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Septická kardiomyopatie

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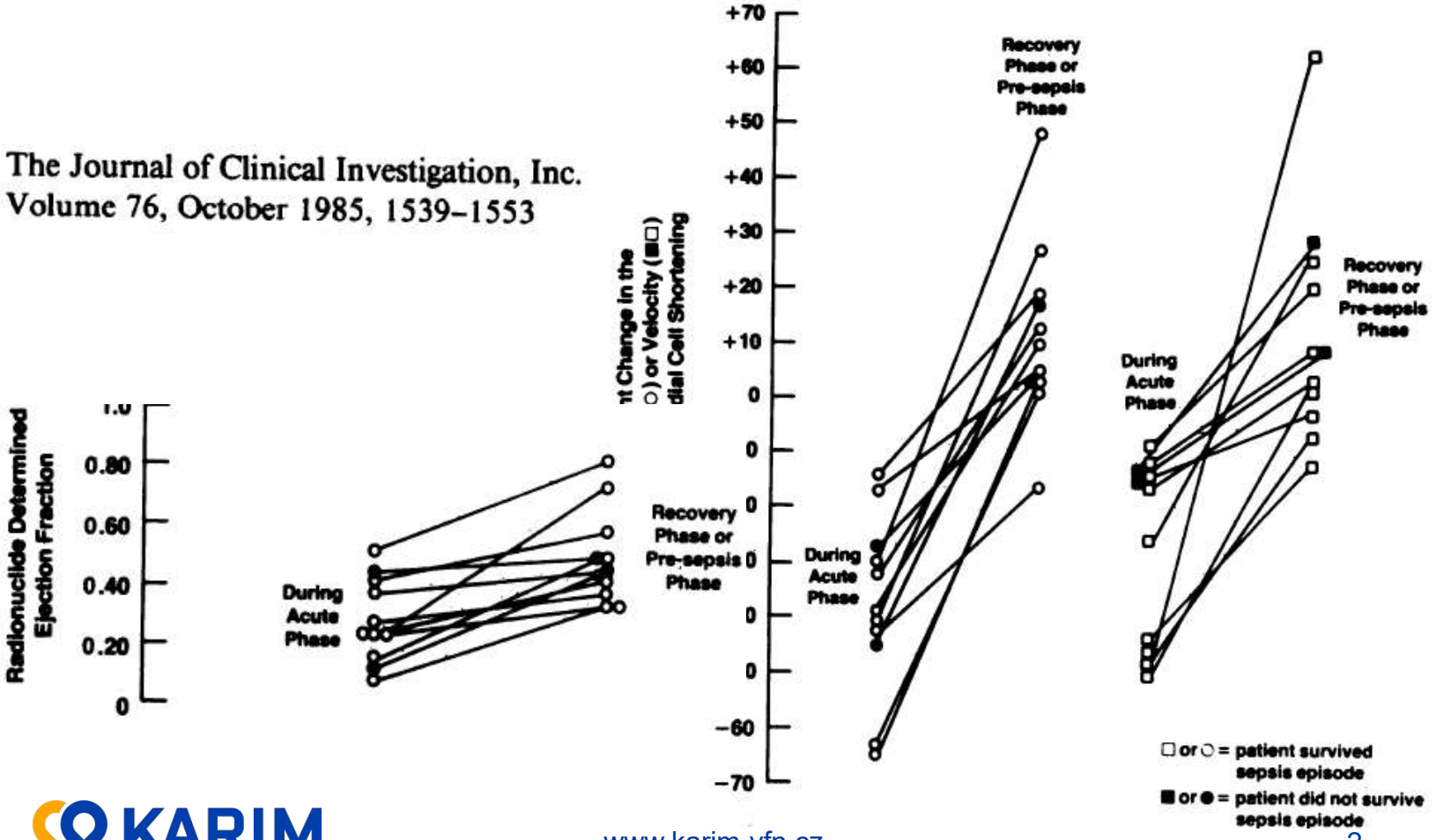
A Circulating Myocardial Depressant Substance in Humans with Septic Shock

Septic Shock Patients with a Reduced Ejection Fraction Have a Circulating Factor That Depresses In Vitro Myocardial Cell Performance

Joseph E. Parrillo, Cynthia Burch, James H. Shelhamer, Margaret M. Parker, Charles Natanson, and William Schuette
Critical Care Medicine Department, Clinical Center, National Institutes of Health, Bethesda, Maryland 20205

The Journal of Clinical Investigation, Inc.
Volume 76, October 1985, 1539–1553



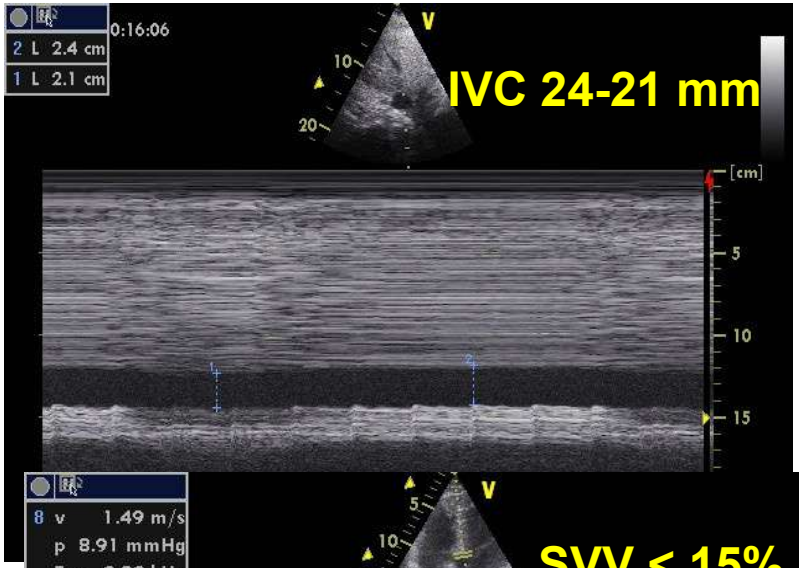
Poruchy srdeční funkce v sepsi a septickém šoku

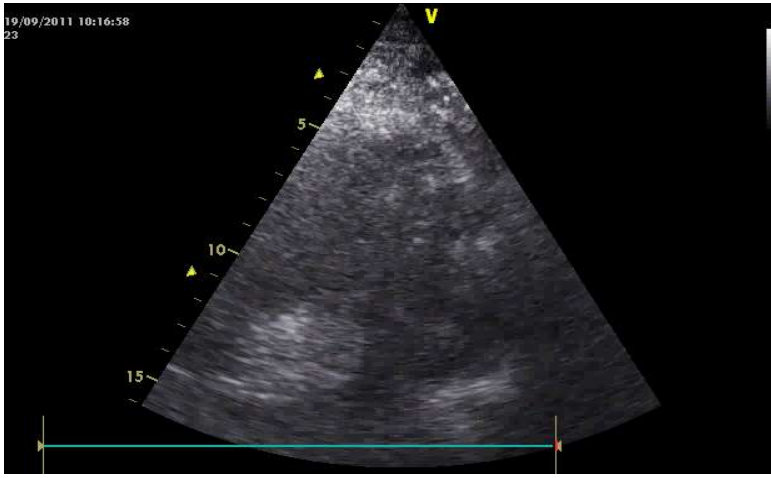
Low SVR, hypotension	Varon J, Marik PE (2008) Irwin and Rippe's intensive care medicine. In: Irwin RS, Rippe JM (eds). 6th edn. Wolters Kluwer Health/Lippincott Williams & Wilkins, Philadelphia, pp 1855-1869
Diastolic and systolic dysfunction: **- 15 to 60% of patients may develop cardiomyopathy**	Rudiger A, Singer M (2007) Mechanisms of sepsis-induced cardiac dysfunction. Crit Care Med 35 (6):1599-1608 Vieillard-Baron A, Caille V, Charron C, Belliard G, Page B, Jardin F (2008) Actual incidence of global left ventricular hypokinesia in adult septic shock. Crit Care Med 36 (6):1701-1706
Autonomic dysfunction **- receptor downregulation**	Cariou A, Pinsky MR, Monchi M, Laurent I, Vinsonneau C, Chiche JD, Charpentier J, Dhainaut JF (2008) Is myocardial adrenergic responsiveness depressed in human septic shock? Intensive Care Med 34 (5):917-922
Chronotropic dysfunction: **- inadequately high HR** **- low HR variability**	Annane D, Trabold F, Sharshar T, Jarrin I, Blanc AS, Raphael JC, Gajdos P (1999) Inappropriate sympathetic activation at onset of septic shock: a spectral analysis approach. Am J Respir Crit Care Med 160 (2):458-465 Schmidt HB, Werdan K, Muller-Werdan U (2001) Autonomic dysfunction in the ICU patient. Curr Opin Crit Care 7 (5):314-322

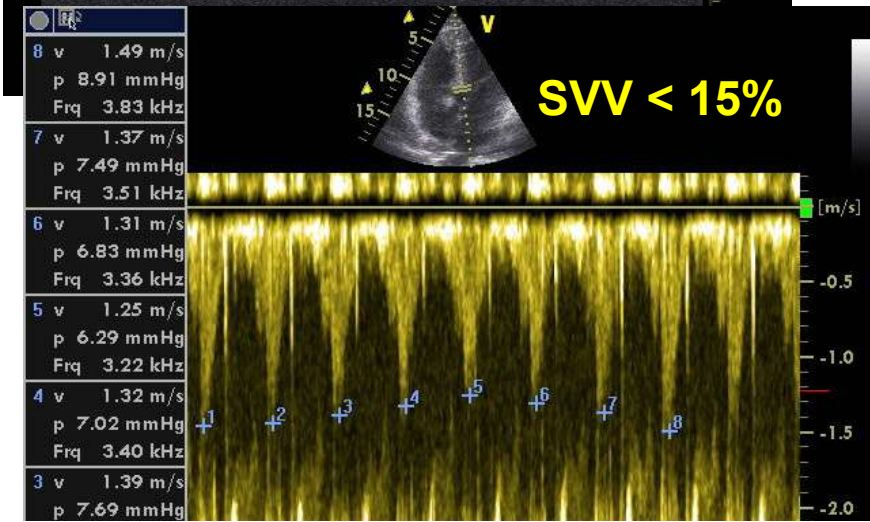
Vazodilatace a nízký komorový endsystolický tlak

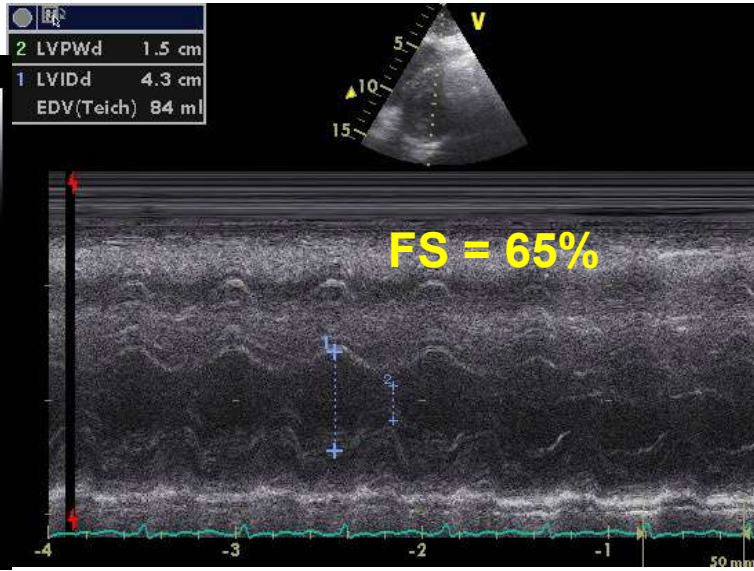
- Low SVR, ESA ⟹ High FS, S_{tdi}, EFLV

- Higher transmitral E









Ztráta ventriculoarterial. coupling v septickém šoku

- Bez ohledu na vysoký CO a CI
- Ees – indikátor systolické funkce
- Ea/Ees ve vztahu k srdeční energetice
- Norm. 1, patol. nad 1.3-1.8
- Ovlivněn vazopresory a inotropiky
- Betablokátory ?

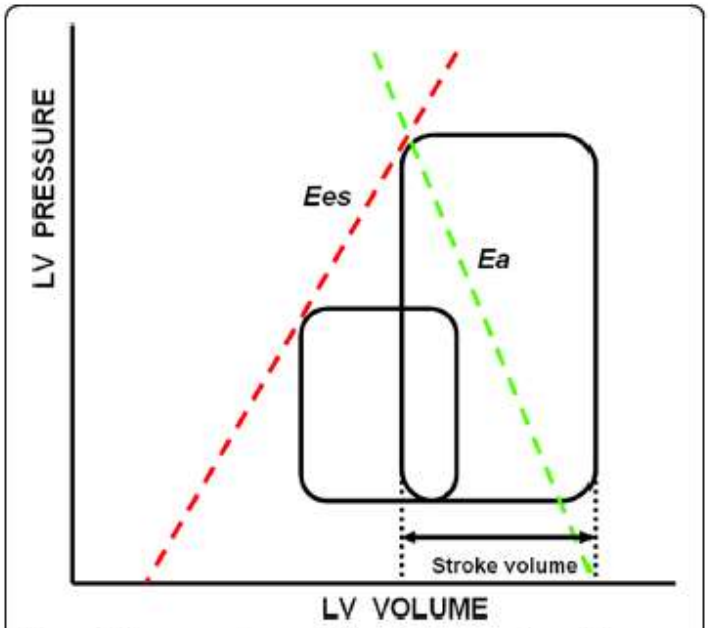
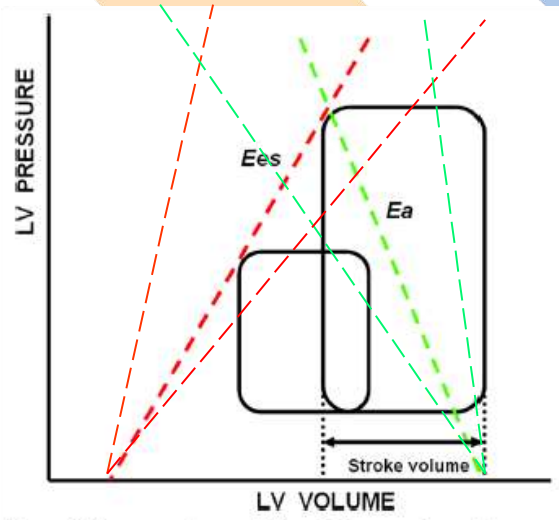
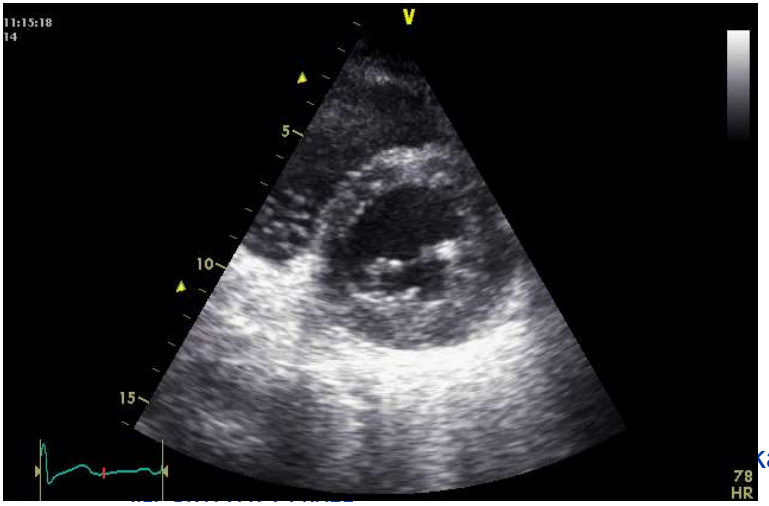


