

# LÉKY, BEZ KTERÝCH SE „NELZE“ OBEJÍT

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Komplexní kardiovaskulární centrum FN Plzeň*

# Cíle zájmu



- Esmolol
- Vasopresin
- Propofol

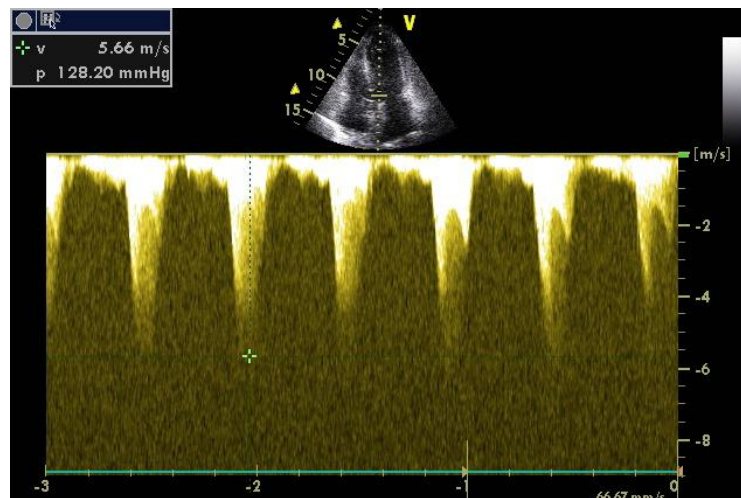
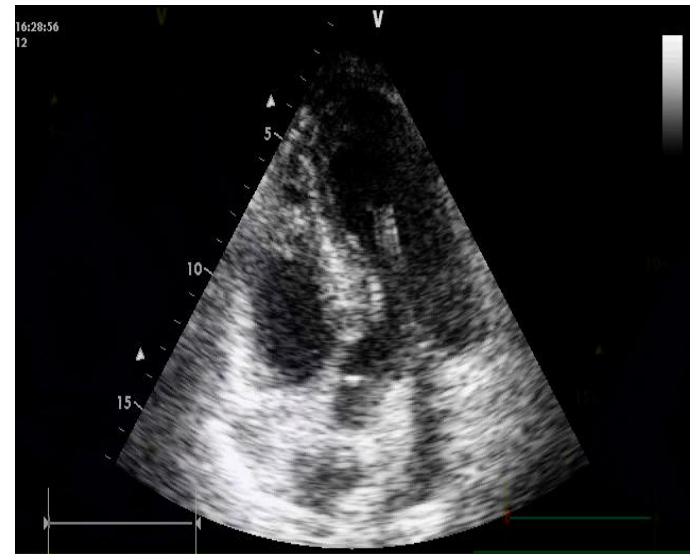
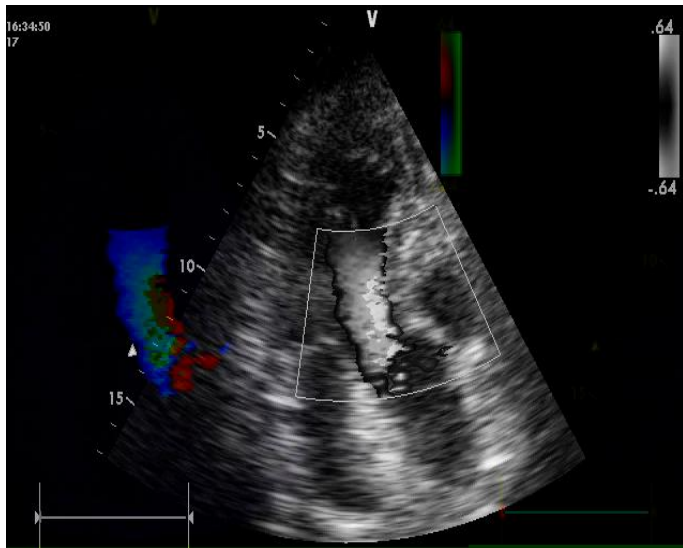
# Esmolol

