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Sinusová tachykardie a supraventrikulární arytmie v septickém šoku

Martin Balík

KARIM 1.LF UK a VFN, Praha

Deklaruji, že nemám střet zájmů

Klinika anesteziologie, resuscitace a intenzivní medicíny
1. lékařské fakulty UK a Všeobecné fakultní nemocnice v Praze

Adresa: U nemocnice 2; 128 08 Praha 2
www.karim-vfn.cz

Hemodynamika v sepsi a septickém šoku

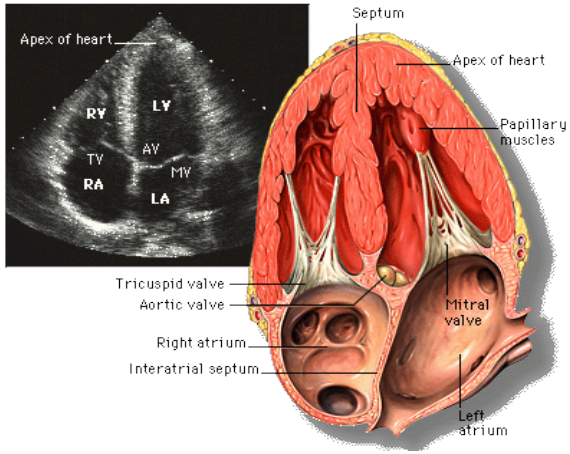
Low SVR, hypotension	Varon J, Marik PE (2008) Irwin and Rippe's intensive care medicine. In: Irwin RS, Rippe JM (eds). 6th edn. Wolters Kluwer Health/Lippincott Williams & Wilkins, Philadelphia, pp 1855-1869
Diastolic and systolic dysfunction: **- 15 to 60% of patients may develop cardiomyopathy**	Rudiger 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

Hlavní determinanty myokardiálního VO_2

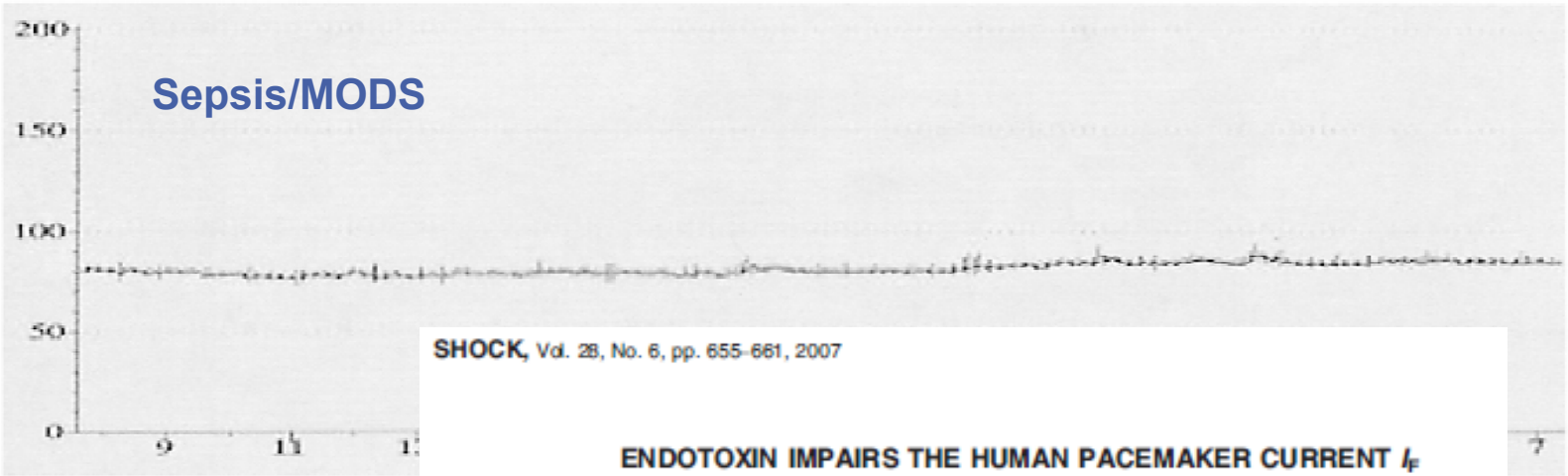
Heart rate (HR)

Contractility Index (dP/dt)

Afterload (T=P.r/h)



Tachykardie a nízká variabilita HR v sepsi (Schmidt H et al: Autonomic dysfunction in the critically ill. Curr Opin Crit Care 2001)