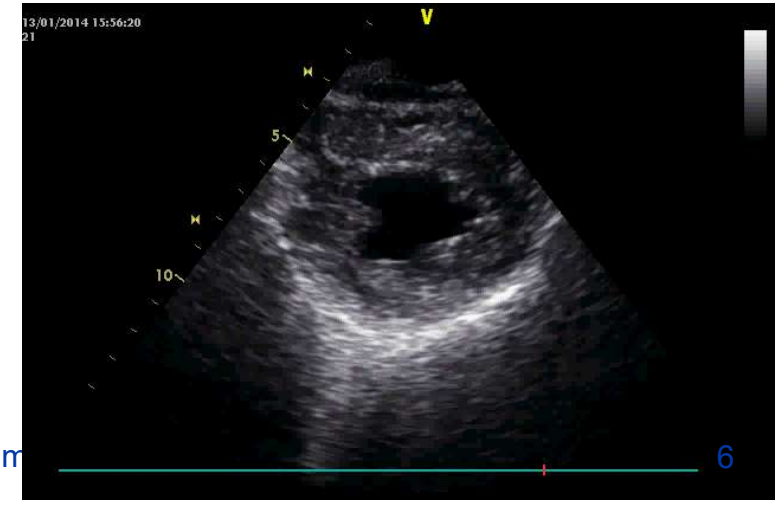
Figure 1 Pressure–volume relationship in a cardiac cycle. The slope of end-systolic elastance (Ees) (red line) represents the end-systolic pressure–volume relationship. The slope of arterial elastance (Ea) (green line) represents the relation between stroke volume (SV) and left ventricular (LV) systolic pressure as SV is varied.

Guarracino *et al. Critical Care* 2014, **18**:R80
http://ccforum.com/content/18/2/R80

Vazodilatace a ventrikulo-arteriální uncoupling



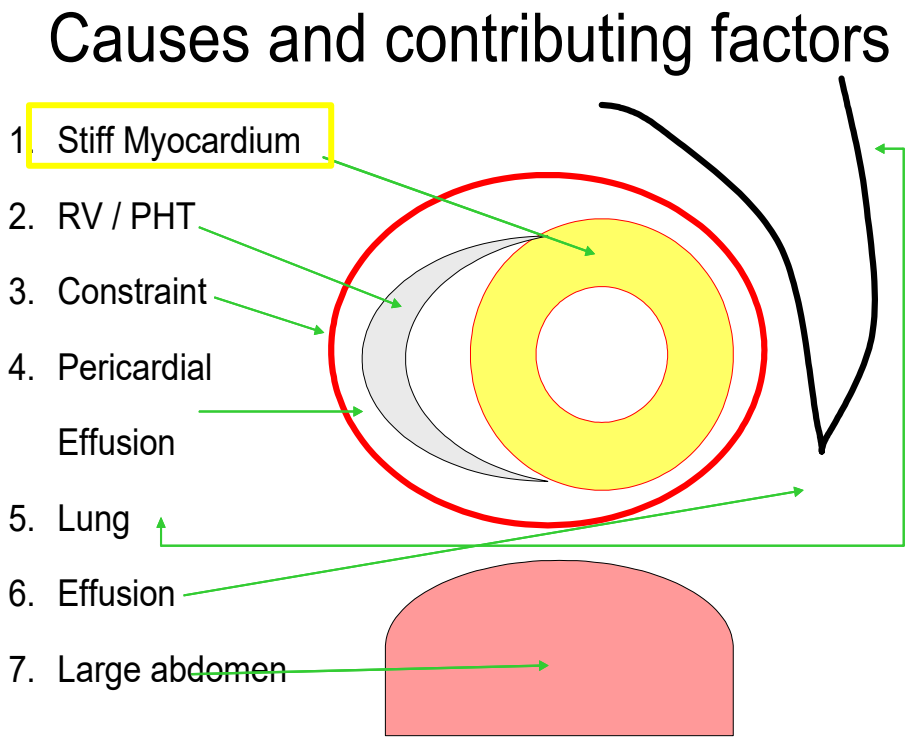




Diastolická dysfunkce: relaxace, kompliance, plnicí tlaky

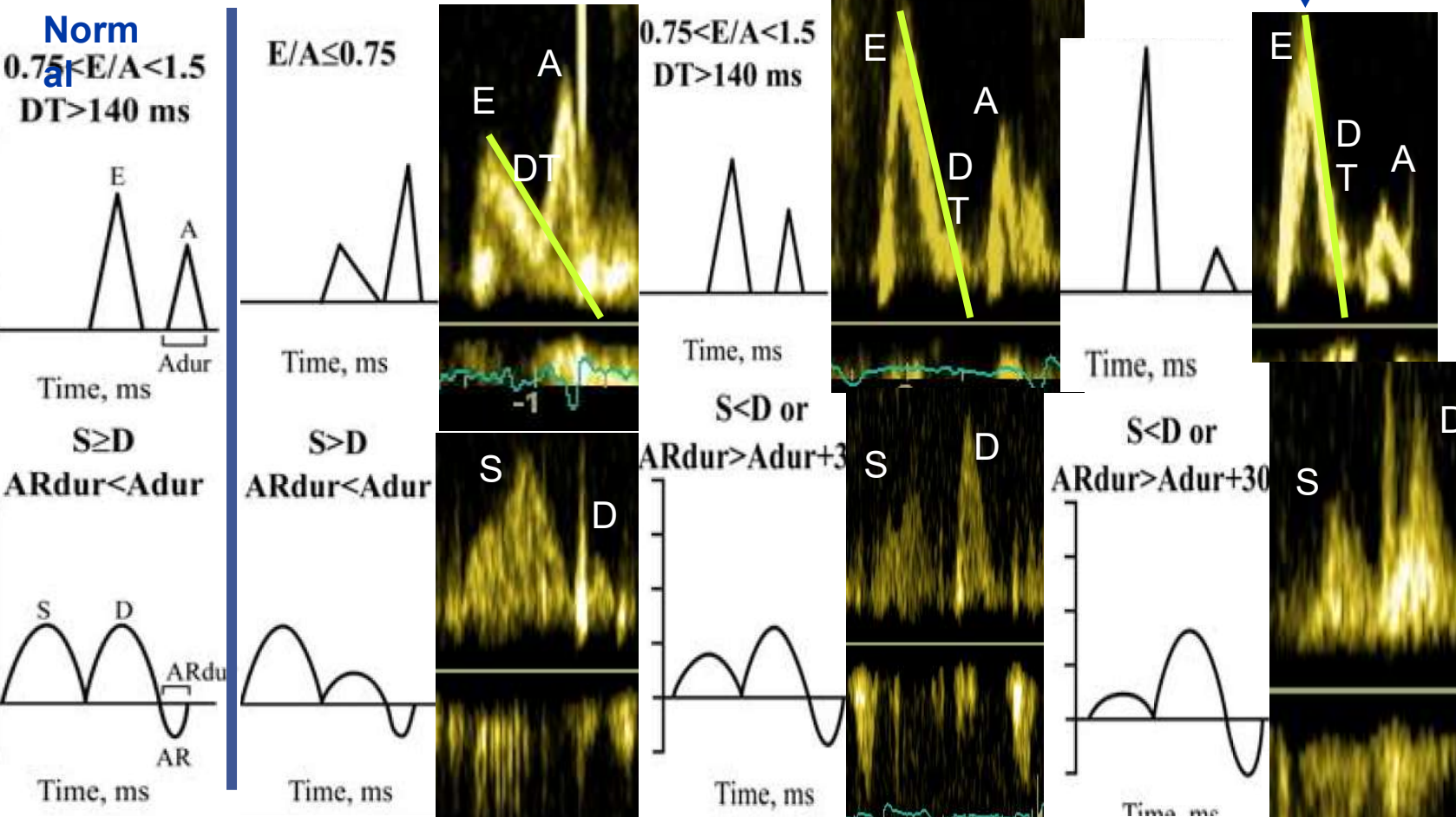
- Téměř 50% srdečních selhání je diastolických, se „zachovanou“ EFLV (Saleh M, Intensive Care Med 2012)
- Dg. s preload a afterload
- LA velikost, stěna LV
- HR a rytmus

  dependentní parametry
- Nagueh SF, et al: Eur J Echocardiography 2009, 10: 165-193

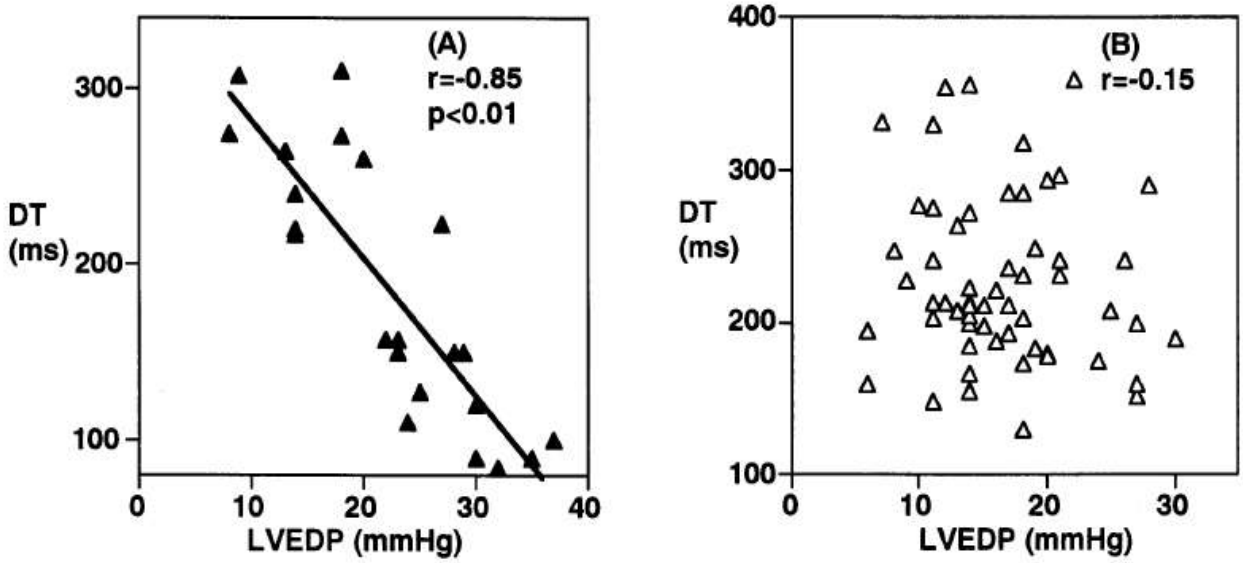


Diastolická funkce v septickém šoku

- Transmitral PW combined with pulmonary vein PW
- Degree of deterioration (relaxation disorder – pseudonormal – restrictive filling) relates to prognosis of septic shock (Poelaert J, Intensive Care Med 1997)



Determination of Left Ventricular Filling Pressure by Doppler Echocardiography in Patients With Coronary Artery Disease: Critical Role of Left Ventricular Systolic Function



Correlation to LVEDP :

