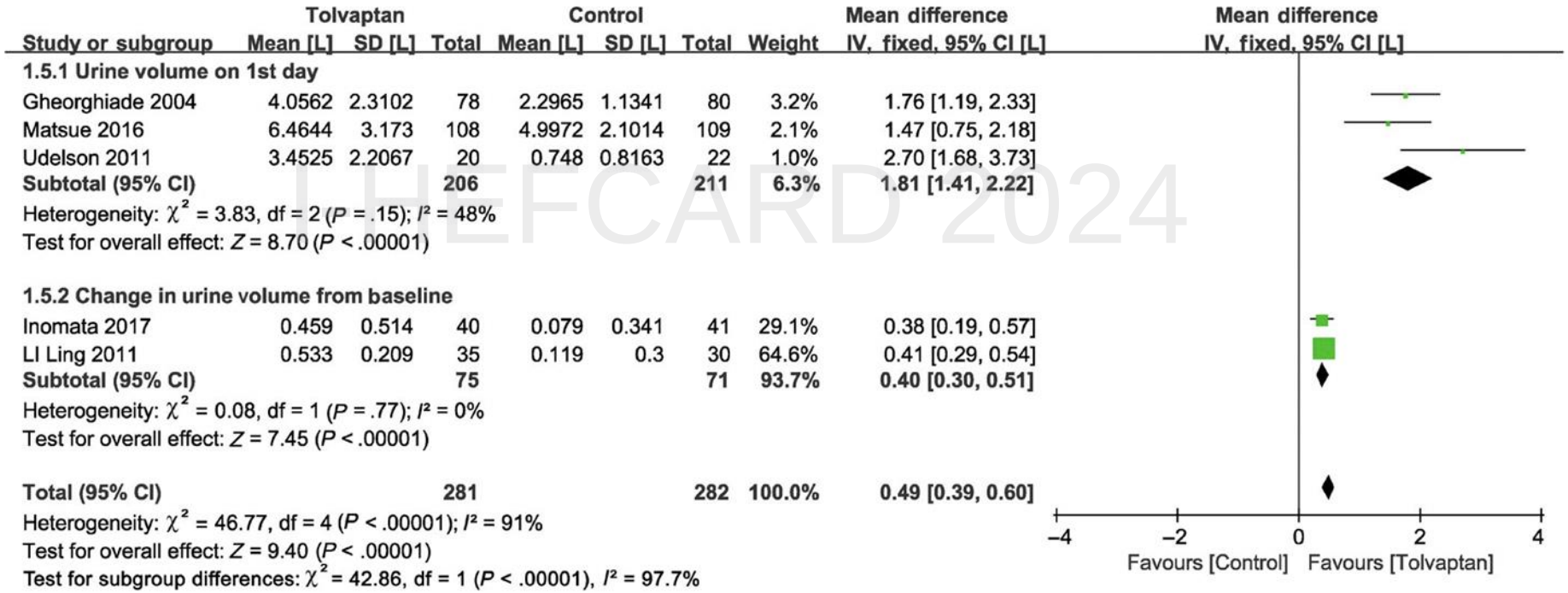


FIGURE 6 Forest plot depicting the effects of tolvaptan on urine volume: tolvaptan was better than traditional diuretics alone at increasing urine output

