Place des Bêta-bloquants dans l'état de choc septique

Pr Raphaël Favory
Pôle de Réanimation CHU de Lille
Département Universitaire de Thérapeutique
raphael.favory@chru-lille.fr

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Review

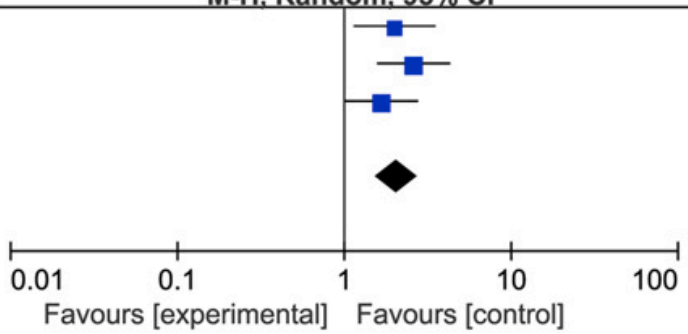
The influence of esmolol on septic shock and sepsis: A meta-analysis of randomized controlled studies

Ping Liu [a], Qi Wu [b], Yu Tang [a], Zhiguo Zhou [a], Malong Feng [b,*]

[a] Department of Respiration, The First Hospital of Changsha, Hunan, China
[b] Department of Emergency, The First Hospital of Changsha

Study or Subgroup	Esmolol group Events	Total	Control group Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Liu 2015	18	24	9	24	28.5%	2.00 [1.14, 3.52]
Morelli 2013	39	77	15	77	35.8%	2.60 [1.57, 4.31]
Wang 2015	20	30	12	30	35.7%	1.67 [1.00, 2.76]
Total (95% CI)		**131**		**131**	**100.0%**	**2.06 [1.52, 2.79]**
Total events	77		36			

Heterogeneity: Tau² = 0.00; Chi² = 1.56, df = 2 (*P* = 0.46); I² = 0%
Test for overall effect: Z = 4.68 (*P* < 0.00001)



*Take home message

En péri-opératoire

The New England
Journal of Medicine

VOLUME 335 DECEMBER 5, 1996 NUMBER 23

EFFECT OF ATENOLOL ON MORTALITY AND CARDIOVASCULAR MORBIDITY AFTER NONCARDIAC SURGERY

DENNIS T. MANGANO, PH.D., M.D., ELIZABETH L. LAYUG, M.D., ARTHUR WALLACE, PH.D., M.D., AND IDA TATEO, M.S.,
FOR THE MULTICENTER STUDY OF PERIOPERATIVE ISCHEMIA RESEARCH GROUP*

atenolol 35/1

EFFECT OF BISOPROLOL ON MORBIDITY AND MORTALITY IN PATIENTS UNDERGOING VASCULAR SURGERY

THE EFFECT OF BISOPROLOL ON PERIOPERATIVE MORTALITY AND MYOCARDIAL INFARCTION IN HIGH-RISK PATIENTS UNDERGOING VASCULAR SURGERY

DON POLDERMANS, PH.D., ERIC BOERSMA, PH.D., JEROEN J. BAX, PH.D., IAN R. THOMSON, PH.D.,
LOUIS L.M. VAN DE VEN, PH.D., JAN D. BLANKENSTEIJN, PH.D., HUBERT F. BAARS, M.D., TIK-IEN YO, PH.D.,
GIUSEPPE TROCINO, M.D., CARLO VIGNA, M.D., JOS R.T.C. ROELANDT, PH.D., AND HERO VAN URK, PH.D.,
FOR THE DUTCH ECHOCARDIOGRAPHIC CARDIAC RISK EVALUATION APPLYING STRESS ECHOCARDIOGRAPHY STUDY GROUP*

The New England Journal of Medicine December 9, 1999

bisoprolol 75/1

Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial

POISE Study Group*

Devereaux PJ, Lancet. 2008 May 31;371(9627):1839-47

	Metoprolol group (n=4174)	Placebo group (n=4177)	Hazard ratio	p value
Cardiovascular death, non-fatal myocardial infarction, or non-fatal cardiac arrest*	244 (5·8%)	290 (6·9%)	0·84 (0·70–0·99)	0·0399
Cardiovascular death	75 (1·8%)	58 (1·4%)	1·30 (0·92–1·83)	0·1368
Non-fatal myocardial infarction	152 (3·6%)	215 (5·1%)	0·70 (0·57–0·86)	0·0008
Non-fatal cardiac arrest	21 (0·5%)	19 (0·5%)	1·11 (0·60–2·06)	0·7436
Total mortality	129 (3·1%)	97 (2·3%)	1·33 (1·03–1·74)	0·0317
Myocardial infarction	176 (4·2%)	239 (5·7%)	0·73 (0·60–0·89)	0·0017
Cardiac revascularisation†	11 (0·3%)	27 (0·6%)	0·41 (0·20–0·82)	0·0123
Stroke	41 (1·0%)	19 (0·5%)	2·17 (1·26–3·74)	0·0053
Non-fatal stroke	27 (0·6%)	14 (0·3%)	1·94 (1·01–3·69)	0·0450
Congestive heart failure†	132 (3·2%)	116 (2·8%)	1·14 (0·89–1·46)	0·3005
New clinically significant atrial fibrillation†	91 (2·2%)	120 (2·9%)	0·76 (0·58–0·99)	0·0435
Clinically significant hypotension†	625 (15·0%)	404 (9·7%)	1·55 (1·38–1·74)	<0·0001
Clinically significant bradycardia†	277 (6·6%)	101 (2·4%)	2·74 (2·19–3·43)	<0·0001
Non-cardiovascular death	54 (1·3%)	39 (0·9%)	1·39 (0·92–2·10)	0·1169

Data are n (%) or hazard ratio or relative risk (95% CI). *Some patients had more than one event. †Relative risks presented, rather than hazard ratios, since we did not collect the actual date patients experienced these events.

Table 3: **Effects of study treatment on primary and secondary outcomes at 30 days**

metoprolol 20/1

Stimulation bêta

Bêta-1

- Cœur: inotrope, chronotrope, dromotrope, bathmotrope, lusitrope
- Rein: sécrétion de rénine
- Tissu adipeux : lipolyse
- Plaquettes: agrégation plaquettaire

Bêta-2:

- Poumons: bronchioles
- Artèrioles: vasodilatation
- Hépatique: glycogénolyse

Quand on parle de « cardiosélectivité », on parle en fait de bêta-1 sélectivité
Quand on augmente la dose, aucun bêta-bloquant n'est « cardiosélectif »

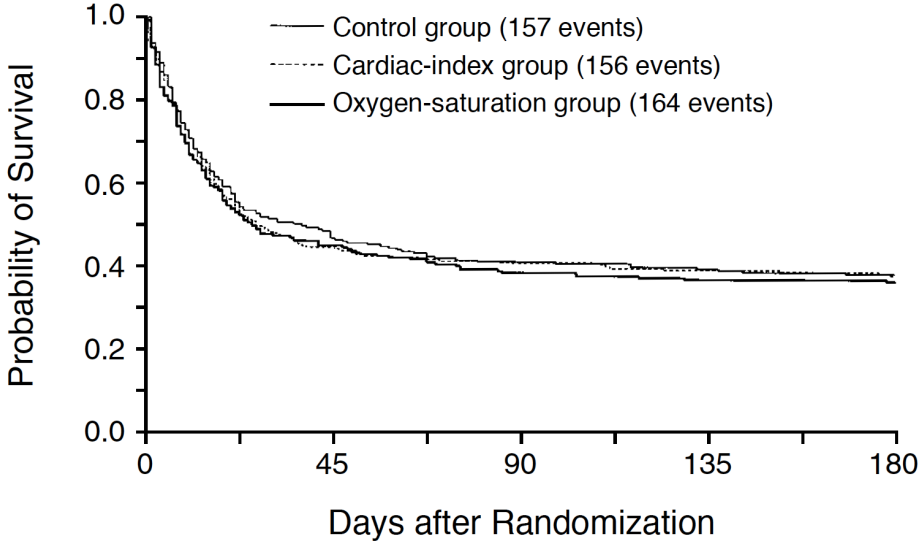

MGM DVD
CLINT EASTWOOD
LE BON
LA BRUTE
ET LE
TRUAND

The New England
Journal of Medicine

Volume 333 OCTOBER 19, 1995 Number 16

A TRIAL OF GOAL-ORIENTED HEMODYNAMIC THERAPY IN CRITICALLY ILL PATIENTS

LUCIANO GATTINONI, M.D., LUCA BRAZZI, M.D., PAOLO PELOSI, M.D., ROBERTO LATINI, M.D., GIANNI TOGNONI, M.D., ANTONIO PESENTI, M.D., AND ROBERTO FUMAGALLI, M.D., FOR THE SvO_2 COLLABORATIVE GROUP*



PATIENTS AT RISK (NO. OF EVENTS)

Control group	252 (129)	108 (13)	94 (4)	90 (3)	87
Cardiac-index group	253 (133)	102 (8)	90 (4)	86 (3)	83
Oxygen-saturation group	257 (133)	106 (16)	89 (4)	85 (1)	84

Figure 2. Survival Curves from Study Entry to the Six-Month Follow-up in the Three Study Groups.

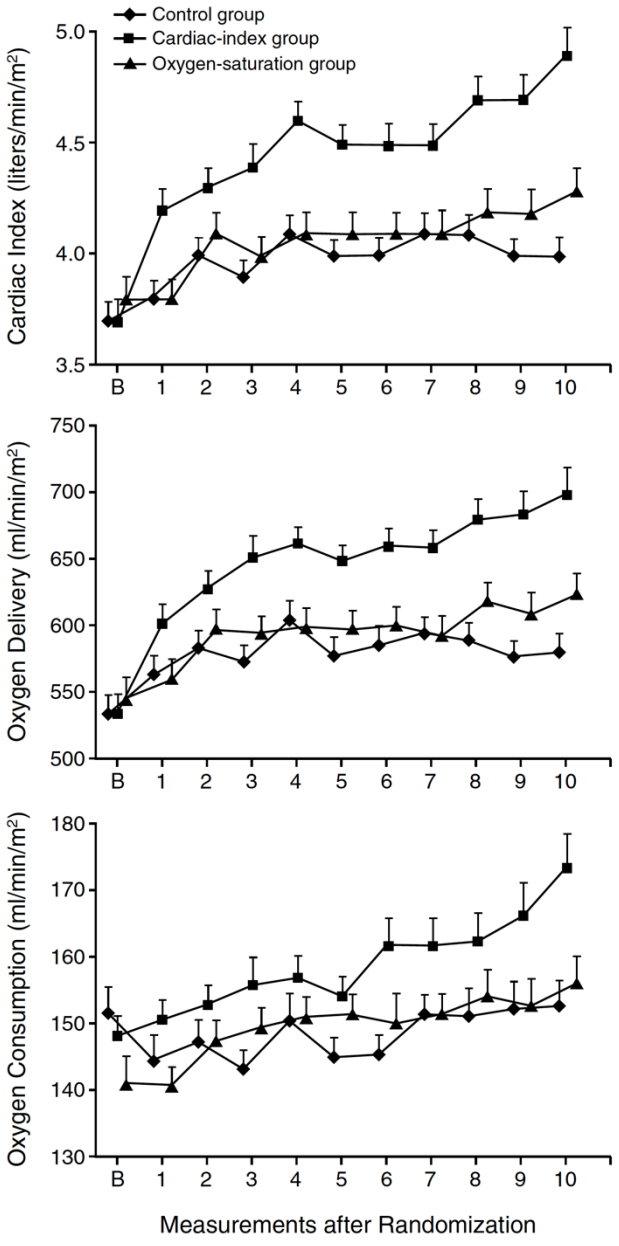


Figure 1. Mean (±SE) Cardiac Index, Oxygen Delivery, and Oxygen Consumption in the Three Study Groups.

For each variable, the incremental area under the curve differed significantly among the three groups ($P<0.001$). B denotes base line. Measurements were made twice a day for five days after randomization.

ELEVATION OF SYSTEMIC OXYGEN DELIVERY IN THE TREATMENT OF CRITICALLY ILL PATIENTS

MICHELLE A. HAYES, F.R.C.A., ANDREW C. TIMMINS, F.R.C.A., ERNEST H.S. YAU, F.R.C.A., MARK PALAZZO, F.R.C.A., CHARLES J. HINDS, F.R.C.A., AND DAVID WATSON, F.R.C.A.

THE NEW ENGLAND JOURNAL OF MEDICINE June 16, 1994

Table 2. Outcome Data.

OUTCOME	CONTROL GROUP (N = 50)	TREATMENT GROUP (N = 50)	NOT RANDOMIZED (N = 9)
Days in unit — median (range)	10 (1–64)	10 (1–48)	10 (1–29)
Ventilation			
No. of days — median (range)	8 (0–54)	8 (0–41)	2 (0–26)
No. of patients	44	46	7
Days in hospital — median (range)	23.5 (1–244)	19 (1–187)	20 (11–102)
Mortality — %			
In intensive care unit	30	50*	—
In hospital	34	54*	—
Predicted risk of death — median % (range)	34 (3–91)	34 (3–85)	6 (3–32)
Cause of death — no. of patients			
Intractable hypotension	4	4	—
Cardiac event	2	4	—
Multiple organ failure	9	17	—

*P = 0.04 for the comparison between the control and treatment groups.

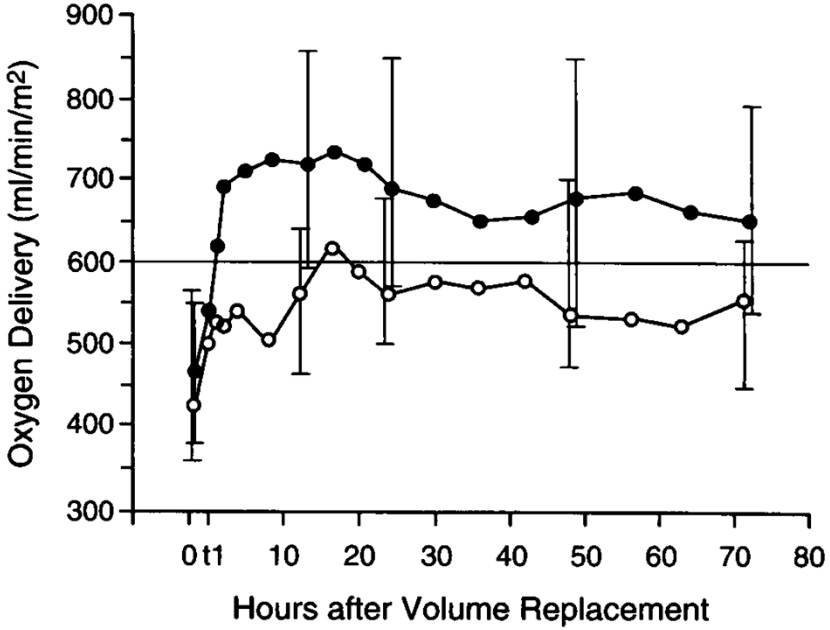


Figure 2. Median Oxygen Delivery in the Treatment and Control Groups.

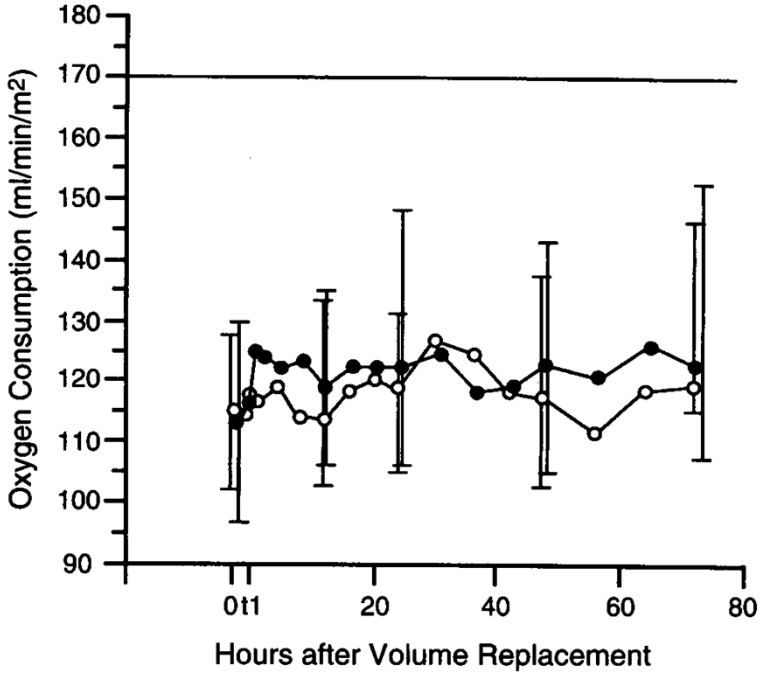


Figure 3. Median Oxygen Consumption in the Treatment and Control Groups.

Dose maximale médiane de dobutamine 25 microgramme/kg/min dans groupe interventionnel

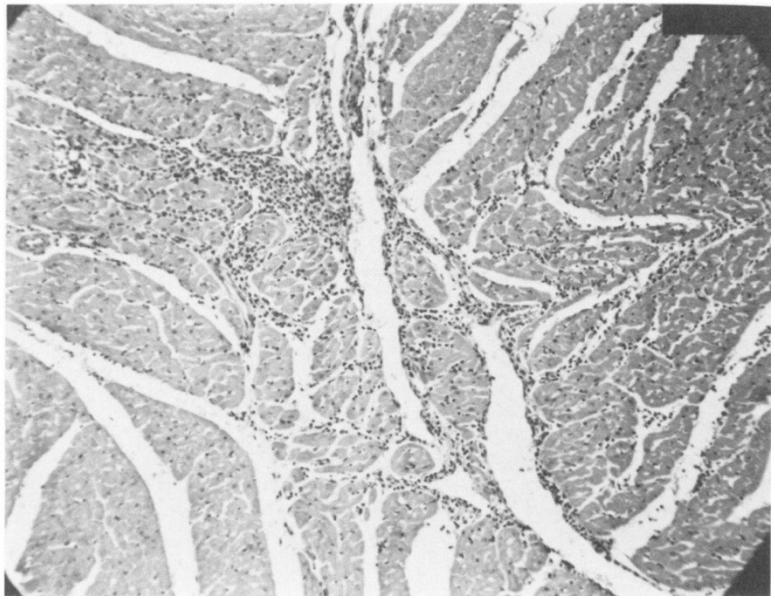
Hayes et al. New England Journal of Medicine 1994

	Moyen diagnostic	Timing	incidence
Vieillard-Baron 2001	ETO	0-6 heures	18%
Bouhemad 2009	ETO	?	20%
Jardin 1990	ETT	0-6 heures	29%
Etchecopar-Chevreuil 2008	ETO	12 heures	46%
Vieillard-Baron 2008	ETO	J1-2-3	60%
Parker 1984	Swan	J1	65%
Pulido 2012	ETT	<24 heures	64%

Dysfonction myocardique septique fréquente, Parfois retardée (iatrogène ?)

Il existe des anomalies structurelles

- Œdème généralisé interstitiel
- Dilatation vasculaire marquée
- Extravasation des leucocytes



SHOCK, Vol. 39, No. 4, pp. 329–335, 2013

HISTOLOGIC PATHOLOGIES OF THE MYOCARDIUM IN SEPTIC SHOCK: A PROSPECTIVE OBSERVATIONAL STUDY

Christian A. Schmittinger,*† Martin W. Dünser,‡ Christian Torgersen,‡ Günter Luckner,‡ Ingo Lorenz,† Stefan Schmid,† Michael Joannidis,§ Patrizia Moser,‖ Walter R. Hasibeder,¶ Milo Halabi,¶ and Christina M. Steger‖

**Department of Anesthesiology, Surgical Intensive Care Medicine, and Rescue Medicine, Lucerne Cantonal Hospital, Lucerne, Switzerland; †Department of Anesthesiology and Intensive Care Medicine, Innsbruck Medical University, Innsbruck; ‡Department of Anesthesiology, Perioperative and General Intensive Care Medicine, General Hospital Salzburg and Paracelsus Private Medical University, Salzburg; §Departments of Internal Medicine, and ‖Pathology, Innsbruck Medical University, Innsbruck; ¶Krankenhaus der Barmherzigen Schwestern, Ried im Innkreis, Austria*

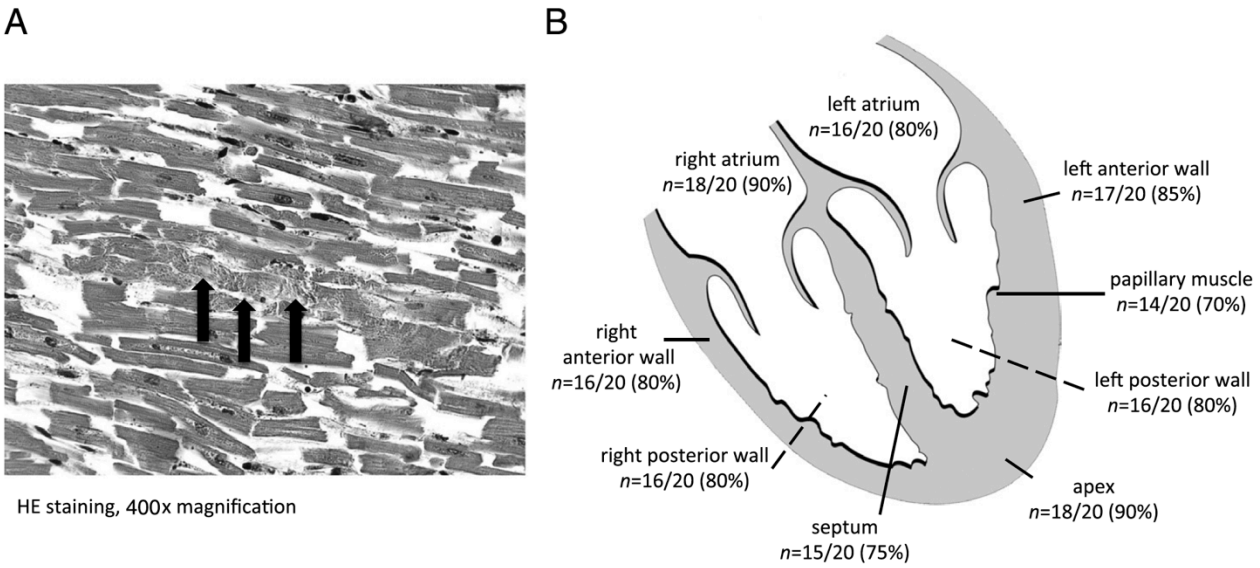


FIG. 1. Histologic appearance of contraction band necrosis (A) and frequency of contraction band necroses (B) in different sections of the heart in all patients.