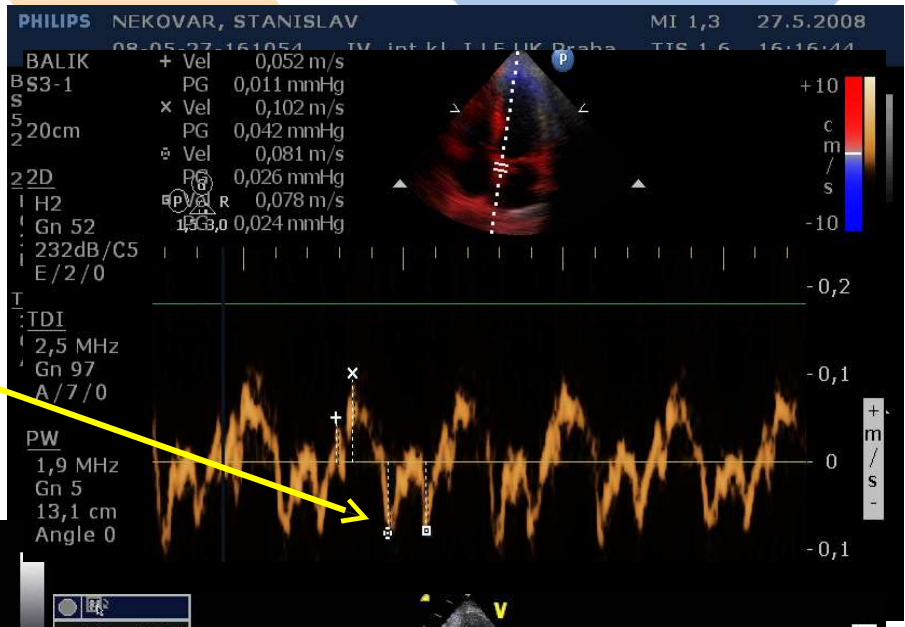
EF < 50% **r= 0,69**

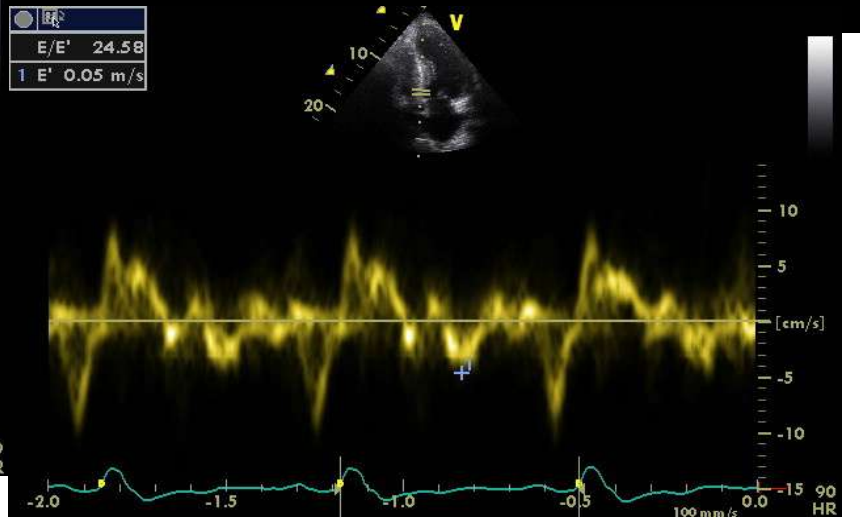
EF ≥ 50% **r= 0,48**

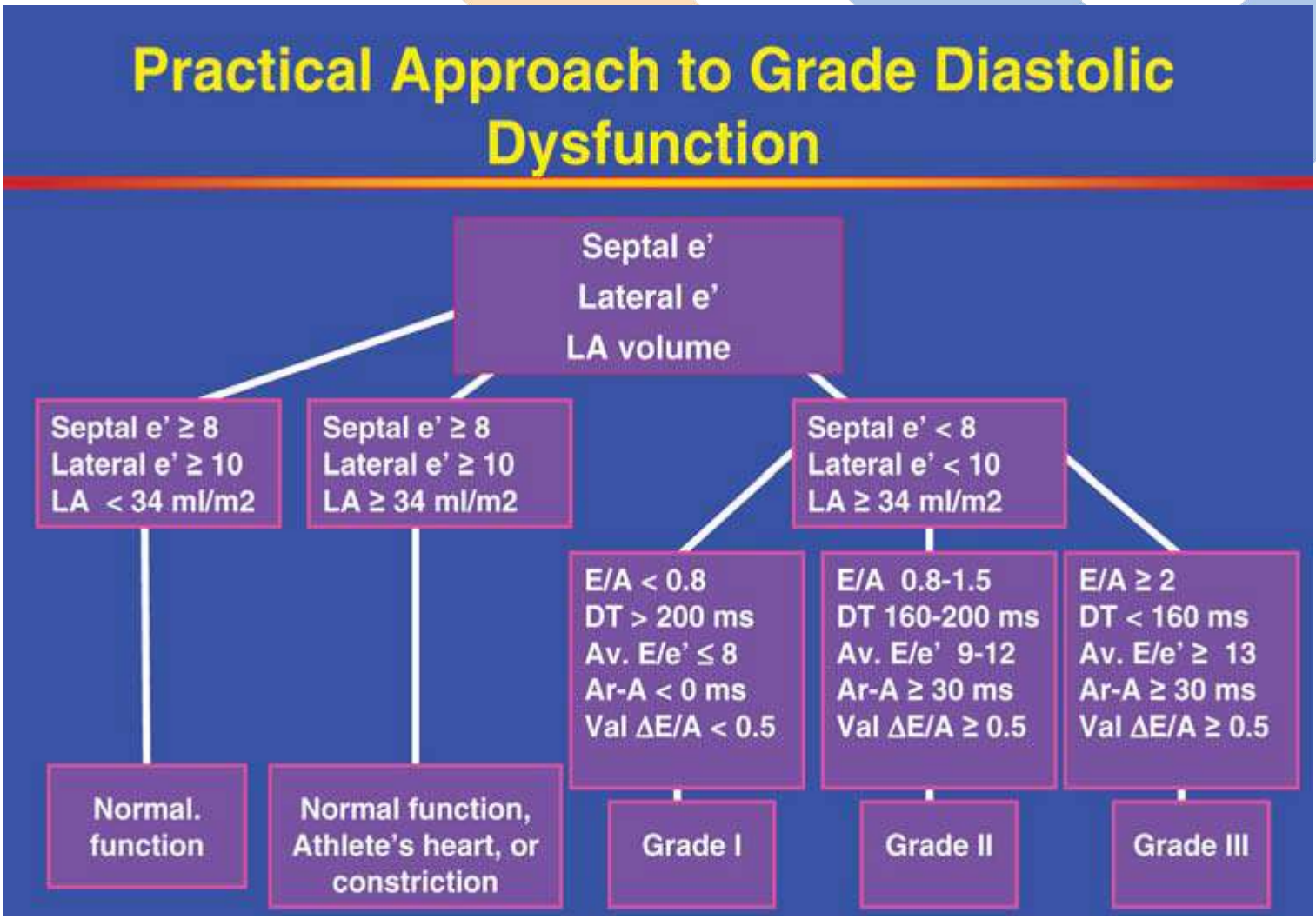
Yamamoto K. et al., JACC 1997

Echo parametry diastolické funkce: TDI (TVI)

- Low frequency signal with higher amplitude produced by myocardium (TVI)
- S_1, S_2, E´, A´
- E/E´<8 - normal LVEDP
- E/E´>13 – elevated LVEDP
- Other parameters if E/E´ 8-13

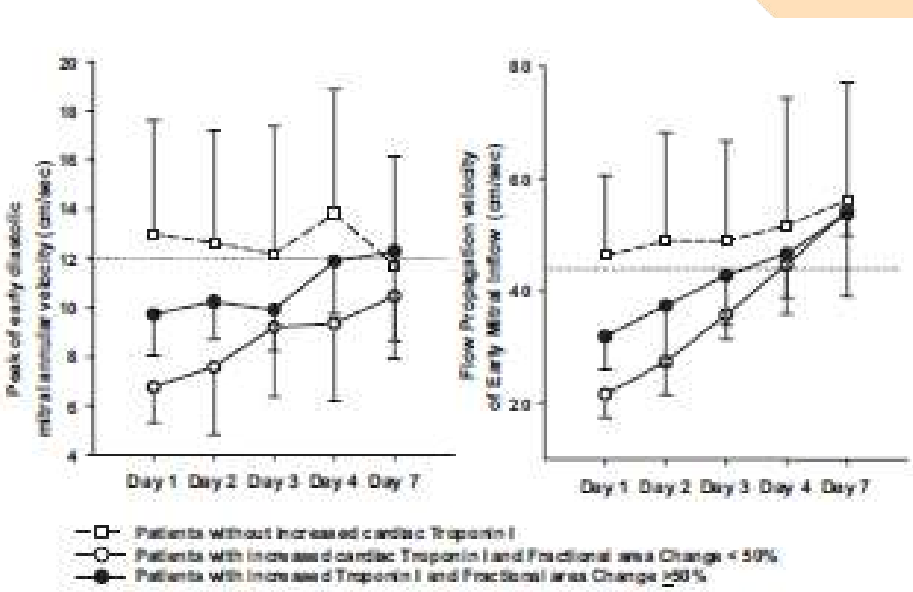


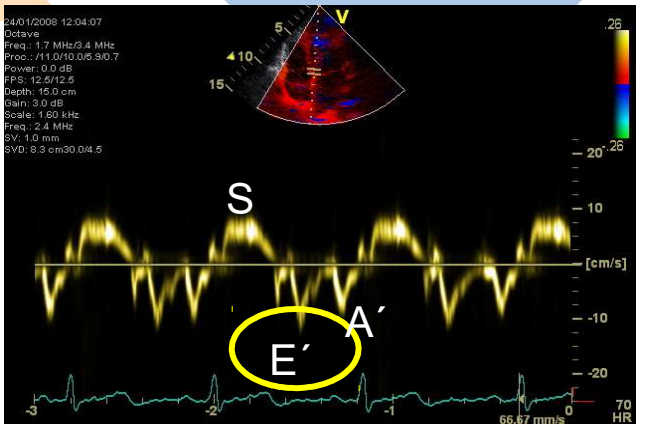


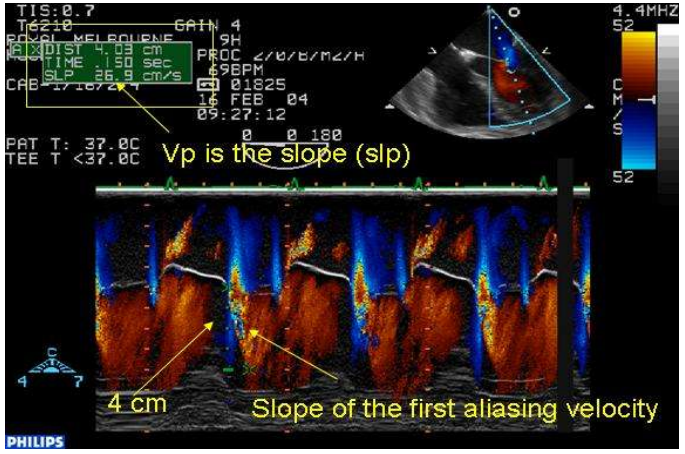


Nagueh SF, et al: Eur J Echocardiography 2009, 10: 165-193

Sepsis induced changes of diastolic function: relaxation, compliance and filling pressures



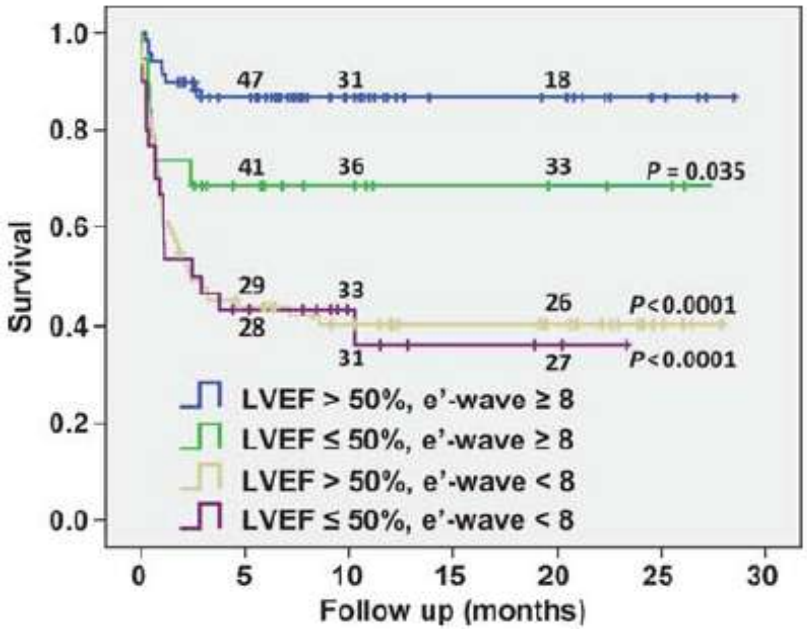


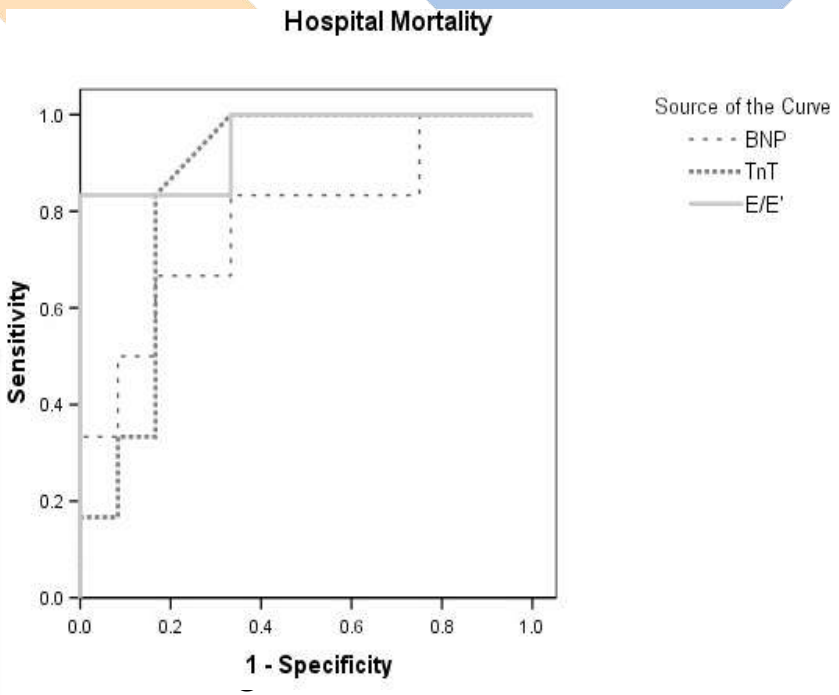


- Reversible impairment in 20%
- Associated with levels of TnI, IL-8, IL-10, TNFα
- Bouhemad B, Crit Care Med 2008

Diastolická dysfunkce a prognoza v sepsi

- Hlavní determinanta přežití srdečního selhání v sepsi (Landesberg G: EHJ 2012)
- Septal diastolic E´ a LVEF

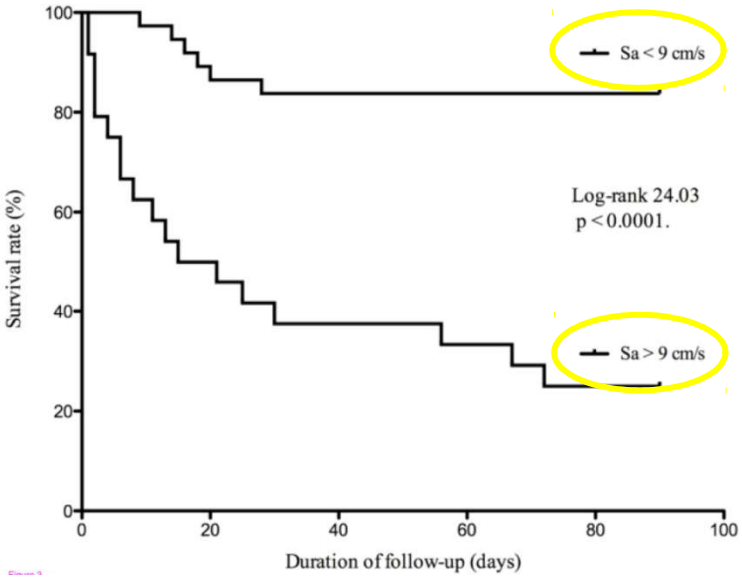




- TDI septal E/E´ jako prognostický indikátor (Sturgess D: Crit Care 2010)
- Lepší než biomarkery (BNP, TnT)

Systolická dysfunkce a prognoza v sepsi

- **Opačný vztah k přežití než diastolická funkce**
- Dilatovaná LV s „nepříliš sníženou“ systolickou funkcí lépe udržuje SV a CO (Parker M, Ann Intern Med, 1984)
- LV rozměry důležitější (Huang SJ, et al: Critical Care 2013)
- Manipulace s preload kritická (Frank-Starling)
- Vliv signifikantní MR (s anulární dilatací)



- Li Weng, et al: Critical Care 2012
- TDI mean septální a laterální **S wave** jako prognostický indikator
- Možný vztah ke kontraktilitě a nízkému afterload v sepsi (?)