Received: 7 May 2020 | Revised: 18 May 2020 | Accepted: 18 May 2020

DOI: 10.1002/prp2.614

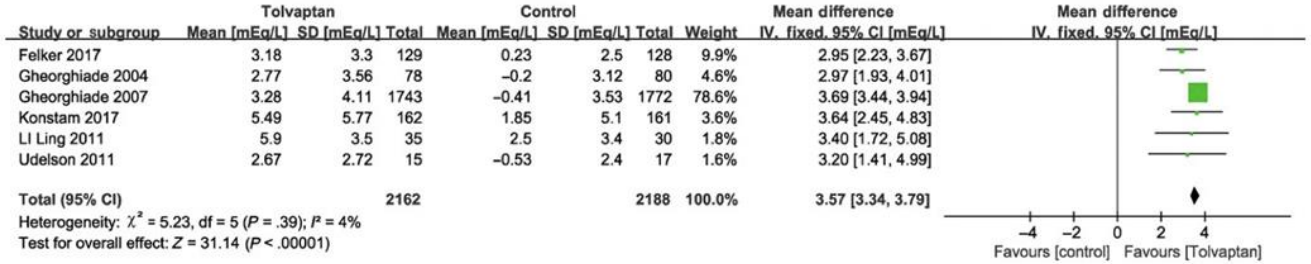


FIGURE 7 Forest plot depicting the effects of tolvaptan on serum sodium concentration: tolvaptan could increase serum sodium concentrations

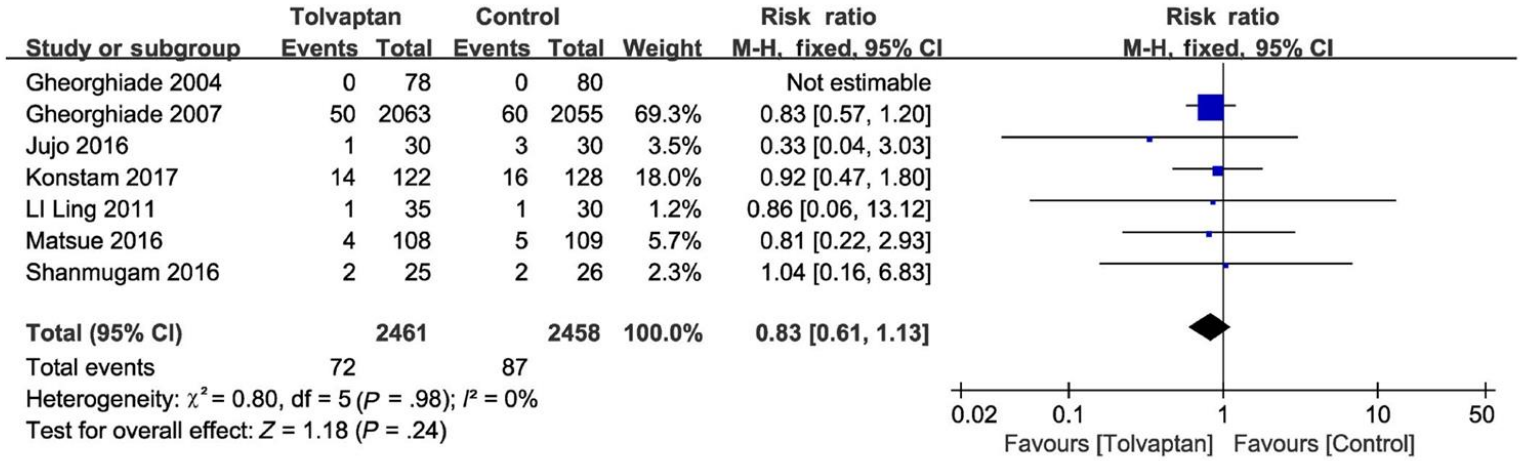


FIGURE 8 Forest plot depicting the effects of tolvaptan on mortality: tolvaptan did not increase mortality during hospitalization more than traditional diuretics alone