TABLE 5. **Microscopic autopsy results of the heart**

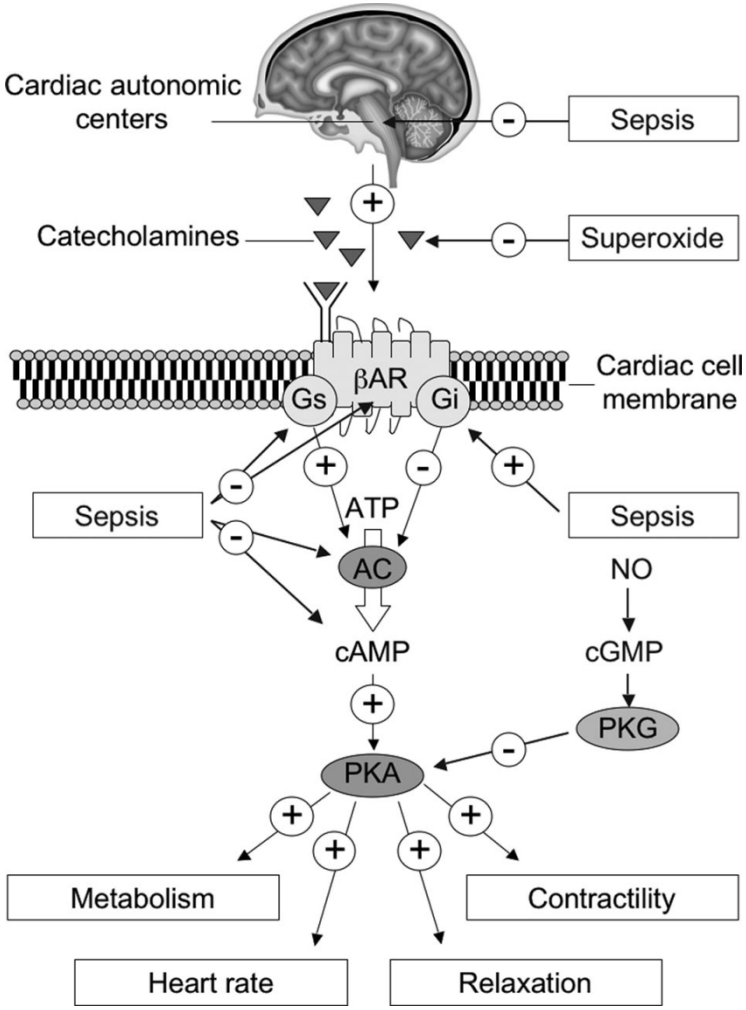
Myocytolysis	n (%)	20 (100)
Percentage involvement of myocardial sections	%	83 (75 – 92)
Interstitial fibrosis	n (%)	20 (100)
Percentage involvement of myocardial sections	%	42 (27 – 56)
Contraction band necrosis	n (%)	19 (95)
Percentage involvement of myocardial sections	%	83 (69 – 98)
Mononuclear infiltrates	n (%)	18 (90)
Percentage involvement of myocardial sections	%	19 (13 – 36)
Interstitial edema	n (%)	18 (90)
Percentage involvement of myocardial sections	%	25 (13 – 36)
Tissue hemorrhage	n (%)	6 (30)
Percentage involvement of myocardial sections	%	6 (6 – 6)

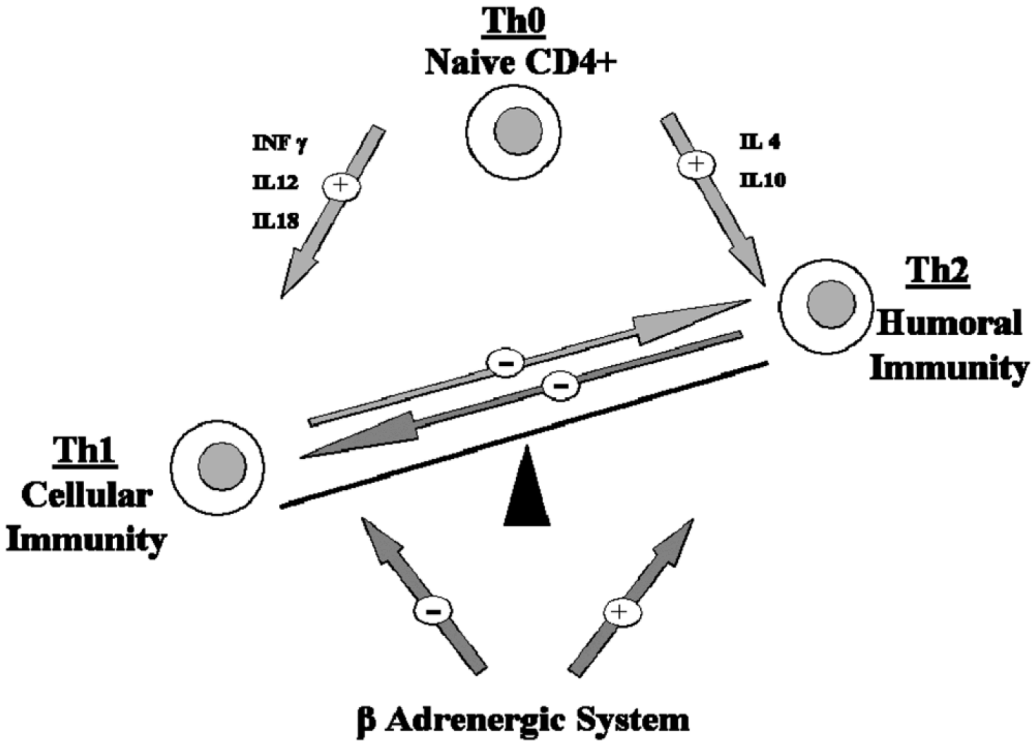
Data are given as median values with interquartile ranges if not otherwise indicated.

Caractéristiques exactes de toxicité aux catécholamines

Schmittinger et al. Shock 2013

Altérations du





T-helper type 1 and T-helper type 2 balance and the adrenergic system. Naive $CD4^+$, T-helper type 0 (Th0) cells are bipotential and are precursors of T-helper type 1 (Th1) cells and T-helper type 2 (Th2) cells. IL-12, produced by antigen-presenting cells, is the major inducer of Th1 differentiation. Th1 and Th2 responses are mutually inhibitory. IL-12 and IFNγ therefore inhibit Th2 cell activity, while IL-4 and IL-10 inhibit the Th1 response. The stimulation of β-adrenergic receptors potently inhibits the production of IL-12 by antigen-presenting cells, and thus inhibits the development of Th1 cells while promoting Th2 cells.

De Montmollin Critical Care 2009

The New England
Journal of Medicine

VOLUME 345 OCTOBER 25, 2001 NUMBER 17

REVERSAL OF CATABOLISM BY BETA-BLOCKADE AFTER SEVERE BURNS

DAVID N. HERNDON, M.D., DAVID W. HART, M.D., STEVEN E. WOLF, M.D., DAVID L. CHINKES, PH.D., AND ROBERT R. WOLFE, PH.D.

TABLE 3. KINETICS OF SKELETAL-MUSCLE PROTEIN AFTER TREATMENT.*

VALUE	CONTROL GROUP (N=12)	PROPRANOLOL GROUP (N=11)	P VALUE
Net balance of protein synthesis and breakdown (μmol/min/100 ml of leg volume)	−0.042±0.016	0.035±0.011†	0.001
Model-derived fluxes‡			
Inflow of phenylalanine into leg through femoral artery (μmol/min/100 ml of leg volume)	0.939±0.175	1.085±0.157	0.69
Outflow of phenylalanine from leg through femoral vein (μmol/min/100 ml of leg volume)	0.982±0.180	1.034±0.147	0.55
Transport of phenylalanine into myocyte (μmol/min/100 ml of leg volume)	0.145±0.020	0.264±0.046	0.18
Transport of phenylalanine from myocyte (μmol/min/100 ml of leg volume)	0.187±0.026	0.214±0.042	0.67
Arteriovenous shunt of phenylalanine past muscle (μmol/min/100 ml of leg volume)	0.795±0.176	0.821±0.127	0.46
Rate of disappearance of phenylalanine, approximating protein synthesis (μmol/min/100 ml of leg volume)	0.060±0.013	0.157±0.027	0.01
Rate of appearance of phenylalanine, approximating protein breakdown (μmol/min/100 ml of leg volume)	0.102±0.015	0.107±0.019	0.67
Muscle-protein synthesis of phenylalanine (μmol/min/100 ml of leg volume)	0.142±0.034	0.337±0.061	0.07
Muscle-protein breakdown of phenylalanine (μmol/min/100 ml of leg volume)	0.184±0.030	0.287±0.048	0.20
Efficiency of protein synthesis (%)§	38.7±5.6	60.7±3.4	0.03
Fractional synthetic rate (percentage of tracer incorporated into muscle/hr)	0.24±0.03	0.34±0.06	

*All values are means ±SE. Leg volume was measured in each study; values per 100 ml of leg volume are shown, to account for different leg sizes.

†The analysis included 12 patients.

‡The model used was the three-compartment model describing protein kinetics in the muscle.[18]

§The efficiency of protein synthesis was calculated for each patient with use of the following equation: muscle-protein synthesis ÷ (transport of phenylalanine into muscle + muscle-protein breakdown).

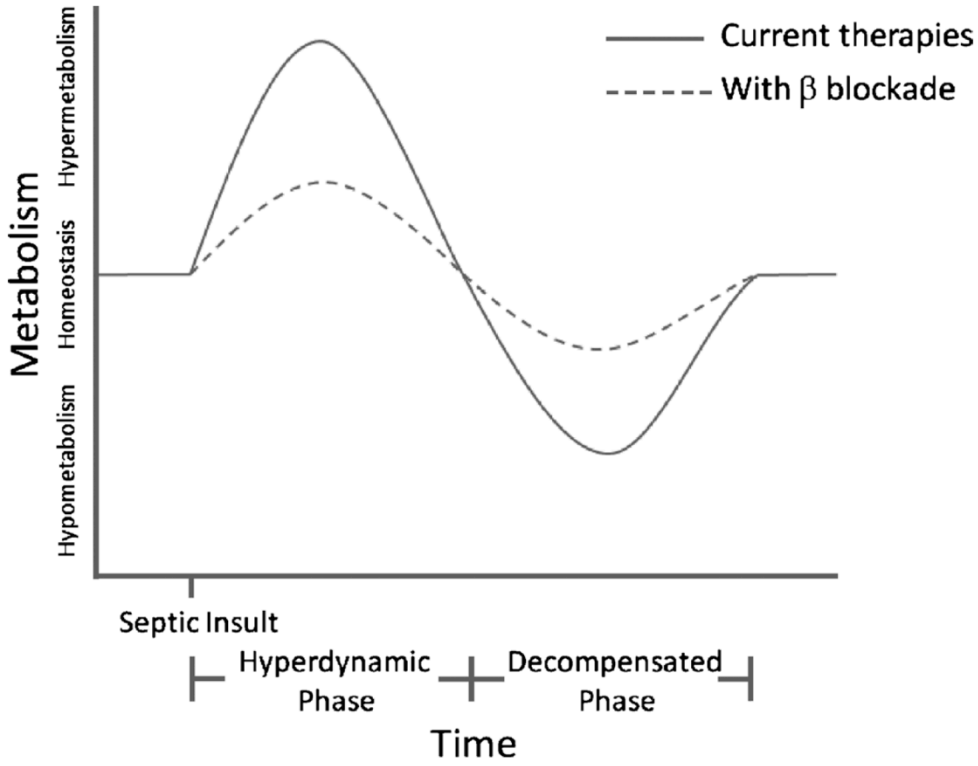
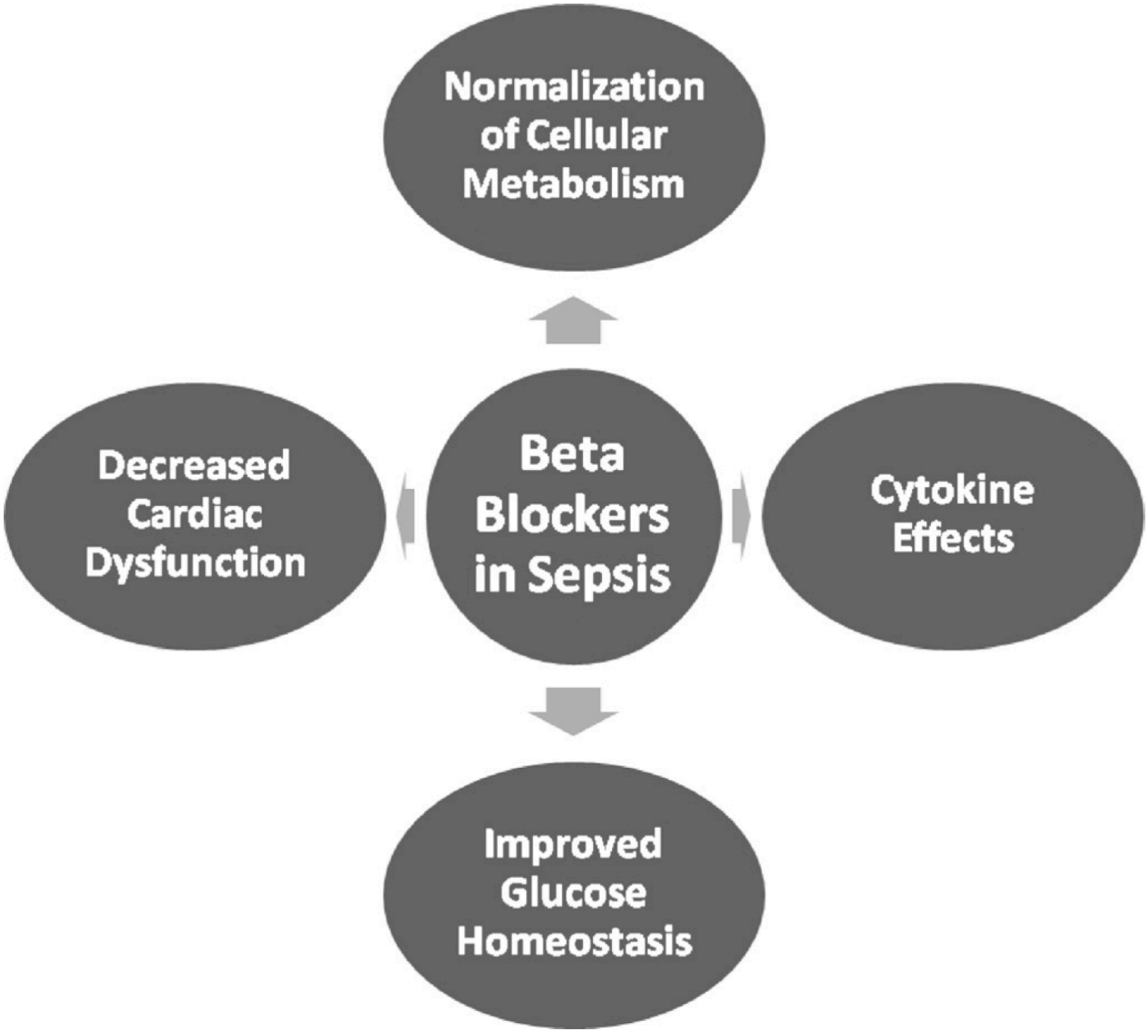


FIG. 1. **Metabolism response in sepsis**. The solid line represents the metabolic response with current therapy alone. The dashed line represents the proposed effect of b-blockade on metabolism in the septic patient.

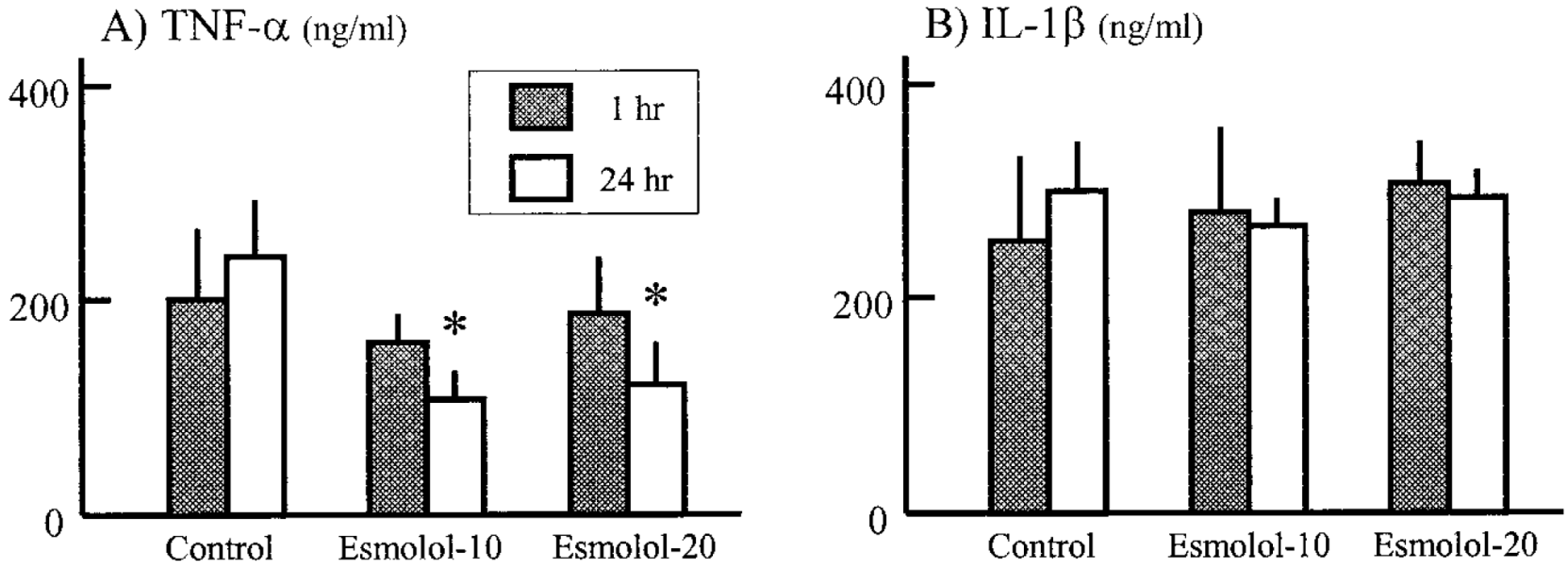
Novotny et al Shock 2009


Normalization of Cellular Metabolism
Decreased Cardiac Dysfunction
Beta Blockers in Sepsis
Cytokine Effects
Improved Glucose Homeostasis


MGM DVD
CLINT EASTWOOD
LE BON
LA BRUTE
ET LE TRUAND

Infusion of the β-adrenergic blocker esmolol attenuates myocardial dysfunction in septic rats*

Takeshi Suzuki, MD; Hiroshi Morisaki, MD; Ryohei Serita, MD; Michiko Yamamoto, BA; Yoshifumi Kotake, MD; Akitoshi Ishizaka, MD; Junzo Takeda, MD



Suzuki et al. Critical Care Medicine 2005

Table 2. Changes of heart rate and the variables of myocardial function in working heart model