Není za lepším přežitím „dilatovaných komor“ v sepsi menší stupeň vazodilatace ?

- LVEDV, LVESV a LV_EF jako afterload dependentní parametry
- Low SVR a hyperdynamická cirkulace udržuje nižší LVESV a vyšší LV_EF
- Kritický pokles SVR a afterload = možná příčina selhání u nedilatovaných LV se zachovanou LV_EF

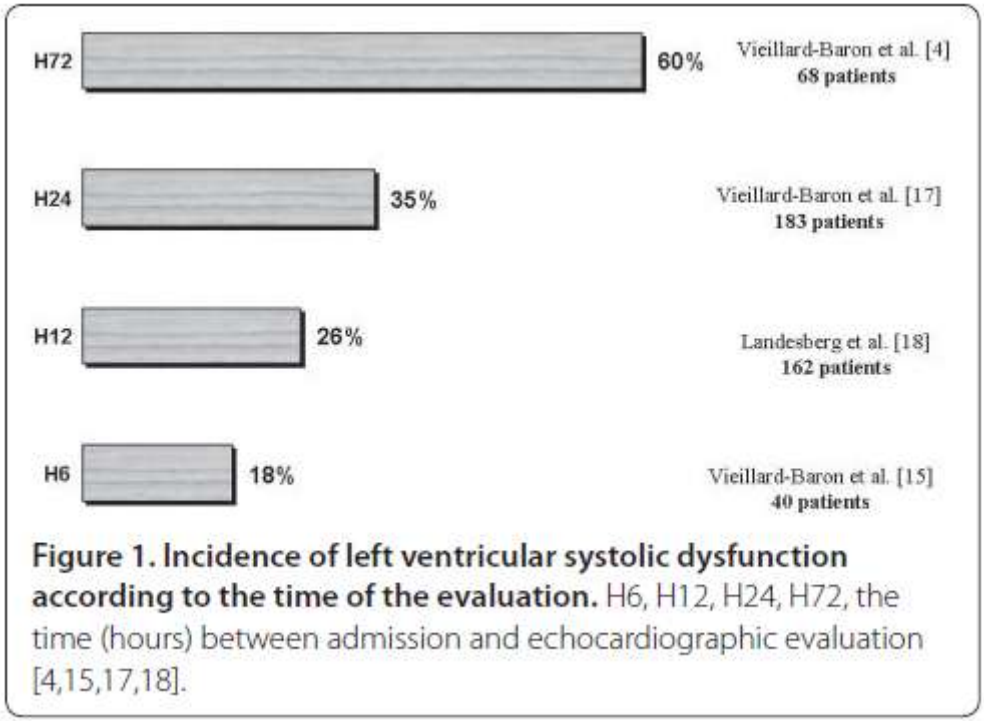


Figure 1. Incidence of left ventricular systolic dysfunction according to the time of the evaluation. H6, H12, H24, H72, the time (hours) between admission and echocardiographic evaluation [4,15,17,18].

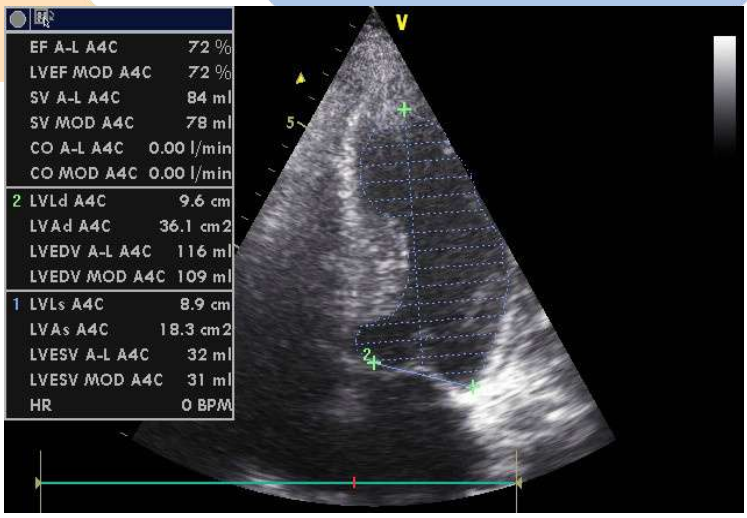
Evaluation of left ventricular systolic function revisited in septic shock

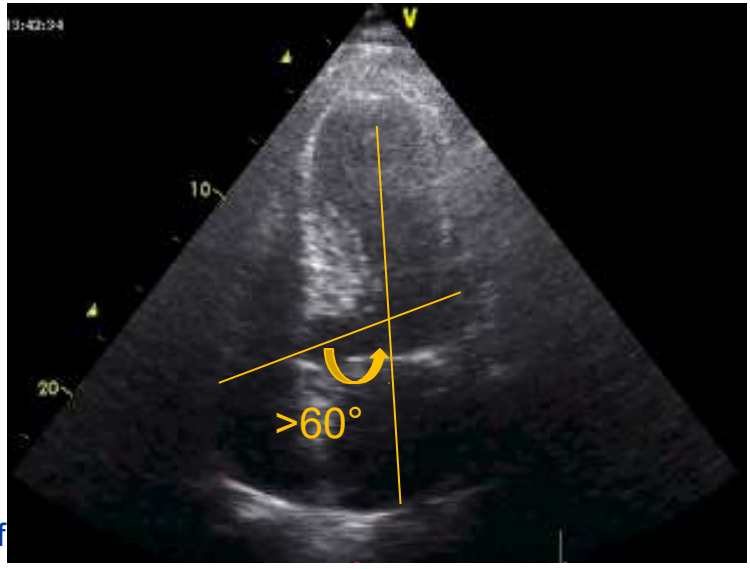
Xavier Repessé[1,2], Cyril Charron[1,2] and Antoine Vieillard-Baron*[1,2]

CRITICAL CARE

Selhání LK: Dynamická LVOT obstrukce v septickém šoku

- LVOT gradient > 30 mmHg při zátěži (Nistri S, et al: Am J Cardiol 2012)
- Septum sigmoideum - angulace subaortálně >15 mm s normální midseptální tloušťkou
- ESLV axis úhel k LVOT > 60°
- Prominentní papilární sval okluduje > ½ LVESD
- Koncentrická hypertrofie





Cha et al. Cardiovascular Ultrasound 2014, 12:23
http://www.cardiovascularultrasound.com/content/12/1/23

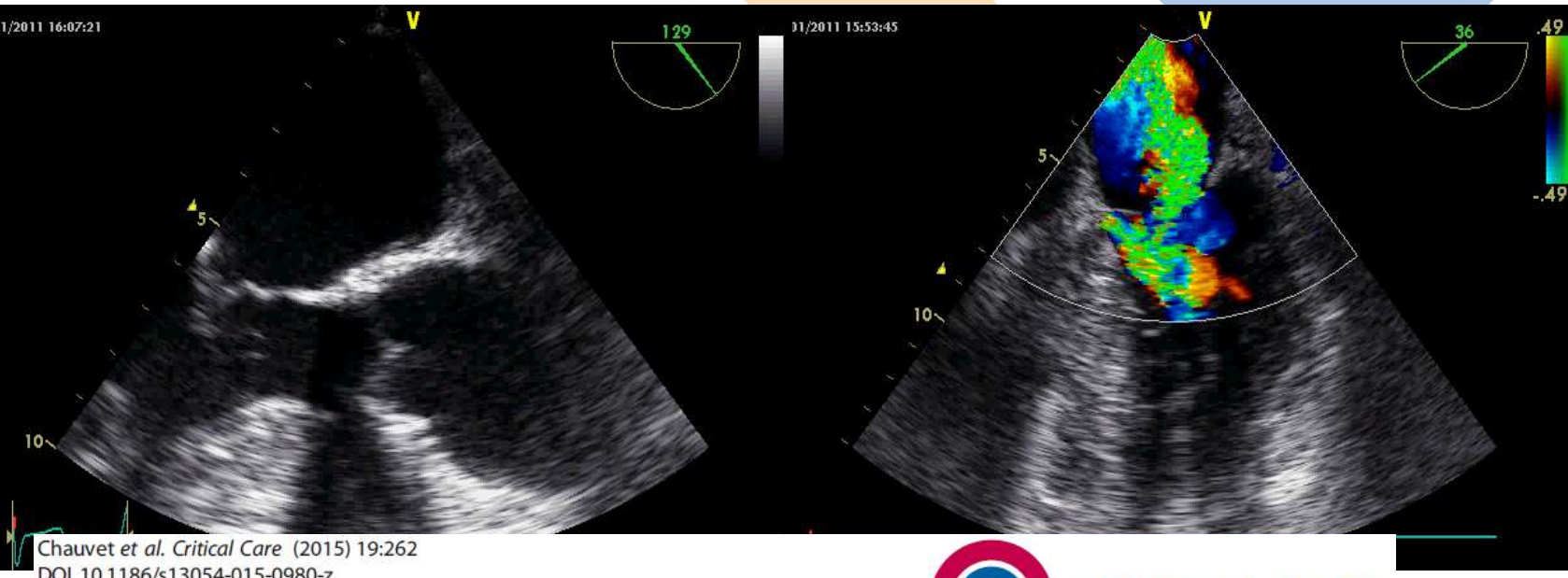
CARDIOVASCULAR ULTRASOUND

RESEARCH Open Access

Diverse geometric changes related to dynamic left ventricular outflow tract obstruction without overt hypertrophic cardiomyopathy

Jung-Joon Cha†, Hyemoon Chung†, Young Won Yoon*, Ji Hyun Yoon, Jong-Youn Kim, Pil-Ki Min, Byoung-Kwon Lee, Bum-Kee Hong, Se-Joong Rim, Hyuck Moon Kwon and Eui-Young Choi*

Insufficient preload and low afterload (sepsis): Dynamic LVOT obstruction causing heart failure



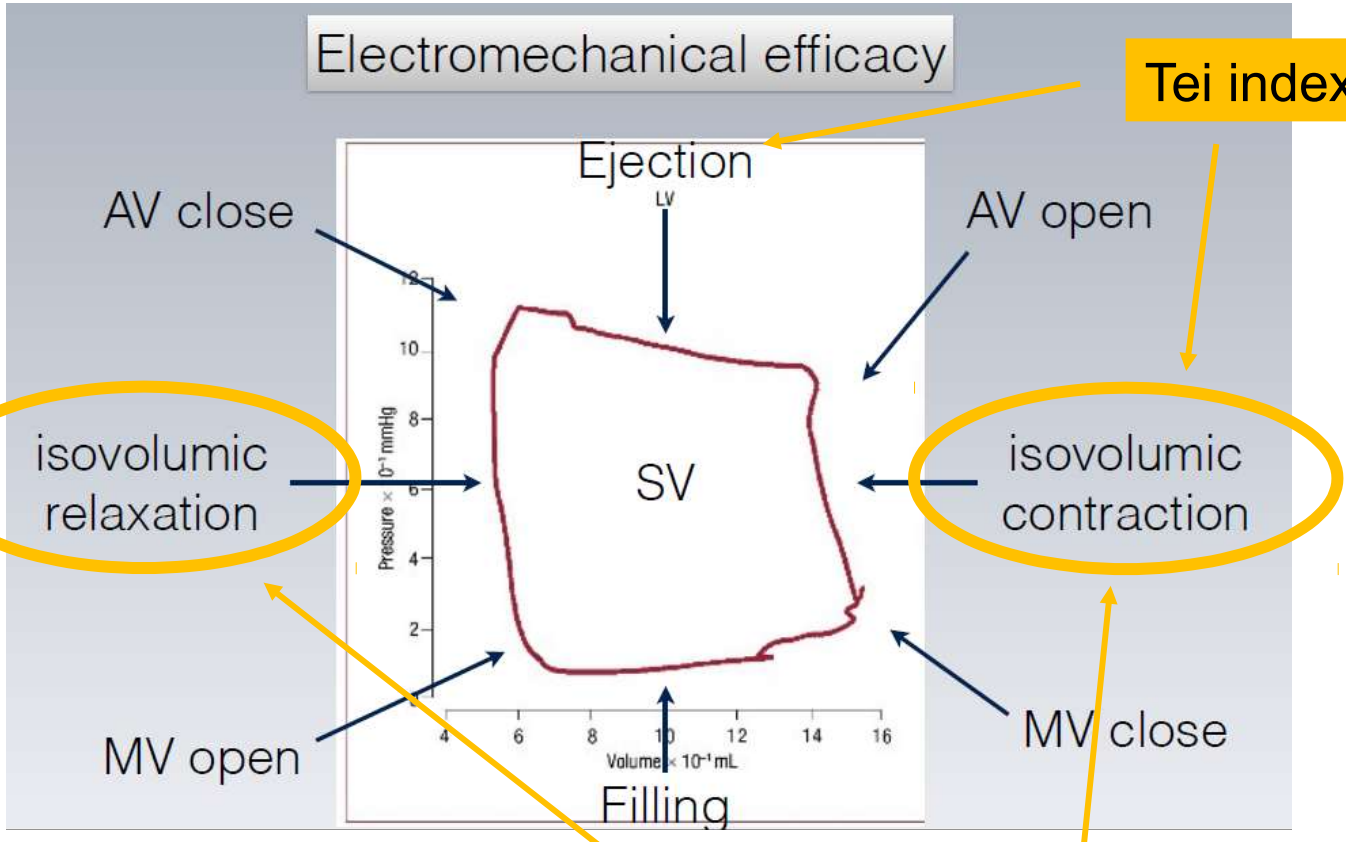
Chauvet *et al. Critical Care* (2015) 19:262
DOI 10.1186/s13054-015-0980-z