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DOI: 10.1002/prp2.614

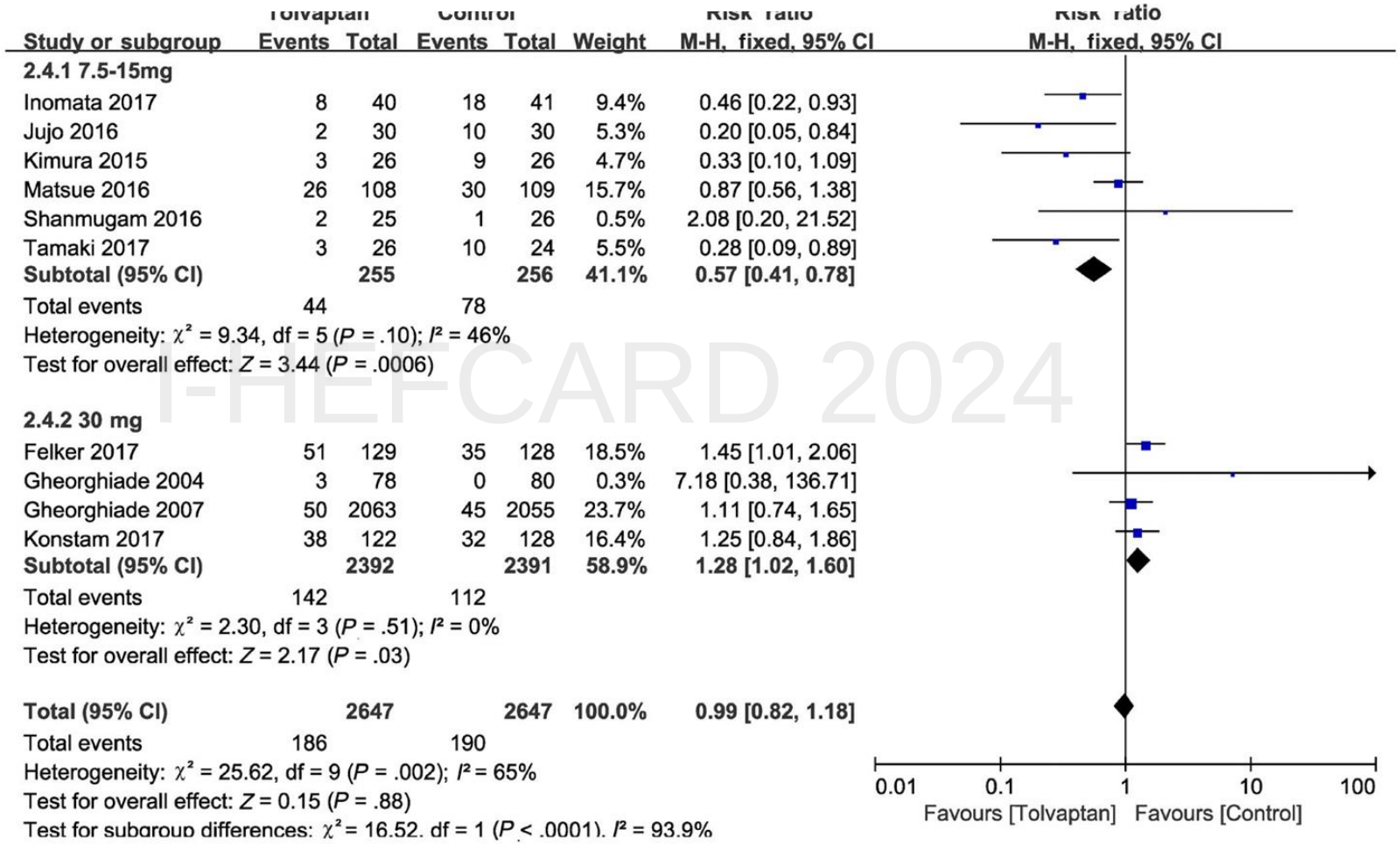


FIGURE 9 Forest plot depicting the effects of tolvaptan on worsening renal function (WRF): The incidence of WRF was associated with the dose of tolvaptan; a low dose of tolvaptan could significantly reduce the incidence of WRF, while a high dose did the opposite

