

Stroke Volume Change after Digoxin Loading in Septic Shock Patients with Transient LV Dysfunction

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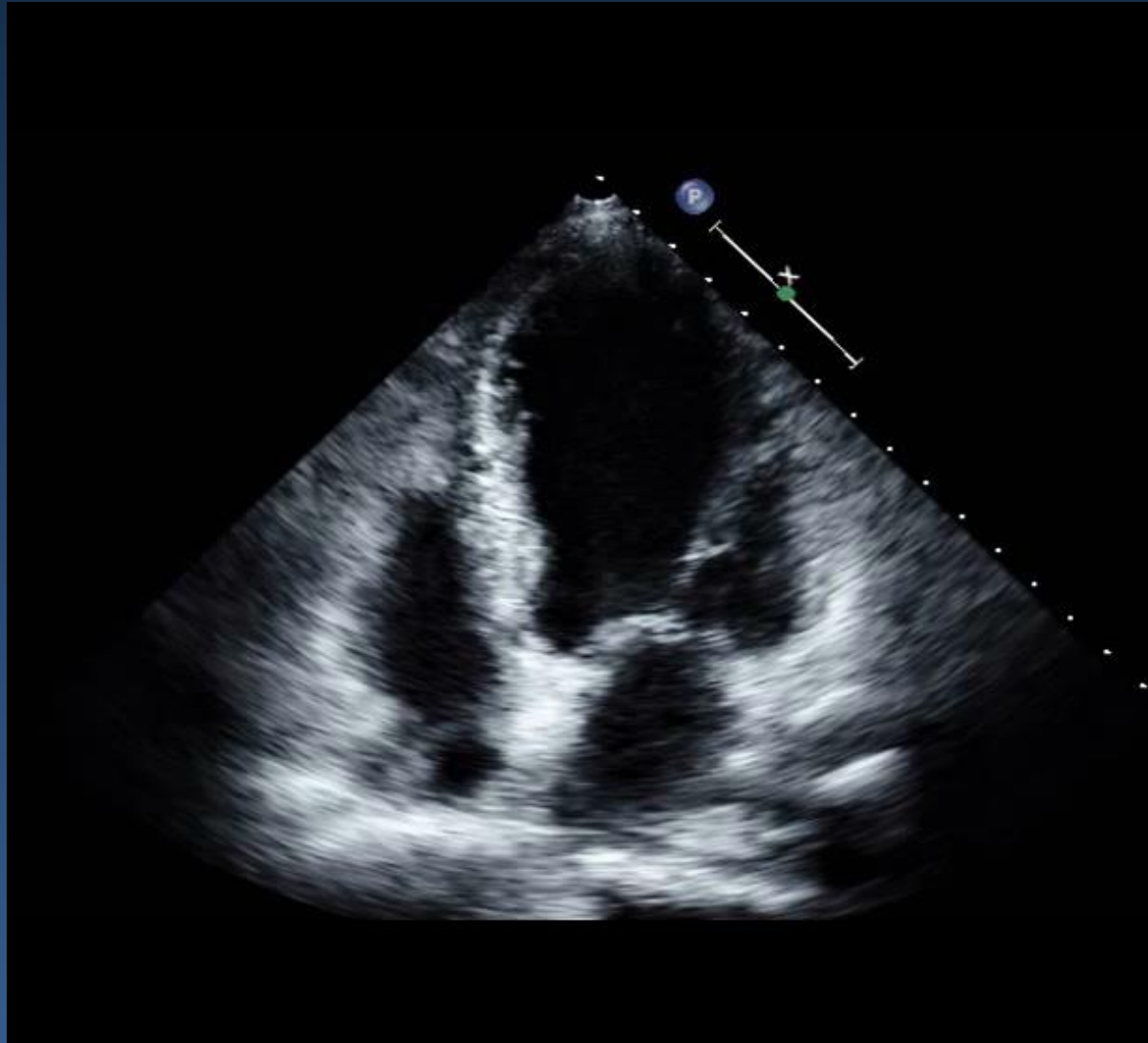
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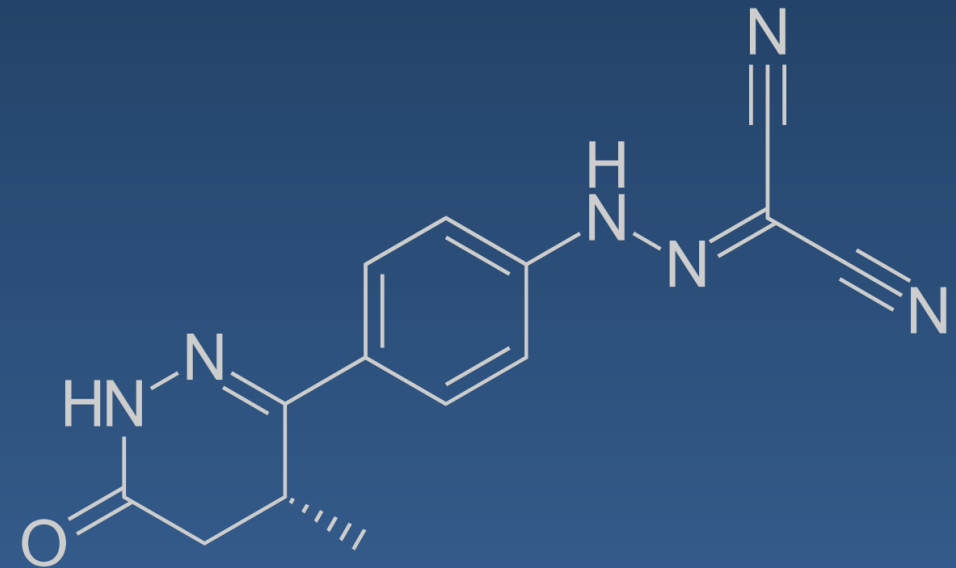
Medical Intensivist