CRITICAL CARE

RESEARCH Open Access

Early dynamic left intraventricular obstruction is associated with hypovolemia and high mortality in septic shock patients

Systolic-diastolic interaction….how to put it all together

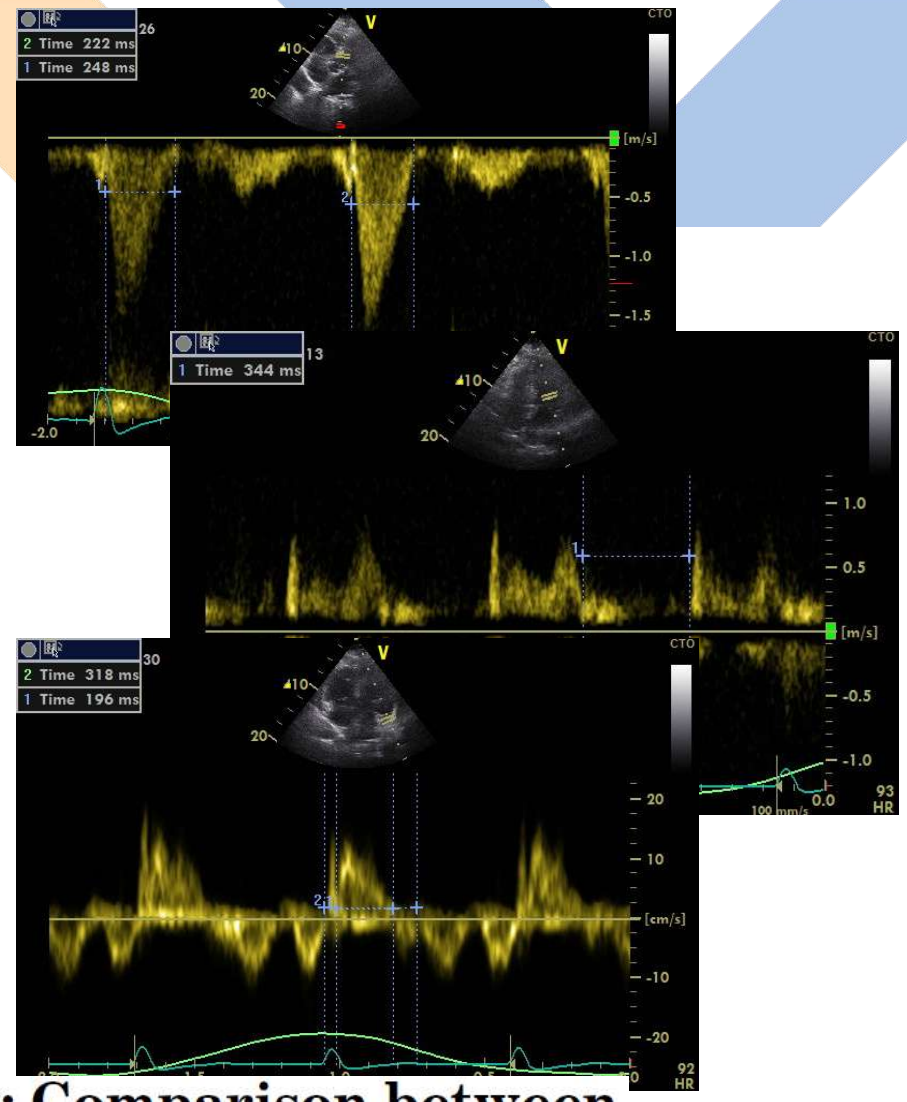


Adapted from Guido Tavazzi, Pavia

Total isovolumic time

Tei index LV/RV

- Isovolemic contraction time is increased in systolic dysfunction
- Time in which LV does not eject
- ↑ Tei index, 344-235/344=0.32
- normal < 0.25-0.28
- Limitation in arrhythmias and valve disoders
- Calculated with TVI less preload dependent (318-196/318=0.38



Left Ventricular Tei Index: Comparison between Flow and Tissue Doppler Analyses

Wen-Chol Voon, M.D., Ho-Ming Su, M.D., Hsueh-Wei Yen, M.D., Tsung-Hsien Lin, M.D., Wen-Ter Lai, M.D., and Sheng-Hsiung Sheu, M.D. *(ECHOCARDIOGRAPHY, Volume 22, October 2005)*

Total isovolumic time (t-IVT) – time in which LV neither ejects nor fills

t-IVT = 60 – (t-FT + t-ET)

> 14s …..marker of global LV mechanical dyssynchrony

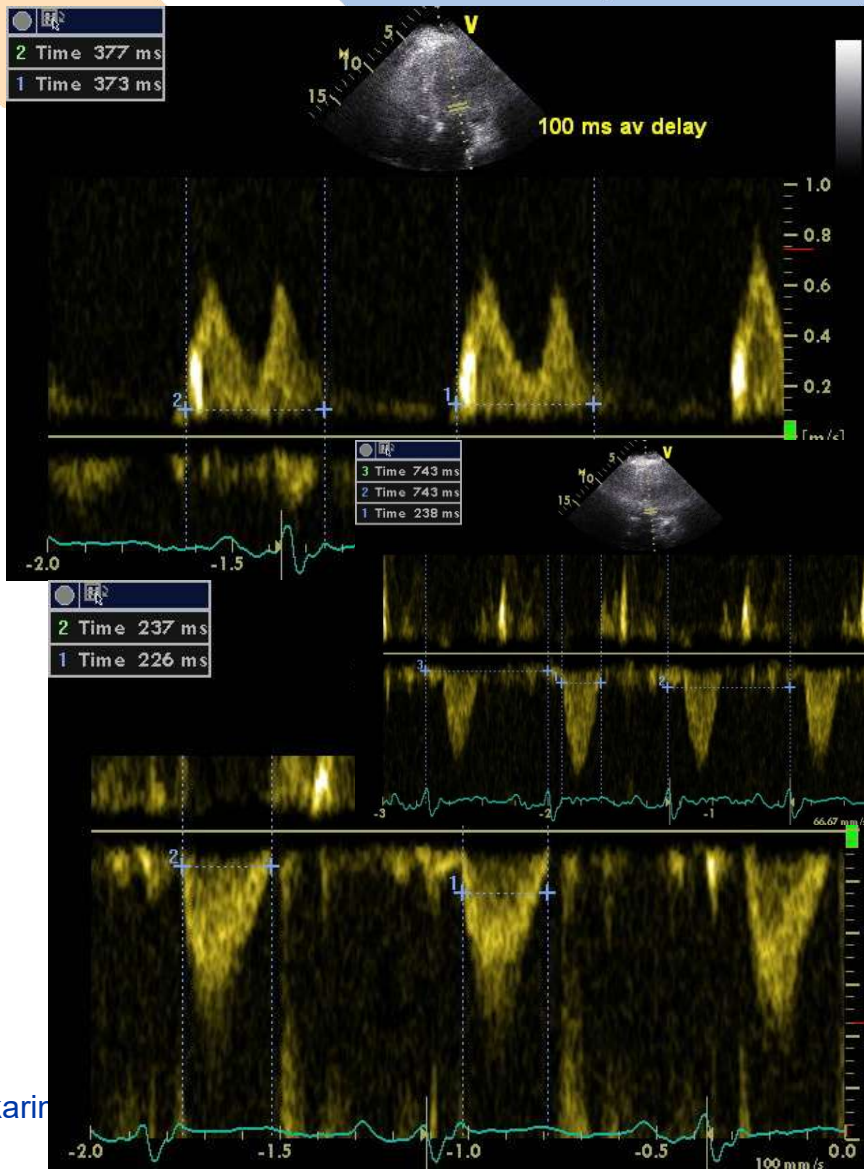
t-Filling Time = FT * 60 / RR

t-Ejection Time = ET * 60 / RR

t-IVT = 60 – (30 + 19) = 11s

Applications in

- ischaemic heart disease
- DDD adjustment
- resynchronisation therapy
- adjustment of inotropes



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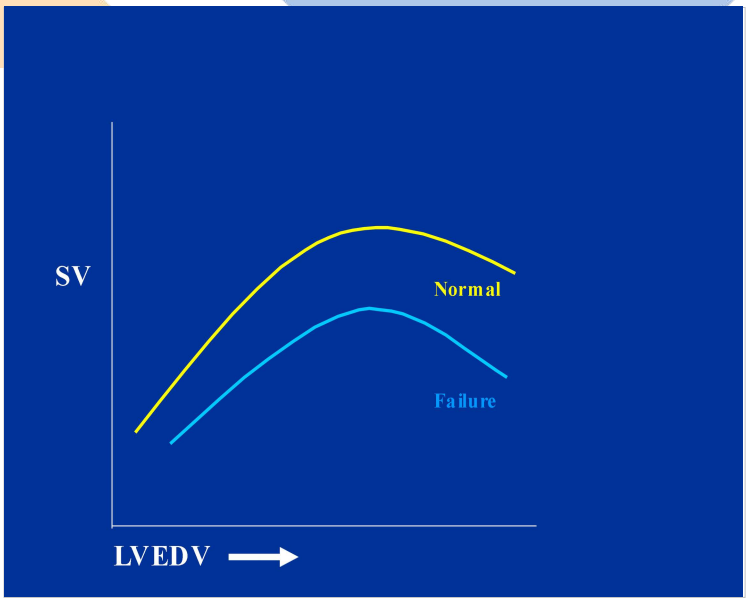
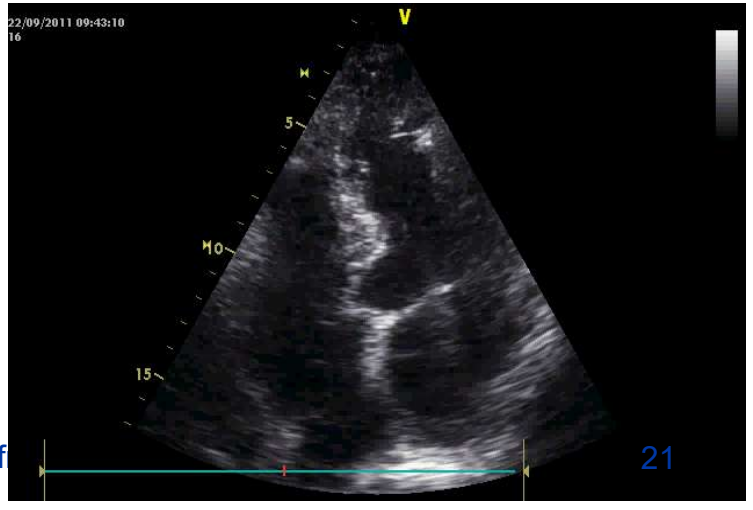
Alterace systolické a diastolické funkce: Implikace pro terapii

- Nenaplněná LV: vliv vysoké dávky katecholaminů na myokard (cAMP, IC calcium, receptor downregulation)