		Preload					
	Group	10 cm H_2O	12 cm H_2O	14 cm H_2O	16 cm H_2O	18 cm H_2O	20 cm H_2O
Heart rate, beats/min	Control	341 ± 69	351 ± 74	360 ± 72	349 ± 69	349 ± 64	352 ± 68
	Esmolol-10	349 ± 48	354 ± 55	356 ± 49	373 ± 55	373 ± 41	376 ± 44
	Esmolol-20	333 ± 59	341 ± 50	359 ± 54	358 ± 50	360 ± 42	379 ± 36
	Sham	318 ± 27	322 ± 23	331 ± 25	342 ± 28	342 ± 24	343 ± 17
Stroke volume, mL	Control	0.10 ± 0.04	0.11 ± 0.04	0.11 ± 0.04	0.11 ± 0.04	0.10 ± 0.04	0.09 ± 0.04
	Esmolol-10	0.18 ± 0.04[a]	0.19 ± 0.04[a]	0.19 ± 0.05[a]	0.18 ± 0.06[a]	0.16 ± 0.06	0.15 ± 0.06
	Esmolol-20	0.18 ± 0.04[a]	0.19 ± 0.03[a]	0.20 ± 0.03[a]	0.21 ± 0.03[a]	0.20 ± 0.04[a]	0.18 ± 0.03[a]
	Sham	0.21 ± 0.03	0.22 ± 0.03	0.22 ± 0.03	0.22 ± 0.02	0.22 ± 0.03	0.21 ± 0.04
Cardiac output, mL/min	Control	28.4 ± 5.6	33.6 ± 7.1	34.7 ± 7.7	34.1 ± 8.9	32.3 ± 9.3	29.7 ± 8.1
	Esmolol-10	61.9 ± 11.6[a]	66.2 ± 12.5[a]	65.9 ± 13.5[a]	64.8 ± 15.3[a]	59.2 ± 18.4[a]	55.7 ± 18.5[a]
	Esmolol-20	58.6 ± 13.1[a]	66.0 ± 13.8[a]	72.4 ± 13.3[a]	73.9 ± 14.1[a]	75.5 ± 9.2[a]	70.0 ± 14.2[a]
	Sham	66.2 ± 9.6	71.0 ± 8.9	74.1 ± 6.8	76.2 ± 6.9	76.7 ± 10.3	74.5 ± 13.4
Left ventricular developed pressure, mm Hg	Control	57 ± 17	60 ± 19	61 ± 16	64 ± 12	61 ± 12	32 ± 10
	Esmolol-10	78 ± 7[a]	78 ± 9[a]	77 ± 8[a]	73 ± 8[a]	70 ± 7	66 ± 8
	Esmolol-20	79 ± 9[a]	78 ± 8[a]	78 ± 6[a]	76 ± 7[a]	74 ± 7[a]	71 ± 7
	Sham	85 ± 5	87 ± 6	85 ± 7	82 ± 5	82 ± 4	80 ± 3
dP/dt_{max}, mm Hg/sec	Control	1557 ± 541	1685 ± 593	1639 ± 489	1725 ± 399	1564 ± 347	1587 ± 300
	Esmolol-10	2293 ± 265[a]	2317 ± 308[a]	2258 ± 250[a]	2138 ± 181[a]	2007 ± 216	1834 ± 177
	Esmolol-20	2289 ± 307[a]	2261 ± 305[a]	2261 ± 256[a]	2153 ± 288[a]	2149 ± 288[a]	1985 ± 305[a]
	Sham	2540 ± 58	2584 ± 206	2459 ± 255	2283 ± 210	2328 ± 203	2260 ± 138
dP/dt_{min}, mm Hg/sec	Control	−1777 ± 370	−1937 ± 338	−1794 ± 429	−1855 ± 275	−1771 ± 212	−1740 ± 225
	Esmolol-10	−2452 ± 324[a]	−2445 ± 352[a]	−2410 ± 257[a]	−2228 ± 174[a]	−2069 ± 84[a]	−1969 ± 167
	Esmolol-20	−2404 ± 364[a]	−2434 ± 306[a]	−2361 ± 282[a]	−2274 ± 320[a]	−2260 ± 224[a]	−2159 ± 308[a]
	Sham	−2806 ± 191	−2792 ± 294	−2698 ± 237	−2482 ± 217	−2568 ± 253	−2444 ± 119
Myocardial oxygen consumption, μLO_2/min	Control	175 ± 15	168 ± 15	158 ± 15	161 ± 15	154 ± 19	148 ± 17
	Esmolol-10	192 ± 40	201 ± 35	189 ± 36	186 ± 38	180 ± 42	185 ± 50
	Esmolol-20	209 ± 35[a]	211 ± 28[a]	215 ± 28[a]	211 ± 34[a]	206 ± 33[a]	200 ± 41[a]
	Sham	210 ± 33	214 ± 39	217 ± 53	210 ± 53	209 ± 54	213 ± 47

dP/dt_{max}, maximum rate of left ventricular pressure increase; dP/dt_{min}, minimum rate of left ventricular pressure increase.
[a] $p < .05$ vs. control group. Data expressed as mean ± SD.

Suzuki et al. Critical Care Medicine 2005

Berk JL, Hagen JF, Dunn JM: The role of beta adrenergic blockade in the treatment of septic shock. Surg Gynecol Obstet 1970; 130: 1025–1034

- 5 patients en choc réfractaire
- Pas de groupe contrôle
- Propanolol (non cardiosélectif) IV 5mg sur 2-3h répété une fois
- FC baisse et PAM monte
- Mortalité 40%
- Traitements concomitants : digoxine, stéroides haute dose, caféine, atropine, entrainement électrique, glucagon…

Hemodynamic and metabolic effects of selective β_1 adrenergic blockade during sepsis

Dennis C. Gore, MD, *and* **Robert R. Wolfe, PhD,** *Galveston, Texas*

Surgery
May 2006

Table I. Patient demographics

Characteristic	*Mean value ± SD*
Age (y)	41 ± 7
Body wt. (kg)	81 ± 18
Body surface area (m^2)	1.87 ± 0.14
Leg volume (100 ml)	9.7 ± 3.2
APACHE II score	17 ± 2
Sepsis severity score	16 ± 1
Hemoglobin concentration (gm/dl)	8.7 ± 0.5
paO_2/FiO_2	186 ± 24
Pulmonary compliance (ml/cmH_2O)	33 ± 4
Plasma creatinine (mg/dl)	0.87 ± 0.16

All patients (n = 6) were diagnosed with pneumonia and required mechanical ventilatory support.

Table II. Hemodynamics

	Basal	*Esmolol*
Cardiac index (L/minute × m^2)		
Normal range (2.5-4.0)	4.89 ± 1.00	3.88 ± 0.88*
Heart rate (beats/minute)		
Normal range (60-100)	114 ± 15	91 ± 12*
Blood pressure (mm Hg)		
Normal range (90-140)	108 ± 14	100 ± 12
Normal range (50-90)	62 ± 6	64 ± 7
Pulmonary artery wedge pressure (mm Hg)		
Normal range (4-12)	14 ± 4	13 ± 6
Systemic vascular resistance index (dyne/sec/cm^{-5}/m^2)		
Normal range (1,300-2,800)	1,366 ± 539	1,360 ± 521
Pulmonary vascular resistance index (dyne/sec/cm^{-5}/m^2)		
Normal range (100-240)	179 ± 94	208 ± 160
Stroke volume index (ml/bt × m^2)		
Normal range (33-47)	43 ± 6	43 ± 11
Leg blood flow (ml/min × 100 ml leg volume)	4.84 ± 1.91	5.07 ± 1.28
Hepatic clearance (ml/min × kg)	2.73 ± 1.32	3.13 ± 1.35

Mean ± SD.

*$P < .05$ comparison to Basal by Student's paired t test.

FC ↘
DC →
VES →
PAM ↘
RVS →

Gore et al. Surgery 2006

Table IV. Oxygen utilization

	Basal	*Esmolol*
Oxygen consumption ($ml/min \times m^2$)	181 ± 27	176 ± 29
Oxygen delivery ($ml/min \times m^2$)	656 ± 101	509 ± 84*
O_2 extraction (%)	28 ± 3	35 ± 4*

Mean ± SD.
*$P < .05$ comparison to Basal by Student's paired t test.

6 patients septiques mais après trauma ou brûlure
Tous ventilés
Aucun sous inotrope
Esmolol pour réduction FC de 20%
Pas de groupe contrôle

Table VI. Glucose/palmitate kinetics

	Basal	*Esmolol*
Arterial glucose concentration (μmol/L)	7.6 ± 1.8	8.9 ± 2.6
Endogenous glucose production (μmol/kg min)	21.0 ± 5.9	22.3 ± 6.5
Glucose clearance (ml/kg × min)	3.18 ± 1.51	3.23 ± 1.65
Glucose oxidation rate (μmol/kg × min)	30.0 ± 8.5	15.3 ± 6.1*
Palmitate oxidation rate (μmol/kg × min)	0.26 ± 2.12	3.84 ± 2.61*

Mean ± SD.
*$P < .05$ comparison to Basal Student's paired t test.

Gore et al. Surgery 2006

Research

Open Access

Combined milrinone and enteral metoprolol therapy in patients with septic myocardial depression

Christian A Schmittinger[1], Martin W Dünser[1], Maria Haller[2], Hanno Ulmer[3], Günter Luckner[1], Christian Torgersen[1], Stefan Jochberger[1] and Walter R Hasibeder[2]

[1]Department of Anaesthesiology and Critical Care Medicine, Innsbruck Medical University, Anichstrasse 35, 6020 Innsbruck, Austria
[2]Department of Anaesthesiology and Critical Care Medicine, Krankenhaus der Barmherzigen Schwestern, Schlossberg 1, 4910 Ried im Innkreis, Austria
[3]Department of Medical Biostatistics, Innsbruck Medical University, Schöpfstrasse 41/1, 6020 Innsbruck, Austria

Corresponding author: Christian A Schmittinger, christian.schmittinger@i-med.ac.at

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This article is online at: http://ccforum.com/content/12/4/R99

Table 1

Characteristics of the study population

Number	40
Age, years	71 ± 13
Male gender, number (percentage)	21 (53)
Body mass index, kg/m²	28 ± 7
Premorbidities, number (percentage)	
Chronic arterial hypertension	23 (58)
Obstructive coronary artery disease	10 (25)
Compensated congestive heart failure	12 (30)
Chronic obstructive pulmonary disease	8 (20)
Chronic renal insufficiency	14 (35)
Chronic liver disease	4 (10)
Neoplasm	3 (8)
Chronic beta-blocker therapy, number (percentage)	15 (38)
Source of infection, number (percentage)	
Liver/Abdomen	21 (53)
Lung	10 (25)
Skin/Soft tissue	3 (8)
Joint/Bone	2 (5)
Catheter/Device	1 (3)
Urogenital tract	1 (3)
Unknown origin	2 (5)
Continuous veno-venous hemofiltration, number (percentage)	28 (70)
Multiple organ dysfunction syndrome score (12), points	9.9 ± 2.3
Simplified Acute Physiology Score II, points	53 ± 16
Intensive care unit length of stay, days	15 ± 11
28-day mortality, number (percentage)	13 (33)

Data are presented as mean value ± standard deviation, if not indicated otherwise.

Schmittinger et al. Critical Care 2008

Table 2

Hemodynamic variables at shock onset and during the observation period

	ICU admission[a]	Baseline	6 hours	12 hours	24 hours	48 hours	72 hours	96 hours	*P* value
Patients, number	40	40	40	39	37	37	35	33	
Heart rate, bpm	110 ± 19	101 ± 18	84 ± 17[b]	84 ± 14[b]	84 ± 13[b]	83 ± 13[b]	79 ± 13[b]	78 ± 14[b]	<0.001[c]
MAP, mm Hg	59 ± 19	85 ± 23	82 ± 15	85 ± 18	87 ± 15	90 ± 20	91 ± 20	90 ± 21	0.16
CVP, mm Hg	14 ± 4	12 ± 3	12 ± 4	12 ± 3	11 ± 3	11 ± 3[b]	10 ± 3[b]	9 ± 3[b]	<0.001[c]
Cardiac index, L/minute per m^2	1.9 ± 0.6	3.1 ± 1.1	3.2 ± 1.0	3.3 ± 0.9	3.4 ± 0.9	3.4 ± 1.0	3.5 ± 1.0	3.5. ± 0.8	0.56
SVI, mL/beat per m^2	18 ± 7	32 ± 12	40 ± 14	40 ± 12	42 ± 12[b]	42 ± 13[b]	42 ± 10[b]	44 ± 9[b]	0.002[c]
CPI, W/m^2	0.24 ± 0.14	0.61 ± 0.32	0.57 ± 0.22	0.60 ± 0.17	0.65 ± 0.18	0.68 ± 0.30	0.71 ± 0.25	0.68 ± 0.23	0.27
$ScvO_2$, percentage	64 ± 12	71 ± 10	72 ± 6	72 ± 11	74 ± 9	77 ± 8	73 ± 11	72 ± 11	0.35
SVRI, dyne-second/cm^5 per m^2	2,041 ± 1,181	2,114 ± 825	1,918 ± 897	1,913 ± 777	1,895 ± 647	2,014 ± 800	2,060 ± 852	1,824 ± 569	0.78
NE, μg/kg per minute	0.12 ± 0.25 (n = 18)	0.17 ± 0.11	0.18 ± 0.11	0.18 ± 0.11	0.17 ± 0.13	0.13 ± 0.13	0.09 ± 0.08[b]	0.06 ± 0.07[b]	<0.001[c]
AVP dosage, IU/hour	NA	2.0 ± 1.6	2.2 ± 1.3	2.1 ± 1.3	2.1 ± 1.2	1.9 ± 1.3	1.3 ± 1.3	0.8 ± 1.1[b]	<0.001[c]
Mil, μg/kg per minute	0.24 ± 0.19 (n = 6)	0.31 ± 0.16	0.34 ± 0.17	0.33 ± 0.16	0.30 ± 0.17	0.24 ± 0.18	0.21 ± 0.19	0.12 ± 0.13[b]	<0.001[c]
Meto, mg	NA	47 ± 19	NA	NA	47 ± 41	52 ± 42	51 ± 42	54 ± 37	NA

[a]Not included in the longitudinal mixed-effects analysis. [b]Significant effects versus baseline. [c]Significant time effect. Data are presented as mean value ± standard deviation. AVP, arginine vasopressin; bmp, beats per minute; CPI, cardiac power index; CVP, central venous blood pressure; ICU, intensive care unit; MAP, mean arterial blood pressure; Meto, metoprolol dosage; Mil, milrinone requirements (n in parentheses indicates the number of patients who received milrinone already at intensive care unit admission); NA, not administered; NE, norepinephrine requirements (n in parentheses indicates the number of patients who received norepinephrine already at intensive care unit admission); $ScvO_2$, central venous oxygen saturation; SVI, stroke volume index; SVRI, systemic vascular resistance index.

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Table 3

Organ function variables during the observation period

	Baseline	6 hours	12 hours	24 hours	48 hours	72 hours	96 hours	*P* value
Patients, number	40	40	39	37	37	35	33	
pH	7.36 ± 0.09	7.37 ± 0.06	7.37 ± 0.1	7.38 ± 0.08	7.38 ± 0.07[a]	7.4 ± 0.06[a]	7.42 ± 0.07[a]	<0.001[b]
Lactate, mg/dL	22 ± 15	24 ± 14	29 ± 32	14 ± 10[a]	12 ± 8[a]	11 ± 7[a]	10 ± 5[a]	<0.001[b]
Creatinine, mg/dL	2.3 ± 1.3	NM	NM	2.0 ± 1.0	1.8 ± 0.7	1.7 ± 0.8	1.6 ± 0.7[a]	0.02[b]
ASAT, IU/L	230 ± 651	NM	NM	143 ± 253	166 ± 320	199 ± 474	153 ± 336	0.97
ALAT, IU/L	128 ± 435	NM	NM	78 ± 222	90 ± 225	101 ± 207	90 ± 157	0.78
Bilirubin, mg/dL	1.7 ± 1.4	NM	NM	1.6 ± 1.3	1.5 ± 1.1	1.5 ± 1.5	1.6 ± 2.2	0.60
C-reactive protein, mg/dL	17.6 ± 8.7	NM	NM	17.8 ± 9.1	15.2 ± 9.3	11.6 ± 8.6	10 ± 8.2	0.001[b]
Troponin I, μg/L	8 ± 40	NM	NM	6 ± 21	3 ± 9	3 ± 7	2 ± 5	0.60
Platelet count, 10^9/L	145 ± 78	NM	NM	132 ± 88	130 ± 106	134 ± 112	133 ± 123	0.95
PaO_2/FiO_2	244 ± 129	NM	NM	243 ± 92	252 ± 102	238 ± 84	262 ± 89	0.87

[a]Significant effects versus baseline. [b]Significant time effect. Data are presented as mean value ± standard deviation. ALAT, alanine aminotransferase; ASAT, aspartate aminotransferase; FiO_2, inspiratory oxygen tension; NM, not measured; PaO_2, arterial oxygen tension.

40 patients
Pas de groupe contrôle
Remplissage ???
31+5 patients sous vasopressine
Mortalité à 28 jours 33 %

FC ↘
DC →
VES ↗
PAM ↘
RVS ↘

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short report

Wien Klin Wochenschr (2012) 124:552–556
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

10 patients
Pas de groupe contrôle
KT droit et ETT
24h de perfusion
Mortalité à 28 jours 10%

Table 1. Esmolol and norepinephrine infusion rates, haemodynamic and calculated parameters, blood draws results and echocardiographic parameters at subsequent time (T) intervals (baseline before esmolol infusion (T0), following esmolol infusion, at 2 (T2), 6 (T6), 12 (T12), 24 h (T24) and 6 h after infusion ceasing (T30)

Time point	T0	T2	T6	T12	T24	T30	*p* value
Infusion							
Esmolol (mg/h)	0	213±64	245±82	255±117	273±90	0	NS
Nor (μg/kg/min)	0.13±0.16	0.14±0.17	0.15±0.14	0.15±0.15	0.17±0.19	0.12±0.12	NS
Hemodynamics, arterial lactate and calculated parameters							
HR (beats/min)	142±11	127±12	120±11	113±7	112± 9	116±11	<0.001
MAP (mmHg)	91±11	89±9	87±11	86±8	84±9	89±8	NS
PAMP (mmHg)	29±4	30±5	29±3	28±3	30±4	28±4	NS
PAWP (mmHg)	16±3	15±2	15±2	15±3	15±2	14±2	NS
CO (l/min)	9.2±1.9	8.8±2.0	8.8±2.1	8.2±1.6	8.2±1.7	8.7±1.6	NS
CI (l/min/m^2]	4.9±0.8	4.7±0.9	4.7±1.0	4.3±0.7	4.4±0.7	4.7±0.7	NS
SV (ml)	67±16	69±14	73±14	72±12	73±15	77±13	NS
SVR (dyn/s/cm^5)	721±212	751±171	733±209	763±203	764±213	749±200	NS
Lactate (mmol/l)	1.7±0.5	1.7±0.4	2.0±0.6	2.1±0.4	1.7±0.3	1.8±0.5	NS
DO_2 (ml/min)	1309±207	1311±206	1314±204	1316±199	1311±185	1308±198	NS
SvO_2 (%)	70±8	67±5	65±5	63±5	60.2±4	64±5	NS
VO_2 (ml/min)	326±130	345±108	367±101	376±101	394±70	385±103	NS
OER (%)	25±8	26±6	28±7	29±7	31±6	30±8	NS
Echocardiography							
LV EF (%)	62.7±12	60.5±11	57.9±10	59.7±9	57.9±6	60.3±9	NS
TAPSE (mm)	21±4	22±3	22±4	21±3	21±3	22±3	NS

Parameters presented as means ± SD. All changes were insignificant except decrease in heart rate ($p<0.001$, repeated measures ANOVA)
Nor norepinephrine, *HR* heart rate, *MAP* mean arterial pressure, *PAMP* mean pulmonary artery pressure, *PAWP* pulmonary artery wedge pressure, *CO* cardiac output, *CI* cardiac index, *SV* stroke volume, *SVR* systemic vascular resistence, DO_2 systemic oxygen delivery, SvO_2 mixed venous oxygen saturation, VO_2 systemic oxygen consumption, *OER* oxygen extraction ratio, *LV EF* left ventricular ejection fraction, *TAPSE* tricuspid annular plane systolic excursion

Microvascular Effects of Heart Rate Control With Esmolol in Patients With Septic Shock: A Pilot Study*

Andrea Morelli, MD[1]; Abele Donati, MD[2]; Christian Ertmer, MD[3]; Sebastian Rehberg, MD[3]; Tim Kampmeier, MD[3]; Alessandra Orecchioni, MD[1]; Annalia D'Egidio, MD[1]; Valeria Cecchini, MD[1]; Giovanni Landoni, MD[4]; Paolo Pietropaoli, MD[1]; Martin Westphal, MD[3]; Mario Venditti, MD[5]; Alexandre Mebazaa, MD[6]; Mervyn Singer, MD, FRCP[7]

Critical Care Medicine

September 2013 • Volume 41 • Number 9

TABLE 2. Hemodynamic Data of the Study Patients ($n = 25$)

Variable	Baseline	24 Hr	p
Cardiac index (L/min/m^2)	4.0 (3.5; 5.3)	3.1 (2.6; 3.8)	< 0.001
Stroke volume index (mL/beat^2/m^2)	34 (27; 46)	40 (31; 46)	0.31
Heart rate (/min)	117 (112; 126)	86 (80; 89)	< 0.001
Mean arterial pressure (mm Hg)	71 (68; 75)	72 (70; 74)	0.67
Mean pulmonary arterial pressure (mm Hg)	31 (28; 34)	31 (28; 34)	0.73
Pulmonary arterial occlusion pressure (mm Hg)	17 (15; 20)	18 (16; 20)	0.50
Central venous pressure (mm Hg)	13 (11; 16)	14 (12; 17)	0.09
Left ventricular stroke work index [g m/beat/m^2]	25 (22; 31)	29 (21; 34)	0.56
Right ventricular stroke work index [g m/beat/m^2]	8.0 (6; 12)	9.0 (6; 12)	0.89
Norepinephrine dosage (µg/kg/min)	0.53 (0.29; 0.96)	0.41 (0.22; 0.78)	0.03

Data are given as median (25th; 75th percentile).