Takotsubo Syndrome



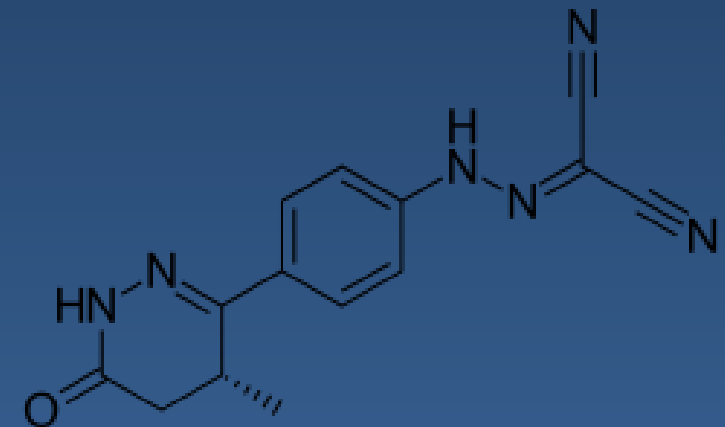
Levosimendan



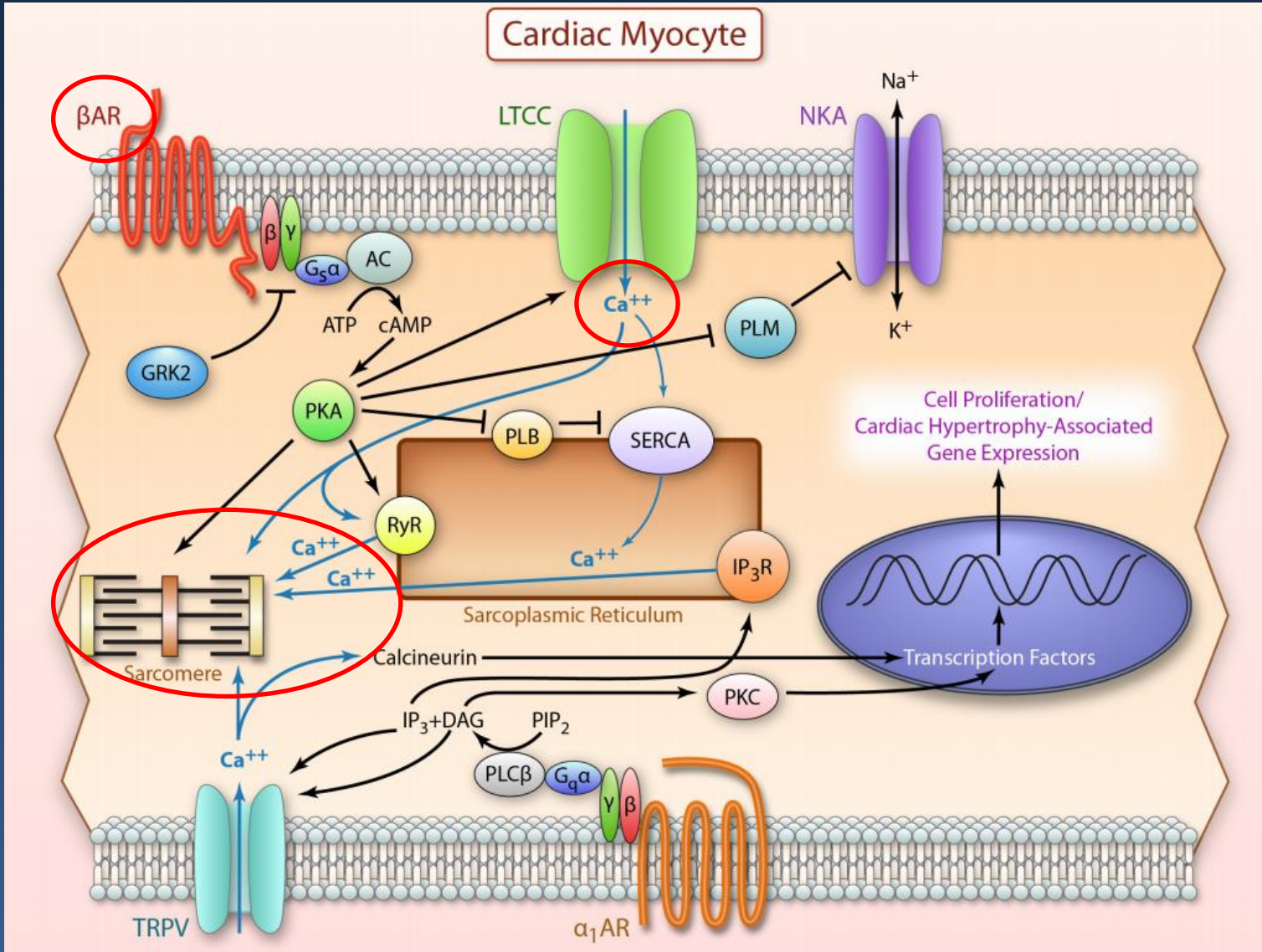
Levosimendan Mechanism

Mechanism of action [\[edit \]](#)

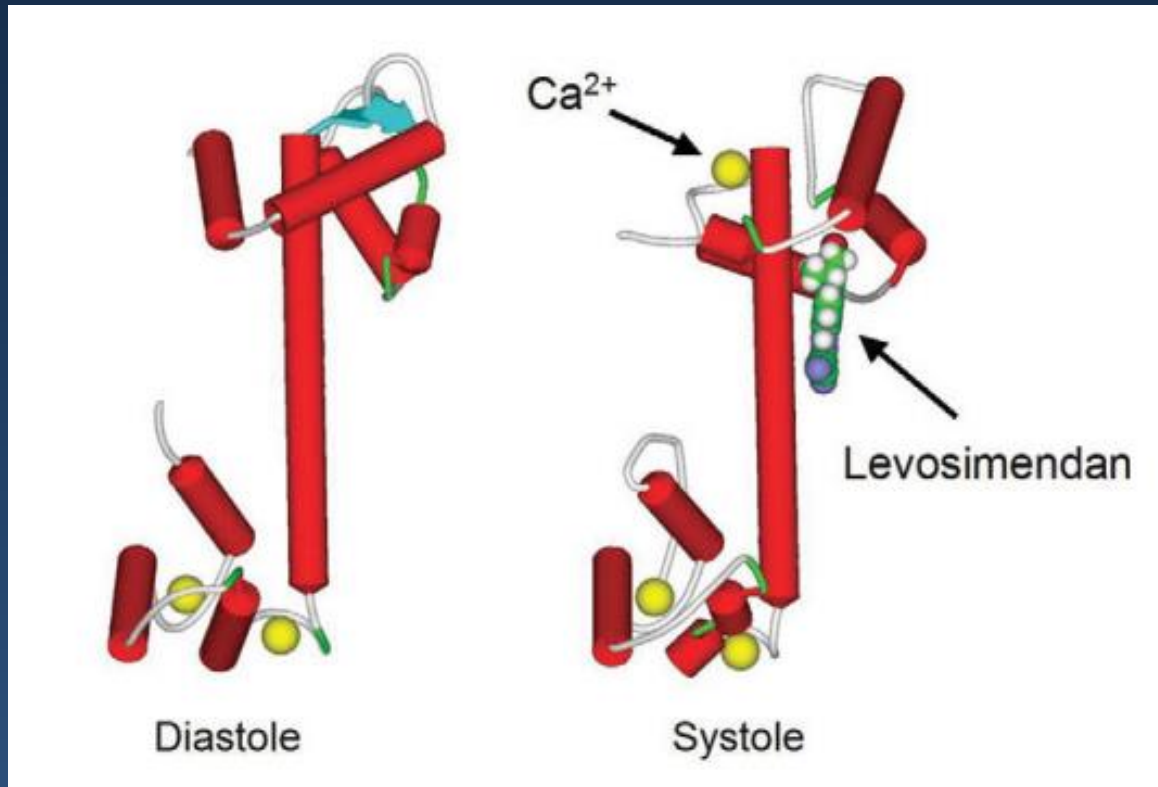
Levosimendan is a **calcium sensitizer**— it increases the sensitivity of the heart to calcium, thus increasing cardiac contractility without a rise in intracellular calcium. Levosimendan exerts its positive inotropic effect by increasing calcium sensitivity of myocytes by binding to cardiac troponin C in a calcium-dependent manner. It also has a vasodilatory effect, by opening adenosine triphosphate (ATP)-sensitive potassium channels in vascular smooth muscle to cause smooth muscle relaxation. The combined inotropic and vasodilatory actions result in an increased force of contraction, decreased preload and decreased afterload. Moreover, by opening also the mitochondrial (ATP)-sensitive potassium channels in cardiomyocytes, the drug exerts a cardioprotective effect.^[1]