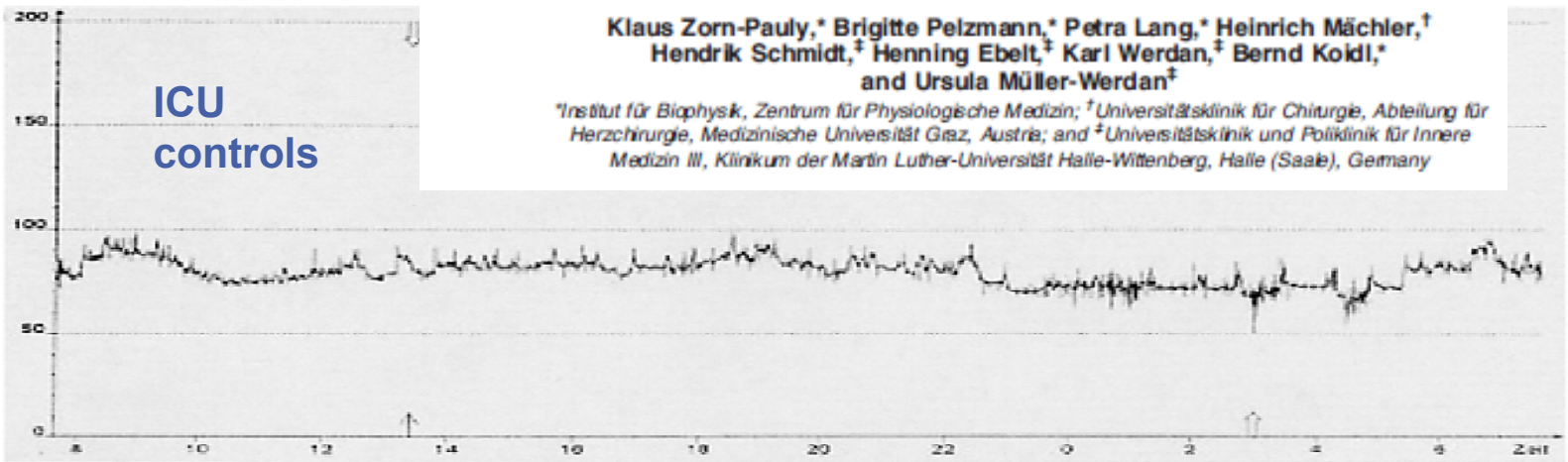


SHOCK, Vol. 28, No. 6, pp. 655-661, 2007

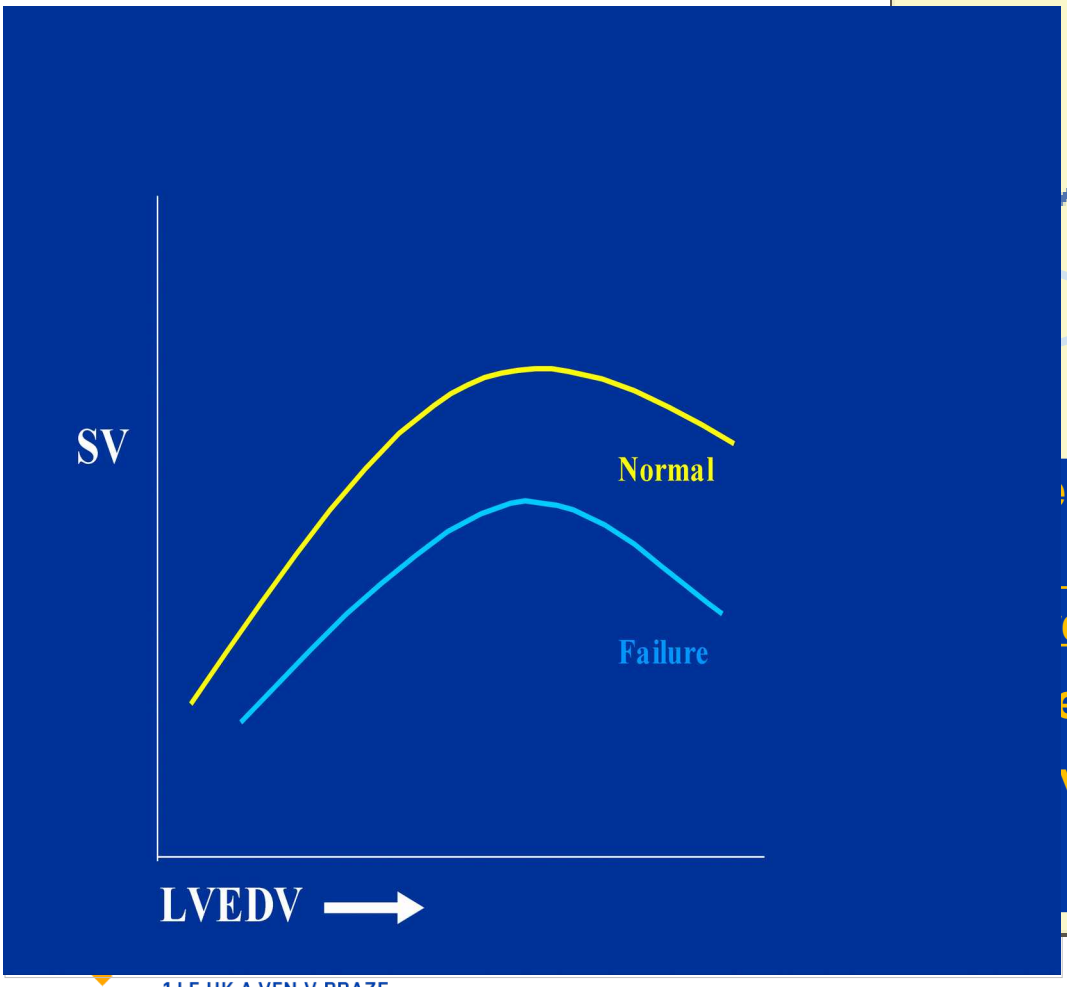
ENDOTOXIN IMPAIRS THE HUMAN PACEMAKER CURRENT I_F

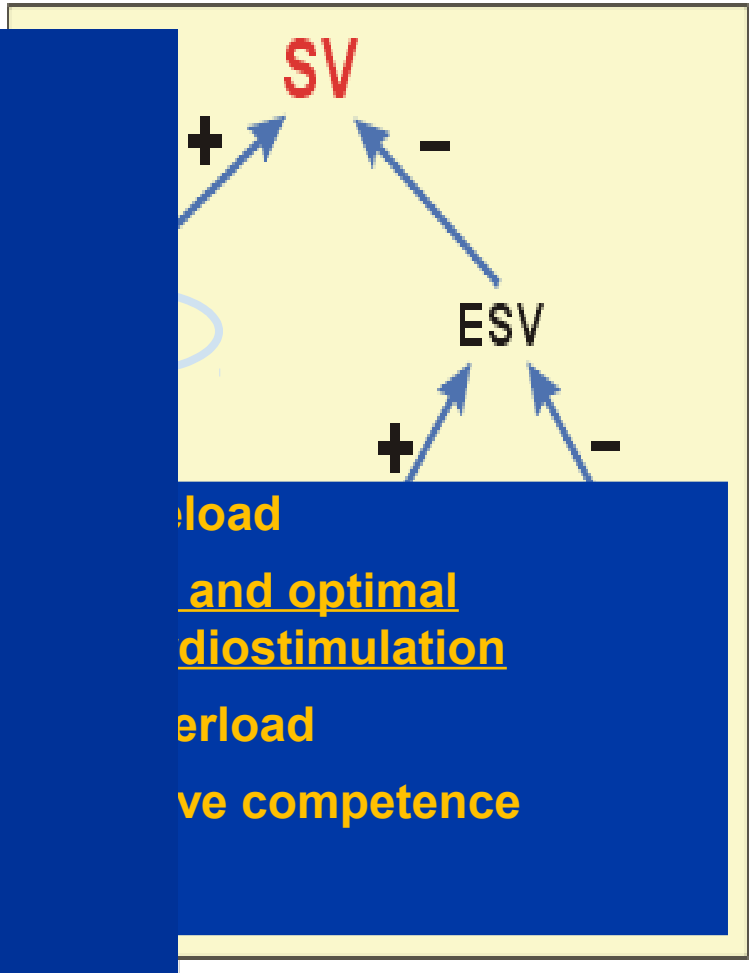
Klaus Zorn-Pauly,* Brigitte Pelzmann,* Petra Lang,* Heinrich Mächler,† Hendrik Schmidt,‡ Henning Ebelt,‡ Karl Werdan,‡ Bernd Koidl,* and Ursula Müller-Werdan‡

*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



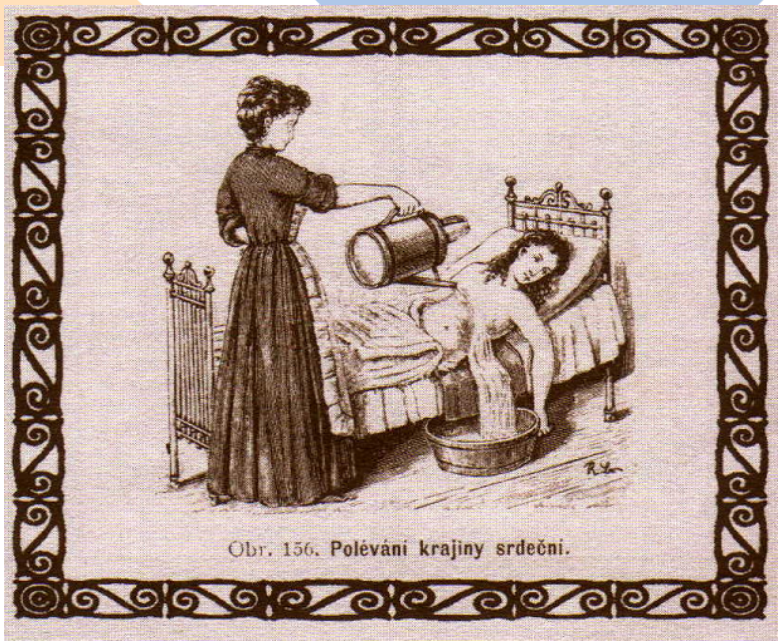
Srdeční frekvence: Diastolický plnicí čas komor jako důležitá proměnná v korekci preload





Odpověď na tekutinovou výzvu: Děláme to dobře ?

	Correlation (r)	AUC
PPV	.78 (.74–.82)	0.94 (0.93–0.95)
SPV	.72 (.65–.77)	0.86 (0.82–0.90)
SVV	.72 (.66–.78)	0.84 (0.78–0.88)
LVEDAI	—	0.64 (0.53–0.74)
GEDVI	—	0.56 (0.37–0.67)
CVP	.13 (−.01–.28)	0.55 (0.48–0.62)



Marik PE, et al: Crit Care Med 2009: 29 studies, 685 pts

56% response to fluid challenge,
only 3 studies used echocardiography

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

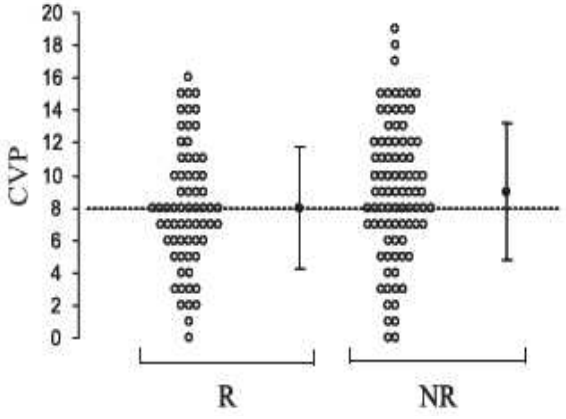
ARTICLE *in* INTENSIVE CARE MEDICINE · JULY 2015

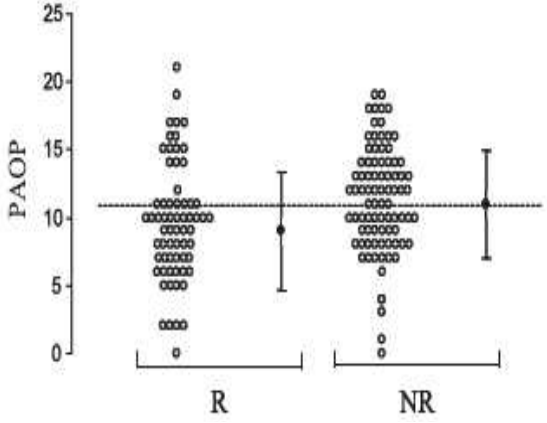
72% volumexpansion with positive effect

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)

EGDT: Problémy s preload a srdeční frekvencí

TABLE 5. Recommendations: Initial Resuscitation and Infection Issues

A. Initial Resuscitation Surviving Sepsis Guidelines: Crit Care Med 2013

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 !
- EGDT preload assessment: 67% fluid overload 1.d, 48% 3.d, OR 1.92 FOR INCREASE OF MORTALITY. Kelm DJ, Shock 2014.