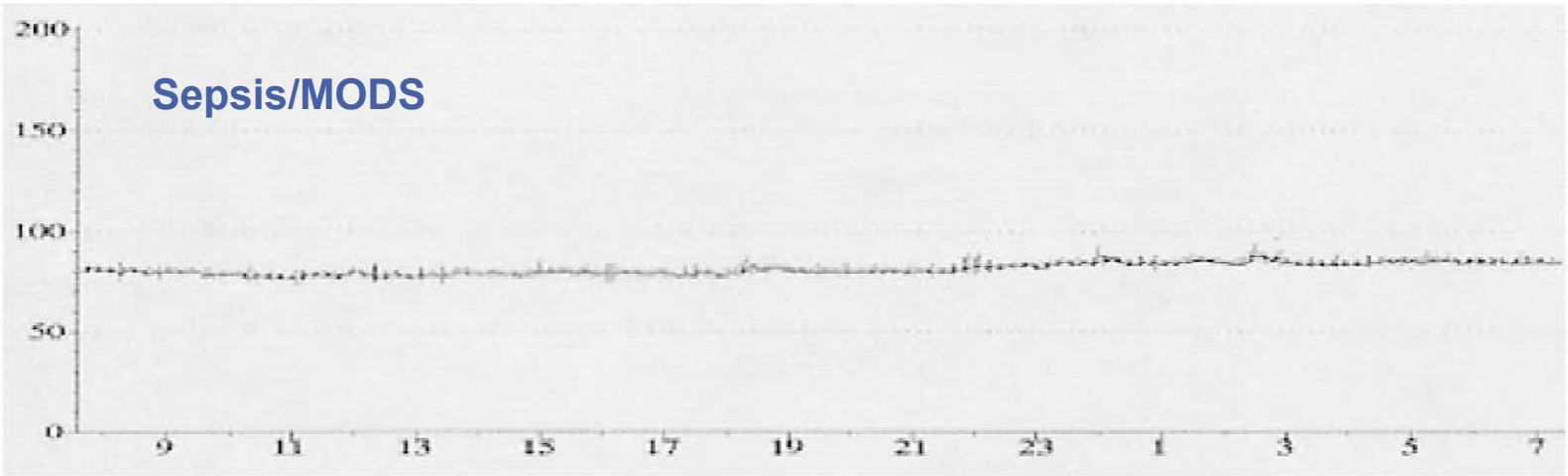
X

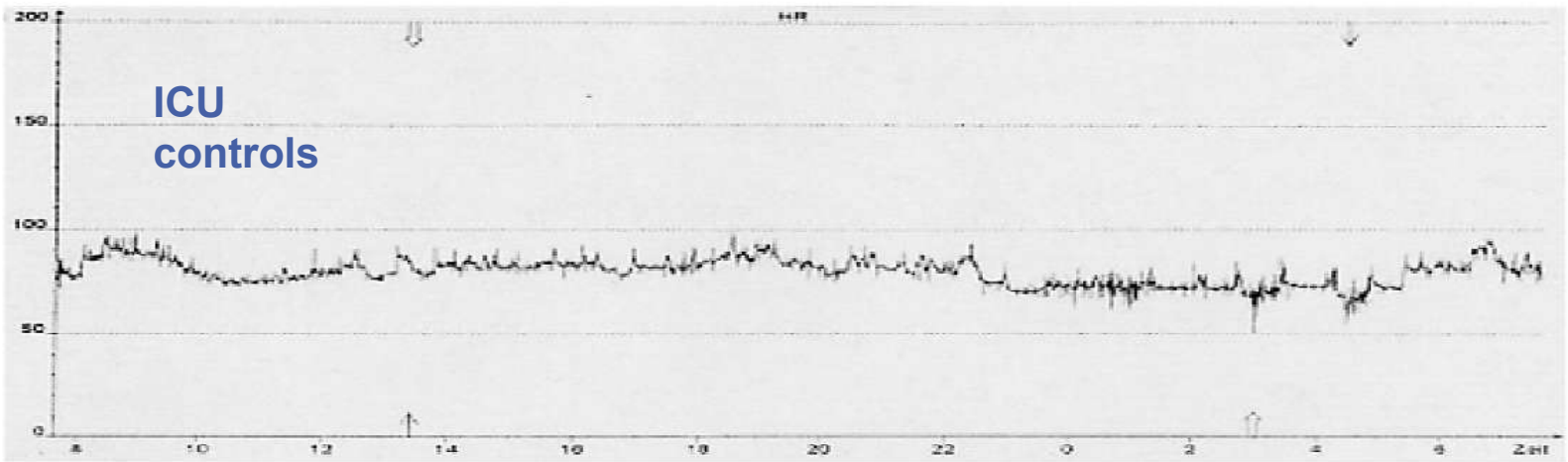
- Elevace EDP při absenci LV systolic. dysfunkce: Diastology !
- „Nepodajné“ komory citlivější k změnám v preload a afterload
- Rychlá infuze tekutin může vyústit v
  - Plicní edém
  - RV dilataci a arytmie
    - Potenciace aggresivní UPV





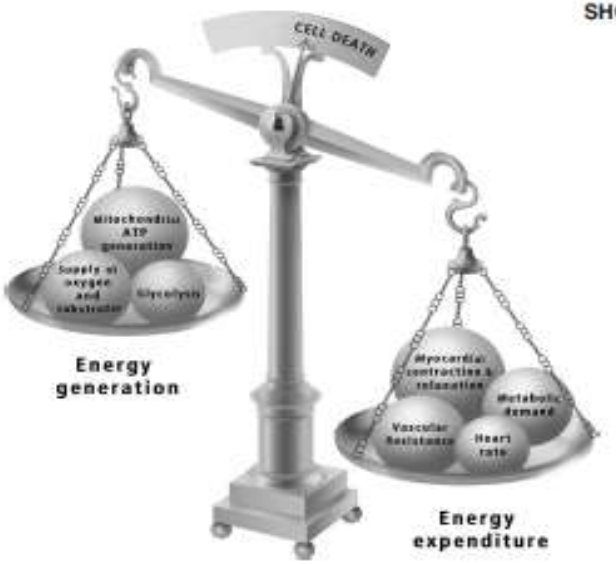
Low HR variability in sepsis (Schmidt H et al: Autonomic dysfunction in the critically ill. Curr Opin Crit Care 2001, 7: 314-322)





High heart rate in septic shock

- Heart rate as one of major determinants of myocardial VO_2
- Septic shock: Any chance of being more cardioprotective….?



Rudiger A: Crit Care Med 2010

SHOCK, Vol. 28, No. 6, pp. 655-661, 2007

ENDOTOXIN IMPAIRS THE HUMAN PACEMAKER CURRENT I_F

Klaus Zorn-Pauly,* Brigitte Pelzmann,* Petra Lang,* Heinrich Mächler,† Hendrik Schmidt,‡ Henning Ebelt,‡ Karl Werdan,‡ Bernd Koidl,* and Ursula Müller-Werdan‡

*Institut für Biophysik, Zentrum für Physiologische Medizin; †Universitätsklinik für Chirurgie, Abteilung für Herzchirurgie, Medizinische Universität Graz, Austria; and ‡Universitätsklinik und Poliklinik für Innere Medizin III, Klinikum der Martin Luther-Universität Halle-Wittenberg, Halle (Saale), Germany

Intensive Care Med
DOI 10.1007/s00134-011-2236-y

EXPERIMENTAL

Jerome Aboab
Veronique Sebille
Mercé Jourdain
Jacques Mangalaboyi
Miloud Gharbi
Arnaud Mansart
Djillali Annane

Effects of esmolol on systemic and pulmonary hemodynamics and on oxygenation in pigs with hypodynamic endotoxin shock

EGDT: a causative link to septic heart involvement ?

TABLE 5. Recommendations: Initial Resuscitation and Infection Issues

Surviving Sepsis Guidelines: Crit Care Med 2013

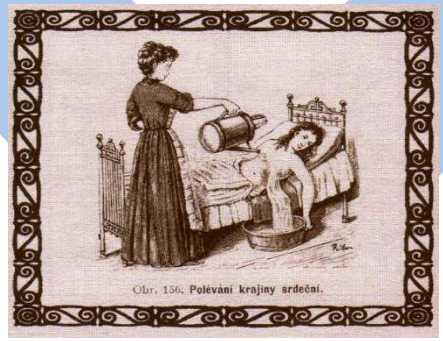
A. Initial Resuscitation

1. Protocolized, quantitative resuscitation of patients with sepsis- induced tissue hypoperfusion (defined in this document as hypotension persisting after initial fluid challenge or blood lactate concentration ≥ 4 mmol/L). Goals during the first 6 hrs of resuscitation:
   a) Central venous pressure 8–12 mm Hg
   b) Mean arterial pressure (MAP) ≥ 65 mm Hg
   c) Urine output ≥ 0.5 mL/kg/hr
   d) Central venous (superior vena cava) or mixed venous oxygen saturation 70% or 65%, respectively (grade 1C).
2. In patients with elevated lactate levels targeting resuscitation to normalize lactate (grade 2C).

- Metaanalysis of EGDT shows ZERO IMPACT on MORTALITY, **2.7-3 x higher use of dobutamine**, red-cell transfusions (SE !). Gu WJ et al: Crit Care 2014
- ARISE (ANZICS CCgroup): NEJM 2014: 51 centers, 1600 pts: Fluid (1964±1415 ml vs. 1713±1401 ml), vasopressor (66.6% vs. 57.8%), red-cell transfusions (13.6% vs. 7.0%), **dobutamine (15.4% vs. 2.6%)** (P<0.001 for all comparisons). NO EFFECT on MORTALITY !

Fluid challenges in intensive care: the FENICE study : A global inception cohort study.

ARTICLE in INTENSIVE CARE MEDICINE · JULY 2015

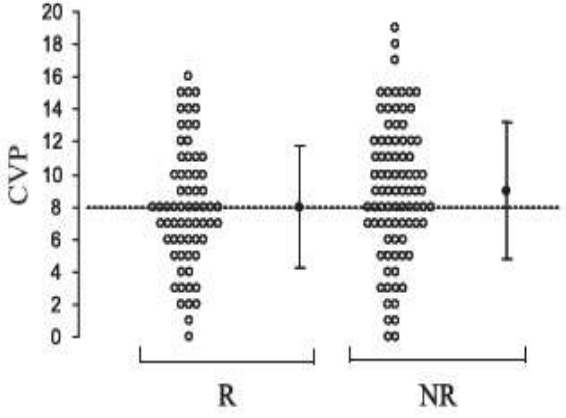


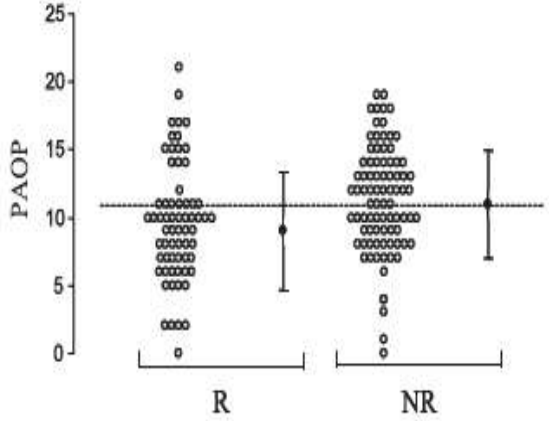
72% volumexpansion with positive effect

45% intensivists have no clear parameters to guide volume challenge

30% indicate according to static parameters of preload

25% indicate according to dynamic parameters incl. echocardiography





- CVP pos. predictive value of 47% (61% in low SVI), OUC 0.56
- PAWP pos. predictive value of 54% (69% in low SVI)

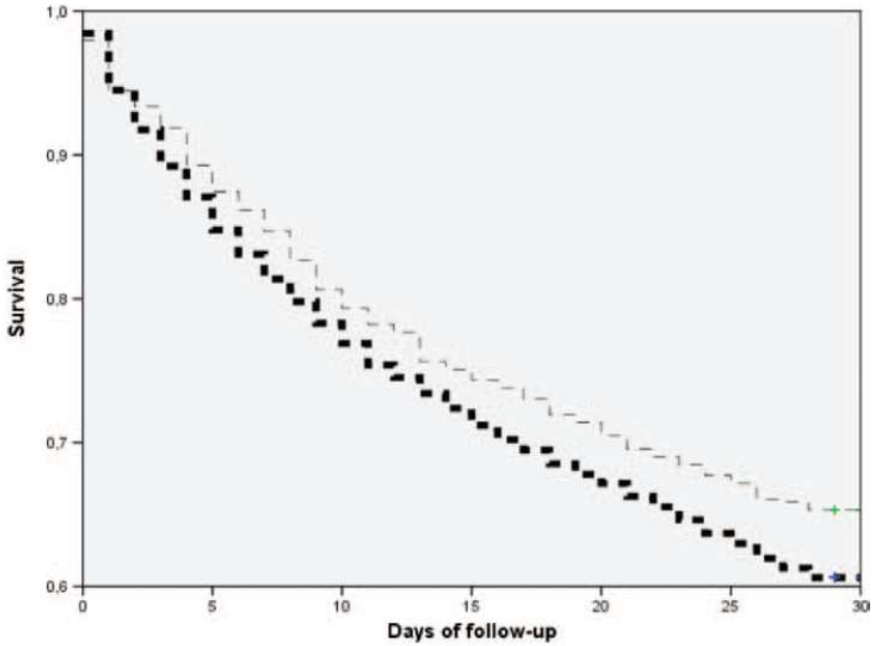
(Osman D, et al: Crit Care Med 2007, Marik PE: Crit Care Med 2013)

Previous prescription of β-blockers is associated with reduced mortality among patients hospitalized in intensive care units for sepsis*

(Crit Care Med 2012; 40:2768–2772)

Alejandro Macchia, MD; Marilena Romero, PhD; Pablo Dino Comignani, MD; Javier Mariani, MD; Antonio D'Ettorre, PhD; Nadia Prini, MD; Mariano Santopinto, MD; Gianni Tognoni, MD

- Retrospective italian database 2003-2008: 9465 pts > 40 years
- 1061 on betablockers (11.2%)
- Lower 28-d mortality (17.7% vs 22%, p=0.025)
- Cohort and prescribtion heterogenity

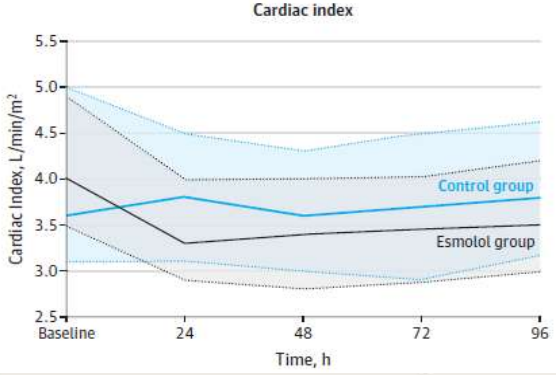


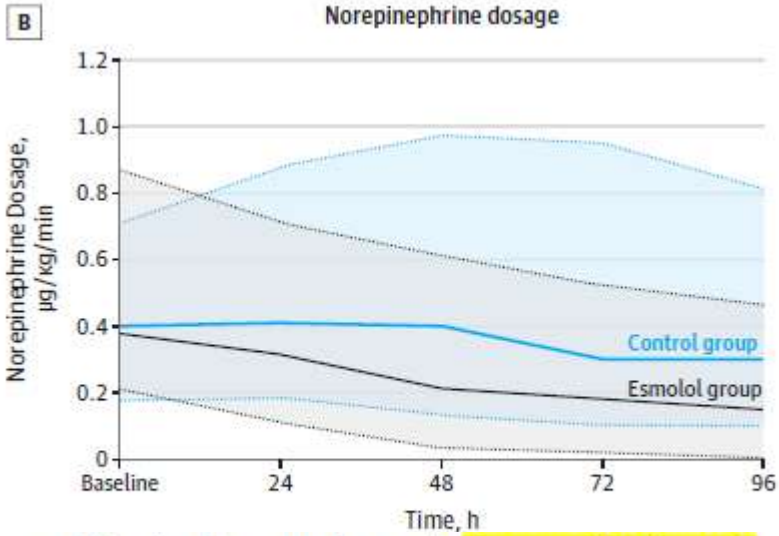
Preliminary Communication | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Heart Rate Control With Esmolol on Hemodynamic and Clinical Outcomes in Patients With Septic Shock

A Randomized Clinical Trial

Surviving Sepsis Guidelines (EGDT) + median esmolol 100 mg/h: HR 80-





($P < .001$; eTable 1 in the Supplement), the need for levosimendan rescue therapy did not differ between groups (49.4% of esmolol patients vs 40.3% control patients; $P = .39$). Fluid

Outcome	No. (%) Esmolol (n = 77)	Control (n = 77)	*P* Value
Mortality			
28 d	38 (49.4)	62 (80.5)	<.001
ICU	44 (57.1)	68 (88.3)	<.001
Hospital	52 (67.5)	70 (90.9)	<.001
Length of ICU stay, d			
Median (IQR)	19 (11-27)	14 (7-25)	.03
Survivors', median (IQR)	17 (9-28)	21 (11-34)	.70
Cause of death, No./total, (%)			
Multiple organ failure	15/52 (28.8)	26/70 (37.1)	.71
Refractory hypotension	32/52 (61.6)	44/70 (62.9)	
Unknown cause	5/52 (9.6%)		

- NO echo
- EGDT static parameters
- 49.4% rescue levosimendan
- Very low dosage esmolol
- Fluid balance ?