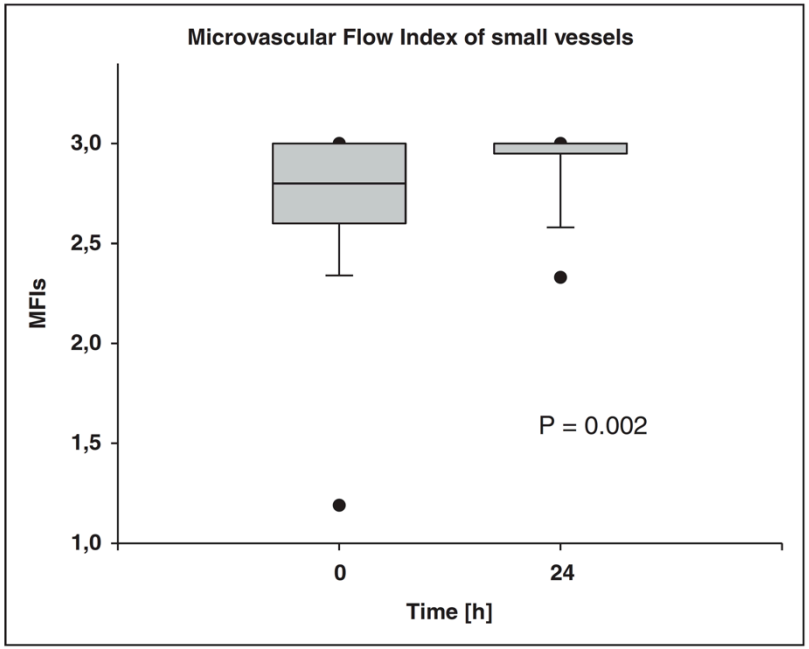


Figure 1. Change in microcirculatory flow index of small vessels (MFIs) after 24 hr of esmolol administration. Small vessels were defined as those with a diameter less than 20 µm. Data are expressed as median (25th; 75th percentile).

Etude pilote non contrôlée
Aucun patient sous support inotrope
Pas de donnée sur la mortalité
Pas de détérioration de la microcirculation malgré baisse du DC

Morelli et al. Critical Care Medicine 2013

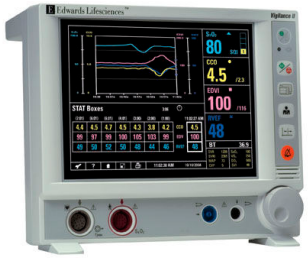

MGM DVD
CLINT EASTWOOD
LE BON LA BRUTE ET LE TRUAND

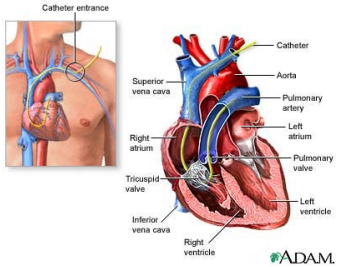
Preliminary Communication | CARING FOR THE CRITICALLY ILL PATIENT

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

Andrea Morelli, MD; Christian Ertmer, MD; Martin Westphal, MD; Sebastian Rehberg, MD; Tim Kampmeier, MD; Sandra Ligges, PhD; Alessandra Orecchioni, MD; Annalia D'Egidio, MD; Fiorella D'Ippoliti, MD; Cristina Raffone, MD; Mario Venditti, MD; Fabio Guarracino, MD; Massimo Girardis, MD; Luigi Tritapepe, MD; Paolo Pietropaoli, MD; Alexander Mebazaa, MD; Mervyn Singer, MD, FRCP

JAMA October 23/30, 2013 Volume 310, Number 16





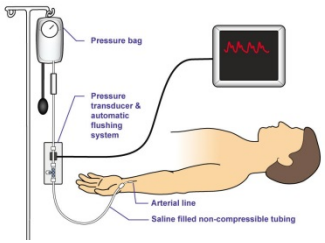
PAM>65
SvO2>65
Noradrénaline après 24h

Sortie de réa ou décès

Esmolol en titration

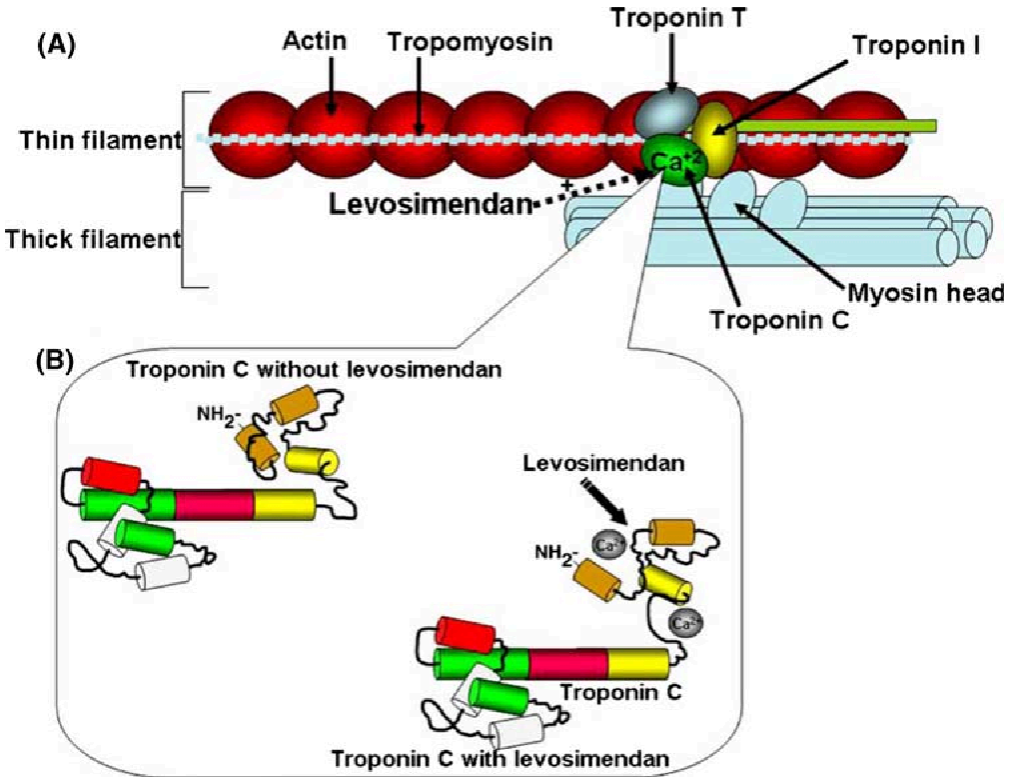
FC >94

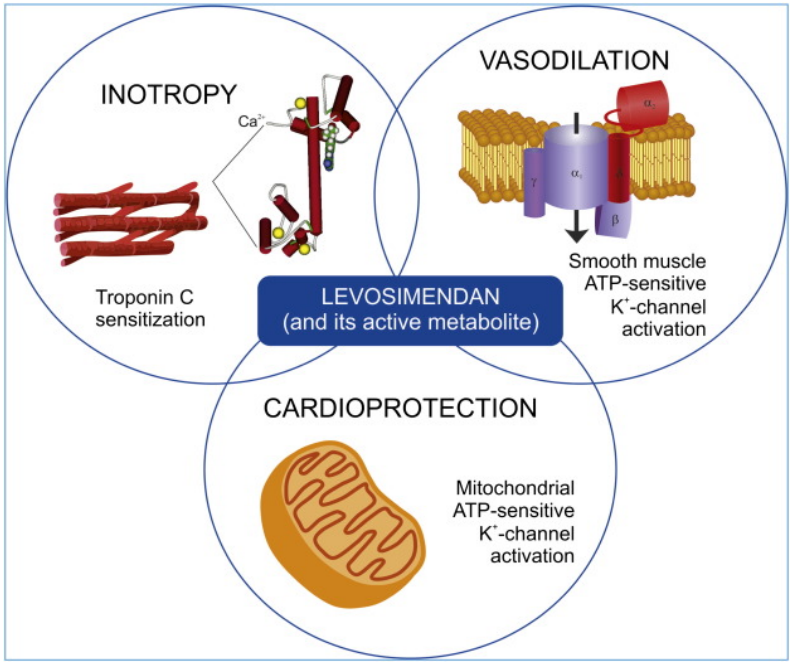
80 < FC < 94



Si SvO2 <65 malgré Sa02>95 et Hb>8g/dl
→ Levosimendan
HSHC 300 mg pour tous

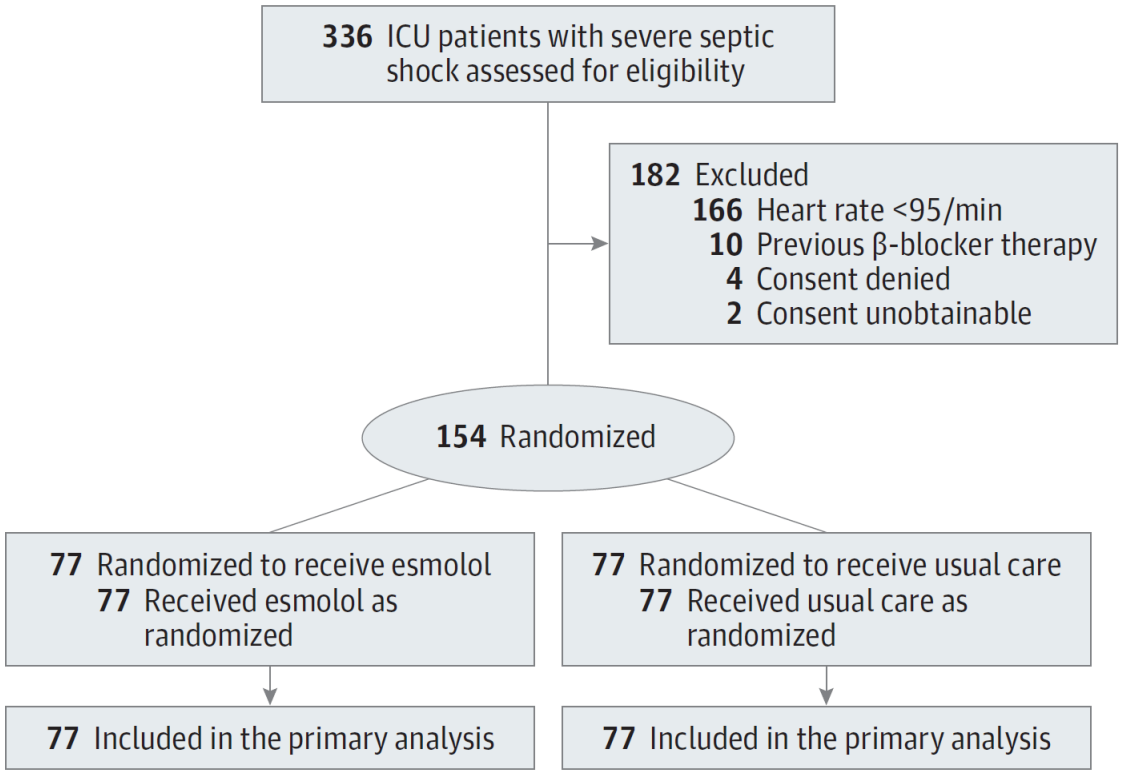
esmolol 30/1 demi-vie 9'





N'augmente pas le calcium dans la cellule MVO2 préservée ?

Figure 1. Flow Chart



ICU indicates intensive care unit.

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Table 1. Baseline Characteristics of the Study Patients

	Esmolol (n = 77)	Control (n = 77)
Age, median (IQR), y	66 (52-75)	69 (58-78)
Men, No. (%)	54 (70)	53 (69)
Body mass index, median (IQR)[a]	29 (26-33)	28 (25-32)
SAPS II score, median (IQR)[b]	52 (47-60)	57 (49-62)
Norepinephrine dosage, median (IQR), μg/kg/min	0.38 (0.21-0.87)	0.40 (0.18-0.71)
Arterial lactate, median (IQR), mmol/L	1.5 (1.1-2.7)	1.9 (1.1-3.1)
Platelet count, median (IQR), × 10^3/μL	178 (126-272)	129 (73-206)
Fluid input, mL, 24 h prior to inclusion, median (IQR),	4700 (4300-5200)	4800 (4100-5325)
Cause of septic shock, No.		
Necrotizing fasciitis	1	2
Pyelonephritis	1	1
Peritonitis	21	30
Pneumonia	54	44
Pathogens, No. (%)		
Klebsiella spp	29 (38.0)	20 (26.0)
Acinetobacter spp	6 (7.8)	6 (7.8)
Acinetobacter spp + *Klebsiella* spp	11 (14.3)	8 (10.4)
Staphylococcus aureus	6 (7.8)	6 (7.8)
Escherichia coli	3 (3.9)	8 (10.4)
Pseudomonas spp	5 (6.5)	4 (5.2)
Aspergillus spp	0 (0.0)	3 (3.9)
Others	17 (22.0)	22 (28.6)
Preexisting conditions, No. (%)		
Coronary artery disease	25 (32.5)	21 (27.3)
Congestive heart failure	11 (14.3)	13 (16.9)
Chronic kidney disease	5 (6.5)	4 (5.2)
Chronic obstructive pulmonary disease	16 (20.8)	20 (26.0)

Abbreviation: IQR, interquartile range.

[a] Calculated as weight in kilograms divided by height in meters squared

[b] The Simplified Acute Physiology Score (SAPS) II is calculated from a point score of 12 routinely measured physiological and biochemical variables within the first 24 hours of intensive care unit admission. The range varies from 0 to 163 points with more extreme values scoring more points.[18]

Patients beaucoup remplis avant Lactate normalisé

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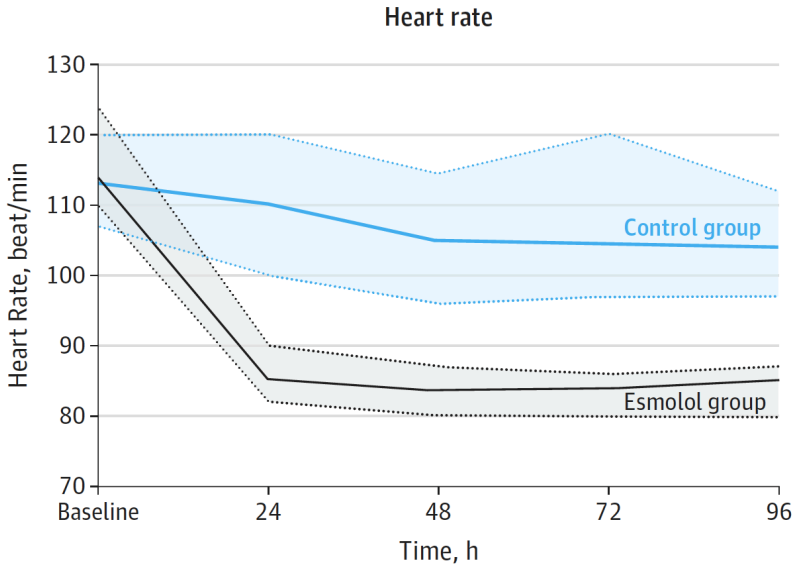
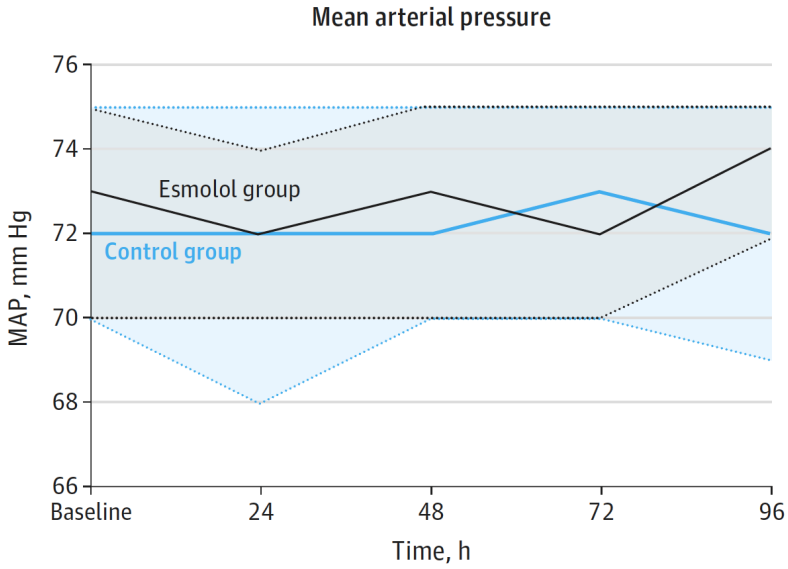


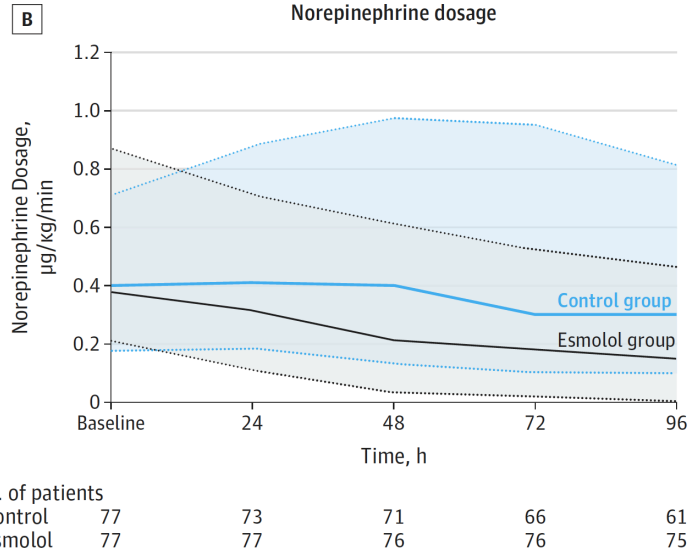
No. of patients

Control	77	73	71	66	61
Esmolol	77	77	76	76	75



No. of patients

Control	77	73	71	66	61
Esmolol	77	77	76	76	75



No. of patients

Control	77	73	71	66	61
Esmolol	77	77	76	76	75

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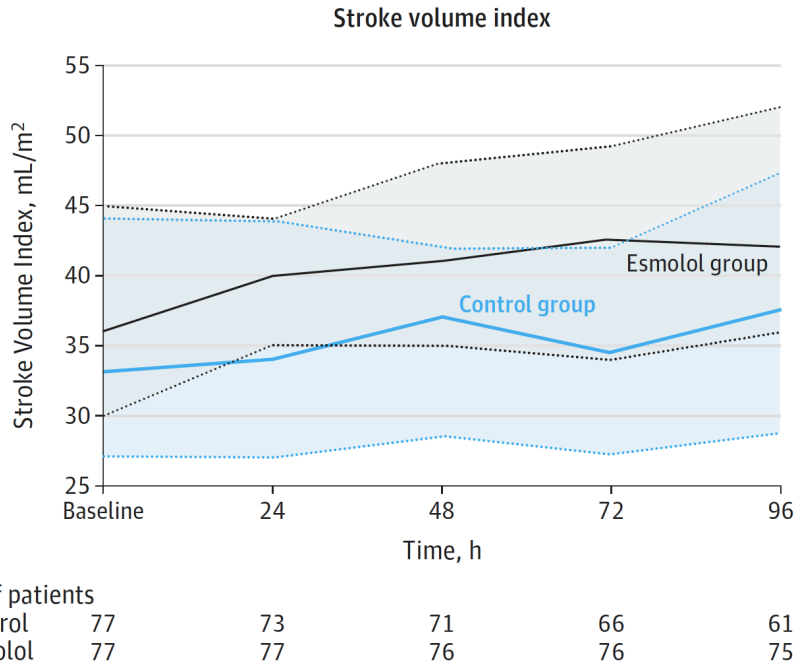

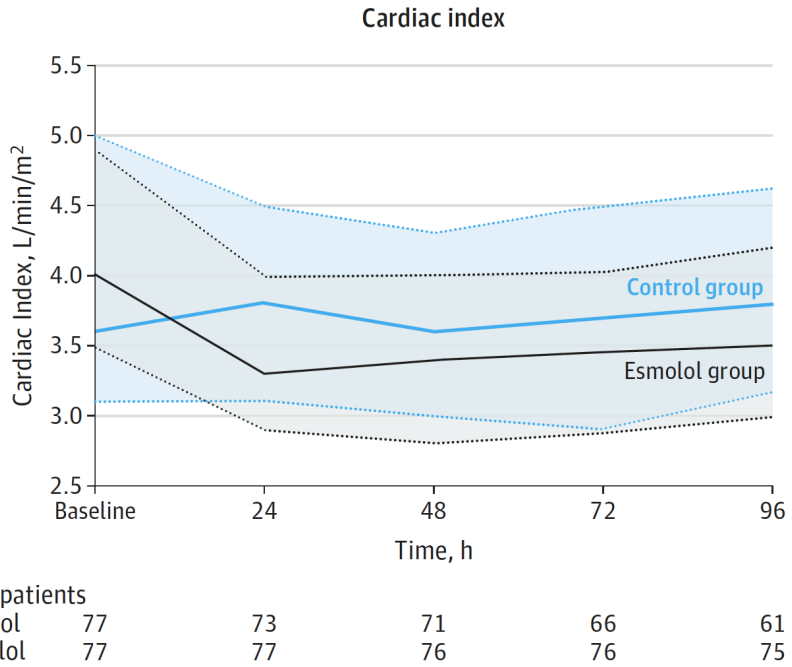

Figure 4. Estimated Glomerular Filtration Rate Using the Modification of Diet in Renal Disease Formula