Ca⁺⁺ in Myocardial Contraction

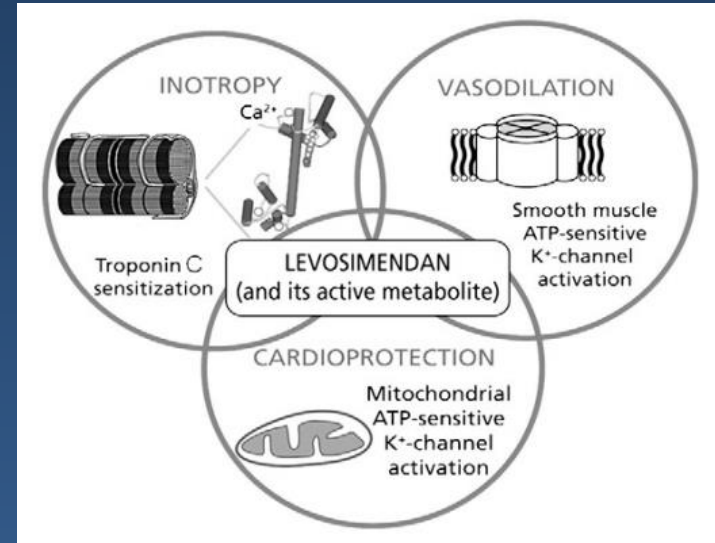


Levosimendan Mechanism



Ca⁺⁺ Sensitizer

Myocardial Contractility



ORIGINAL ARTICLE

Levosimendan for Hemodynamic Support after Cardiac Surgery

G. Landoni, V.V. Lomivorotov, G. Alvaro, R. Lobreglio, M.G. Calabrò, E.V. Grigoryev, V.V. Likhvantsev, M.F. V.V. Pasyuga, M. Baiocchi, F. Pappalardo, F. Mo M.N. Abubakirov, B. Amantea, R. Lembo, L. Brazzi, A.M. Scandroglio, T. Bove, A. Belletti, M.G. Mich T.S. Zabelina, R. Bellomo, and A. Zangrillo, for the C

ORIGINAL ARTICLE

Levosimendan in Patients with Left Ventricular Dysfunction Undergoing Cardiac Surgery

R.H. Mehta, J.D. Leimberger, S. van Diepen, J. Meza, A. Wang, R. Jankowich, R.W. Harrison, D. Hay, S. Femes, A. Duncan, E.G. Soltesz, J. Lubner, S. Park, M. Argenziano, E. Murphy, R. Marcel, D. Kalavrouziotis, D. Nagpal, J. Bozinovski, W. Toller, M. Heringlake, S.G. Goodman, J.H. Levy, R.A. Harrington, K.J. Anstrom, and J.H. Alexander, for the LEVO-CTS Investigators*

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Levosimendan Versus Dobutamine in Myocardial Injury Patients with Septic Shock: A Randomized Controlled Trial

[Zhonghua Wei Zhong Bing Ji Jiu Yi Xue](#). 2014 Oct;26(10):692-6. doi: 10.3760/cma.j.issn.2095-4352.2014.10.002.

[Effects of levosimendan on hemodynamics and cardiac function in patients with septic shock].

[Article in Chinese]

[Fang M¹](#), [Dong S](#).

Open Access

Research

BMJ Open Effect of levosimendan on mortality in severe sepsis and septic shock: a meta-analysis of randomised trials

Wei Chang, Jian-Feng Xie, Jing-Yuan Xu, Yi Yang

Levosimendan accelerates recovery in patients with takotsubo cardiomyopathy.

Yaman M¹, Arslan U, Kaya A, Akyol A, Ozturk E, Okudan YE, Bayramoglu A, Bektas O.

Levosimendan: The Inotrope of Choice in Cardiogenic Shock Secondary to Takotsubo Cardiomyopathy?

Laven Padayachee, MBBS, FACEM, FJFICM*

Cardiol J. 2016;23(6):616-617. doi: 10.5603/CJ.2016.0101.

Levosimendan: New hope therapy for takotsubo syndrome.

Hering D¹, Jaguszewski M.