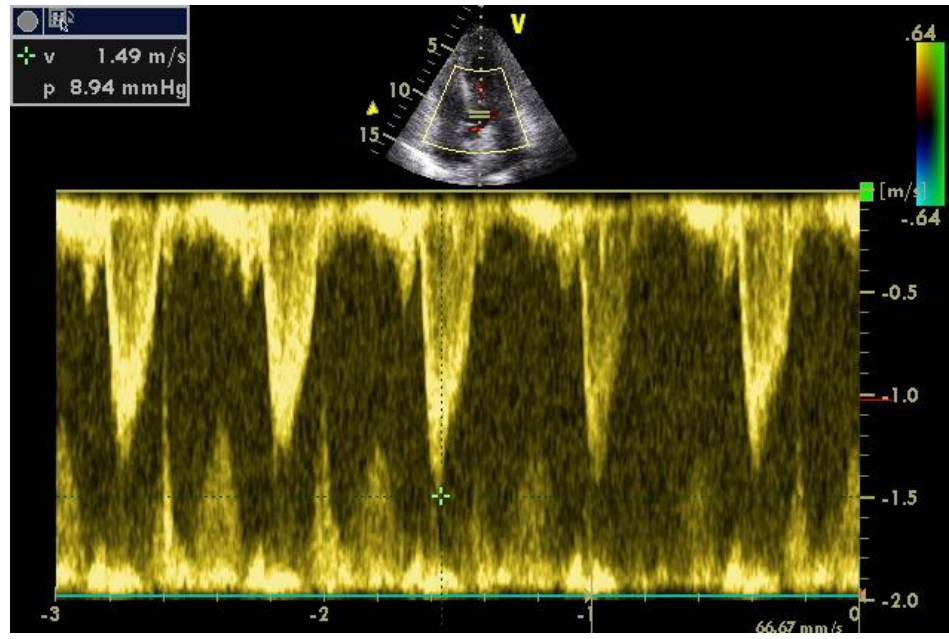


- je vysoce kardioselektivní betablokátor, beta1-selektivita je udávána hodnotou 1 : 34-43
- i.v. aplikace
- po podání vysycovacího bolusu 500 µg/kg a následném kontinuálním i.v. podáváníí se objevuje efekt do 2 minut a maximálního efektu a vyrovnaného stavu je dosaženo z 90 % již během 5 minut
- poločas eliminace je přibližně 9 minut (4–16 minut), plné odeznění betablokády nastává do 18–30 minut po zastavení léčby
- využití v emergentních situacích pro kontinuální léčbu tachykardií, tachyarytmií a hypertenze při hemodynamické nestabilitě a vyšším riziku nežádoucích nebo nadměrných účinků betablokátorů

# Indikace

- zpomalení neadekvátní sinusové tachykardie s negativním hemodynamickým dopadem
- zpomalení komorové odpovědi při fibrilaci a flutteru síní a AVNRT
- léčba tachyarytmií při digitalisové intoxikaci
- léčba arytmií při vrozeném dlouhém QT intervalu
- léčba atrioventrikulárních nodálních a atrioventrikulárních tachykardií (bez zjevné preexcitace)
- léčba / prevence komorových arytmií
- léčba emergentních hypertenzních stavů
- léčba krátkodobých perioperačních hypertenzních reakcí
- řízená hypotenze při disekujícím aneurysmatu aorty
- akutní koronární stavy





# Kontraindikace

- šokový stav
- závažné poruchy vodivosti AV uzlu a AV blok 2. nebo 3.stupně bez zajištění kardiostimulací
- tachyarytmie při syndromu preexcitace (s rizikem zablokování pomalé dráhy a navozením rezistentní tachyarytmie
- feochromocytom bez současné léčby alfablokátorem
- dekompenzovaný bronchospastický stav
- těžší metabolická acidoza
- přecitlivělost na esmolol