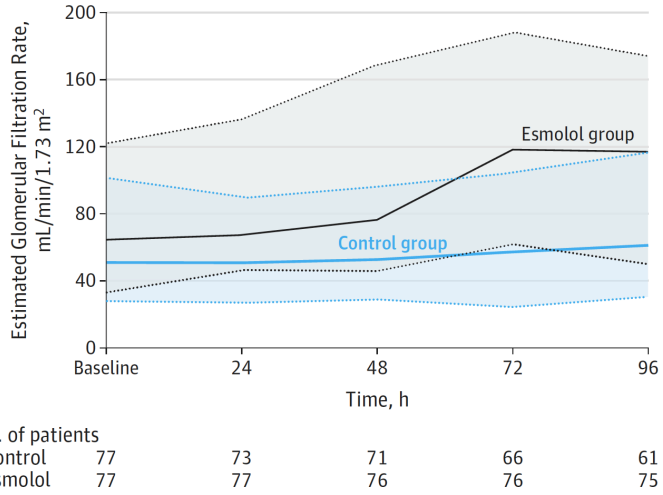

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Table 2. Hemodynamic Variables of Study Patients

Group	Median (Interquartile Range)						*P* Value, Wilcoxon-Mann-Whitney
	Baseline	24 Hours	48 Hours	72 Hours	96 Hours	Area Under the Curve	
Pressure, mm Hg							
RAP							
Esmolol	12 (10 to 15)	14 (11 to 16)	14 (11 to 15)	13 (10 to 15)	13 (11 to 15)	1 (−1 to 3)	.17
Control	13 (9 to 15)	12 (10 to 15)	12 (10 to 15)	13 (9 to 15)	12 (9 to 15)	0 (−2 to 2)	
PAWP							
Esmolol	17 (14 to 20)	17 (15 to 20)	17 (15 to 19)	17 (14 to 19)	16 (14 to 18)	0 (−2 to 2)	.48
Control	17 (14 to 20)	17 (14 to 20)	17 (15 to 19)	17 (14 to 19)	17 (14 to 19)	0 (−2 to 1)	
MPAP							
Esmolol	31 (28 to 34)	30 (27 to 33)	29 (27 to 32)	30 (26 to 32)	29 (25 to 32)	−1 (−1 to 0)	.34
Control	31 (27 to 34)	29 (27 to 34)	30 (27 to 32)	30 (25 to 33)	28 (25 to 33)	−1 (−2 to 1)	
Resistance pressure, dyn.s/cm^5/m^2							
SVRI							
Esmolol	1148 (970 to 1362)	1382 (1171 to 1653)	1370 (1149 to 1668)	1403 (1141 to 1708)	1411 (1137 to 1616)	264 (33 to 439)	<.001
Control	1271 (967 to 1548)	1265 (1031 to 1608)	1326 (1086 to 1614)	1359 (1026 to 1678)	1276 (985 to 1586)	90 (−74 to 231)	
PVRI							
Esmolol	253 (188 to 309)	293 (206 to 393)	270 (195 to 415)	281 (198 to 385)	286 (197 to 360)	38 (−12; 84)	.02
Control	282 (214 to 347)	289 (197 to 389)	286 (231 to 348)	286 (216 to 384)	261 (221 to 326)	8 (−24 to 40)	
Stroke work index, mL/m^2							
Left ventricle							
Esmolol	27 (23 to 33)	31 (24 to 34)	32 (26 to 37)	32 (25 to 39)	34 (28 to 41)	3 (−1 to 8)	.03
Control	24 (19 to 31)	26 (19 to 31)	28 (21 to 34)	27 (21 to 32)	31 (23 to 36)	1 (−3 to 5)	
Right ventricle							
Esmolol	9 (6 to 12)	9 (7 to 12)	9 (7 to 11)	9 (7 to 12)	9 (7 to 12)	0 (−2 to 2)	.69
Control	8 (6 to 10)	9 (7 to 10)	8 (7 to 12)	8 (6 to 11)	8 (7 to 11)	0 (−1 to 1)	
Fluid infusion, mL/24 h							
Esmolol		5000 (4300 to 5400)	4600 (4300 to 5000)	4300 (4000 to 4600)	4000 (3600 to 4300)	3975 (3663 to 4200)	<.001
Control		5200 (4700 to 5800)	5400 (4900 to 5700)	5200 (4800 to 5600)	5400 (4725 to 6000)	4425 (4038 to 4775)	

Abbreviations: MPAP, mean pulmonary arterial pressure; PAWP, pulmonary artery wedge pressure; PVRI, pulmonary vascular resistance index; RAP, right atrial pressure; RVSWI, right ventricular stroke work index; SVRI, systemic vascular resistance index.

Morelli et al. JAMA 2013

Table 3. Outcome Data of Study Patients

Outcome	No. (%) Esmolol (n = 77)	No. (%) 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%)		

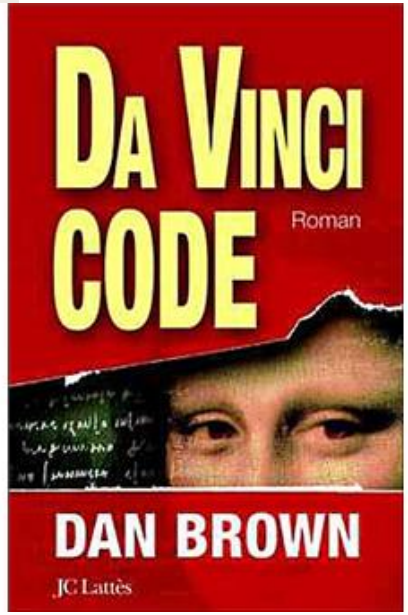
Abbreviations: ICU, intensive care unit; IQR, interquartile range.

Morelli et al. JAMA 2013

Mortalité groupe contrôle très élevée
49% des patients du groupe esmolol sous levosimendan
Patients remplis de façon majeure,
Dans ce contexte peut-être que les bêta-bloquants limitent la mortalité

Table 3. Outcome Data of Study Patients

Outcome	No. (%) Esmolol (n = 77)	Control (n = 77)	*P* Val
Mortality			
28 d	38 (49.4)	62 (80.5)	<.00
ICU	44 (57.1)	68 (88.3)	<.00
Hospital	52 (67.5)	70 (90.9)	<.00
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)	
Refractory hypotension	32/52 (61.6)	44/70 (62.9)	.71
Unknown cause	5/52 (9.6%)		



Veni Vidi Vinci

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

Jean-Louis Chauvet[1], Shari El-Dash[2,3], Olivier Delastre[1], Bernard Bouffandeau[1], Dominique Jusserand[1], Jean-Baptiste Michot[1], Fabrice Bauer[4], Julien Maizel[2,5] and Michel Slama[2,5*]

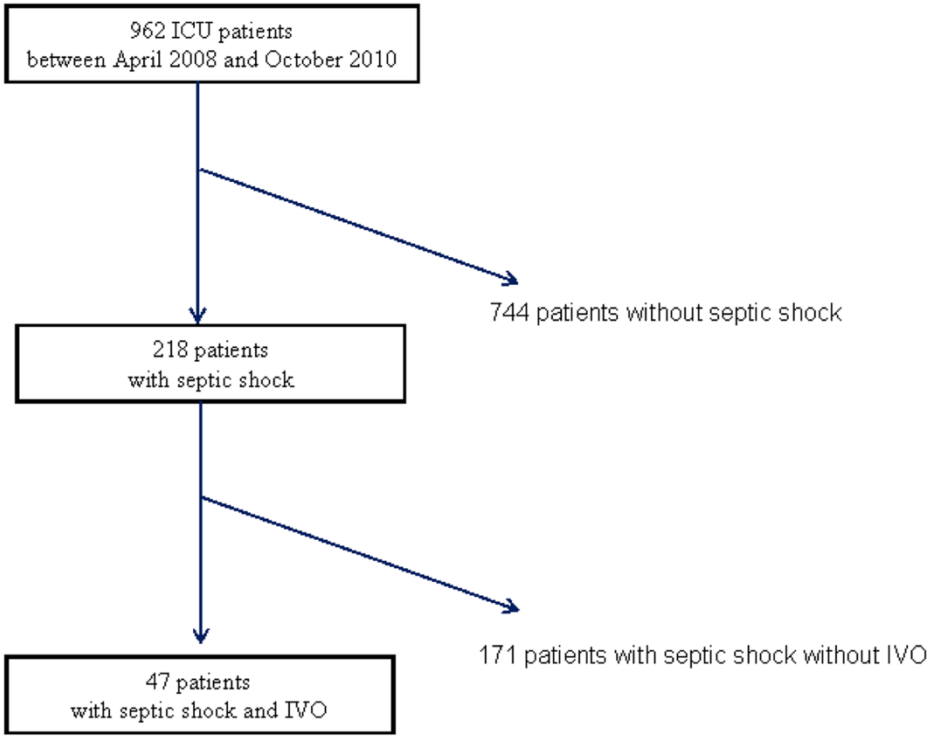


Fig. 1 Flow chart. *IVO* intraventricular obstruction

Table 1 Characteristics of patients with septic shock with and without IVO

	Septic shock patients without IVO (n = 171)	Septic shock patients with IVO (n = 47)	*p* value
Age (years)	62 ± 15	69 ± 11	ns
Males	106 (62 %)	27 (57 %)	ns
SAPS II	54 ± 21	59 ± 16	ns
Mechanical ventilation	149 (87 %)	39 (83 %)	ns
ICU stay duration (days)	11 ± 27	12 ± 10	ns
Medical patients	109 (64 %)	32 (68 %)	ns
Surgical patients	62 (36 %)	15 (32 %)	ns
ICU mortality	41 (24 %)	25 (53 %)	<0.01
Mortality at 28 days	57 (33 %)	26 (55 %)	<0.01

Values are shown as n (%) or mean ± SD. *IVO* intraventricular obstruction, *ns* not significant, *SAPS* Simplified Acute Physiology Score

Pas d'utilisation de bêta-bloquant
Remplissage

Chauvet et al. Critical Care 2015

Table 2 Hemodynamic and echocardiographic characteristics of patients with intraventricular obstruction before and after fluid infusion

	Before	After	*p* value
Heart rate (beats/minute)	109 ± 25	102 ± 22	ns
Systolic arterial pressure (mmHg)	110 ± 28	141 ± 32	<0.01
Diastolic arterial pressure (mmHg)	54 ± 11	65 ± 14	<0.01
Mean arterial pressure (mmHg)	71 ± 16	89 ± 1	<0.01
Cardiac output (l/minute)	4.6 ± 1.9	5.8 ± 2.1	<0.01
Cardiac index (l/minute/m^2)	2.4 ± 0.9	3 ± 1	<0.01
Stroke volume (ml)	43 ± 18	58 ± 22	<0.01
Indexed stroke volume (ml/m^2)	23 ± 10	31 ± 11	<0.01
Intraventricular obstruction (m/s)	1.9 ± 0.9	1 ± 1	<0.01
Intraventricular obstruction (mmHg)	18 ± 18	8 ± 13	<0.01
Inferior vena cava diameter (mm)	16 ± 6.4	18 ± 6.6	ns
E/A	0.8 ± 0.46	0.9 ± 0.3	ns
E′ (cm/s)	14 ± 5	16 ± 5	ns
E′/A′	0.77 ± 0.26	0.87 ± 0.37	ns
E/E′	5.8 ± 2.1	6.8 ± 1.8	ns

A late velocity of diastolic mitral flow, *A′* late velocity of diastolic mitral annulus motion, *E* early diastolic velocity of mitral flow, *E′* early velocity of diastolic mitral annulus motion, *ns* not significant

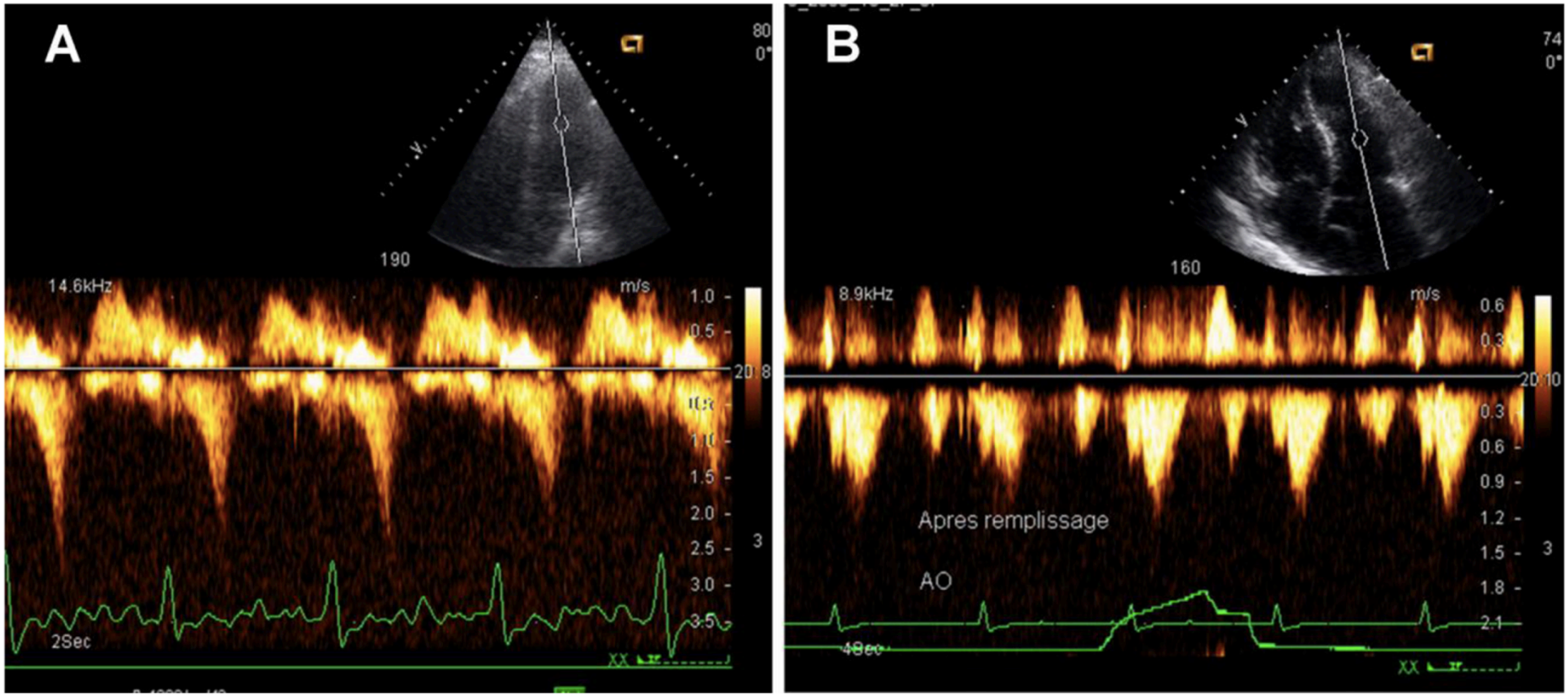


Fig. 2 Left intraventricular obstruction. **a** Pulsed-wave Doppler curve showing the characteristic late peaking saber-shape indicating a LV outflow obstruction (IVG). **b** After fluid replacement, the flow profile returns to normal symmetrical shape

Chauvet et al. Critical Care 2015

Original Article

Efficacy and Safety of Esmolol in Treatment of Patients with Septic Shock

Wei Du, Xiao-Ting Wang, Yun Long, Da-Wei Liu

Department of Critical Care Medicine, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing 100730, China

Chinese Medical Journal ¦ July 20, 2016 ¦ Volume 129 ¦ Issue 14

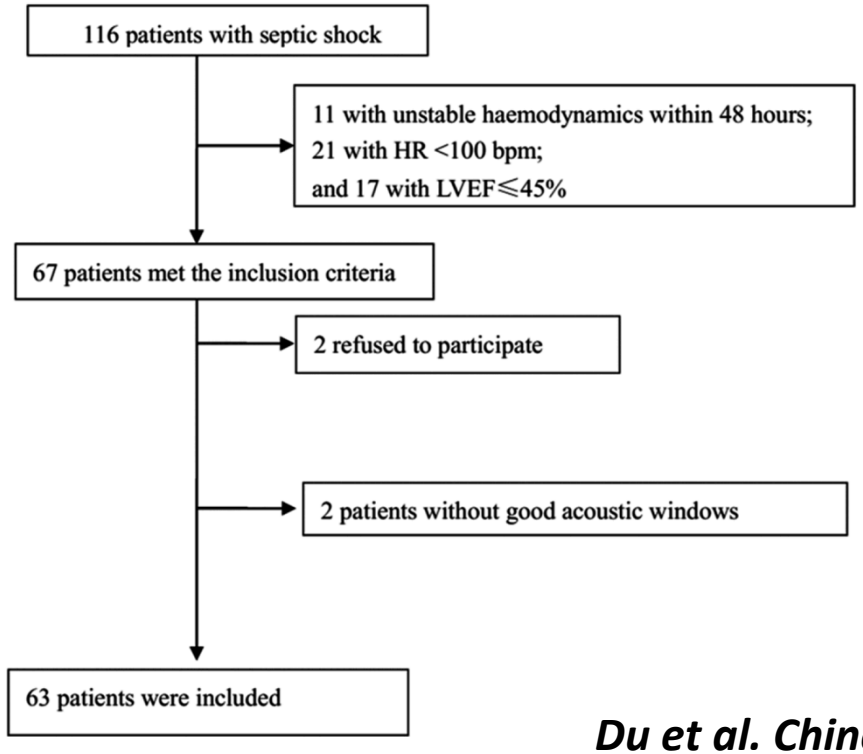


Figure 1: Flow chart of the study.

Du et al. Chinese Medical Journal 2016

Table 4: General characteristics and outcomes of the patients with and without an increase in stroke volume

Variables	With SV increase (n = 42)	Without SV increase (n = 21)	t	P
Age (years)	49.4 ± 17.0	52.4 ± 13.0	−0.2	0.474
Sex (male, %)	47.6	47.6	−0.1	0.924
APACHE II	16.1 ± 5.5	14.3 ± 4.2	0.3	0.542
Mechanical ventilation (%)	73.5	66.9	0.1	0.679
Baseline cardiac function (%)			−0.1	0.982
NYHA I	54.8	52.4		
NYHA II	35.7	38.1		
NYHA III	9.5	9.5		
NE dose ($\mu g \cdot kg^{-1} \cdot min^{-1}$)	0.45 ± 0.18	0.48 ± 0.19	−0.1	0.487
Maximum dose of esmolol (mg/h)	110.6 ± 76.8	116.4 ± 89.9	−0.2	0.237
Total dose of esmolol (mg)	197.6 ± 108.7	184.5 ± 113.9	0.2	0.458
Time to achieve target heart rate (h)	1.7 ± 0.3	1.7 ± 0.5	0.1	0.786

SV: Stroke volume; APACHE: Acute Physiology and Chronic Health Evaluation; NYHA: New York Heart Association; NE: Norepinephrine.

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Table 2: Changes in vital signs, tissue oxygen metabolism, and myocardial enzymes after the usage of esmolol

Variables	Before the usage of esmolol (n = 63)	After the usage of esmolol (n = 63)	t	P
Systolic blood pressure (mmHg)	130.5 ± 16.7	126.4 ± 18.8	1.5	0.146
Diastolic blood pressure (mmHg)	72.8 ± 12.3	72.6 ± 12.4	0.1	0.926
Mean arterial pressure (mmHg)	90.0 ± 13.8	88.7 ± 13.9	0.6	0.548
Pulse pressure (mmHg)	57.7 ± 13.3	53.8 ± 16.8	1.7	0.109
Central venous pressure (mmHg)	6.5 ± 2.1	7.5 ± 2.5	−3.0	0.007
Heart rate (beats/min)	107.8 ± 8.7	86.2 ± 10.2	20.8	<0.001
Left ventricular outflow tract cardiac output (L/min)	5.0 ± 1.8	4.3 ± 1.7	5.2	<0.001
Lactate (mmol/L)	1.4 ± 0.8	1.1 ± 0.6	2.6	0.015
Pcv-a CO_2 (mmHg)	5.6 ± 3.3	4.3 ± 2.2	2.6	0.019
$ScvO_2$ (%)	78.99 ± 7.95	78.06 ± 7.59	0.5	0.480
Arterial pH	7.42 ± 0.06	7.44 ± 0.06	−1.3	0.192
HCO_3^- (mmol/L)	26.4 ± 4.7	26.6 ± 4.5	−0.6	0.537
Anion gap correction (mmol/L)	10.8 ± 4.0	10.2 ± 4.4	1.0	0.362
Urine output (ml/h)	102.5 ± 88.6	106.8 ± 107.7	−0.3	0.760
Peripheral perfusion index	2.4 ± 1.6	2.1 ± 1.4	1.8	0.079
Creatine kinase (U/L)	316.1 ± 522.7	321.9 ± 580.8	−0.2	0.880
Creatine kinase isoenzyme (ng/ml)	1.8 ± 2.0	2.8 ± 6.1	−0.9	0.403
Troponin I (ng/ml)	1.5 ± 7.0	1.5 ± 7.0	−0.9	0.370
NT-proBNP (pg/ml)	8825.8 ± 6583.1	9313.3 ± 7049.8	−0.6	0.553

Pcv-a CO_2: Central venous-to-arterial carbon dioxide difference; NT-proBNP: N-terminal pro-brain natriuretic peptide.