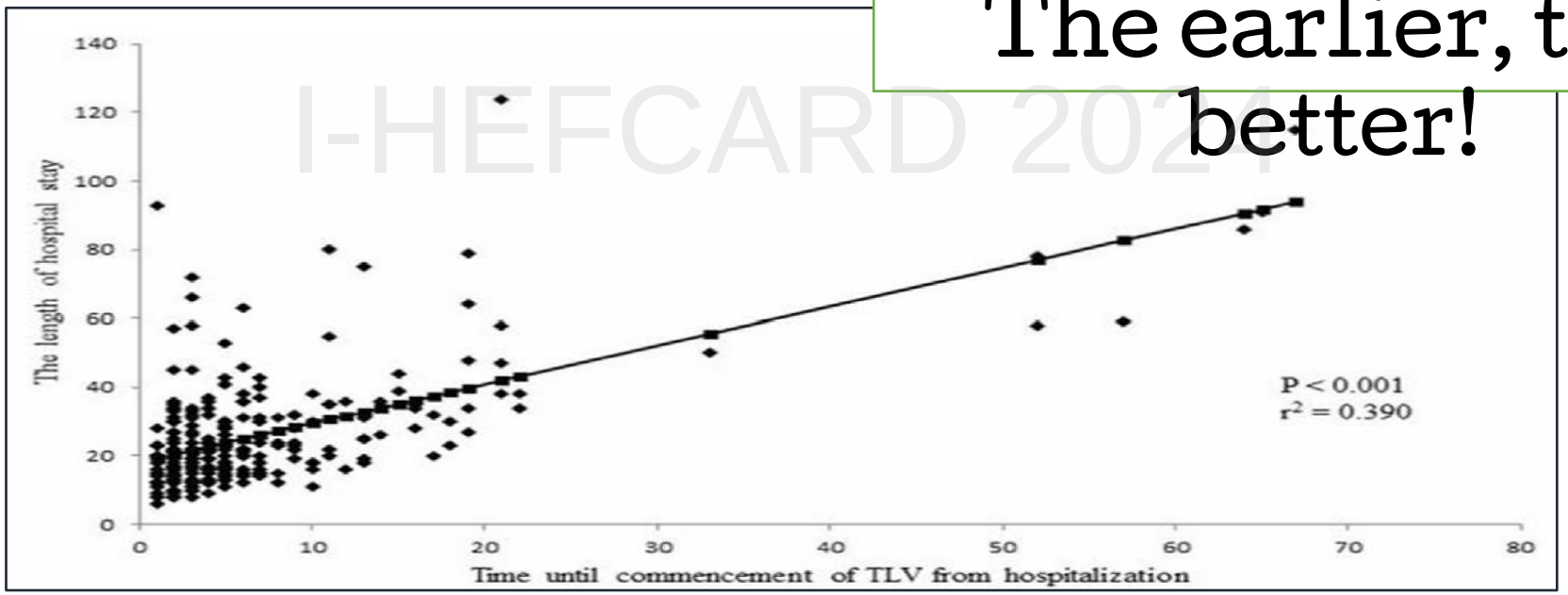
Observational Study > Heart Vessels. 2018 Apr;33(4):367-373.
doi: 10.1007/s00380-017-1067-3. Epub 2017 Nov 11.

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

Shunsuke Kiuchi [1], Shinji Hisatake [2], Takayuki Kabuki [2], Takashi Oka [2], Shintaro Dobashi [2], Takahiro Fujii [2], Takanori Ikeda [2]

Multivariate analysis : TLV initiated days was **independently related** to the long-term hospitalization (odds ratio 1.32, 95% CI 1.13-1.53, P < 0.001). Early use of TLV was related to the length of hospital stay for ADHF patients.

The earlier, the better!



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.

Kiuchi *et al. BMC Cardiovascular Disorders* (2022) 22:202
https://doi.org/10.1186/s12872-022-02640-7

RESEARCH Open Access

Early initiation of tolvaptan is associated with early discharge in patients with heart failure regardless of age

Shunsuke Kiuchi*, Shinji Hisatake, Takayuki Kabuki, Takashi Oka, Shintaro Dobashi, Yoshiki Murakami, Takahide Sano and Takanori Ikeda

Conclusions:
The early initiation of TLV after hospitalization was associated with a shorter length of hospital stay in patients with HF **regardless of age**.