# Dávkování

Konverzní tabulka: **mikrogramy/kg/min** → **ml/h** (esmolol naředěný na koncentraci 10 mg/ml)

|           | 500 µg/kg/min             | 50 µg/kg/min | 100 µg/kg/min | 150 µg/kg/min | 200 µg/kg/min | 250 µg/kg/min | 300 µg/kg/min |
|-----------|---------------------------|--------------|---------------|---------------|---------------|---------------|---------------|
|           | <b>pouze<br/>minuta 1</b> |              |               |               |               |               |               |
| <b>kg</b> | <b>ml/h</b>               | <b>ml/h</b>  | <b>ml/h</b>   | <b>ml/h</b>   | <b>ml/h</b>   | <b>ml/h</b>   | <b>ml/h</b>   |
| 40        | 120                       | 12           | 24            | 36            | 48            | 60            | 72            |
| 45        | 135                       | 13,5         | 27            | 40,5          |               |               |               |
| 50        | 150                       | 15           | 30            | 45            |               |               |               |
| 55        | 165                       | 16,5         | 33            | 49,5          |               |               |               |
| 60        | 180                       | 18           | 36            | 54            |               |               |               |
| 65        | 195                       | 19,5         | 39            | 58,5          |               |               |               |
| 70        | 210                       | 21           | 42            | 63            |               |               |               |
| 75        | 225                       | 22,5         | 45            | 67,5          |               |               |               |
| 80        | 240                       | 24           | 48            | 72            |               |               |               |
| 85        | 255                       | 25,5         | 51            | 76,5          |               |               |               |
| 90        | 270                       | 27           | 54            | 81            |               |               |               |
| 95        | 285                       | 28,5         | 57            | 85,5          |               |               |               |
| 100       | 300                       | 30           | 60            | 90            |               |               |               |
| 105       | 315                       | 31,5         | 63            | 94,5          |               |               |               |
| 110       | 330                       | 33           | 66            | 99            |               |               |               |
| 115       | 345                       | 34,5         | 69            | 103,5         |               |               |               |
| 120       | 360                       | 36           | 72            | 108           |               |               |               |

Diagram postupu při zahájení a pokračování léčby

Počáteční dávka 500 mikrogramů/kg/min v průběhu první minuty,  
pak 50 mikrogramů/kg/min po 4 minuty

Nedostatečná odpověď v průběhu 5 minut.  
Opakujte dávku 500 mikrogramů/kg/min  
během první minuty.  
Zvyšte udržovací dávku na 100 mikrogramů/kg/min  
po 4 minuty.

Nedostatečná odpověď v průběhu 5 minut.  
Opakujte dávku 500 mikrogramů/kg/min  
v průběhu první minuty.  
Zvyšte udržovací dávku na 150 mikrogramů/kg/min  
po 4 minuty.

Nedostatečná odpověď.  
Opakujte dávku 500 mikrogramů/kg/min  
v průběhu první minuty.

Zvyšte udržovací dávku na 200 mikrogramů/kg/min a zůstaňte na této hladině.

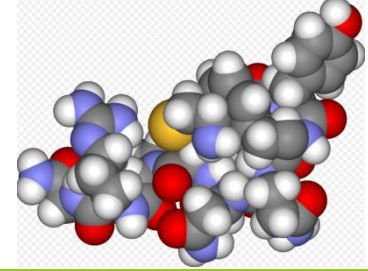
Příznivá reakce:  
Udržujte infuzi na  
50 mikrogramech/kg/min.