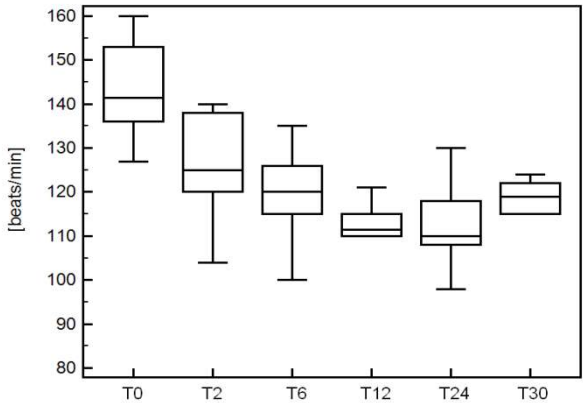
Echo guided betablockers in shock

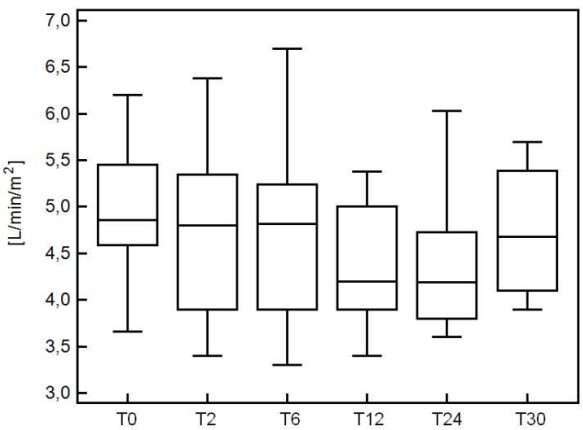
Wien Klin Wochenschr
DOI 10.1007/s00508-012-0209-y

Wiener klinische Wochenschrift
The Central European Journal of Medicine

Concomitant use of beta-1 adrenoreceptor blocker and norepinephrine in patients with septic shock

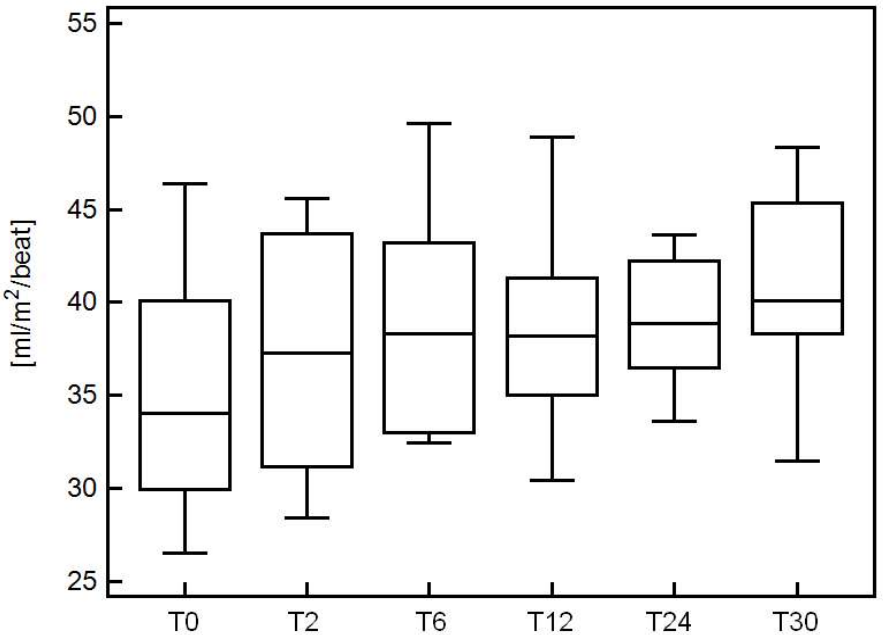
Martin Balik, Jan Rulisek, Pavel Leden, Michal Zakharchenko, Michal Otahal, Hana Bartakova, Josef Korinek





Cardiac output
Stroke volume

HR × SV
(if SV unchanged)



Esmolol: 213±64 mg/h - 273±90 mg/h (ve 24h)

Wien Klin Wochenschr
DOI 10.1007/s00508-013-0487-z

Wiener klinische Wochenschrift
The Central European Journal of Medicine

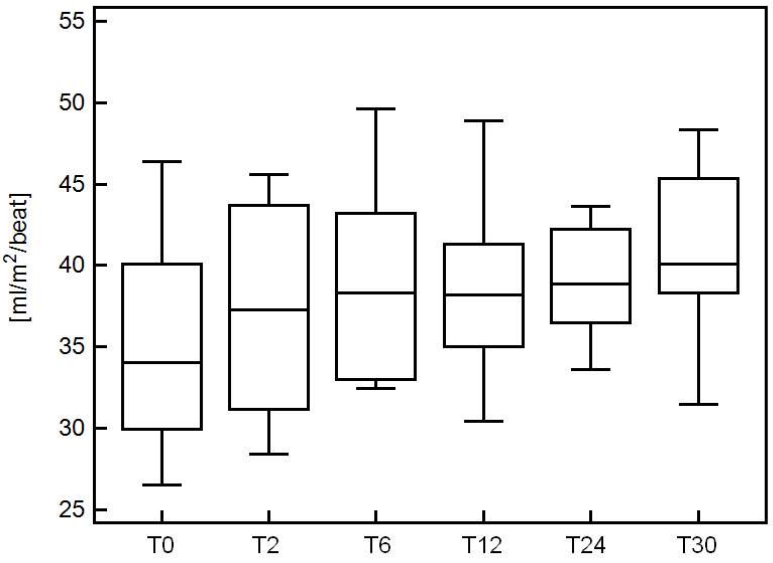
Concomitant use of beta-1 adrenoreceptor blocker and norepinephrine in patients with septic shock. Reply to a letter to the authors

Martin Balik · Jan Rulisek · Pavel Leden · Michal Zakharchenko · Michal Otahal · Hana Bartakova · Josef Korinek

No need for rescue levosimendan !

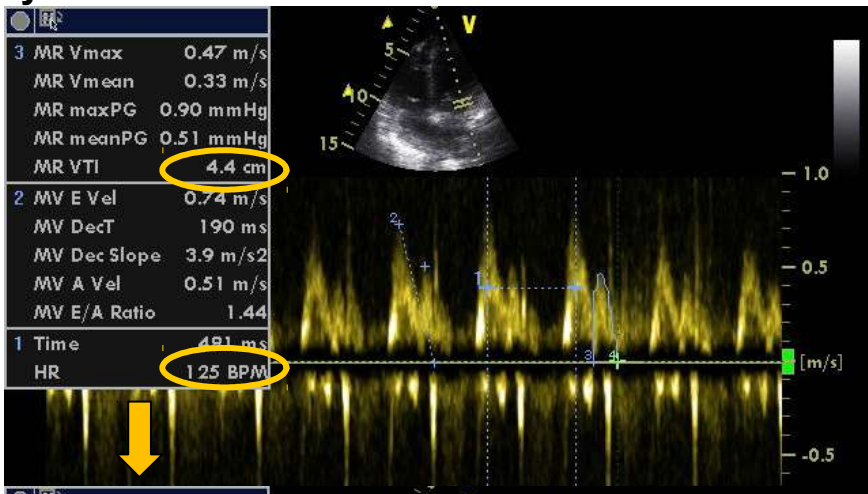
Betablocker and diastolic function in shock

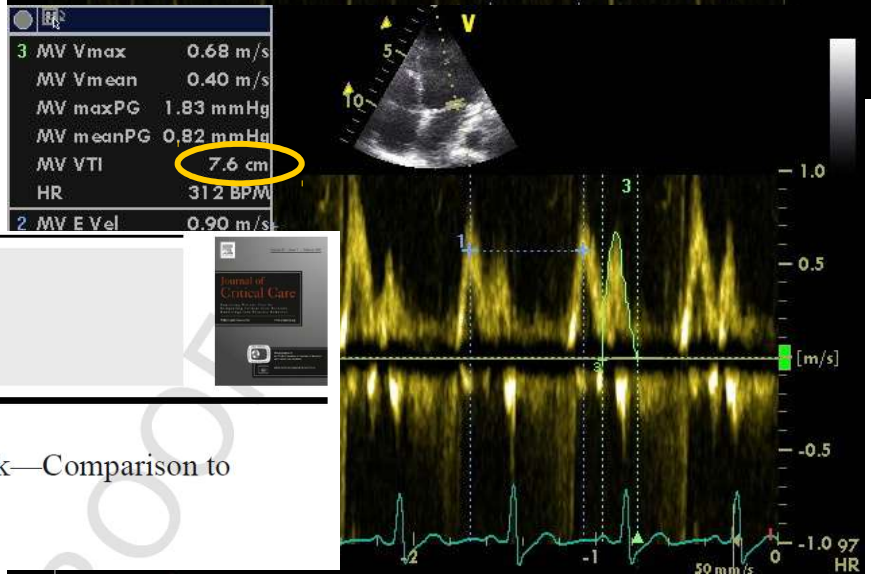
Stroke volume index: ⇧



140……110/min – tendency to increase SV

Změny diastolické funkce: A vlna





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Propafenone for supraventricular arrhythmias in septic shock—Comparison to amiodarone and metoprolol. The authors reply☆

M. Balik*, M. Maly, T. Brozek, P. Brestovansky

Journal of Critical Care 41 (2017) 16–23

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Propafenone for supraventricular arrhythmias in septic shock—Comparison to amiodarone and metoprolol☆,☆☆

M. Balik [a,*], I. Kolnikova [a], M. Maly [a], P. Waldauf [b], G. Tavazzi [c], J. Kristof [a]

234 patients with septic shock and SV arrhythmias
163 (69.7%) atrial fibrillation
34 (14.5%) chronic atrial fibrillation
27 (11.5%) SVT
10 (4.3%) atrial flutter

Phase I: Antiarrhythmic efficacy (24h)

Chronic AF excluded

Primary agent and after change within 24h

Concomitant electric cardioversion rates (23.7% amiodarone, 35.5% propafenone, ns)

Cardioversion rates: 73.5% amiodarone, 88.9% propafenone, 92.3% metoprolol

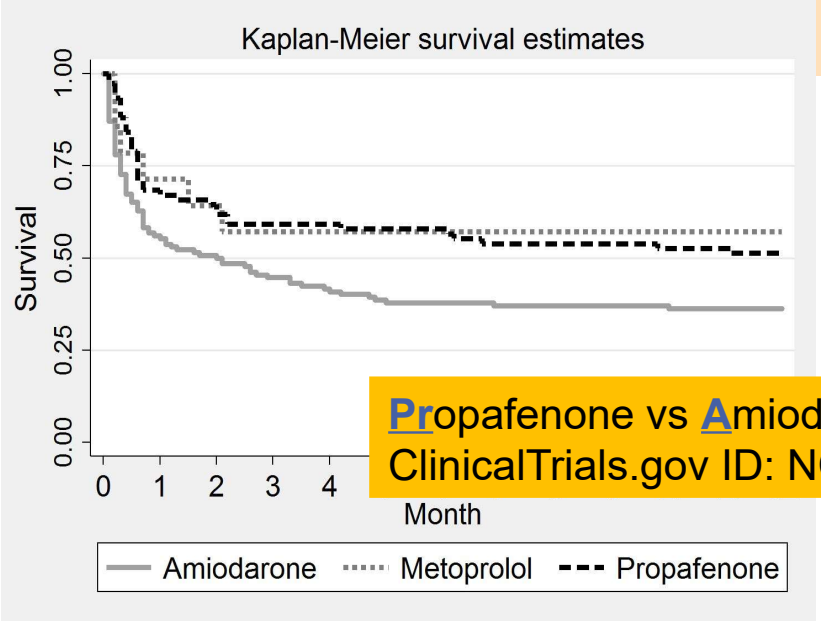
Phase II: Outcome analysis

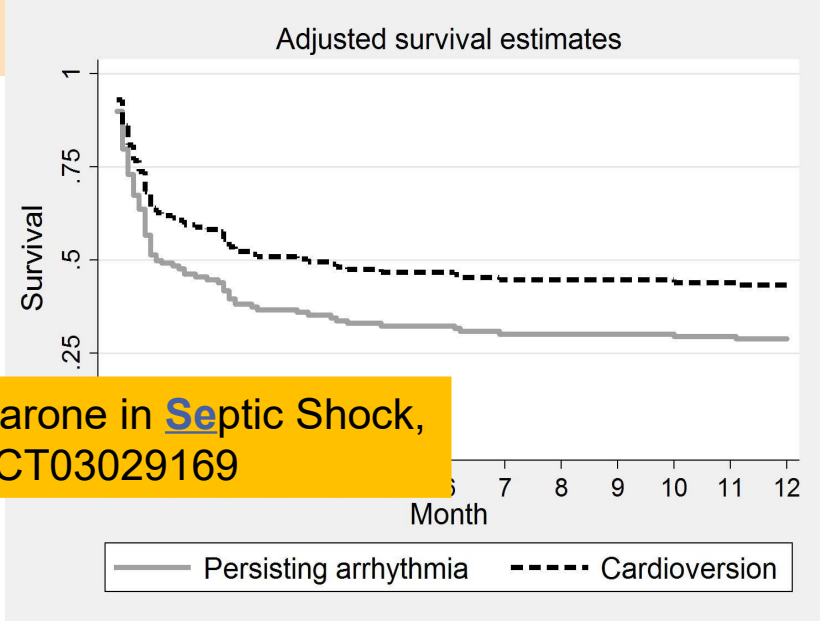
Started at 24h (amiodarone n=142, propafenone n=78, metoprolol n=14)

ICU mortality: amiodarone 40.4%, propafenone 30.4%, metoprolol 21.4% (all ns)

28-day mortality: amiodarone 49.6%, propafenone 39.5%, metoprolol 21.4% (all ns)

Outcome analysis at 12 months





Propafenone vs **A**miodarone in **Se**ptic Shock, ClinicalTrials.gov ID: NCT03029169

Survival in propafenone similar to metoprolol, higher than amiodarone

NAD dosage not related to 12m mortality when adjusted (p=0.138).