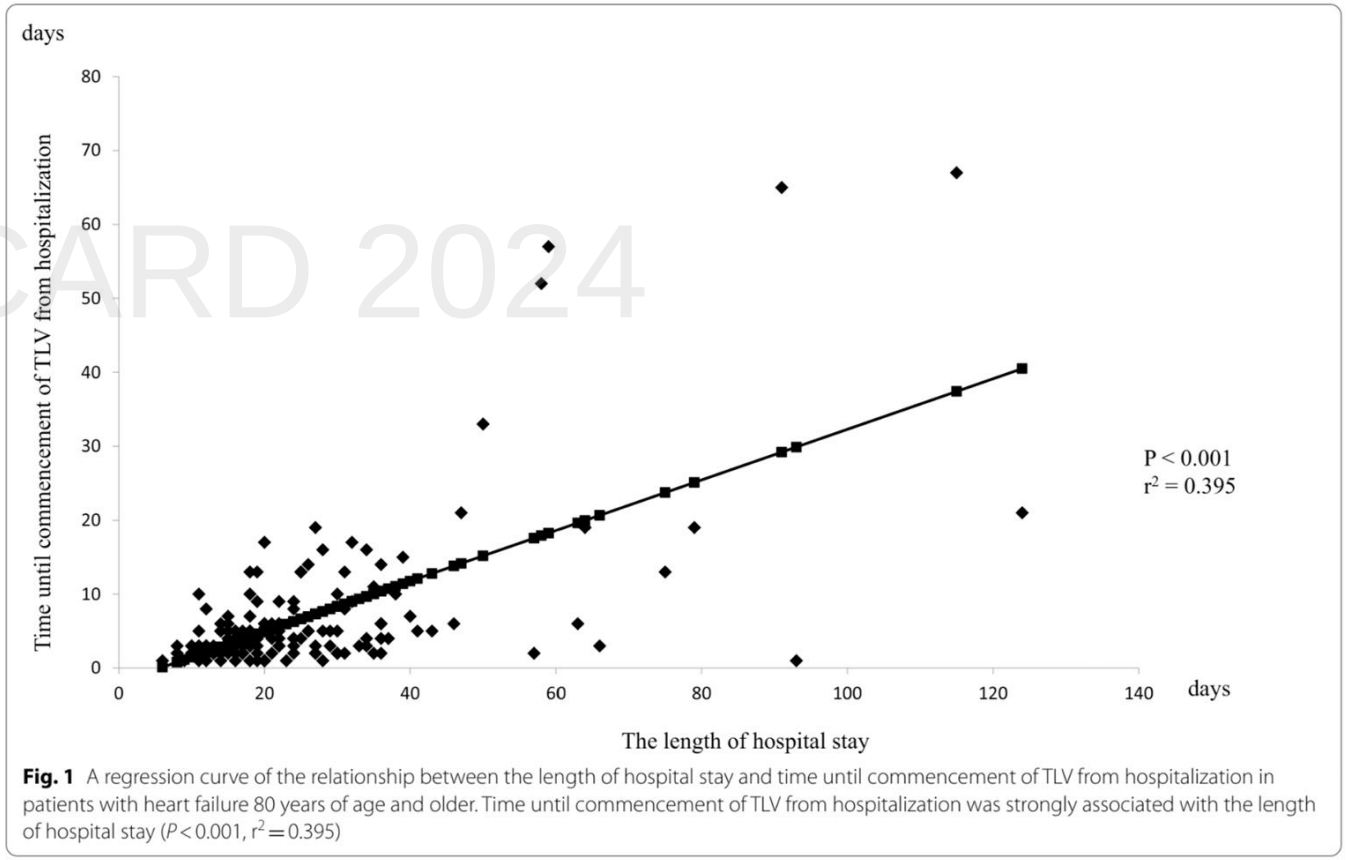


Fig. 1 A regression curve of the relationship between the length of hospital stay and time until commencement of TLV from hospitalization in patients with heart failure 80 years of age and older. Time until commencement of TLV from hospitalization was strongly associated with the length of hospital stay ($P < 0.001$, $r^2 = 0.395$)

Circulation Journal
Circ J 2019; 83: 2084–2184
doi:10.1253/circj.CJ-19-0342

JCS GUIDELINES

Tolvaptan?