Příznivá reakce:  
Udržujte infuzi na  
100 mikrogramech/kg/min

Příznivá reakce:  
Udržujte infuzi na  
150 mikrogramech/kg/min

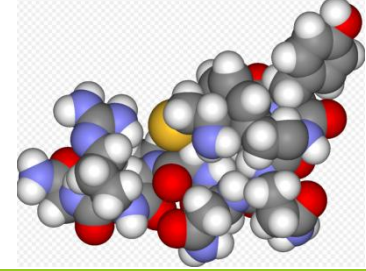


# Vasopresin



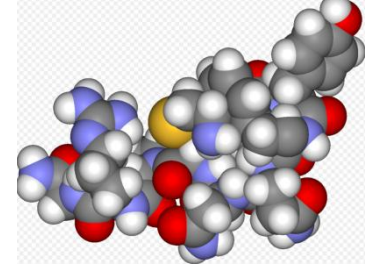
- ADH – hormon, který se tvoří v hypotalamu a do krve je uvolňován ze zadního laloku hypofýzy
- zvyšuje zpětnou resorpci vody v ledvinách, jeho výdej proto stoupá při nedostatku tekutin.
- vysoké dávky: vasokonstrikce a zvýšení TK
- nízké dávky: snížení diurézy bez vlivu na cirkulaci (antidiuretický hormon)

# Vasopresin



| receptor       | tkáň  | efekt                                  |
|----------------|---|--|
| V <sub>1</sub> | bb. hladké svaloviny<br>cév, ledvin, jater; PLT | vasokonstrikce                         |
| V <sub>2</sub> | endoteliální bb.<br>sběrných kanálků            | ↑ permeability<br>pro H <sub>2</sub> O |
| V <sub>3</sub> | hypofýza  | ↑ sekrece ACTH                         |
| OTRs           | uterus, aorta, PA...                            | vasodilatace                           |

# Vasopresin



Serpa Neto *et al.* *Critical Care* 2012, **16**:R154

RESEARCH

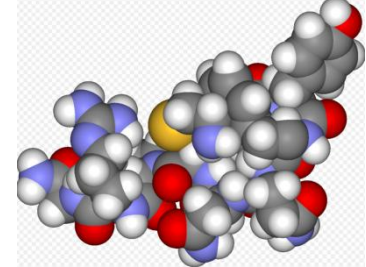
Open Access

## Vasopressin and terlipressin in adult vasodilatory shock: a systematic review and meta-analysis of nine randomized controlled trials

Ary Serpa Neto<sup>1\*</sup>, Antônio P Nassar Júnior<sup>2</sup>, Sérgio O Cardoso<sup>1</sup>, José A Manetta<sup>1</sup>, Victor GM Pereira<sup>1</sup>, Daniel C Espósito<sup>1</sup>, Maria CT Damasceno<sup>1</sup> and James A Russell<sup>3</sup>

- oba preparáty **významně snižují potřebu noradrenalinu**
- kombinace **vasopressin + NOR** je spojená s nižší mortalitou
- kombinace **terlipresin + NOR** nemá vliv na mortalitu