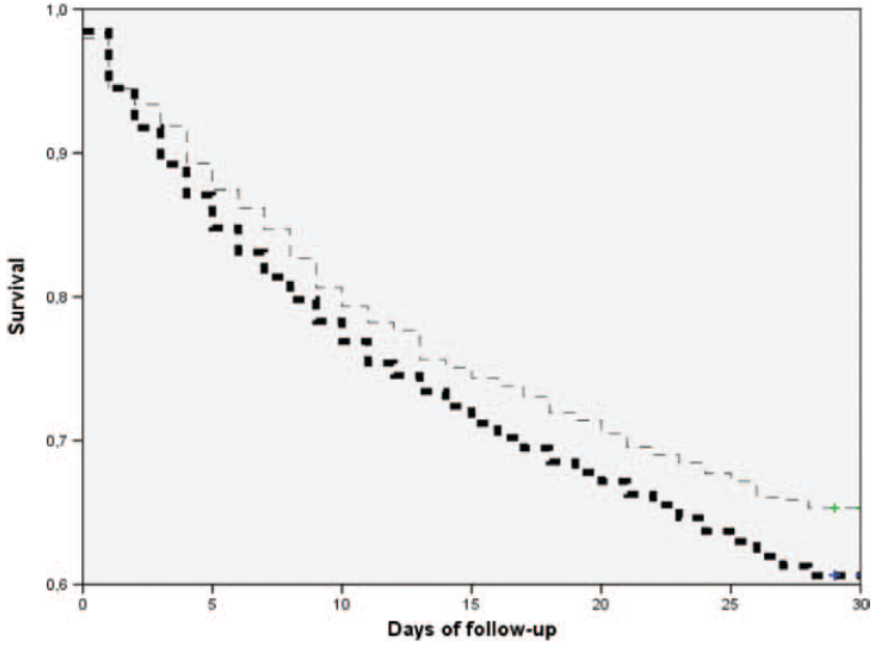
Pacienti na chronické betablokádě

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

- Retrospektivní italská databáze 2003-2008: 9465 pts > 40 let
- Z nich 1061 na betablokátorech (11.2%)
- Nižší 28-d mortalita (17.7% vs 22%, p=0.025)
- Heterogenita souboru i preskripce



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β1 selektivní titrovatelné betablokátory

Esmolol: $T_{1/2}$ 2 min, čas do maximálního efektu 6 až 10 min a odeznívá do 9 min po přerušení infuze, dávky 200-300 mg/h

Landiolol: $T_{1/2}$ 3-4 min, je 8x více β1 selektivní než esmolol, rychlejší nástup účinku, dávky 50-200 mg/h

当前位置：药品说明书与价格首页 >> 心血管系统 >> 新药推荐 >> 西药 >> 注射用盐酸兰地洛尔(Landiolol Hydrochloride)

注射用盐酸兰地洛尔(Landiolol Hydrochloride)

2011-10-05 11:59:34 作者： 来源：互联网 浏览次数：62 文字大小：

简介：【效构类别】抗心律失常药>美托洛尔类【通用药名】LANDIOLOL【中文译名】兰地洛尔,注射用盐酸兰地洛尔(Landiolol Hydrochloride)【别　　名】【CA登记号】[133242-30-5] * 一般名 ランジオロール塩酸塩

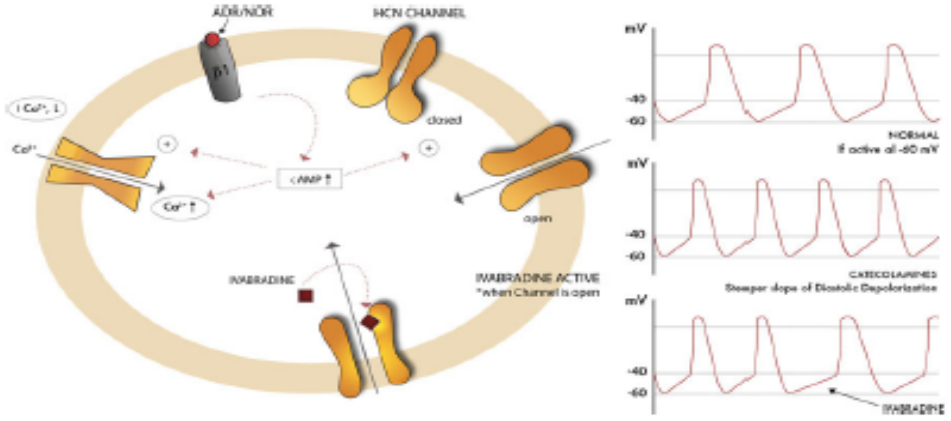
Ivabradine

Clin Res Cardiol (2013) 102:171–178
DOI 10.1007/s00392-012-0516-3

REVIEW

Ivabradine: potential clinical applications in critically ill patients

Vincenzo De Santis · Domenico Vitale · Anna Santoro · Aurora Magliocca · Andrea Giuseppe Porto · Cecilia Nencini · Luigi Tritapepe



- If kanál: Na-K, aktivace hyperpolarizací a cAMP
- Ivabradine brání dosažení depolarizace (slope potenciálu)
- Efekt závislý na HR
- Selektivně chronotropní v SA uzlu

Clin Res Cardiol (2011) 100:915–923
DOI 10.1007/s00392-011-0323-2

ORIGINAL PAPER

Reducing elevated heart rate in patients with multiple organ dysfunction syndrome by the I_f (funny channel current) inhibitor ivabradine

MODI_fY Trial

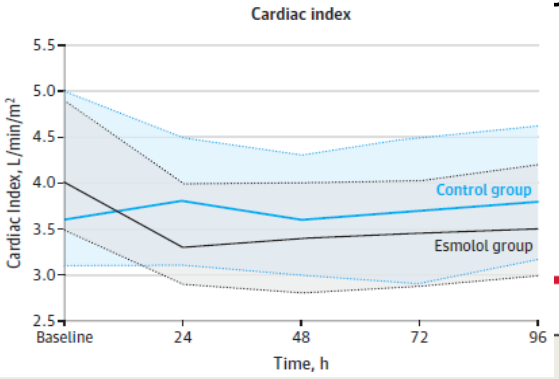
Sebastian Nuding · Henning Ebelt · Robert S. Hoke · Annette Krummenerl · Andreas Wienke · Ursula Müller-Werdan · Karl Werdan

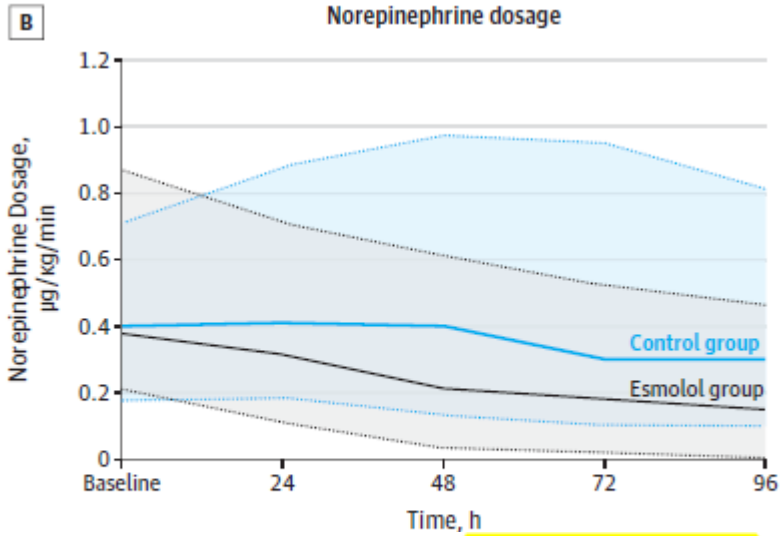
Preliminary Communication | CARING FOR THE CRITICALLY ILL PATIENT

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%)		

Limitace snižování srdeční frekvence

1.) Minimální „bezpečná HR“ ?

2.) Maximální „bezpečné dávkování vasopresorů“ ?

3.) Globální a periferní hemodynamika

4.) Preload - korekce

5.) Dysfunkční pravá komora ?

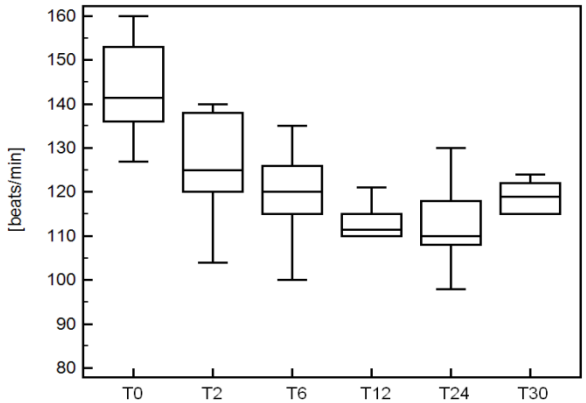
Betablokátory v septickém šoku

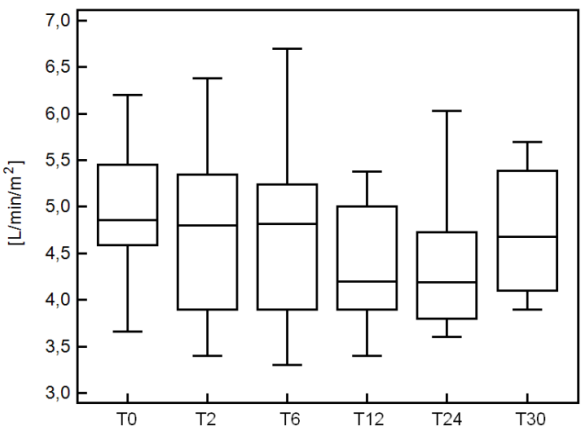
Wien Klin Wochenschr
DOI 10.1007/s00508-012-0209-y

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





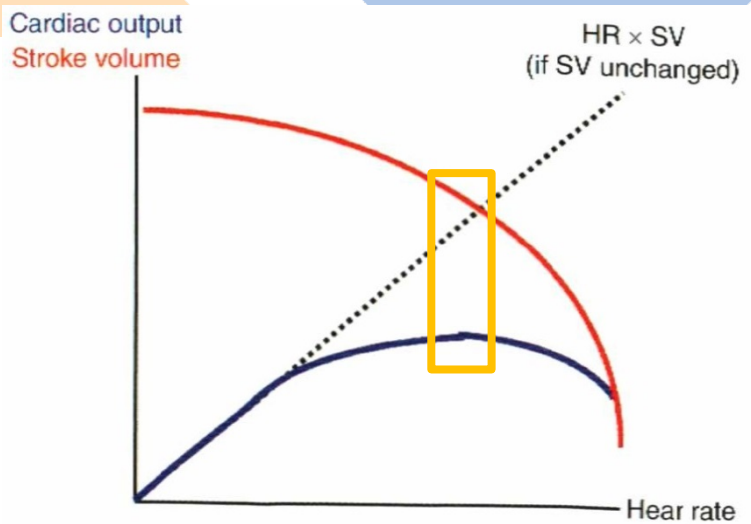


Fig. 9.1 Relationship between heart rate (HR) and stroke volume (SV) or cardiac output

Maizel J, Slama M: Haemodynamic Evaluation in the Patient with Arrhythmias. In: De Backer D, et al (eds) Hemodynamic Monitoring Using Echocardiography in the Critically Ill, Springer 2011, pp 89-95.