– what the **Guideline** recommend…

JCS 2017/JHFS 2017 Guideline on Diagnosis and Treatment of Acute and Chronic Heart Failure

Table 23. Recommendations and Levels of Evidence for Medications for HFrEF

	Class of Recommendation	Level of Evidence	Grade of Recommendation (MINDS)	Level of Evidence (MINDS)
ACE inhibitors				
Use in all patients (including asymptomatic patients) unless contraindicated	I	A	A	I
ARBs				
Use in patients intolerable ACE inhibitors	I	A	A	I
Concomitant use with ACE inhibitors	IIb	B	C2	II
β-blockers				
Use in symptomatic patients to improve prognosis	I	A	A	I
Use in asymptomatic patients with left ventricular systolic dysfunction	IIa	B	A	II
Use for rate control in patients with atrial fibrillation with a rapid ventricular response	IIa	B	B	II
MRAs				
Use in patients with NYHA Class II-IV, LVEF <35% who are receiving loop diuretics and ACE inhibitors	I	A	A	I
Loop diuretics, thiazide diuretics				
Use in patients with symptoms of congestion	I	C	C1	III
Vasopressin V_2 receptor antagonists				
Start treatment during hospitalization to relieve symptoms of fluid retention due to heart failure in patients who do not respond well to other types of diuretics including loop diuretics	IIa	B	B	II

Diuretics	
Furosemide	40 to 80 mg/day once daily
Azosemide	60 mg/day once daily
Torasemide	4 to 8 mg/day once daily
Tolvaptan	7.5 to 15 mg/day once daily
Trichlormethiazide	2 to 8 mg/day once daily

Circulation Journal
Circ J 2019; 83: 2084–2184
doi:10.1253/circj.CJ-19-0342

JCS GUIDELINES

Tolvaptan?

– what the **Guideline** recommend…

JCS 2017/JHFS 2017 Guideline on Diagnosis and Treatment of Acute and Chronic Heart Failure

Table 26. Recommendations and Levels of Evidence for Medications for HFpEF

	Class of Recommendation	Level of Evidence	Grade of Recommendation (MINDS)	Level of Evidence (MINDS)
Diuretics				
Use of diuretics to relieve symptoms of congestion	I	C	C1	VI
Preference of long-acting drugs when using loop diuretics	IIb	C	C1	III
Out-patient use of tolvaptan introduced during hospitalization for acute heart failure to control congestion*	IIa	C	C1	IVb
ACE inhibitors/ARBs				
Increasing the dose of ACE inhibitors/ARBs to maximum tolerable level to reduce the risk of clinical events	IIb	C	C1	III
β-blockers				
Increasing the dose of β-blockers to maximum tolerable level to reduce the risk of clinical events	IIb	C	C1	III
MRAs				
Increasing the dose of MRAs to maximum tolerable level to reduce the risk of clinical events	IIb	C	C1	III
Nitrates				
Use of nitrates to improve prognosis and increase activities of daily living	III	B	D	II

*Tolvaptan must be introduced during hospitalization. There are no data on the efficacy and safety of long-term treatment with tolvaptan. ARB, angiotensin II receptor blocker; ACE, angiotensin converting enzyme; MRA, mineralocorticoid receptor antagonist.

Diuretics	
Furosemide	40 to 80 mg/day once daily
Azosemide	60 mg/day once daily
Torasemide	4 to 8 mg/day once daily
Tolvaptan	7.5 to 15 mg/day once daily
Trichlormethiazide	2 to 8 mg/day once daily

CLINICAL PRACTICE GUIDELINE: FULL TEXT

2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure

Recommendations for Diuretics and Decongestion Strategies in Patients With HF
Referenced studies that support the recommendations are summarized in the Online Data Supplements.

COR	LOE	RECOMMENDATIONS
1	B-NR	1. In patients with HF who have fluid retention, diuretics are recommended to relieve congestion, improve symptoms, and prevent worsening HF (1-5).
1	B-NR	2. For patients with HF and congestive symptoms, addition of a thiazide (e.g., metolazone) to treatment with a loop diuretic should be reserved for patients who do not respond to moderate- or high-dose loop diuretics to minimize electrolyte abnormalities (6).

Recommendations for Diuretics in Hospitalized Patients: Decongestion Strategy
Referenced studies that support the recommendations are summarized in the Online Data Supplements.