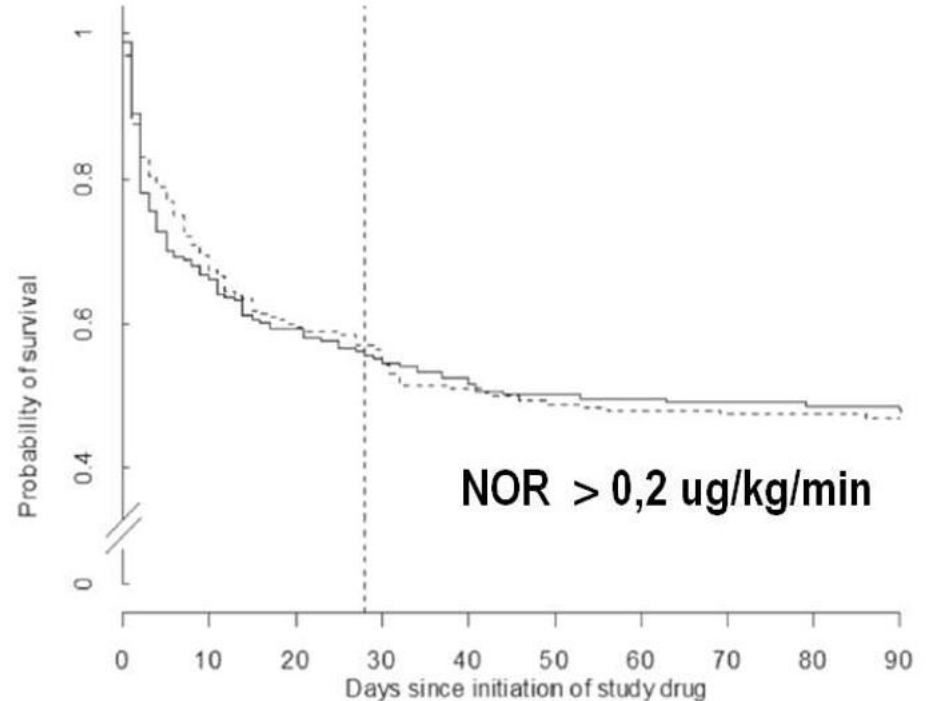
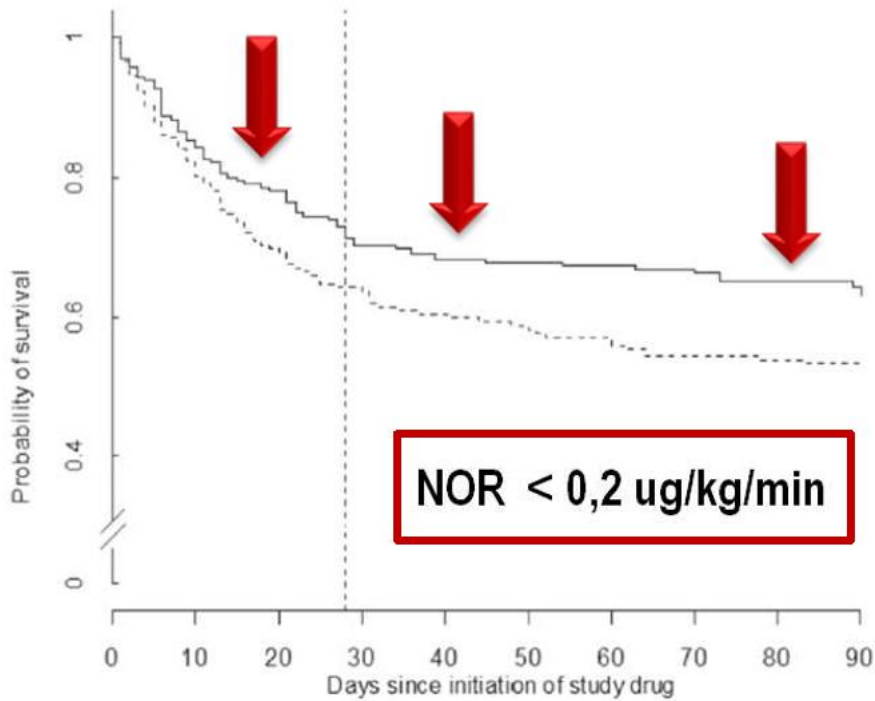
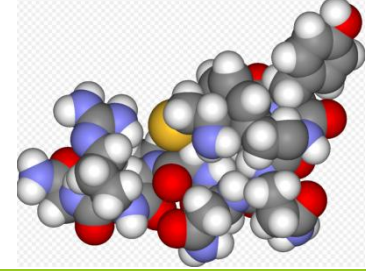
# Vasopresin



- 2) Použití vasopresinu lze zvážit u pacientů se septickým šokem, kde nelze dosáhnout cílových hodnot krevního tlaku i přes použití vysokých dávek noradrenalinu. V těchto případech doporučujeme přidání vasopresinu do maximální dávky 4 IU/h, což odpovídá přibližně 0,04 IU/kg.h, s cílem dosažení cílové hodnoty krevního tlaku nebo snížení dávky noradrenalinu (2-5) a to při kontrole periferní perfuze (akra, splanchnicus). Vasopresin považujeme na základě současného stavu odborného poznání za látku druhé volby v uvedené indikaci.