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

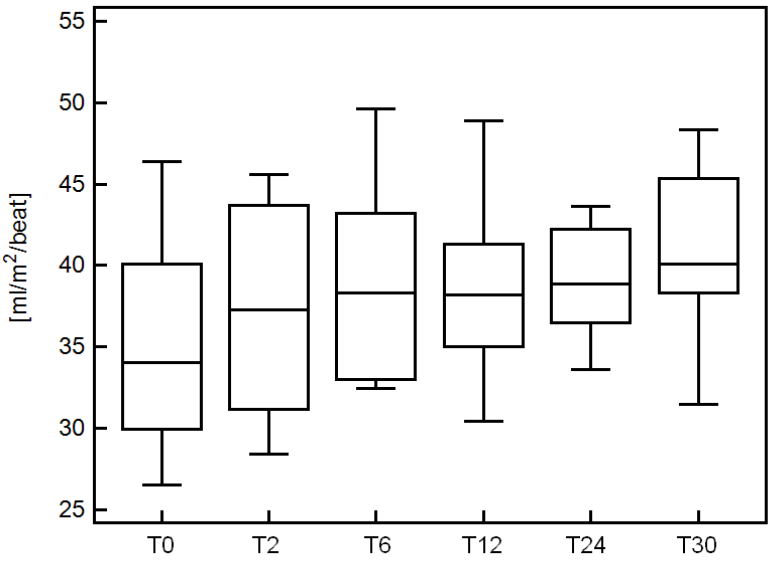
Concomitant use of beta-1 adrenoreceptor blocker and norepinephrine in patients with septic shock. Reply to a letter to the authors

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

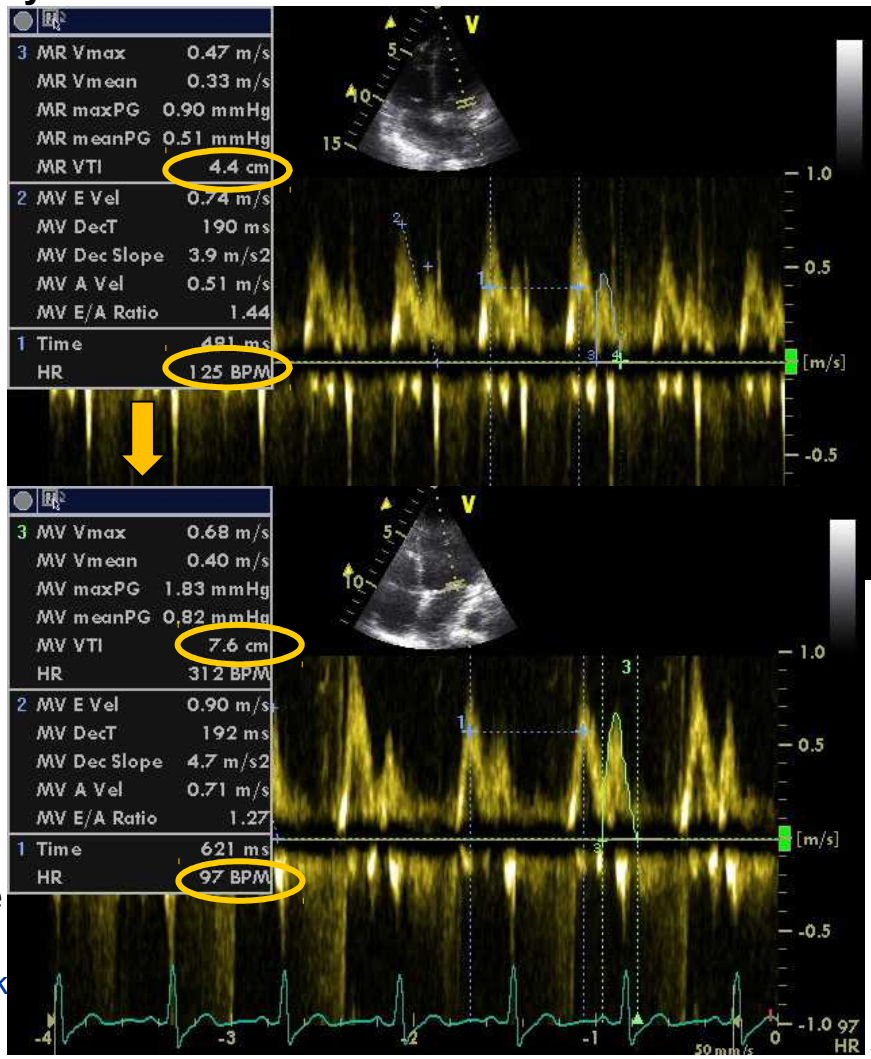
No need for rescue levosimendan !

Betablokátor a diastolická funkce v septickém šoku

Stroke volume index: ⇧



Změny diastolické funkce: A vlna



Pokles ze 140 na 110/min – tendence k vzestupu SV

Pokles pod 95/min (80-95 /min) – SV nestoupá = klesá CI

Vhodné jen u hyperkinetické cirkulace

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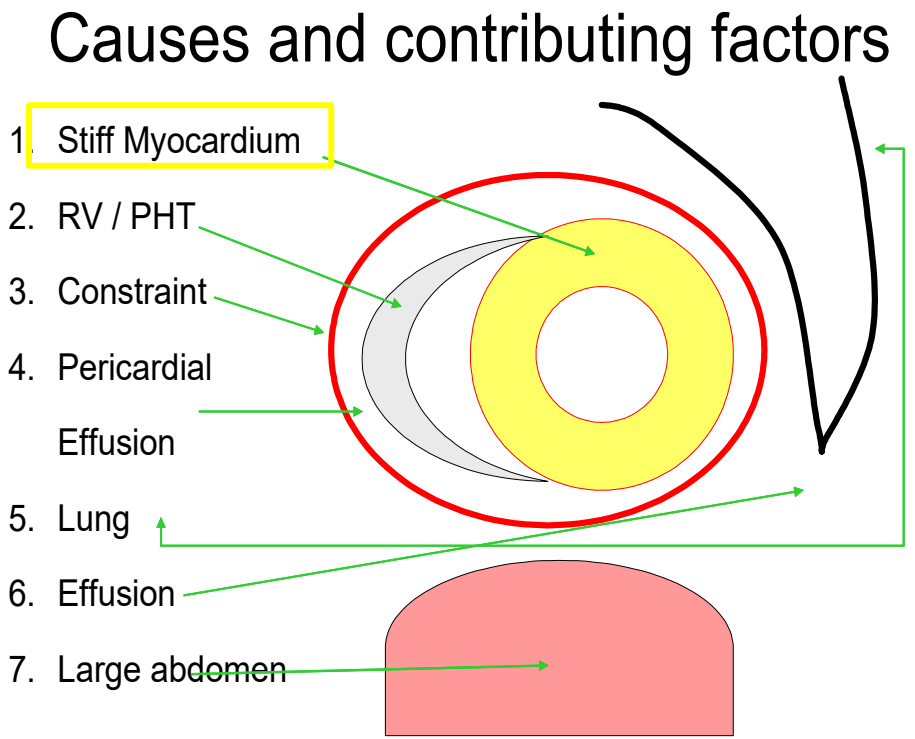
www.k