COR	LOE	RECOMMENDATIONS
1	B-NR	1. Patients with HF admitted with evidence of significant fluid overload should be promptly treated with intravenous loop diuretics to improve symptoms and reduce morbidity (1).
1	B-NR	2. For patients hospitalized with HF, therapy with diuretics and other guideline-directed medications should be titrated with a goal to resolve clinical evidence of congestion to reduce symptoms and rehospitalizations (1-6).
1	B-NR	3. For patients requiring diuretic treatment during hospitalization for HF, the discharge regimen should include a plan for adjustment of diuretics to decrease rehospitalizations (7).
2a	B-NR	4. In patients hospitalized with HF when diuresis is inadequate to relieve symptoms and signs of congestion, it is reasonable to intensify the diuretic regimen using either: a. higher doses of intravenous loop diuretics (1,3); or b. addition of a second diuretic (3).

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

Review

Update of acute and long-term tolvaptan therapy

Teruhiko Imamura (MD, PhD, FJCC)[a], Koichiro Kinugawa (MD, PhD, FJCC)[b,*]

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[b] Second Department of Internal Medicine, Toyama University, Toyama, Japan

Acute Phase

Optimal Timing

- ✔ Within 3 days : better response to tolvaptan (urine volume), earlier initiation of ambulatory cardiac rehabilitation, shorter hospital stay, and lower rate of in-hospital death
- ✔ May be considered in the second 60-min when the furosemide iv is refractory in the first 60-min in AHF

  (class IIa and evidence level A)

Optimal Dose

- ✔ Favourable outcome in preserving renal function at 7.5–15mg/day
- ✔ Advantage in renal function disappeared at dose 30 mg/day
- ✔ Dose **7.5 mg to 15 mg** is recommended

Concomitant Diuretic Usage

- ✔ Reduce the dose of concomitant diuretics may be recommended for the better clinical outcome sufficient **after** decongestion is ideal before discharge

4th I-HEF CARD

The 4th Indonesian Symposium on Heart Failure and Cardiometabolic Disease

TAKE HOME POINTS

- ✔ Lack of trials on Diuretic; no direct effect on mortality
  - Door-to-diuretic time predicts in-hospital mortality
  - Net fluid loss in the first 24h predicts WRF
- ✔ Several challenges did occurred with conventional loop diuretic
- ✔ Ineffective decongestion :
  - Combination therapy (Class IIa)

- ✔ **Yes, I HAVE A TRUF CARD for Decongestion!**
- ✔ **Tolvaptan** combination in acute □ favored in meta-analysis
  - optimal timing (earlier-better)
  - optimal dose (7.5-15 mg/day, avoid 30 mg/day)
  - concomitant diuretic (wean out)
- ✔ PERKI 2023 : Kombinasi Furosemide dan Tolvaptan bila UO tidak sesuai target

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7th SCF & SOC-HF

SOLO CARDIOVASCULAR FORUM &
SOLO COURSE ON HEART FAILURE
26th-28th July 2024

Great Disruption in Cardiovascular Disease Management: Winner Takes All

Hotel Grand Mercure, Solo Baru, Surakarta
July 26th-28th 2024

Symposium | In-Depth Course | Abstract Submission | Plenary Lecture
Arrhythmia Special Session | Memorial Lecture

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dr. Hawani Sasmaya, Sp.JP (K), FIHA, FHFA | Dr. dr. Sally Aman Nasution, Sp.PD-KKV, FINASIM, FACP
dr. Siti Elkana Nauli, Sp.JP(K), FIHA, FAsCC, FHFA | dr. Rarsari Soerarso, Sp.JP(K), MARS, FIHA, FHFA
dr. Irnizarifka, Sp.JP (K), FIHA, FAPSC, FAsCC, FHFA | Prof. Dr. dr. Trisulo Wasyanto, Sp.JP(K), FIHA, FAPSC, FAsCC

and many more

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7th SCF & SOC-HF

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SOLO COURSE ON HEART FAILURE
26th-28th July 2024

Arrhythmia Special Session:
Live Demo