 Author information

PMID: 27976790 DOI: [10.5603/CJ.2016.0101](https://doi.org/10.5603/CJ.2016.0101)

[Indexed for MEDLINE]



SHORT COMMUNICATION

Safety and Feasibility of Levosimendan Administration in Takotsubo Cardiomyopathy: A Case Series

Francesco Santoro, Riccardo Ieva, Armando Ferraretti, Vincenzo Ienco, Giuseppe Carpagnano, Michele Lodispoto, Luigi Di Biase, Matteo Di Biase & Natale Daniele Brunetti

Department of Cardiology, University of Foggia, Foggia, Italy

Case Report

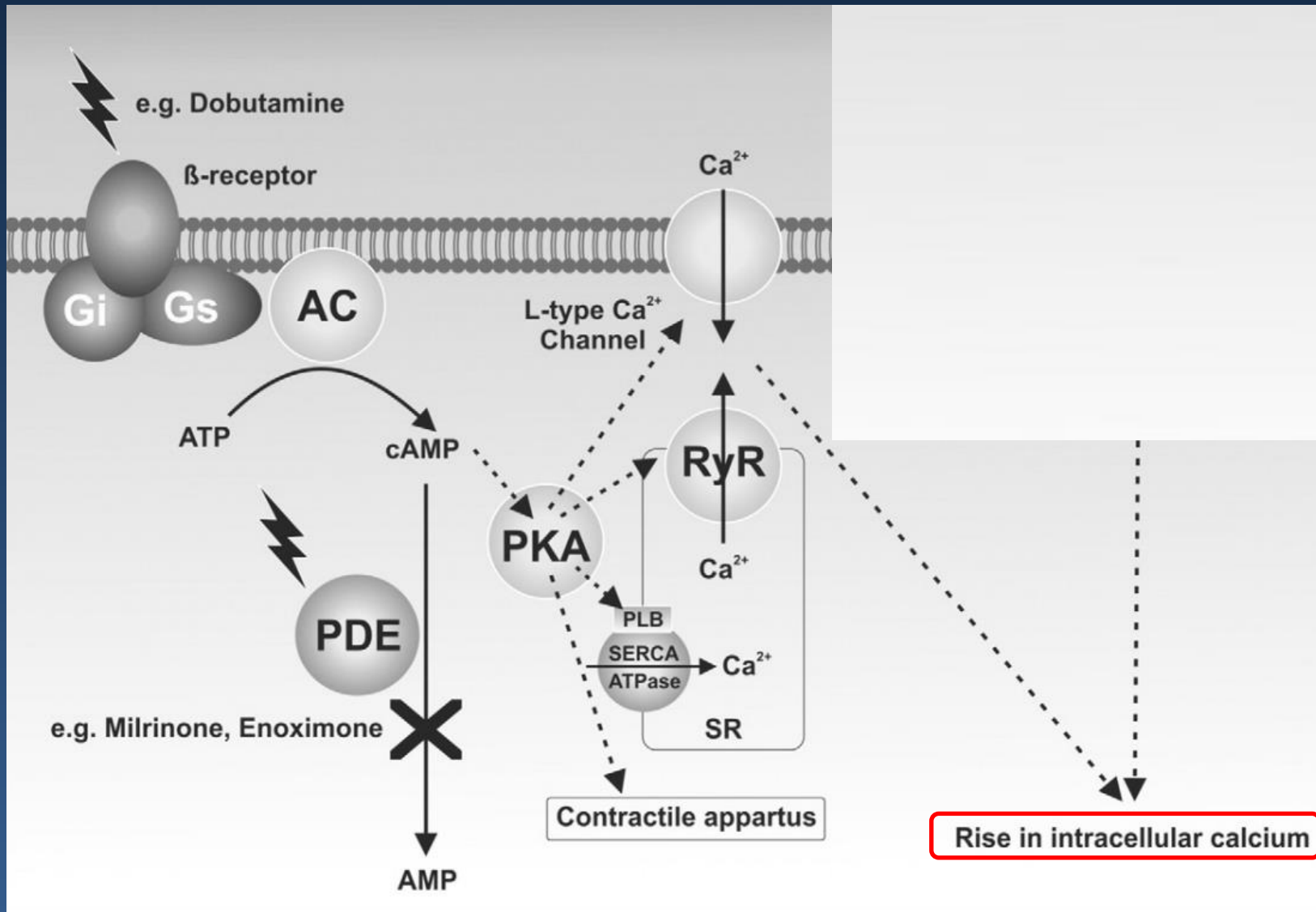
Sepsis-associated takotsubo cardiomyopathy can be reversed with levosimendan☆

Efficacy of levosimendan in Takotsubo-related cardiogenic shock

doi: 10.1111/j.1399-6576.2009.02105.x

Cardiovascular
Therapeutics

Cardiac Inotropes and Receptors





2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Digoxin

Digoxin may be considered in symptomatic patients in sinus rhythm despite treatment with an ACE-I (or ARB), a beta-blocker and an MRA, to reduce the risk of hospitalization (both all-cause and HF-hospitalizations).

IIb

B

185

For patients in NYHA Class IV, in addition to treatment for AHF, an intravenous bolus of amiodarone or, in digoxin-naïve patients, an intravenous bolus of digoxin should be considered to reduce the ventricular rate.

IIa

B

348,349

For patients in NYHA Class I–III, digoxin, should be considered when ventricular rate remains high^d despite beta-blockers or when beta-blockers are not tolerated or contra-indicated.