Adjusted 12m survival: HR amiodarone vs propafenone 1.58 (1.04; 2.4), p=0.03

Multivariate analysis: 12m HR cardioversion versus acute arrhythmia: HR 0.67, p=0.113

Septická kardiomyopatie a ECMO

- VA-ECMO or VAV-ECMO při poklesu CO/CI se vzestupem laktátu
- Definice neadekvátního CO ?
- McLaren G: VA-ECMO in meningitis, Pediatr Crit Care Med 2007, BW<35 kg
- U dospělých a adolescentů nutnost *centrálního* ECMO, kanyly až 50F

Pediatr Crit Care Med 2013 Jun;14:S1-2
Joint statement on mechanical circulatory support in children: a consensus review from the Pediatric Cardiac Intensive Care Society and Extracorporeal Life Support Organization.

VV nebo VA-ECMO ?

Viral pneumonitis (2009…)

Pneumococcal or G- sepsis (2011…)

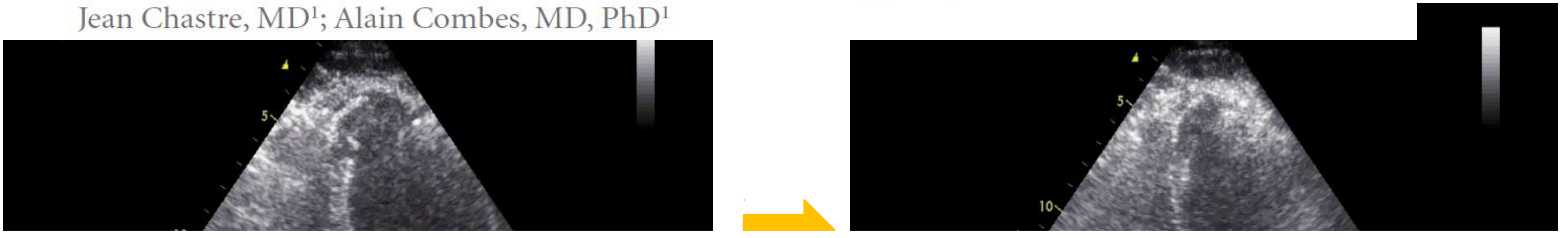
-typically in imunocompromised

-2-3 days after viremia

Venoarterial Extracorporeal Membrane Oxygenation Support for Refractory Cardiovascular Dysfunction During Severe Bacterial Septic Shock*

-d-

Nicolas Bréchot, MD, PhD[1]; Charles-Edouard Luyt, MD, PhD[1]; Matthieu Schmidt, MD[1]; Pascal Leprince, MD, PhD[2]; Jean-Louis Trouillet, MD[1]; Philippe Léger, MD[2]; Alain Pavie, MD[2]; Jean Chastre, MD[1]; Alain Combes, MD, PhD[1]

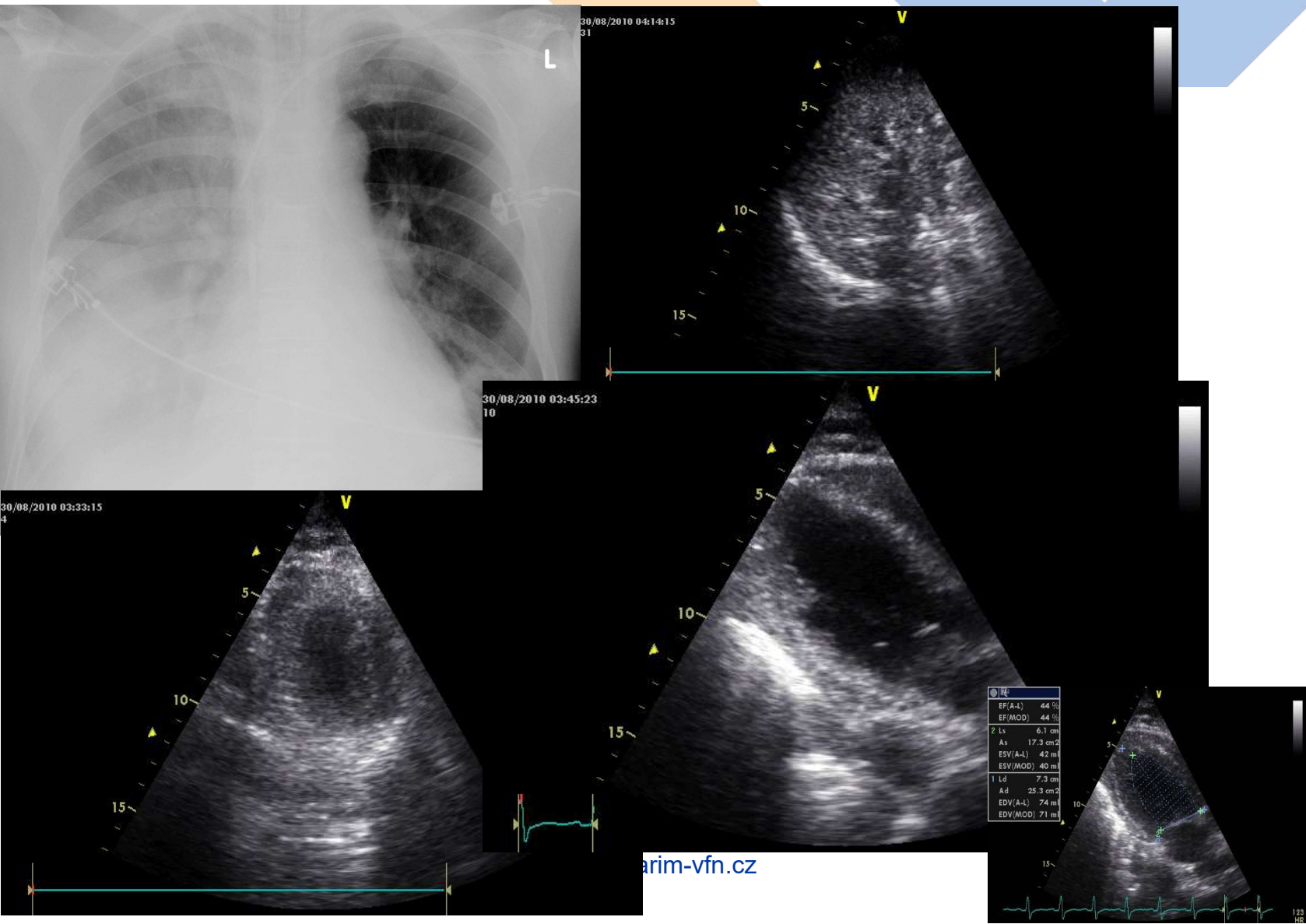


Successful Use of Extra-corporeal Membrane Oxygenation in a Patient with Streptococcal Sepsis: A Case Report and Review of Literature

Pořízka M.[1], Kopecký P.[1], Prskavec T.[2], Kunstýř J.[1]., Rulíšek J.[1], Balík M.[1]

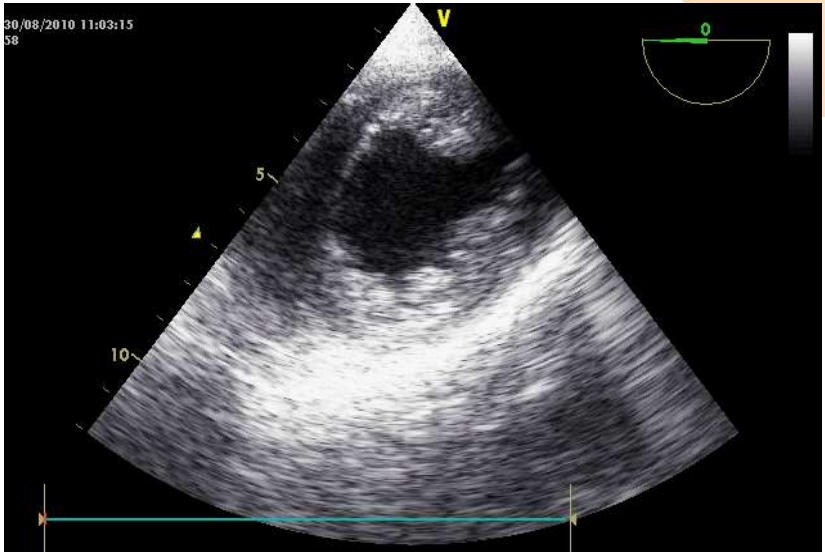
Prague Medical Report 2015, 116(1):57-63.

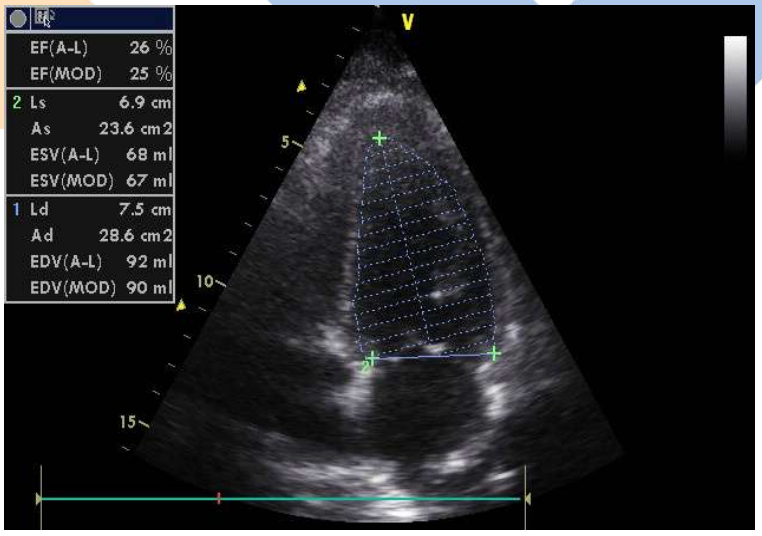
ECMO bridge to recovery in septic heart (HAP, Kl.pn.)



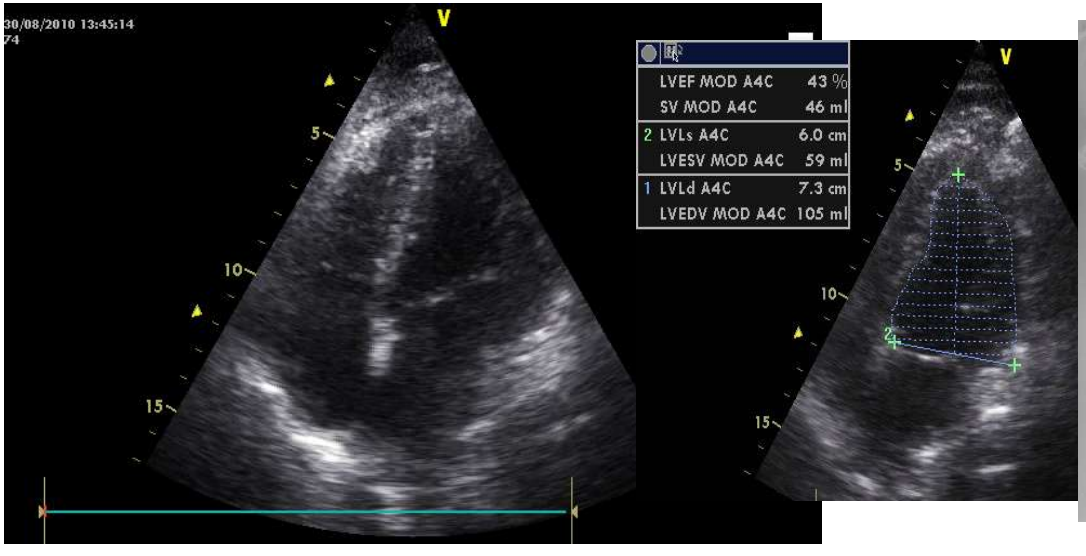
arim-vfn.cz

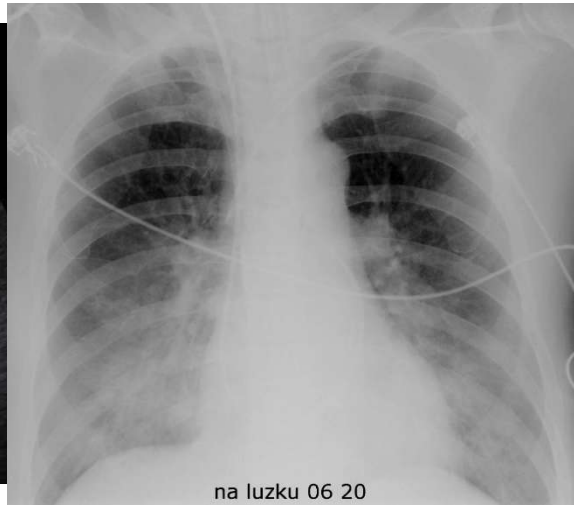
7 h later……EFLV 26%, NAD 1.2 ug/kg.min….





24 h later…EFLV 43%, NAD 0.3, DBX 3.0 ug/kg.min





Separation of the VV and VA techniques not feasible

- **If admitted to an ICU with only VV facility, i.e.„only respiratory support“ the patient would have died**
- **Unified „code ECLS“ !**
- **Most frequent indications to VA-ECMO (….VAV, VVA) in „respiratory failure“**
  - Septic cardiomyopathy
  - Myocarditis
  - ACP on an aggressive IPPV with circulatory failure (LCO)
  - Septic embolisations (ACP)
  - Embolisations of „post-ECMO“ thrombi (ACP)

Závěry pro praxi

- Problém PRELOAD: používat funkční hemodynamiku, dynamické parametry, echokardiografii
- Dg. plnicí tlaky (diastologie)
- CO až CCO v kombinaci s echo u pokračující nestability
- Terapie arytmií
- AS cílová < 125/min, opatrně <110/min
- Dekatecholaminizace (AVP…..)
- Terapie zdroje + časná identifikace agens
- Časný záchyt hypodynamické sepse a indikace k EC podpoře oběhu (VA-ECMO)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