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Table 3: Effects of esmolol on cardiac contractility and overall cardiac function

Variables	Before the usage of esmolol (n = 63)	After the usage of esmolol (n = 63)	t	P
Parameter reflecting cardiac contractility and overall cardiac functions				
Left ventricular Tei index	0.43 ± 0.27	0.56 ± 0.34	−1.9	0.062
Left ventricular outflow tract VTI (cm)	15.2 ± 3.6	16.1 ± 4.0	−2.6	0.031
SV (ml)	43.6 ± 22.7	49.9 ± 23.7	−2.3	0.047
Left ventricular outflow tract CO (L/min)	5.0 ± 1.8	4.3 ± 1.7	5.2	<0.001
EF %	63.8 ± 13.9	59.6 ± 13.5	2.4	0.023
FS %	34.7 ± 10.2	31.1 ± 8.1	2.6	0.015
TAPSE (cm)	2.1 ± 0.7	1.9 ± 0.6	1.7	0.106
MAPSElat (cm)	1.3 ± 0.3	1.3 ± 0.3	0.7	0.209
MAPSEmed (cm)	1.3 ± 0.3	1.2 ± 0.3	1.3	0.213
Parameters reflecting cardiac preload				
Lateral E/Ea	7.1 ± 2.6	6.9 ± 2.3	0.5	0.601
Septal E/Ea	8.9 ± 4.2	9.1 ± 3.3	−0.4	0.712
LVIDd (cm)	4.7 ± 0.6	4.9 ± 0.7	−2.8	0.009
EDV (ml)	103.3 ± 29.7	119.2 ± 34.1	−3.0	0.005

SV: Stroke volume; CO: Cardiac output; EF: Ejection fraction; FS: Shortening fraction; TAPSE: Tricuspid annular plane systolic excursion; MAPSElat: Mitral lateral annular plane systolic excursion; MAPSEmed: Mitral septal annular plane systolic excursion; Ea: Early diastolic velocity by tissue Doppler; LVIDd: Left ventricular end-diastolic diameter; EDV: End-diastolic volume; VTI: Velocity time integral.

FC ↘
DC ↘
VES ↗
PAM →
RVS →

Effet « précharge »

Du et al. Chinese Medical Journal 2016

Intensive Care Med (2016) 42:1528–1534
DOI 10.1007/s00134-016-4351-2

ORIGINAL

Heart rate reduction with esmolol is associated with improved arterial elastance in patients with septic shock: a prospective observational study

A. Morelli[1*], M. Singer[2], V. M. Ranieri[1], A. D'Egidio[1], L. Mascia[4], A. Orecchioni[1], F. Piscioneri[1], F. Guarracino[3], E. Greco[1], M. Peruzzi[4], G. Biondi-Zoccai[4,5], G. Frati[4,5] and S. M. Romano[6]

Table 1 Characteristics of the study patients ($n = 45$)

Age (years)	61 ± 18
Gender, male	73 %
SAPS II	54 ± 7
28-day mortality	51 %
ICU length of stay (days)	18 ± 17

Data are given as mean and standard deviation

SAPS II simplified acute physiology score II, *ICU* intensive care unit

Table 2 Hemodynamic, echocardiographic, and arterial waveform data

Variable	Baseline	4 h	*p* value
CO^{th} (L min^{-1})	5.4 ± 1.3	5.1 ± 1.4	0.11
SV^{th} (mL)	48 ± 14	59 ± 18	**<0.001**
CO^{p} (L min^{-1})	5.1 ± 1.3	5.0 ± 1.3	0.77
SV^{p} (mL)	47 ± 12	59 ± 16	**<0.001**
HR (min^{-1})	115 ± 11	88 ± 9[a]	**<0.001**
SVR (Dyn s^{-1} cm^{-5})	1234 ± 293	1102 ± 260	**0.001**
MAP (mmHg)	80 ± 12	75 ± 10	**0.005**
MPAP (mmHg)	30 ± 7	28 ± 6	**0.001**
PAOP (mmHg)	16 ± 3	16 ± 4	0.74
CVP (mmHg)	12 ± 3	12 ± 3	0.86
Ea^{p} (mmHg l^{-1})	2.2 ± 0.7	1.7 ± 0.5	**<0.001**
Ea^{th} (mmHg l^{-1})	2.0 ± 0.6	1.55 ± 0.5	**<0.001**
LVEF (%)	52 ± 11	53 ± 11	0.17
Art. dP/dt_{max} (mmHg ms^{-1})	1.08 ± 0.32	0.89 ± 0.29	**0.0009**
CCE (units)	−0.15 ± 0.5	−0.01 ± 0.4	**0.002**
CPwO (W)	0.53 ± 0.14	0.63 ± 0.24	**0.007**
NE dosage (μg kg^{-1} min^{-1})	0.7 ± 0.7	0.58 ± 0.55	**0.01**
P_{sys} (mmHg)	119 ± 18	110 ± 18	**0.0003**
P_{dia} (mmHg)	61 ± 12	57 ± 9	**0.0004**
P_{dic} (mmHg)	72 ± 15	70 ± 12	0.45
MAP − P_{dic} (mmHg)	9.4 ± 9	4.3 ± 8	**<0.0001**

Data given as mean and standard deviation

CO^{th} cardiac output obtained with thermodilution, *SV^{th}* stroke volume obtained with thermodilution, *CO^{p}* cardiac output obtained with the pulse contour analysis, *SV^{p}* stroke volume obtained with the pulse contour analysis, *HR* heart rate, *MAP* mean arterial pressure, *MPAP* mean pulmonary arterial pressure, *PAOP* pulmonary arterial occlusion pressure, *CVP* central venous pressure, *Ea^{p}* arterial elastance obtained with the pulse contour analysis, *Ea^{th}* arterial elastance obtained with thermodilution, *LVEF* left ventricular ejection fraction, *CCE* cardiac cycle efficiency, *CPwO* cardiac power output, *NE* norepinephrine, *P_{sys}* systolic pressure, *P_{dia}* diastolic pressure, *P_{dic}* dicrotic pressure

[a] See Fig. 2

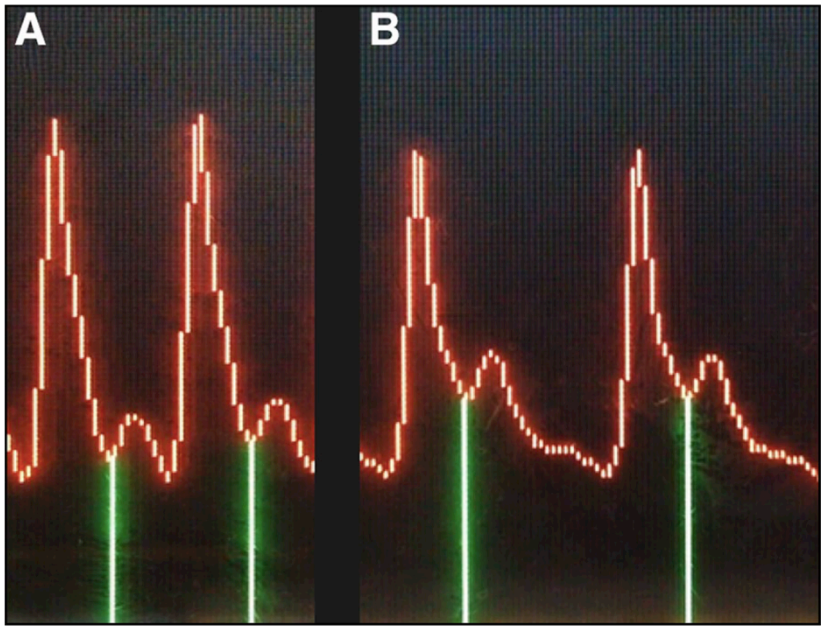

Fig. 3 Example of an arterial waveform before (**a**) and after (**b**) reducing heart rate. Note the biphasic nature of the flow pattern during tachycardia and the more physiological waveform after reducing heart rate with esmolol. Changes were achieved through an increase in SV as well as the ability of the cardiovascular system to increase arterial tone in response to an augmented SV

Morelli et al. Intensive Care Medicine 2016

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EDITORIAL

Beta-blockers in septic shock to optimize hemodynamics? No

Anthony S. McLean[1*], Fabio S. Taccone[2] and Antoine Vieillard-Baron[3,4]

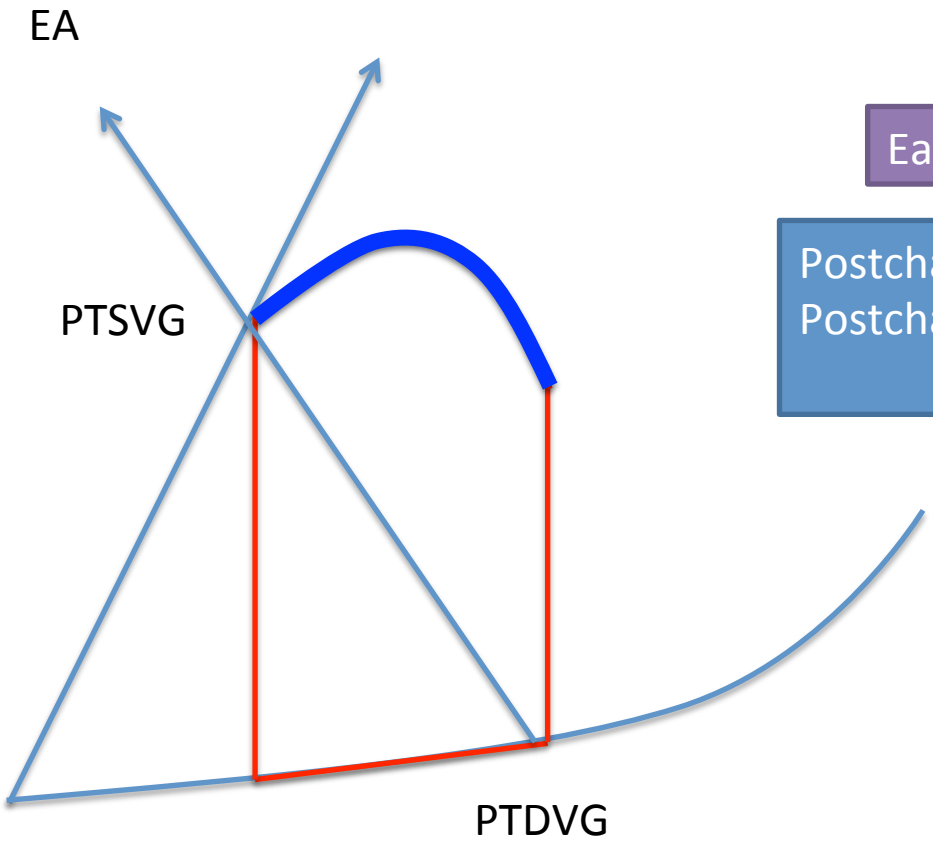
Intensive Care Med (2016) 42:1607–1609
DOI 10.1007/s00134-016-4414-4

EDITORIAL

Beta-blockers in septic shock to optimize hemodynamics? Yes

Daniel A. Reuter[1*], James A. Russell[2,3] and Armand Mekontso Dessap[4,5]

Post charge



Ea= PTSVG/VES = FC x RVS

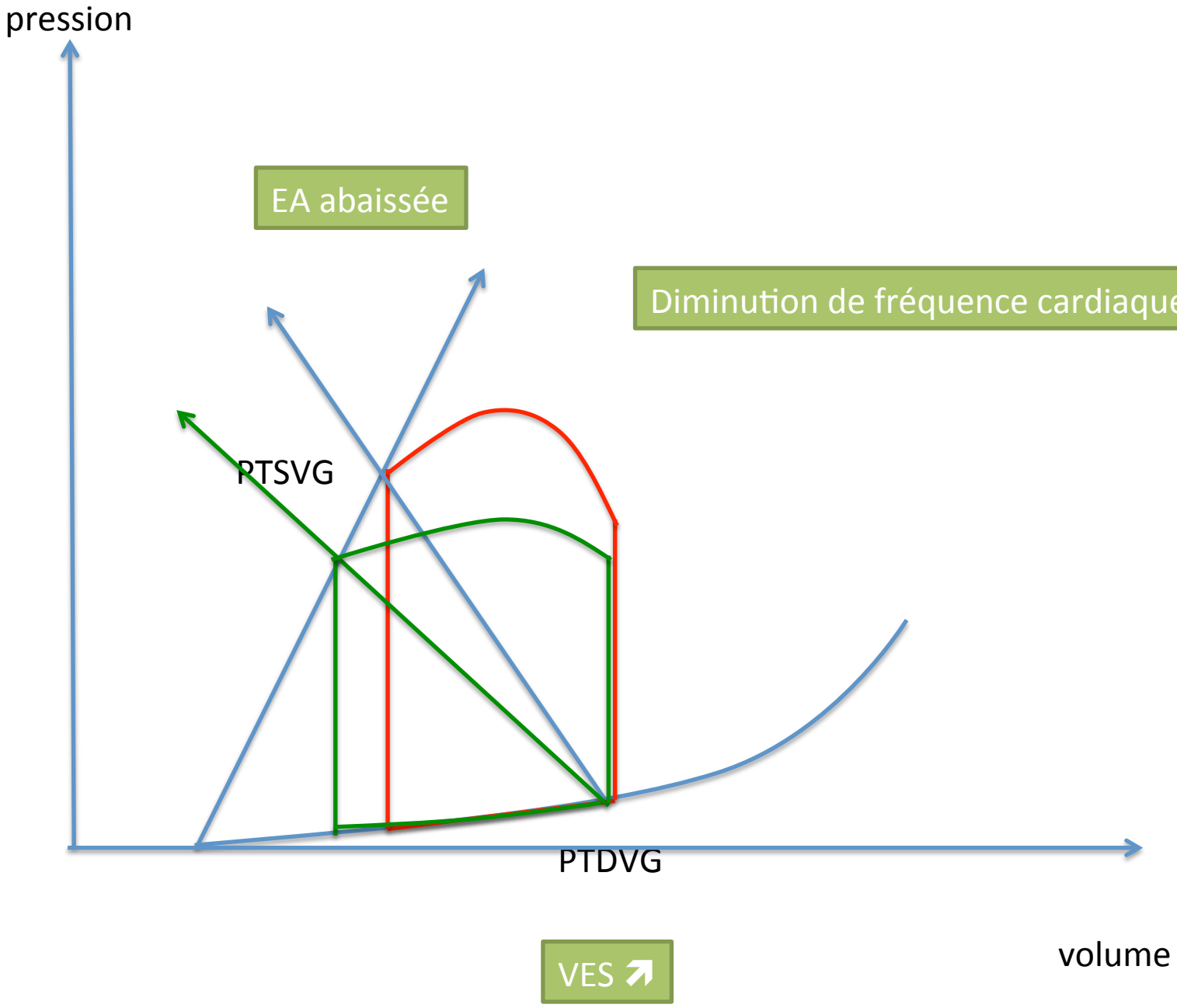
Postcharge = wall stress pendant éjection

$$\text{Postcharge} = \frac{\text{Pej x rayon Vgej}}{\text{2 wej}}$$

Pej

contactilité

précharge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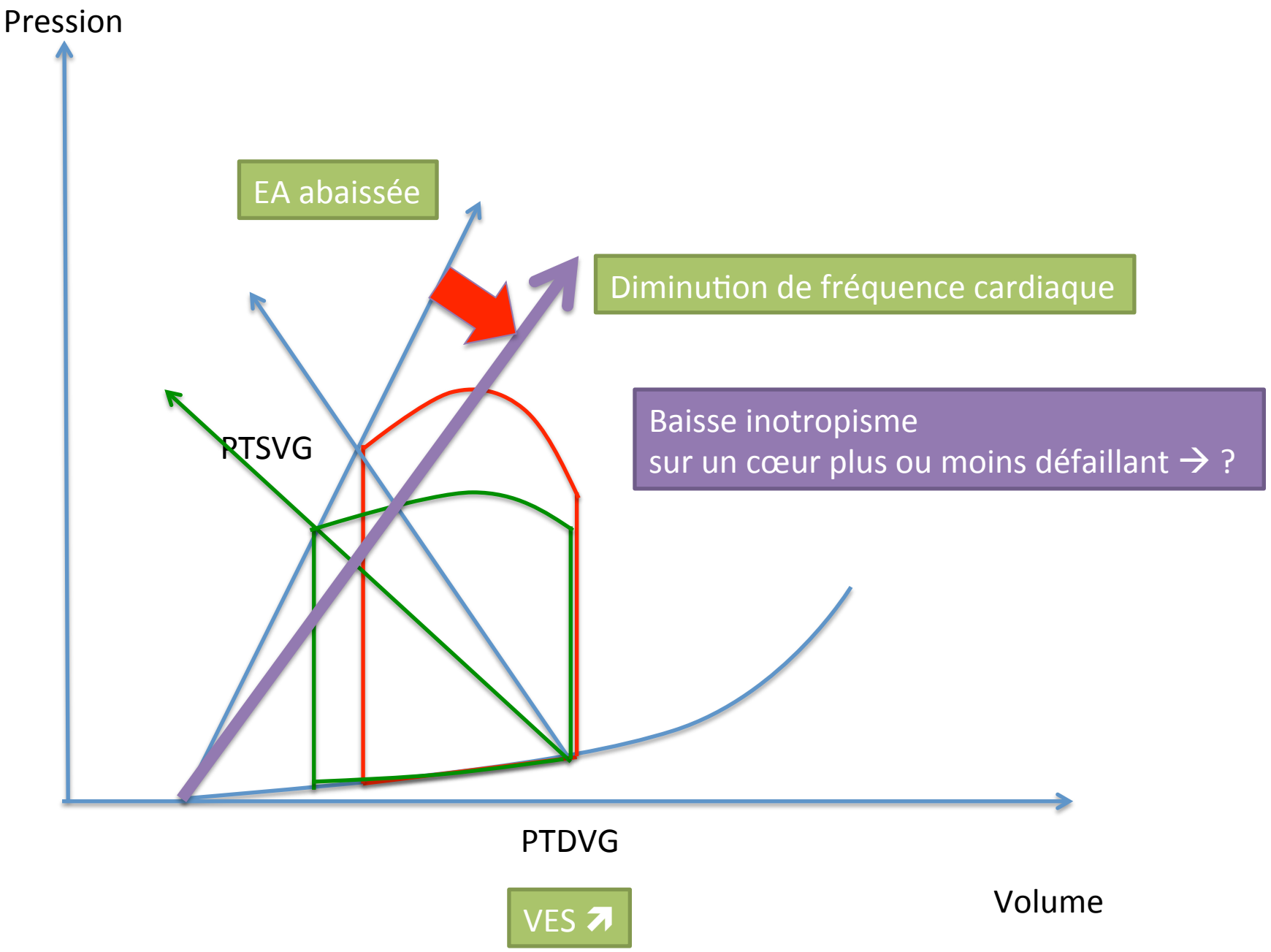
EA abaissée
Diminution de fréquence cardiaque
PTSVG
PTDVG
VES ↗
volume


Pression
EA abaissée
Diminution de fréquence cardiaque
Baisse inotropisme
sur un cœur plus ou moins défaillant → ?
PTSVG
PTDVG
VES ↗
Volume

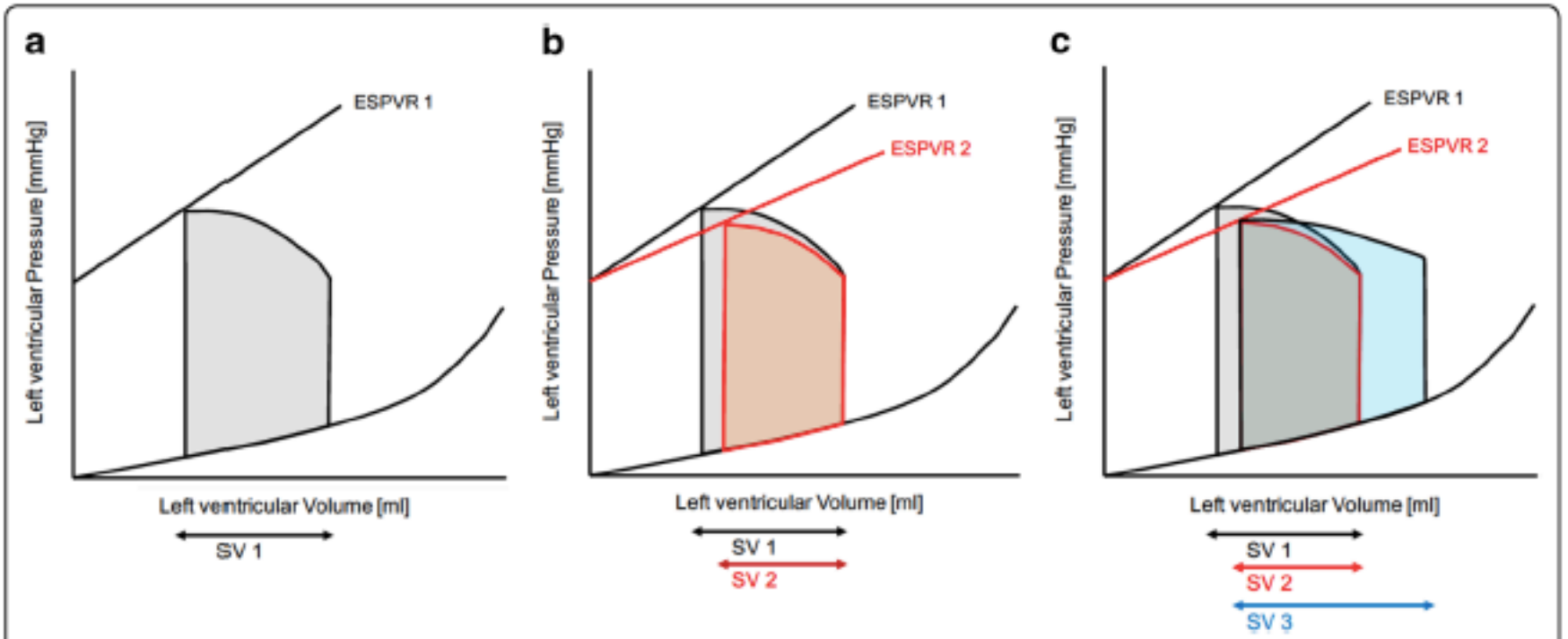


Fig. 1 Pressure–volume loops of the left ventricle are depicted. **a** Pressure–volume loop prior to β-blockade; **b** β-blockade leads to a decrease of inotropy, which is reflected by the reduced angle of the ESPVR 2. Accordingly, the resulting SV 2 is diminished; **c** If venous return to the left ventricle is high enough, the prolonged duration of diastole caused by heart rate reduction will allow increased left ventricular filling, which, in combination with decreased afterload, will result in an increased SV 3. *SV* stroke volume, *ESPVR* end-systolic pressure volume relation