Diastolická dysfunkce: relaxace, kompliance, plnicí tlaky

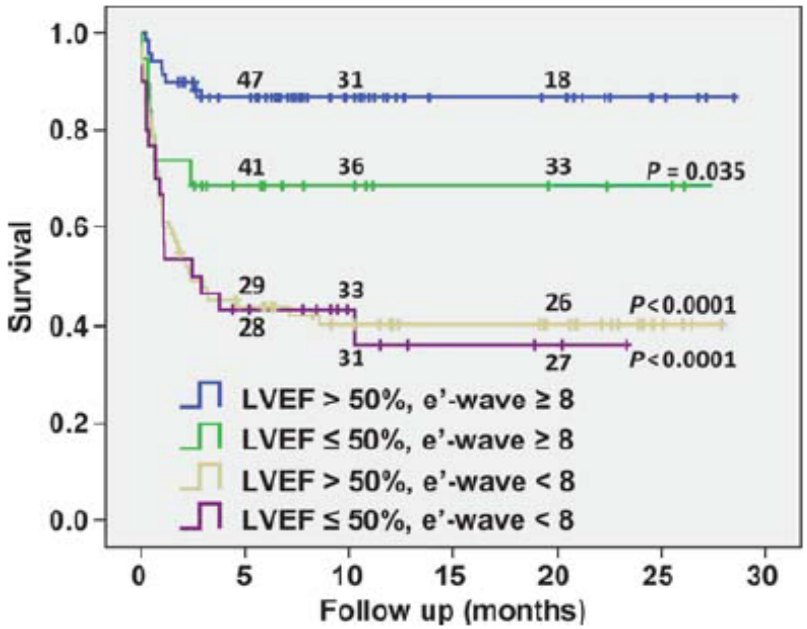
- Téměř 50% srdečních selhání je diastolických, se „zachovanou“ EFLV (Saleh M, Intensive Care Med 2012)
- Dg. s preload a afterload
- LA velikost, stěna LV
- HR a rytmus

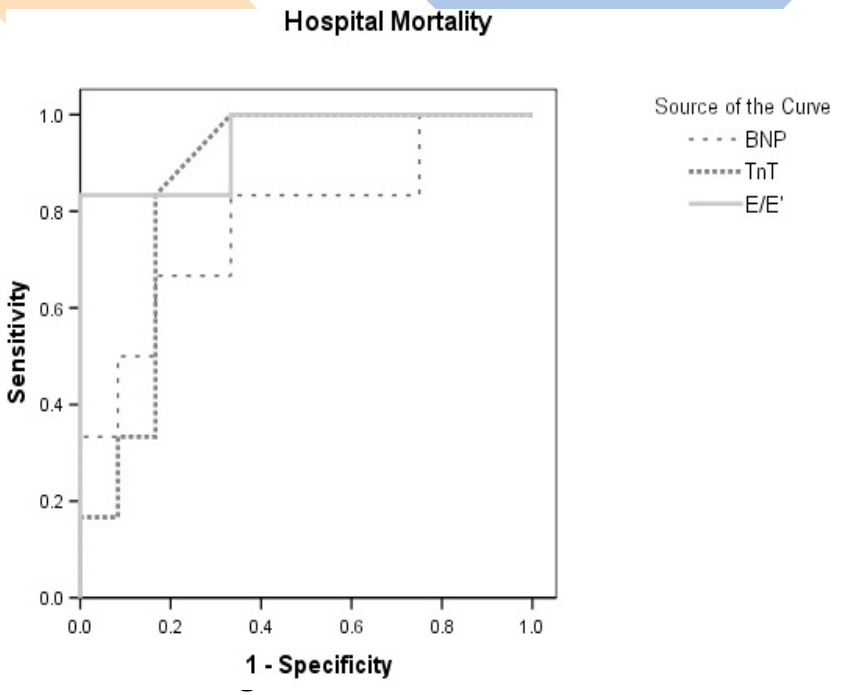
  dependentní parametry
- Nagueh SF, et al: Eur J Echocardiography 2009, 10: 165-193



Diastolická dysfunkce a prognoza v sepsi

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

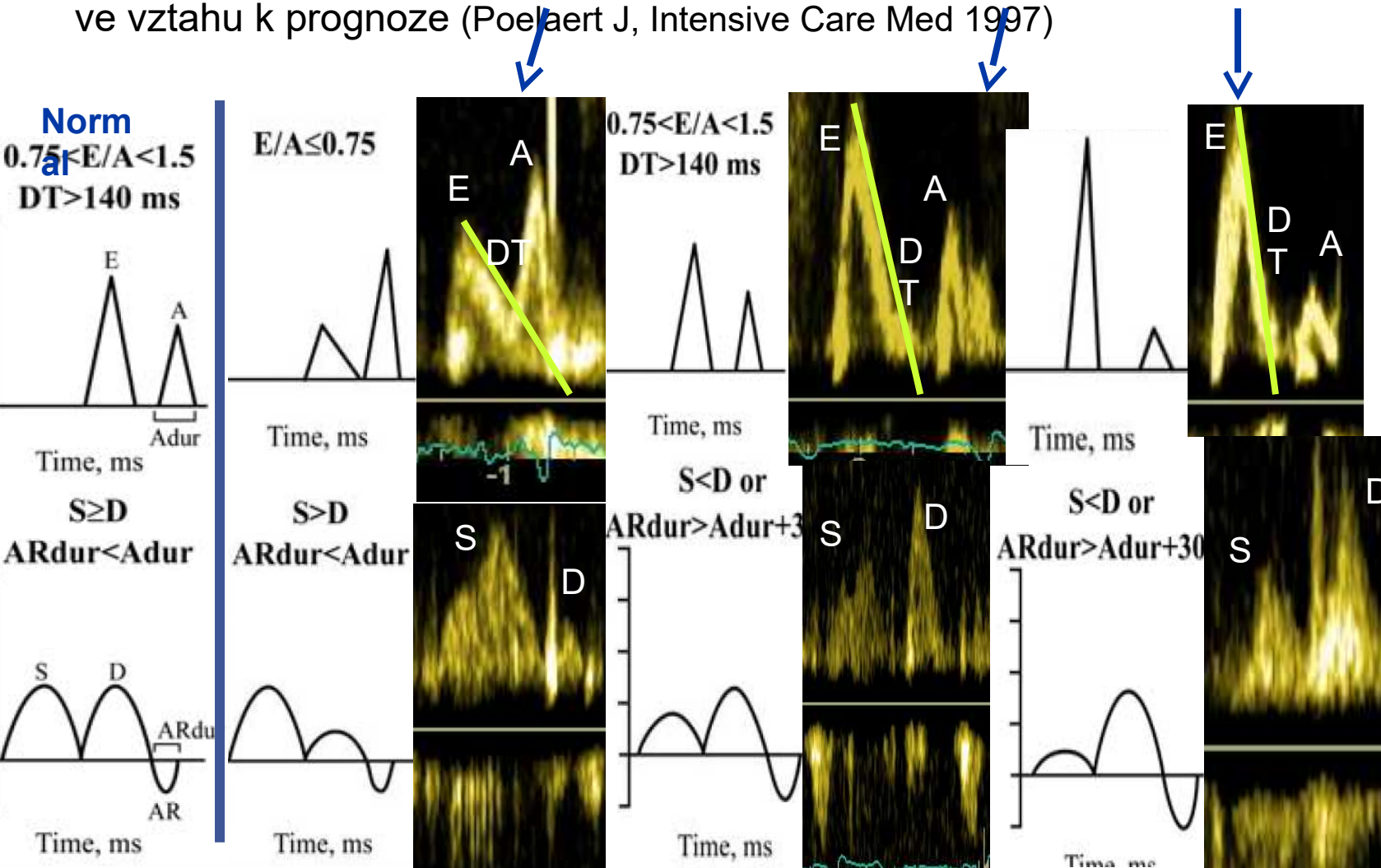




- TDI septal E/E´ jako prognostický indikátor (Sturgess D: Crit Care 2010)
- Lepší než biomarkery (BNP, TnT)

Diastolická funkce a SV arytmie: ztráta 10-40% plnění LK v diastole, alterace ventrik. funkce……

- Stupeň zhoršení (relaxation disorder – pseudonormal – restrictive filling) ve vztahu k prognoze (Poelaert J, Intensive Care Med 1997)

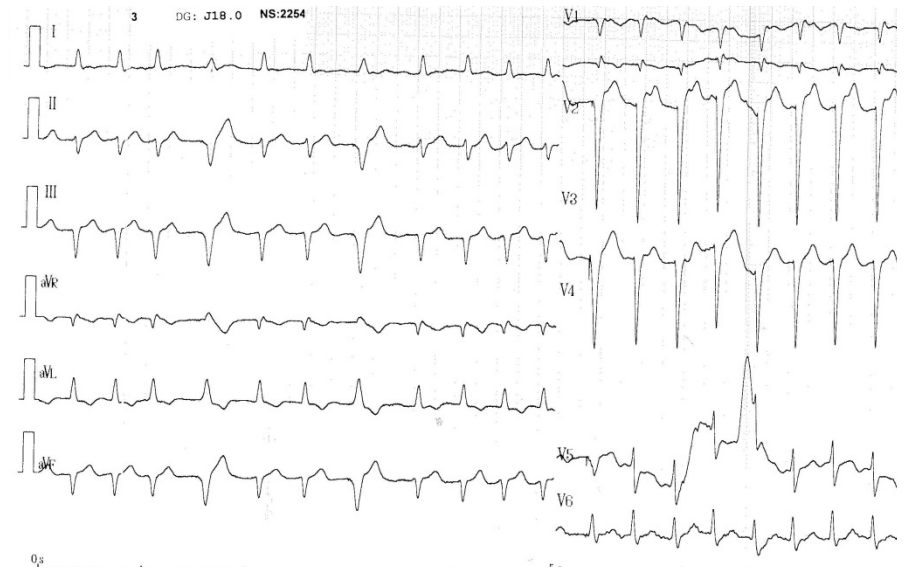


Incidence, risk factors and outcomes of new-onset atrial fibrillation in patients with sepsis: a systematic review

Critical Care 2014, **18**:688 doi:10.1186/s13054-014-0688-5

Sanne Kuipers (s.kuipers@students.uu.nl)
Peter MC Klein Klouwenberg (p.m.c.kleinklouwenberg@umcutrecht.nl)
Olaf L Cremer (o.l.cremer@umcutrecht.nl)

- Arytmie jako nejčastější příčina diastolického srdečního selhání
- 11 studií v metaanalýze: Incidence nově vzniklé AF je
  - **8% (0-14%) v sepsi**
  - **10% (4-23%) severe sepsis**
  - **23% (6-46%) v sept šoku**
- general ICU population
  - 4-9-11% (age dep.)
  - 30-40% postcardiotomy



Rhythm control or rate control ?