IIa

B

197

Suggested wording to use

Is recommended/is indicated

Since a given treatment or procedure is beneficial, useful, effective.

Class II
Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.

Class IIa
Weight of evidence/opinion is in favour of usefulness/efficacy. Should be considered

Class IIb
Usefulness/efficacy is less well established by evidence/opinion. May be considered

Class III
Evidence or general agreement that the given treatment or procedure is not useful/effective; and in some cases may be harmful. Is not recommended

Digitalis in Takotsubo Syndrome



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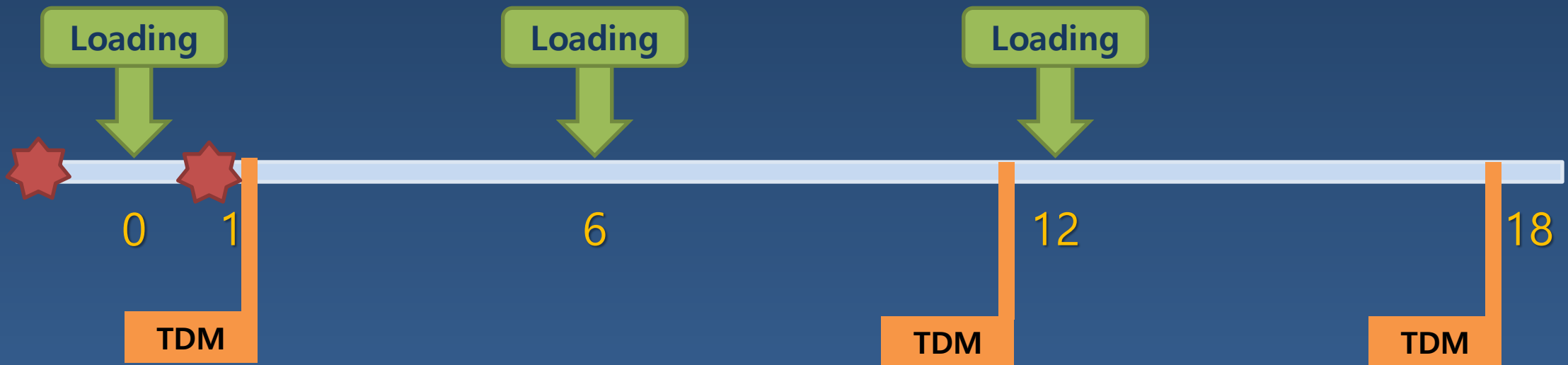
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Digoxin Loading Protocol for Transient LV Dysfunction

- Digoxin 1A (0.25 mg) IV infusion for 30 mins
- 3 times q 6 hr

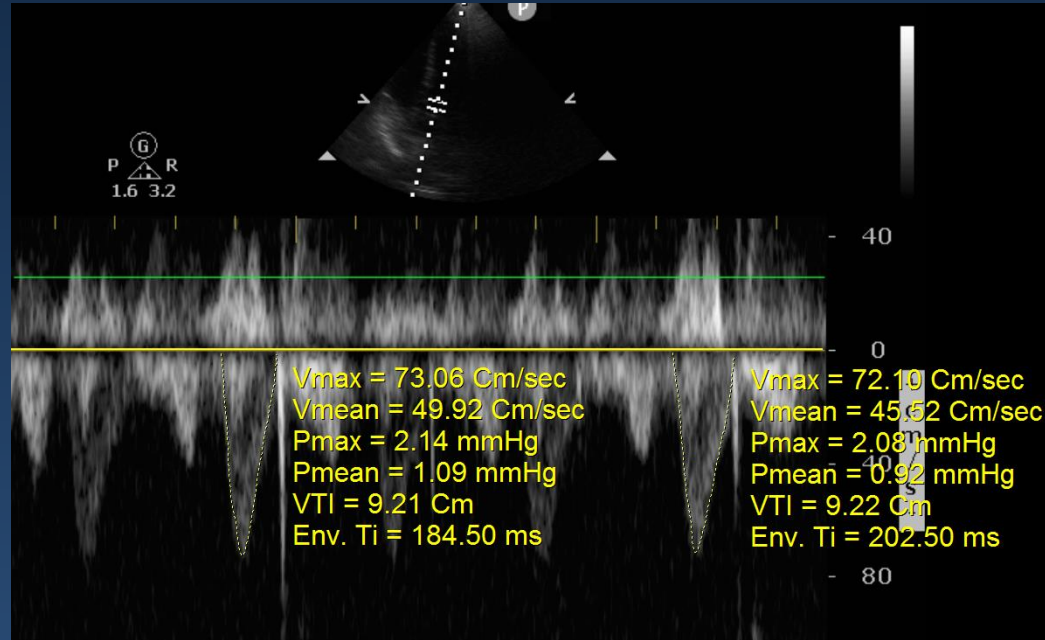
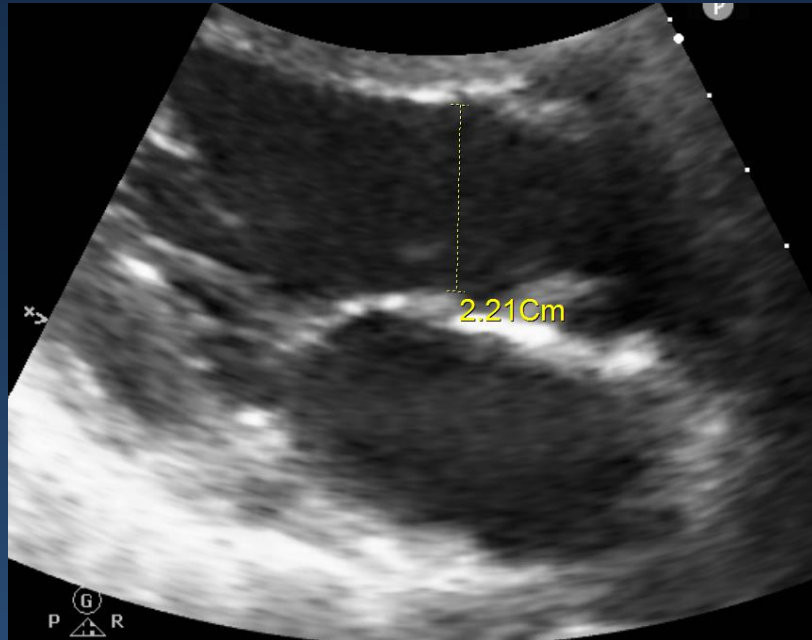
● Intravenous loading – For ventricular rate control in atrial fibrillation and flutter, the most rapid means of digitalization is the intravenous route. An initial intravenous dose of 0.25 to 0.5 mg of digoxin is given over several minutes, followed by 0.25 mg every 6 hours for a total loading dose of 0.75 to 1.5 mg (10 to 12 mcg/kg lean body weight) ([calculator 1](#) and [calculator 2](#)). Intravenous digoxin begins to act in 15 to 30 minutes with a peak effect in 1 to 5 hours.