Poznámka: Určení "vysoké" dávky noradrenalinu je klinické rozhodnutí, ve vztahu k plicnicové cirkulaci se jedná obvykle o dávku nad 0,5  $\mu\text{g}/\text{kg}\cdot\text{min}$ . Vasopresin na rozdíl od terlipresinu a noradrenalinu nezvyšuje tlak v plicnici, současné snížení dávek noradrenalinu v septickém šoku může mít příznivý dopad na funkci pravé komory srdeční, zvláště u pacientů s primární dysfunkcí pravé komory a/nebo plicní hypertenzí (6,7). V podmínkách intenzivní péče jde nejčastěji o pacienty se septickým šokem na umělé plicní ventilaci, obvykle na vysoké dávce noradrenalinu, s plicní hypertenzí a dysfunkcí pravé komory srdeční. Snížení dávky noradrenalinu je vhodné i u dynamické obstrukce výtokového traktu levé komory srdeční nebo u septické kardiomyopatie.

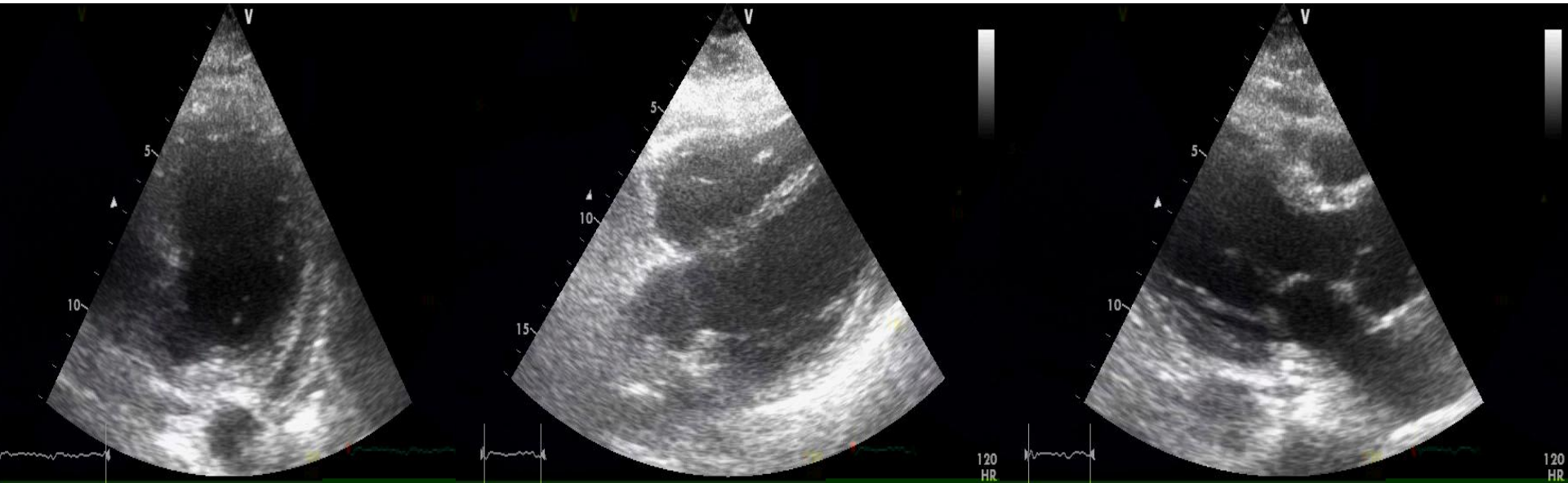
# Vasopresin



Russell J et al., *N Engl J Med* 2008, 358:877-887



# Tako-tsubo kardiomyopatie



# Tako-tsubo kardiomyopatie



Research

JAMA. 2016;316(5):509-518

JAMA | **Original Investigation**

# Effect of Early Vasopressin vs Norepinephrine on Kidney Failure in Patients With Septic Shock

## The VANISH Randomized Clinical Trial

Anthony C. Gordon, MD; Alexina J. Mason, PhD; Neeraja Thirunavukkarasu, MSc; Gavin D. Perkins, MD; Maurizio Cecconi, MD; Magda Cepkova, MD; David G. Pogson, MB BCH; Hollmann D. Aya, MD; Aisha Anjum, BSc; Gregory J. Frazier, MSc; Shalini Santhakumaran, MSc; Deborah Ashby, PhD; Stephen J. Brett, MD; for the VANISH Investigators

... **nepotvrdila inferioritu vazopresinu jako vazopresoru „PRVNÍ VOLBY“ u pacientů v septickém šoku ve srovnání s noradrenalinem**