- **U hemodynamicky stabilních bez zn diastolického selhání ?**
- **U kardiotorakálních pacientů ?**
- **U septických pacientů ?**
- **U pacientů v septickém šoku ?**

Conclusion on rate control or rhythm control

There are insufficient data in ICU patients to justify a choice
ontrol or on rhythm
advantage above rate
/ or mortality, in non-

The NEW ENGLAND JOURNAL of MEDICINE

Review Article

Management of Atrial Fibrillation in Critically Ill Patients

Mattia Arrigo, Dominique Bettex, and Alain Rudiger

Ztráta síňového příspěvku plnění komor u 6-21% na ICU - asociuje s 2-5x zvýšenou mortalitou !

Echocardiography in arrhythmia

TTE as first choice:

- LV size, contractility ?
- LVEDP, preload ⟶ catecholamines ?
- Valves: MS, MR, AS – sig. ?
- Dilated LA ?
- Spont. echocontrast ?

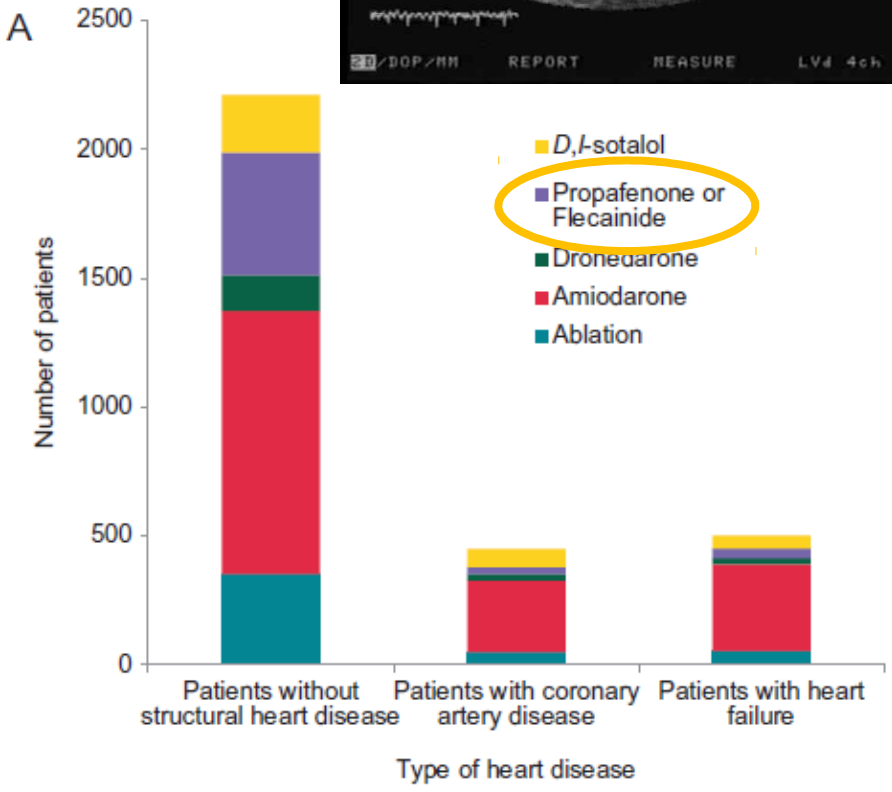
Rhythm or rate control ?

Electric cardioversion ?

>48h ?: TEE

Predictors of cardioversion – transmitral A wave 6h after

Anticoagulation setting



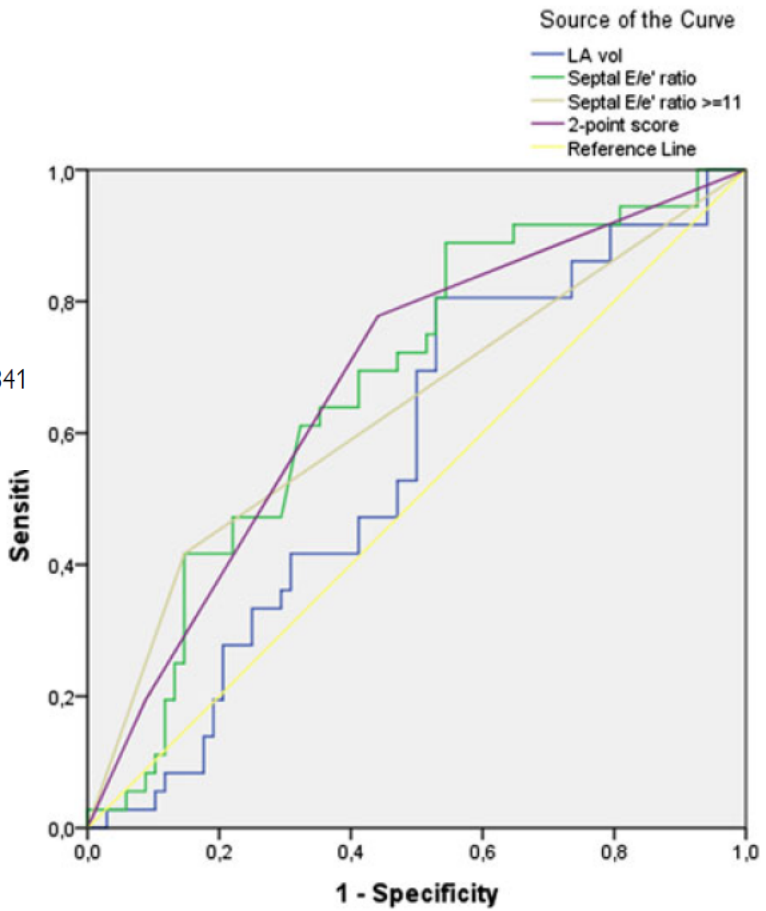
Europace (2014) **16**, 6–14
doi:10.1093/europace/eut263

CLINICAL RESEARCH
Atrial fibrillation

Preload a objem LS – vliv na udržení sinus rytmu

- Vzestup LAVi + 1 ml/m2 BSA….. +21% riziko návratu AF (OR 1.21, CI 1.11-1.30, p<0.001)

Marchese P, et al: Eur J Echocardiogr 2011



European Heart Journal – Cardiovascular Imaging (2015) **16**, 335–341
doi:10.1093/ehjci/jeu193

- U dilatované LS s LAVi>34 ml/m2 spíše vliv LAP
- Nejlépe predikuje septální E/E ´>11
- Plus chronicita anamn (90 dní…)

Worried of 1c class agents ?

VIA MEDICA

CASE REPORT

Cardiology Journal
2013, Vol. 20, No. 2, pp. 203–205
DOI: 10.5603/CJ.2013.0035
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ISSN 1897–5593

Arrhythmogenic effect of flecainide toxicity

Pierre-Yves Courand[1], Franck Sibellas[1], Sylvain Ranc[1], Audrey Mullier[2], Gilbert Kirkorian[1], Eric Bonnefoy[1]

The New England
Journal of Medicine

Volume 324 MARCH 21, 1991 Number 12

MORTALITY AND MORBIDITY IN PATIENTS RECEIVING ENCAINIDE, FLECAINIDE, OR PLACEBO

The Cardiac Arrhythmia Suppression Trial

- CAST trial – IHD exposed to 1c class vs placebo
- 1c class higher mortality, incl. EF_LV < 30%
- Cardiology outpatients – follow up 10 months
- Study not applicable for critically ill in 2016 !!!

Journal of the American College of Cardiology
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Published by Elsevier Science Inc.