METHODS

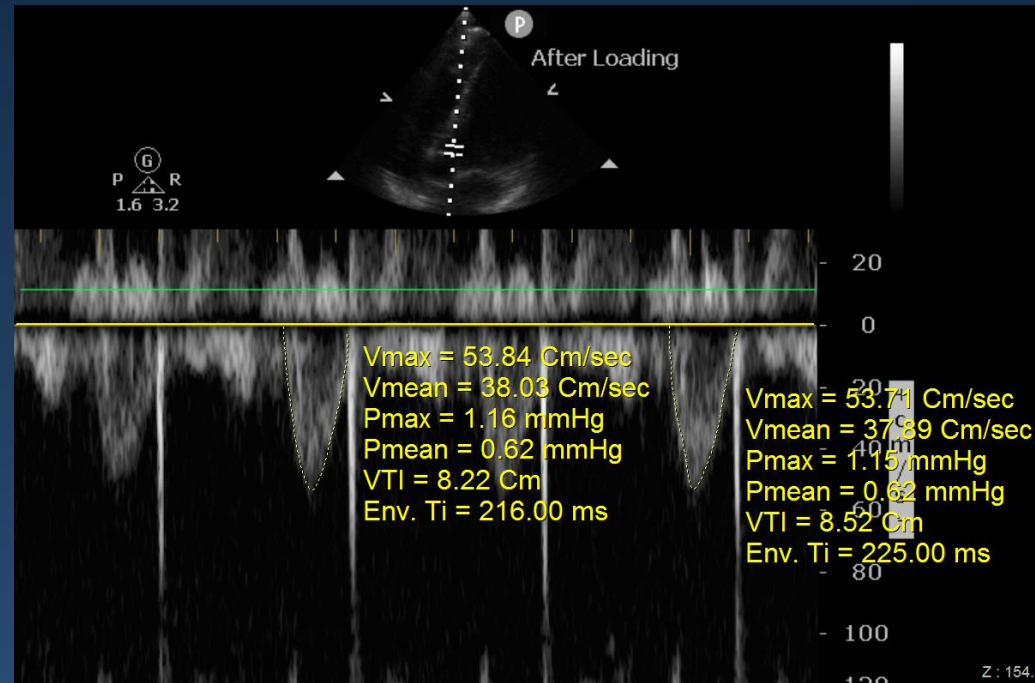
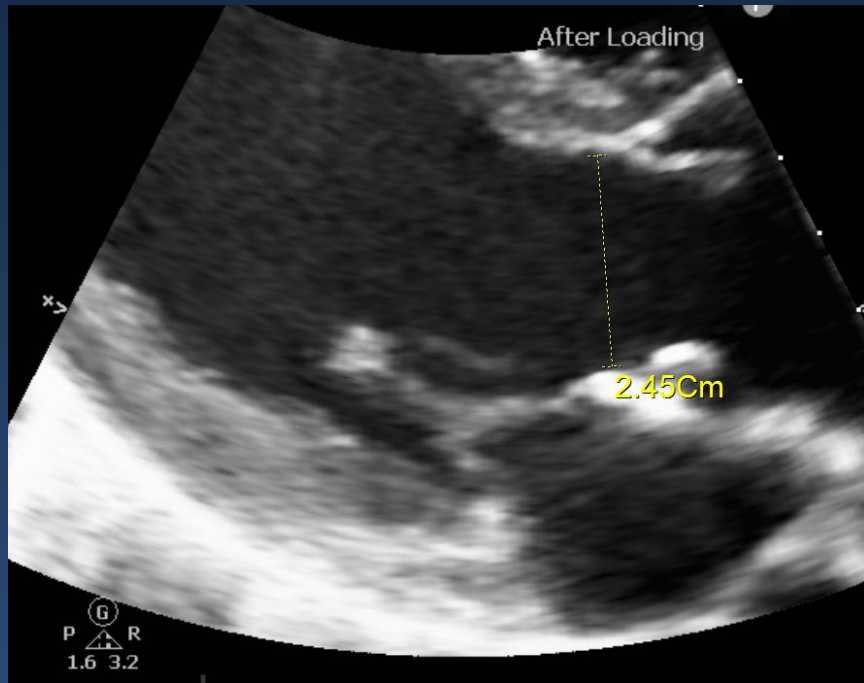
- Retrospective observational study
- Adult
- Septic Shock
- ICU
- Vasopressor
- Transient LV dysfunction
 - Bedside echo
 - Typical Takotsubo shape wall motion abnormality
 - Atypical Takotsubo shape → Confirmed spontaneous recovery