Reuter et al. Intensive Care Medicine 2016

Brown *et al. Pilot and Feasibility Studies* (2018) 4:132
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Pilot and Feasibility Studies

RESEARCH Open Access

Esmolol infusion in patients with septic shock and tachycardia: a prospective, single-arm, feasibility study

Samuel M. Brown[1,2,7*], Sarah J. Beesley[1,2], Michael J. Lanspa[1,2], Colin K. Grissom[1,2], Emily L. Wilson[1], Samir M. Parikh[3], Todd Sarge[4], Daniel Talmor[4], Valerie Banner-Goodspeed[4], Victor Novack[4], B. Taylor Thompson[5], Sajid Shahul[6] for The Esmolol to Control Adrenergic Storm in Septic Shock-ROLL-IN (ECASSS-R) study

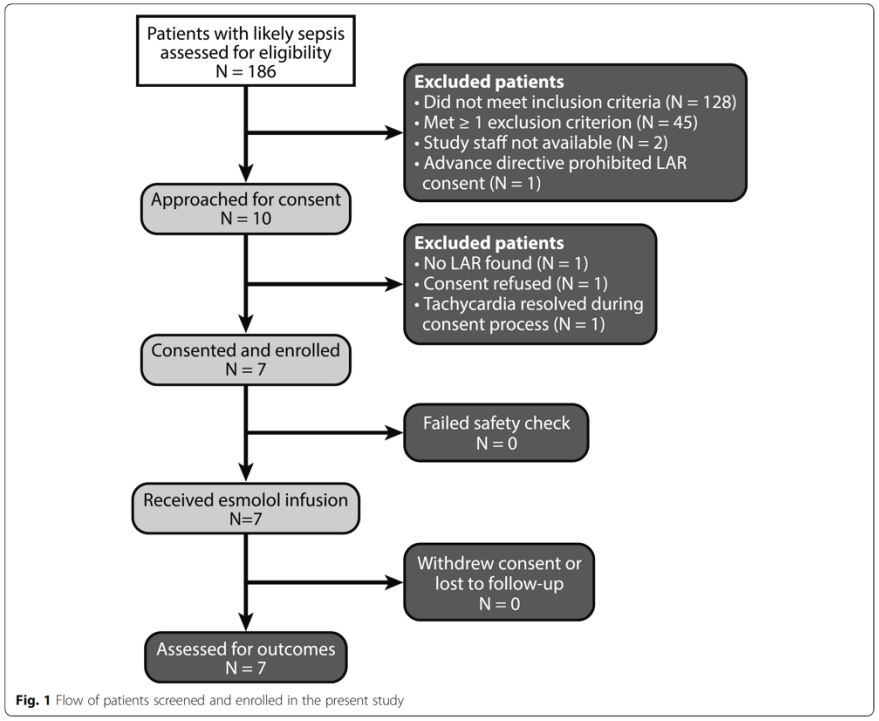

Fig. 1 Flow of patients screened and enrolled in the present study

- 2/7 patients ventilés
- 15+/-9h après début noradrénaline
- Noradrénaline : 0,20

(0,14–0,23) µg/kg/min

- Esmolol perfusé pendant 13 +/- 10h
- Critères d'arrêt:
  - Sécurité
  - FC<80
  - Vasopresseurs sevrés depuis 3 heures

Table 2 Clinical outcomes

Variable	Esmolol-treated patients ($n = 7$)
OFFD among all patients (units)	26 (24.5–26)
OFFD among 28-day survivors (days)	26 (24.5–26)
ICU LOS among survivors (days)	3.3 (3.1–5.4)
Hospital LOS among survivors (days)	8.2 (7.1–17.3)
Mortality	
In-hospital mortality, *n* (%)	0 (0%)
28-day all-cause mortality, *n* (%)	0 (0%)
90-day all-cause mortality, *n* (%)	0 (0%)

OFFD organ-failure-free days, *ICU* intensive care unit, *LOS* length of stay

Brown et al. Pilot and feasibility studies 2018

Table 1 Patient attributes at beginning of esmolol infusion

Variable	Esmolol-treated patients ($n = 7$)
Age (years)	46 (± 19)
Female sex	5 (71%)
Cause of sepsis *n* (%)	
Pneumonia	2 (29%)
Skin/soft tissue	3 (43%)
Urinary source	1 (14%)
Abdominal	1 (14%)
Duration of vasopressor therapy (hours)[a]	15.1 (± 9)
Norepinephrine infusion rate (μg/kg/min)	0.20 (± 0.09)
Receiving vasopressin *n* (%)	2 (29%)
Heart rate (/min)	109 (± 15)
Mean arterial pressure (mmHg)	71 (± 7)
Lactate (mmol/L)[b]	4.8 (± 3.3)
Intravenous crystalloid prior to enrollment (L)	3.5 (3.4–9.0)
Admission APACHE II score (points)	28 (± 8)
Admission SOFA score (points)	11 (± 2)

Values are reported as central tendency and variation, expressed as mean (± standard deviation) or median (inter-quartile range), as appropriate

[a]At time of initiating esmolol infusion

[b]Peak lactate on day of enrollment

Variable	Mean (standard deviation)
$ScvO_2$ (%)	76 (5)
LVEF (%)	55 (8)
Cardiac index (L/min/m2)	3.6 (1.3)
Adequacy of volume expansion (%)*	100%
Passive leg raise (n=4) Graded volume expansion (n=4) Central venous catheter (n=1) Clinical assessment (n=1) Dynamic measures on ventilator (n=0)	Change in cardiac index: 3.2 (4.0) % Change in cardiac index: 5.3 (1.5) % CVP: 18mmHg Stroke volume variability: NA
*Two patient were assessed with multiple modalities, so modalities sum to 10 rather than 7.	

Variable	Change
Cardiac index (L/min/m^2 BSA)	-0.1 L/min/m^2 BSA
Heart Rate (min^{-1})	-6 min^{-1}
Norepinephrine infusion rate (mcg/kg/min)	+0.02 mcg/kg/min
Mean arterial pressure (mmHg)	-4 mmHg
*Average effect observed with an esmolol titration of 10 mcg/kg/min, at initial doses BSA: body surface area	

Parameter	Enrollment TTE	Day 1 TTE	P value
LV GLS (%)	-11.5 (-19.6, -9.4)	-15.8 (-20.1, -13.5)	0.62
LV EF (%)	59 (48, 60)	56 (49, 62)	0.8
LV tMPI	0.58 (0.50, 0.62)	0.56 (0.46, 0.84)	1
LV: left ventricular; GLS: global longitudinal strain; EF: ejection fraction; tMPI: tissue Myocardial Performance Index			

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Variable	No STOP event (N=4)	STOP event (N=3)	p-value*
Age (years)	51 (42-61)	30 (26-46)	0.38
Maximum esmolol infusion rate (mcg/kg/min)	25 (18-35)	50 (50-75)	**0.10**
Admission APACHE II	23 (23-25)	28 (27-36)	0.21
Norepinephrine dose at esmolol initiation[a] (mcg/kg/min)	0.14 (0.10-0.20)	0.22 (0.21-0.30)	0.21
Arterial elastance[b] (mmHg/ml)	1.0 (0.9-1.1)	1.8 (1.6-2.2)	**0.05**
Left ventricular EF[b] (%)	59 (57-60)	46 (40-54)	0.37
$ScvO_2$[b] (%)	78 (77-80)	73 (70-75)	0.11
Left ventricular GLS[b]	-19.6 (-22.1- -15.6)	-9.7 (-10.6- -8.1)	0.22
Shannon entropy of heart rate[b]	4.4 (4.3-4.7)	4.1 (4.0-4.4)	0.60
DFA ratio[b]	0.53 (0.43-0.78)	0.90 (0.87-0.94)	0.38
Angiopoietin-2[b] (ng/ml)	23 (18-38)	17 (14-26)	0.86
Stroke volume[b]	75 (70-75)	39 (32-46)	**0.05**
Fluid administered prior to enrollment (L)	6.2 (3.2-9.0)	3.5 (3.5-6.4)	0.59
MAP[a] (mmHg)	70 (68-75)	69 (67-70)	0.59

[a]At time of esmolol initiation
[b]At time of enrollment
EF: ejection fraction; GLS: global longitudinal strain; DFA ratio: ratio of fractal exponents from detrended fluctuation analysis; MAP: mean arterial pressure.

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Effects of the β-blockers on cardiac protection and hemodynamics in patients with septic shock: a prospective study oct 2014 Yang et al

Zhonghua Wei Zhong Bing Ji Jiu Yi Xue

OBJECTIVE:
To investigate the effects of β-blockers on cardiac protection and hemodynamic in patients with septic shock.

METHODS:
A prospective randomized controlled trial was conducted. Forty-one patients with septic shock in accordance with early goal directed treatment and met the target within 6 hours, and admitted to intensive care unit (ICU) of Affiliated Huxi Hospital of Jining Medical College from January 2012 to January 2014 were enrolled. The patients were divided into treatment group (n=21) and control group (n=20) by random number table. The patients in both groups were given the standard treatment, esmolol was giving to patients in treatment group in order to control the heart rate(HR) below 100 bpm within 2 hours, and the patients in control group only received standard treatment. The changes in hemodynamic parameters [mean arterial pressure (MAP), central venous pressure (CVP), HR, cardiac index (CI), stroke volume index (SVI), systemic vascular resistance (SVRI), global end diastolic volume index (GEDVI)], biochemistry metabolic of tissue [central venous oxygen saturation ($ScvO_2$), lactic acid (Lac)], and cardiac markers [troponin I (cTnI)] before and 12, 24, 48, 72 hours after the treatment were recorded.

RESULTS:
(1) Before treatment, the hemodynamic parameters, tissue metabolism index and cTnI had no significant differences in both groups (all P>0.05). (2) The hemodynamic parameters after treatment in the control group showed no significant difference compared with that before treatment. HR and CI in the treatment group were gradually declined after treatment, SVRI and GEDVI were gradually increased. There were significant differences in HR, CI, SVRI, and GEDVI between treatment group and control group from 12 hours on [HR (bpm): 93 ± 4 vs. 118 ± 13, CI ($L \times min^{-1} \times m^{-2}$): 3.3 ± 0.8 vs. 4.5 ± 0.6, SVRI ($kPa \times s \times L^{-1} \times m^{-2}$): 159.2 ± 27.4 vs. 130.5 ± 24.2, GEDVI (mL/m^2): 668 ± 148 vs. 588 ± 103, P<0.05 or P<0.01]. MAP, CVP and SVI in the treatment group showed no significant changes. (3) Lac after treatment in both groups was decreased slowly, Lac (mmol/L) at 12 hours after treatment was significantly decreased compared with that before treatment (control group: 8.8 ± 3.2 vs. 9.8 ± 3.4, treatment group: 9.5 ± 3.1 vs. 10.5 ± 4.1, both P<0.05). The Lac of control group and treatment group were 2.5 ± 1.2 and 2.7 ± 1.1 at 72 hours after treatment, and there was no significant difference between two groups (all P>0.05). The $ScvO_2$was not decreased in both groups. (4) Compared with before treatment, cTnI in the control group was gradually increased, peaked at 72 hours, and that in the treatment group was gradually increased, peaked at 24 hours and then gradually declined. Compared with control group, the cTnI (μg/L) in the treatment group was decreased significantly at 24, 48, 72 hours (1.15 ± 0.57 vs. 1.74 ± 0.77, 0.93 ± 0.52 vs. 2.15 ± 1.23, 0.52 ± 0.36 vs. 2.39 ± 1.17, all P<0.01).

CONCLUSIONS:
β-blockers (esmolol) can improve cardiac function and myocardial compliance, reduce the myocardial injury in patients with sepsis shock. Although β-blockers can decrease cardiac output, it has no influence on the circulation function and tissue perfusion.

表 2　艾司洛尔对脓毒性休克患者血流动力学参数的影响($\bar{x} \pm s$)

组别	时间点	例数(例)	MAP(mmHg)	CVP(mmHg)	HR(次/min)	CI($L \cdot min^{-1} \cdot m^{-2}$)	SVI(mL/m^2)	SVRI($kPa \cdot s \cdot L^{-1} \cdot m^{-2}$)	GEDVI(mL/m^2)
对照组	治疗前	20	79.0 ± 7.0	10.5 ± 1.6	121 ± 21	4.4 ± 1.2	37.0 ± 9.1	131.5 ± 34.4	602 ± 141
	治疗 12 h 点	20	78.0 ± 7.4	10.2. ± 1.4	118 ± 13	4.5 ± 0.6	38.0 ± 5.1	130.5 ± 24.2	588 ± 103
	治疗 24 h 点	20	79.0 ± 7.3	10.4 ± 1.4	113 ± 14	4.4 ± 1.2	38.0 ± 9.0	143.5 ± 18.6	618 ± 111
	治疗 48 h 点	20	76.0 ± 7.4	10.7 ± 1.5	108 ± 14	4.0 ± 0.9	37.0 ± 6.3	149.8 ± 20.5	606 ± 95
	治疗 72 h 点	20	75.0 ± 8.4	10.7 ± 1.3	99 ± 13	3.9 ± 0.8	39.0 ± 6.2	154.5 ± 18.8	626 ± 87
治疗组	治疗前	21	77.0 ± 9.6	10.4 ± 1.5	119 ± 22	4.5 ± 1.2	38.0 ± 8.8	127.8 ± 30.7	592 ± 121
	治疗 12 h 点	21	75.0 ± 7.2	10.5 ± 1.2	93 ± 4[ac]	3.3 ± 0.8[ac]	36.0 ± 8.5	159.2 ± 27.4[ac]	668 ± 148[bd]
	治疗 24 h 点	21	77.0 ± 8.5	10.6 ± 1.3	89 ± 8[ac]	3.3 ± 0.7[ac]	37.0 ± 7.8	163.6 ± 20.1[ac]	720 ± 119[ac]
	治疗 48 h 点	21	77.0 ± 8.6	10.3 ± 1.3	91 ± 7[ac]	3.3 ± 0.7[ac]	36.0 ± 6.1	175.1 ± 25.7[ac]	730 ± 144[ac]
	治疗 72 h 点	21	76.0 ± 7.9	11.1 ± 1.3	89 ± 7[ac]	3.4 ± 0.6[ad]	38.0 ± 5.7	170.7 ± 21.5[ad]	760 ± 97[ac]

注:MAP 为平均动脉压,CVP 为中心静脉压,HR 为心率,CI 为心排血指数,SVI 为每搏量指数,SVRI 为外周血管阻力指数,GEDVI 为全心舒张期末容积指数;1 mmHg=0.133 kPa;与本组治疗前比较,[a]$P<0.01$,[b]$P<0.05$;与对照组同期比较,[c]$P<0.01$,[d]$P<0.05$

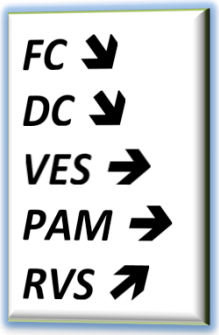

表 3　艾司洛尔对脓毒性休克患者组织代谢指标及心肌标志物的影响($\bar{x} \pm s$)

组别	时间点	例数(例)	$ScvO_2$	Lac(mmol/L)	cTnI(μg/L)
对照组	治疗前	20	0.769 ± 0.063	9.8 ± 3.4	1.08 ± 0.41
	治疗 12 h 点	20	0.783 ± 0.063	8.8 ± 3.2[a]	1.14 ± 0.40
	治疗 24 h 点	20	0.778 ± 0.057	6.8 ± 2.8[b]	1.74 ± 0.77[a]
	治疗 48 h 点	20	0.764 ± 0.060	3.6 ± 1.9[b]	2.15 ± 1.23[b]
	治疗 72 h 点	20	0.788 ± 0.065	2.5 ± 1.2[b]	2.39 ± 1.17[b]
治疗组	治疗前	21	0.791 ± 0.065	10.5 ± 4.1	1.06 ± 0.46
	治疗 12 h 点	21	0.794 ± 0.071	9.5 ± 3.1[a]	1.08 ± 0.37
	治疗 24 h 点	21	0.771 ± 0.053	6.3 ± 2.6[b]	1.15 ± 0.57[c]
	治疗 48 h 点	21	0.786 ± 0.062	3.9 ± 2.2[b]	0.93 ± 0.52[ac]
	治疗 72 h 点	21	0.798 ± 0.064	2.7 ± 1.1[b]	0.52 ± 0.36[bc]

注:$ScvO_2$ 为中心静脉血氧饱和度,Lac 为乳酸,cTnI 为心肌肌钙蛋白 I;与本组治疗前比较,[a]$P<0.01$,[b]$P<0.05$;与对照组同期比较,[c]$P<0.01$

The β-Blocker Esmolol Restores the Vascular Waterfall Phenomenon After Acute Endotoxemia*

Wei Du, MD; Dawei Liu, MD; Yun Long, MD; Xiaoting Wang, MD

Critical Care Medicine

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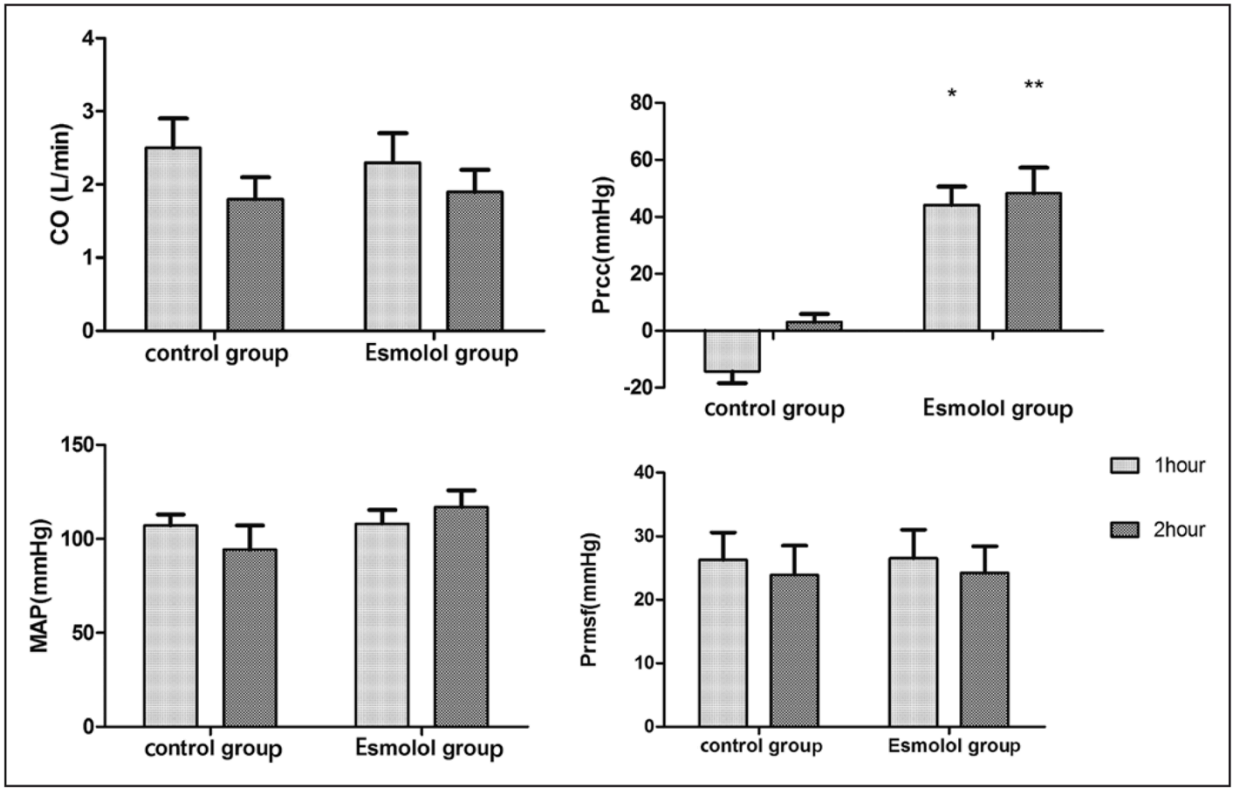


Figure 2. Esmolol treatment after acute endotoxemia increases renal critical closing pressure (Prcc) and restores the waterfall phenomenon. CO = cardiac output, MAP = mean arterial pressure, Prmsf = renal mean filling pressure. *$p < 0.05$ versus controls in 1 hr; **$p < 0.05$ vs control in 2 hr.

Anesth Analg. 2012 April ; 114(4): 803–810. doi:10.1213/ANE.0b013e318247fa44.