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Amiodarone Versus Placebo and Class Ic Drugs for Cardioversion of Recent-Onset Atrial Fibrillation: A Meta-Analysis

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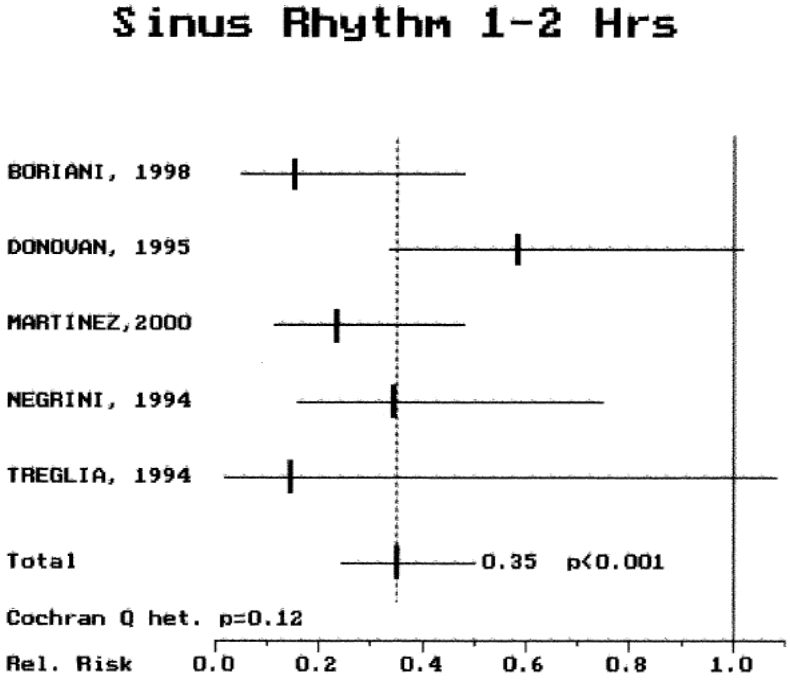
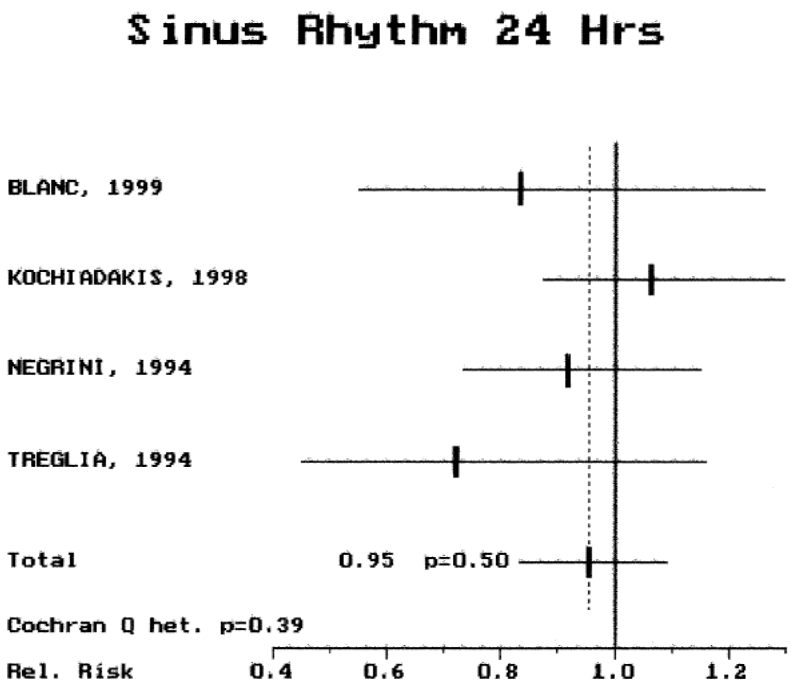
- 6 studií amiodarone vs placebo a 6 studií 1c class vs placebo
- Propafenon nejúčinnější v 1-2h, stejně ve 24h jako amiodarone





Flowchart

Phase I:

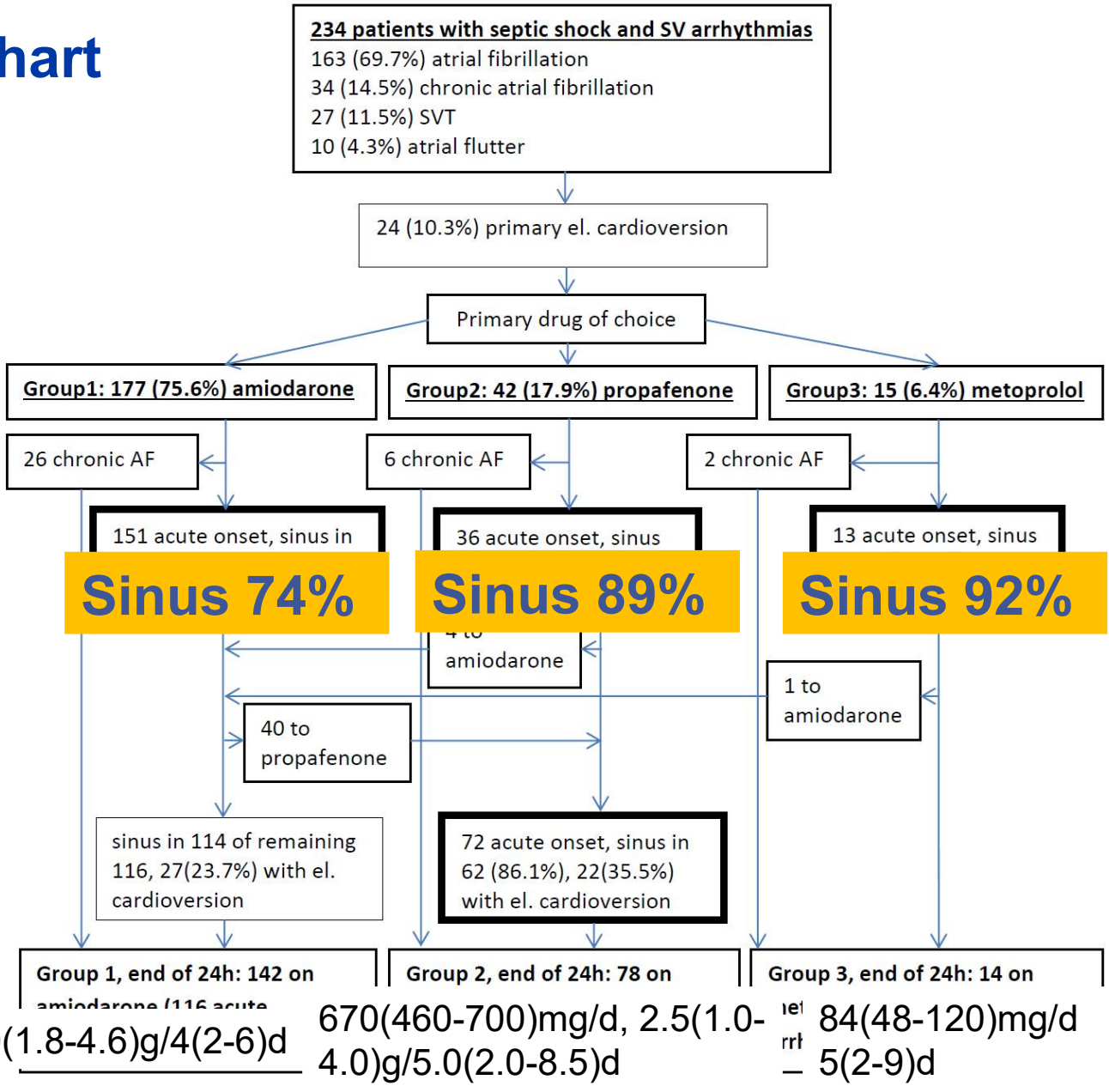
Antiarrhythmic efficacy (24h)

- chronic AF excluded
- primary agent
- after change within 24h
- 74.4% overall cardioversion, 87% without chronic AF

Phase II:

- starts at 24h
- incl. chronic AF

Outcome analysis



3.0(1.8-4.6)g/4(2-6)d

670(460-700)mg/d, 2.5(1.0-4.0)g/5.0(2.0-8.5)d

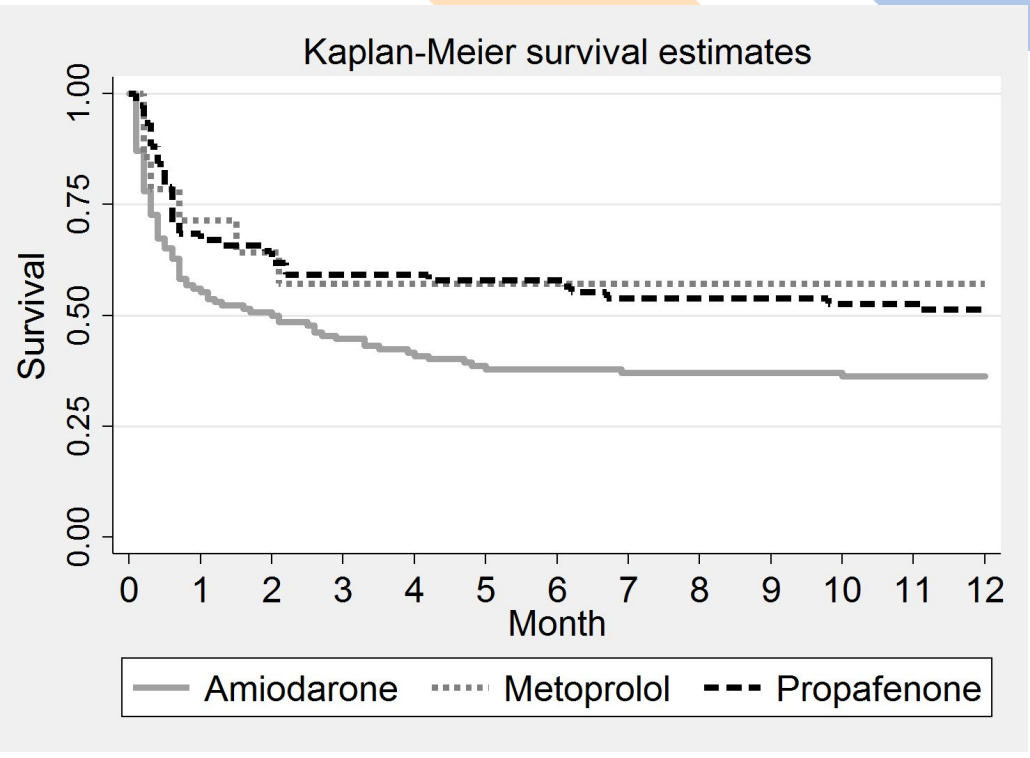
84(48-120)mg/d

5(2-9)d

LOS and ICU mortality

Parameter	G1: Amiodarone (N=142)	G2: Propafenone (N=78)	G3: Betablocker (metoprolol, N=14)	Comparisons
LOS [days][1]	9 (6-15)	15 (8-23)	8 (8-13)	G1 vs G2: p=0.002 G1 vs G3: ns G2 vs G3: p=0.08
LOS [days] without dead pts[1]	11.5 (7-17.5)	13 (8-23)	8 (7-11.5)	ns
LOS(A-on) [days][1]	8 (4-13)	10 (5-18)	7 (6-10)	G1 vs G2: p=0.005 G1 vs G3: ns G2 vs G3: p=0.08
LOS(A-on) [days] – without dead pts[1]	9 (6-15)	10 (4-21)	7 (6-11)	ns
ICU mortality	40.4%	30.4%	21.4%	ns
28-day mortality	49.6%	39.5%	21.4%	ns