Stroke Volume before DGX Loading



$$3.14 \times (2.21/2)^2 \times 9.22 = 35.3$$

Stroke Volume after DGX Loading



$$3.14 \times (2.45/2)^2 \times 8.52 = 40.1$$

RESULTS

- 2016.09 ~ 2017.12
- Digoxin loading protocol: 16 patients
- Echocardiography available: 6 patients

- Mean age: 65.0 ± 10.2 yo
- Female: 4 patients (66.7%)

RESULTS

- CAG: 2 patients
 - no significant lesion
- Echo
 - Typical Takotsubo type RWMA: 4 patients
 - Reversed Takotsubo type RWMA: 1 patients → CAG: no lesion
 - Global hypokinesia: 1 patients → CAG: no lesion

Observed Patient Information

No	Sex	Age	Dx	Echo Finding	CAG	Echo F/U	Outcome
1	F	60	Deep neck infection	Typical TS	(-)	Normalized WM	Alive D/C, 32d
2	F	60	Pneumonia	Global hypokinesia	(+)	Normalized WM	Alive D/C, 29d
3	M	73	Ischemic colitis	Typical TS	(-)	None	Alive D/C, 24d
4	F	56	Pneumonia	Reversed TS	(+)	Normalized WM	Alive D/C, 13d
5	F	82	Pneumonia	Typical TS	(-)	None	Dead, 0d
6	M	59	Pneumonia	Typical TS	(-)	None	Dead, 5d

Hemodynamic Parameters between LD of Digoxin

	Before DL	After DL	p
HR (bpm)	127.8 ± 14.1	118.8 ± 24.3	0.544
EF (%)	20.2 ± 9.4	22.2 ± 10.4	0.327
TVI (cm)	10.8 ± 3.1	12.3 ± 4.6	0.093
LVOT diameter (cm)	1.82 ± 0.24	1.88 ± 0.26	0.025
SV (mL)	27.6 ± 7.9	33.7 ± 11.9	0.048
CO (L/m)	3.5 ± 1.1	3.9 ± 1.1	0.459

Adverse Event (16 patients with DL)

- No adverse event
 - Overdose in TDM result: none
 - Digitalis toxicity on EKG: none
 - Significant bradycardia: none

DISCUSSION

- Retrospective observational study
- Hemodynamic effect of digoxin loading in sepsis with transient LV dysfunction

- Increased SV & LVOT diameter
- Not increased TVI & CO

LIMITATION

- Small patient number
- Retrospective observational design
- Observer: bias (TVI)
- Other hemodynamic parameters: N-A
- CAG in selected patients

Conclusion

- Digoxin loading in septic shock patients with transient LV dysfunction such as Takotsubo syndrome might increase stroke volume significantly.
- Digoxin can be a feasible medical treatment
 - Takotsubo SD
 - Septic cardiomyopathy
 - Myocarditis
 - Myocardial stunning in AMI
 - Toxin/drug induced cardiomyopathy
- Further controlled study to reveal hemodynamic effect in Takotsubo syndrome is needed.