Determination of Vascular Waterfall Phenomenon by Bedside Measurement of Mean Systemic Filling Pressure and Critical Closing Pressure in the Intensive Care Unit

Jacinta J. Maas, M.D.,
Department of Intensive Care, Leiden University Medical Center, Leiden, The Netherlands

Rob B. de Wilde, Ph.D.,
Department of Intensive Care, Leiden University Medical Center, Leiden, The Netherlands

Leon P. Aarts, M.D., Ph.D.,
Department of Anesthesiology, Leiden University Medical Center, Leiden, The Netherlands

Michael R. Pinsky, M.D., Dr hc, FCCM, and
Department of Critical Care Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania

Jos R. Jansen, Ph.D.
Department of Intensive Care, Leiden University Medical Center, Leiden, The Netherlands

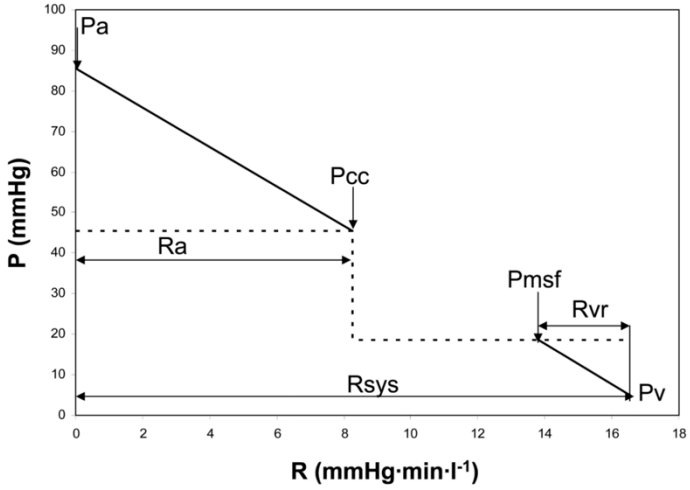


Figure 4.
Schematic graph of the pressure trend from arterial blood pressure (Pa) to critical closing pressure (Pcc), mean systemic filling pressure (Pmsf) to venous pressure (Pv). The pressure decrease between Pcc and Pmsf (the vascular waterfall) shows that total systemic vascular resistance (Rs) does not exist. Instead vascular resistance can be divided in a resistance upstream of the waterfall (arterial resistance Ra) and downstream (venous resistance Rv). The dotted line between the waterfall and Pmsf indicates that it is unknown how close to the waterfall Pmsf is located.

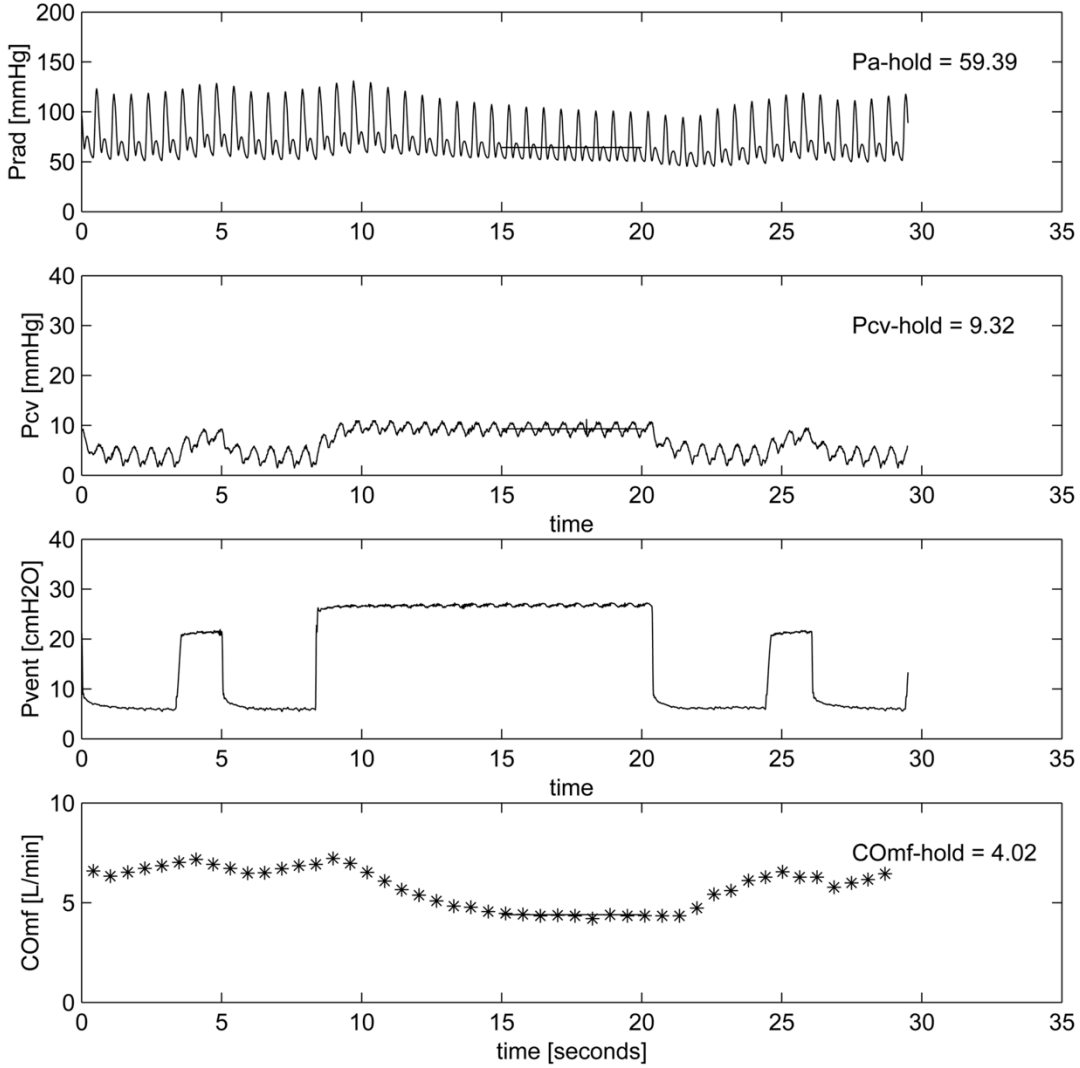


Figure 1.
Effects of an inspiratory hold maneuver on arterial pressure (Prad), central venous pressure (Pcv), airway pressure (Pvent) and beat to beat cardiac output (COmf). Preceding the hold maneuver the effects of a normal ventilatory cycle are plotted. Note the rapid restoration to baseline (within 4 seconds).

Maas et al. Anesthesia Analgesia 2012

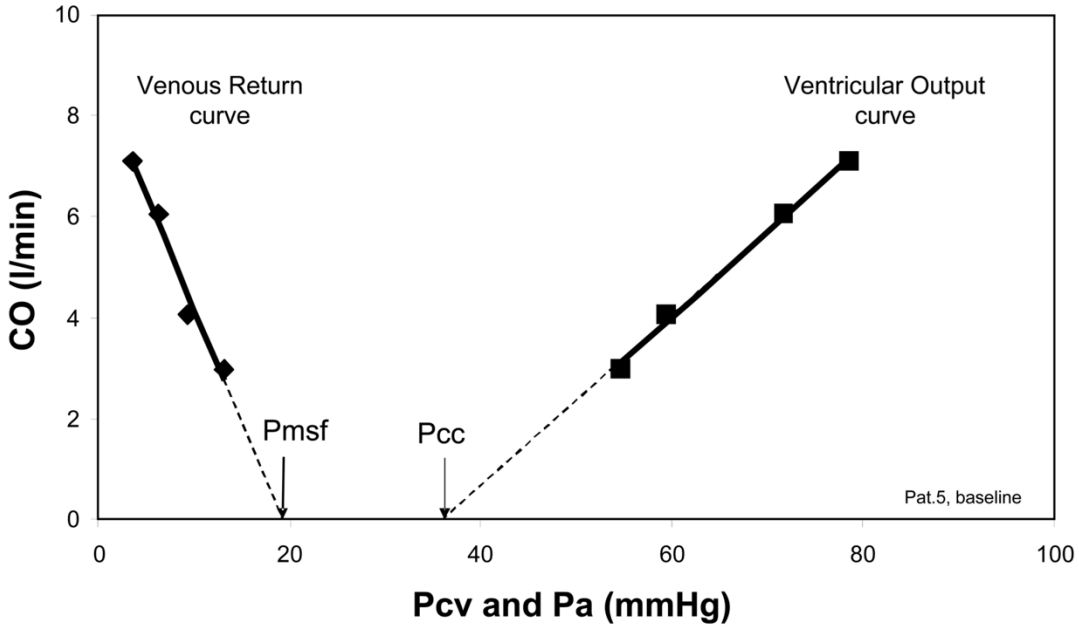


Figure 2.
Relationship between cardiac output (CO) and central venous pressure (Pcv) in a venous return curve and between CO and arterial blood pressure (Pa) in a ventricular output curve for an individual patient. Extrapolation to the zeroflow intercept leads to mean systemic filling pressure (Pmsf) for the venous return curve and to critical closing pressure (Pcc) for the ventricular output curve.

Ra = (PAM − Pcc) /DC

Rv = (Psmf − PVC)/DC

Maas et al. Anesthesia Analgesia 2012

Perspectives

V. Future directions

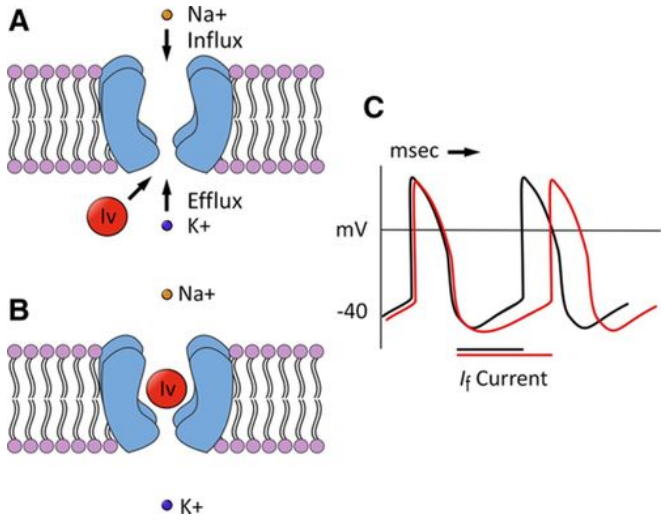
A. Esmolol to treat the hemodynamic effects of septic shock[57]
   i. Randomized open label efficacy study sponsored by Beth Israel Deaconess Medical Center in collaboration with American Heart Association enrolling patients between March 2015 to January 2019
   ii. Primary outcome: determine if esmolol reduces need for vasopressor support six hr after initiation
   iii. Secondary outcomes: time to shock reversal, change in lactate levels, difference in HR, need for vasopressor support at 24 hrs
   iv. Clinicaltrials.gov identifier: NCT02369900

B. Esmolol effects on heart and inflammation in septic shock (ESMOSEPSIS)[58]
   i. Open-label study sponsored by Central Hospital (Nancy, France) in collaboration with Baxter Healthcare Corporation enrolling patients between December 2013 and January 2016
   ii. Primary outcome: compare mean CI before and after esmolol administration
   iii. Secondary outcomes: effect of esmolol on vasopressor requirements, microcirculatory effects of esmolol, changes in cytokine patterns in esmolol patients, echocardiography assessment of ventricular function during esmolol administration
   iv. Clinicaltrials.gov identifier: NCT02068287

A priori très difficile…

Ivabradine

- NCT03367026: Pekin
  70 patients en choc septique
  double aveugle
  4 jours de traitement
  CJP= baisse FC
- NCT01186783:
  70 patients en choc septique
  Open label
  CJP: proportion avec baisse FC d'au moins 10 points dans les 4 premiers jours



PER OS
PHARMACOCINETIQUE COMPLIQUÉE

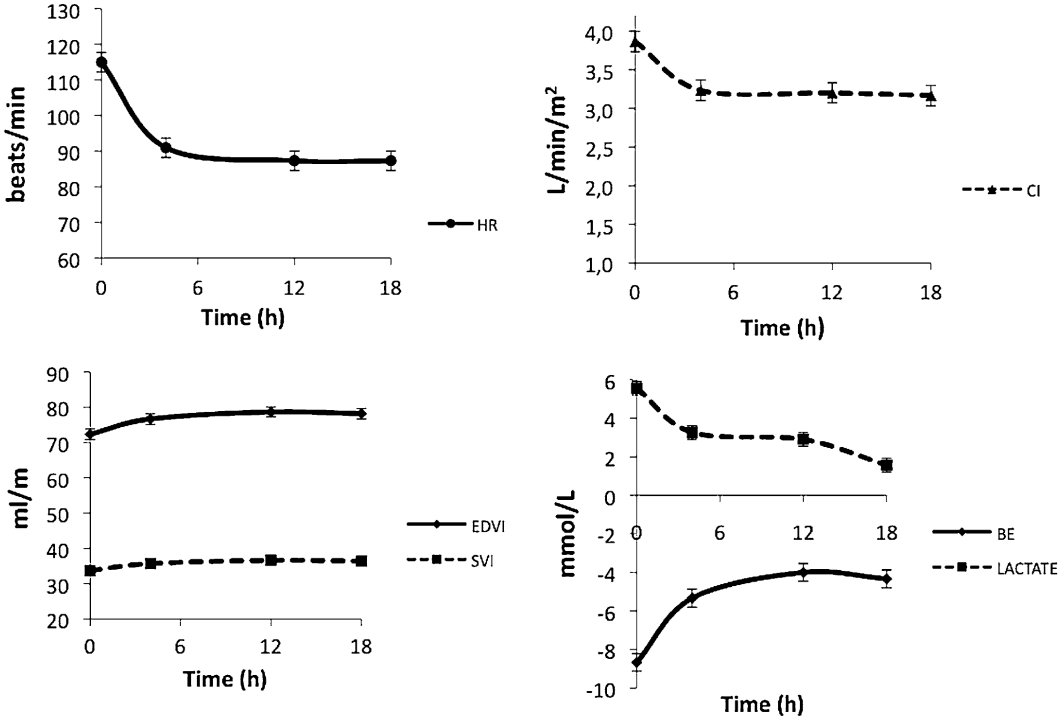
Clin Res Cardiol (2014) 103:831–834
DOI 10.1007/s00392-014-0722-2

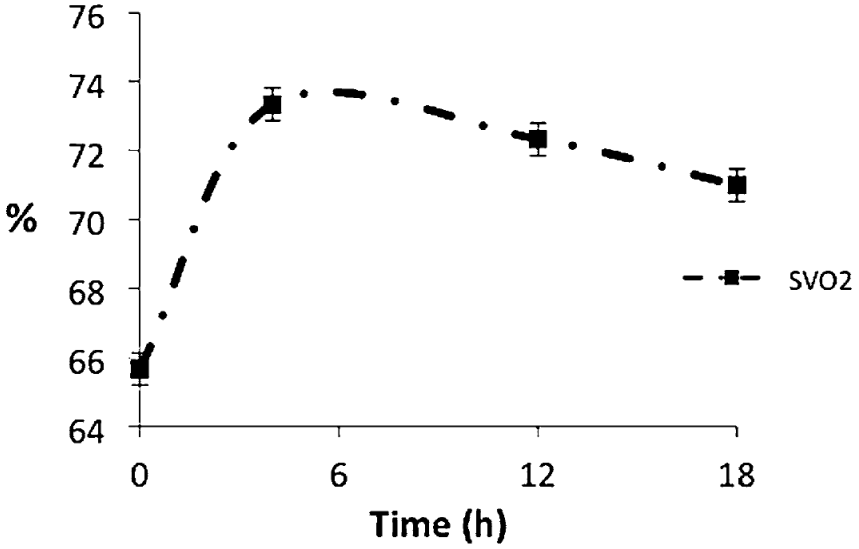
LETTER TO THE EDITORS

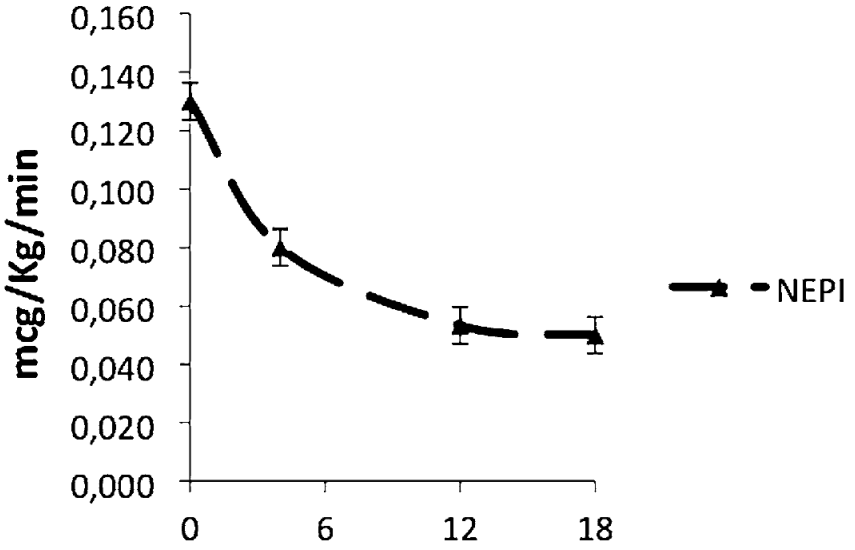
Ivabradine: a preliminary observation for a new terapeutic role in patients with multiple organ dysfunction syndrome

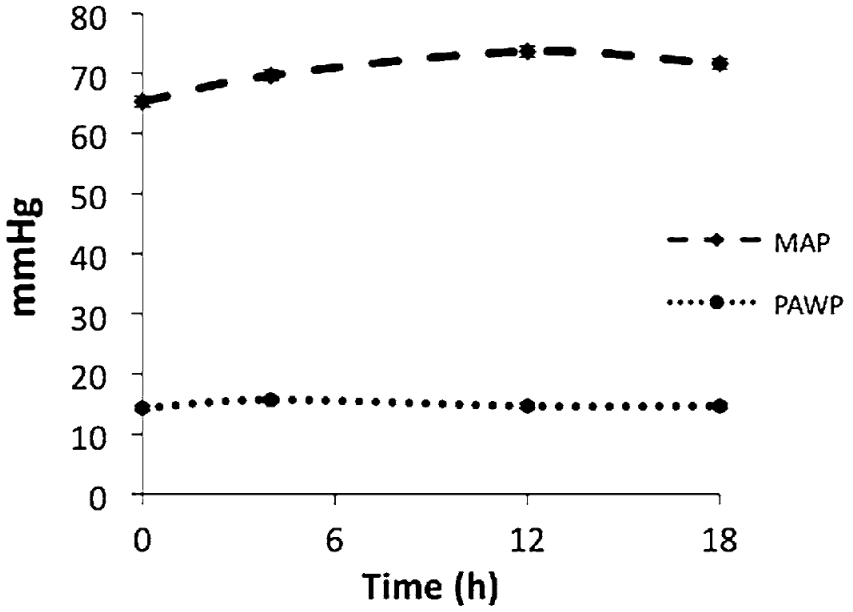
Vincenzo De Santis · Giacomo Frati · Ernesto Greco · Luigi Tritapepe

3 patients









De santis et al. Clin Res Cardiol 2014

Unger et al. Trials (2018) 19:637
https://doi.org/10.1186/s13063-018-3024-6

Trials

STUDY PROTOCOL Open Access

Landiolol in patients with septic shock resident in an intensive care unit (LANDI-SEP): study protocol for a randomized controlled trial

Martin Unger[1*], Andrea Morelli[2], Mervyn Singer[3], Peter Radermacher[4], Sebastian Rehberg[5], Helmut Trimmel[6], Michael Joannidis[7], Gottfried Heinz[8], Vladimír Cerny[9], Pavel Dostál[10], Christian Siebers[11], Fabio Guarracino[12], Francesca Pratesi[13], Gianni Biancofiore[14], Massimo Girardis[15], Pavla Kadlecova[16], Olivier Bouvet[17], Michael Zörer[1], Barbara Grohmann-Izay[1], Kurt Krejcy[1], Christoph Klade[1] and Günther Krumpl[1]

Landiolol 225/1
1er patient inclus février 2018

Abstract

Background: In patients with septic shock, the presence of an elevated heart rate (HR) after fluid resuscitation marks a subgroup of patients with a particularly poor prognosis. Several studies have shown that HR control in this population is safe and can potentially improve outcomes. However, all were conducted in a single-center setting. The aim of this multicenter study is to demonstrate that administration of the highly beta1-selective and ultrashort-acting beta blocker landiolol in patients with septic shock and persistent tachycardia (HR ≥ 95 beats per minute [bpm]) is effective in reducing and maintaining HR without increasing vasopressor requirements.

Methods: A phase IV, multicenter, prospective, randomized, open-label, controlled study is being conducted. The study will enroll a total of 200 patients with septic shock as defined by The Third International Consensus Definitions for Sepsis and Septic Shock criteria and tachycardia (HR ≥ 95 bpm) despite a hemodynamic optimization period of 24–36 h. Patients are randomized (1:1) to receive either standard treatment (according to the Surviving Sepsis Campaign Guidelines 2016) and continuous landiolol infusion to reach a target HR of 80–94 bpm or standard treatment alone. The primary endpoint is HR response (HR 80–94 bpm), the maintenance thereof, and the absence of increased vasopressor requirements during the first 24 h after initiating treatment.

Discussion: Despite recent studies, the role of beta blockers in the treatment of patients with septic shock remains unclear. This study will investigate whether HR control using landiolol is safe, feasible, and effective, and further enhance the understanding of beta blockade in patients with septic shock.

Trial registration: EU Clinical Trials Register; EudraCT, 2017-002138-22. Registered on 8 August 2017.

Conclusions

- Pas encore…
- Que fréquence cardiaque ? (ivabradine ?)
- Combien de temps ?
- Que bêta-1 ?
- Quels patients ?
- Test thérapeutique ?