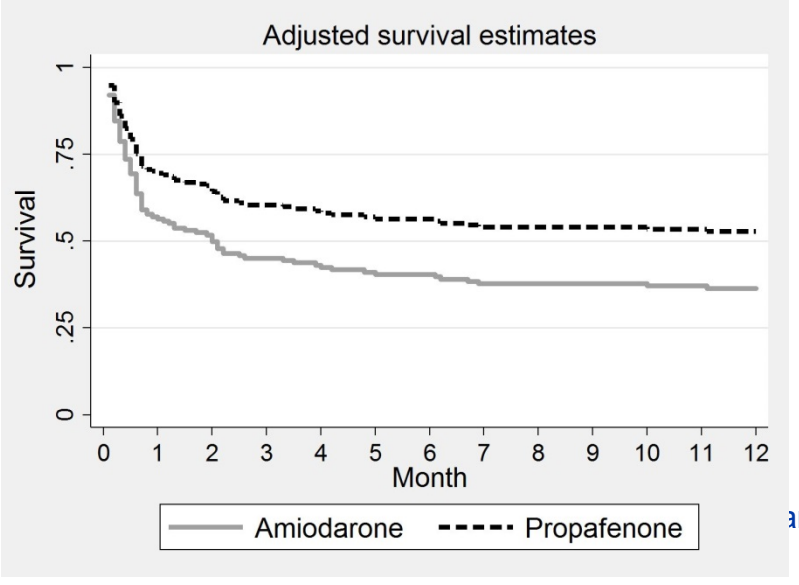
12 months outcome



- Long term survival of the propafenone Group 2 similar to long term survival of the metoprolol Group 3.
- Unadjusted hazard long term mortality ration amiodarone vs propafenone: 1.76 (1.06; 2.3), p=0.024.

12 Month survival (Cox regression)

	unadjusted (univariate)			adjusted (multivariate)		
Parameter	HR	95%CI	P	HR	95%CI	p
Amiodarone vs propafenone	1.76	(1.06;2.3)	0.024	1.58	(1.04;2.4)	0.03
Standardized age (SD=11 yrs)	1.51	(1.24;1.85)	<0.001	1.63	(1.28;2.07)	<0.001
Standardized NAD (SD=0,4 ug/kg/min)	1.51	(1.26;1.8)	<0.001	1.18	(0.95;1.46)	0.138
Standardized SOFA (SD=4)	1.76	(1.43;2.16)	<0.001	1.75	(1.35;2.26)	<0.001
Standardized APACHE (SD=11)	1.31	(1.1;1.56)	<0.001			
CRRT (yes vs no)	2.32	(1.61;3.34)	<0.001	1.6	(1.02;2.53)	0.041



- Propafenone mortality lower than amiodarone in univariate and in multivariate analysis.
- Dosage of noradrenaline not related to 12 month mortality when adjusted for co-variates.
- Adjusted 12 months survival: HR amiodarone vs propafenone 1.58 (1.04; 2.4), p=0.03.

Outcome analysis: SR vs arrhythmia ?

Cardioverted

ICU mortality 33.5%,

28-day mortality 43.6%

Chronic AF

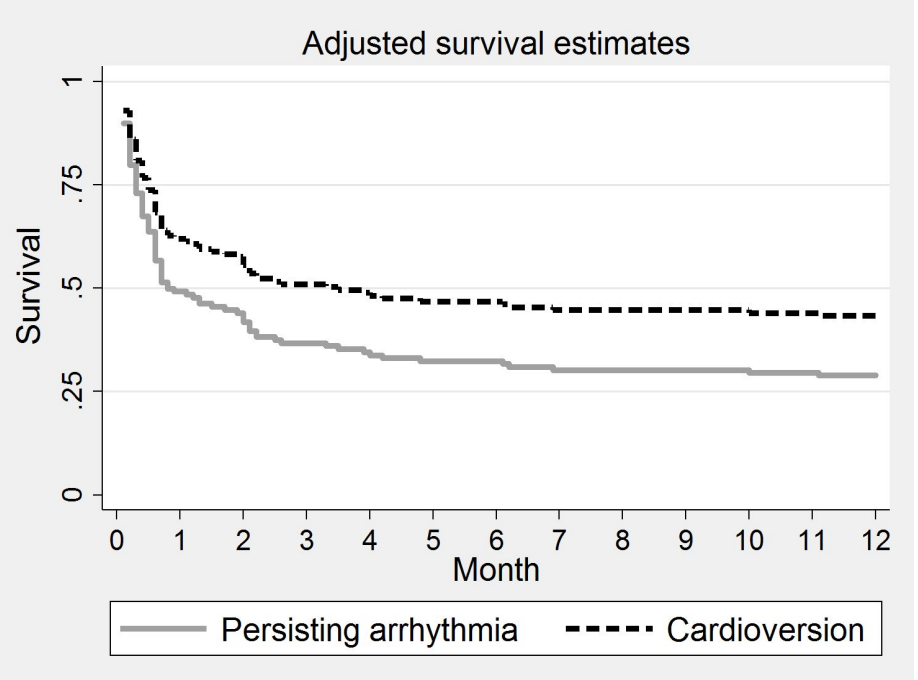
ICU mortality 38.2% (ns)

28-day mortality 41.1% (ns)

Acute SV arrhythmia

ICU mortality 48.3% (p=0.129)

28-day mortality 55.2% (p=0.252)



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

Digoxin

- Rate control pro chron. deblok. AF
- Nástup 5-20 min
- Digitalizace 0,75-1,0 mg i.v – na ideální komor odpověď (NE hladinu !)
- Aditivní antiarytmikum u těžké syst dysfunkce a nedost. efektu amiodarone + Mg
- S omezením u renální dysfunkce – terap index
- Bez vlivu na mortalitu, snižuje frekvenci hospitalizací

Safety and efficacy of digoxin: systematic review and meta-analysis of observational and controlled trial data

Oliver J Ziff,[1,2] Deirdre A Lane,[1,3] Monica Samra,[2] Michael Griffith,[4] Paulus Kirchhof,[1,3] Gregory Y H Lip,[1,3] Richard P Steeds,[4] Jonathan Townend,[1,4] Dipak Kotecha[1,3,4,5]

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THE EFFECT OF DIGOXIN ON MORTALITY AND MORBIDITY IN PATIENTS WITH HEART FAILURE

THE DIGITALIS INVESTIGATION GROUP*

Vernakalant

- Limitace pro ambulanty s recivující SV arytmií (AF)
- Teoreticky nejrychlejší farm kardioverze (10 min…)
- NE u strukturálních poruch myokardu
- 3mg/kg bolus (10 min) plus opakovat ev. 2 mg/kg
- 53% kardioverze do 6h u kardiochir. pacientů
- 34% s mírným poklesem MAP po aplikaci - vazodilatace
- Cena léku

Critical Care Research and Practice
Volume 2014, Article ID 826286, 7 pages
http://dx.doi.org/10.1155/2014/826286

Hindawi

Clinical Study

Suitability, Efficacy, and Safety of Vernakalant for New Onset Atrial Fibrillation in Critically Ill Patients

Alain Rudiger,[1] Alexander Breitenstein,[1,2] Mattia Arrigo,[1,2] Sacha P. Salzberg,[3] and Dominique Bettex[1]

Závěry pro praxi

- Septický šok s vyšším výskytem tachykardií a SV arytmií
- Medián ICU populace 60-65 let, diastolická dysfunkce (HT)……

Cílem je udržení sinus rytmu a diastolického plnění LK

- Rate control pouze u chronické AF, nebo při neudržitelnosti sinus rytmu na vysokých dávkách vasopresorů

Elektrická kardioverze u nestabilních a absenci KI

Problém PRELOAD: používat funkční hemodynamiku, echo

Echokardiografie esenciální pro určení léčby

- Ic class (propafenon) jako lék první volby – plus Mg^{2+}, K^{+} substituce – echo guided stejně bezpečný jako amiodarone
- III class (amiodarone) u kontraindikací propafenon
- II class (betablokátory) u absence KI, sinus > 125/min

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