*Anesthesiology* 2017; 126:85-93

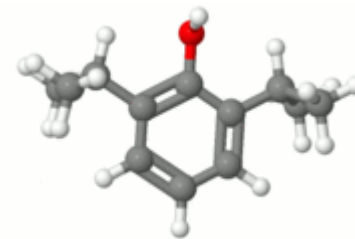
## **Vasopressin versus Norepinephrine in Patients with Vasoplegic Shock after Cardiac Surgery**

*The VANCS Randomized Controlled Trial*

Ludhmila Abrahao Hajjar, M.D., Ph.D., Jean Louis Vincent, M.D., Ph.D.,  
Filomena Regina Barbosa Gomes Galas, M.D., Ph.D., Andrew Rhodes, M.D., Ph.D.,  
Giovanni Landoni, M.D., Eduardo Atsushi Osawa, M.D., Ph.D., Renato Rosa Melo, M.D.,  
Marcia Rodrigues Sundin, M.D., Solimar Miranda Grande, M.D., Fabio A. Gaiotto, M.D., Ph.D.,  
Pablo Maria Pomerantzeff, M.D., Ph.D., Luis Oliveira Dallan, M.D., Ph.D., Rafael Alves Franco, M.D.,  
Rosana Ely Nakamura, M.D., Luiz Augusto Lisboa, M.D., Ph.D., Juliano Pinheiro de Almeida, M.D., Ph.D.,  
Aline Muller Gerent, M.D., Dayenne Hianae Souza, M.D., Maria Alice Gaiane, M.D.,

- ... **potvrdila SUPERIORITU vazopresinu jako vazopresoru „PRVNÍ VOLBY“ u pacientů s vazoplegickým šokem po použití „mimotěláku“, ve srovnání s noradrenalinem**

# PROPOFOL



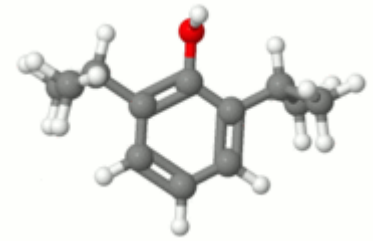
- 2,6-DIISOPROPYLFENOL
- VYROBEN 1976, V KLINICKÉ PRAXI OD 11/1989 (USA)
- LIPOFILNÍ (SÓJOVÁ EMULZE): 100mg/ml (P 1%) či 50mg/ml (P 2%)
- ADITIVA: EDTA nebo BENZYLALKOHOL nebo METABISULFIT – inhibice mikrobiálního růstu až 12hod.



Wo Propofol Wirklich Herkommt...



# PROPOFOL



REVIEW

CNS Neuroscience & Therapeutics

## The Experimental and Clinical Pharmacology of Propofol, an Anesthetic Agent with Neuroprotective Properties

Yoshinori Kotani<sup>1,2</sup>, Masamitsu Shimazawa<sup>1</sup>, Shinichi Yoshimura<sup>2</sup>, Toru Iwama<sup>2</sup> and Hideaki Hara<sup>1</sup>

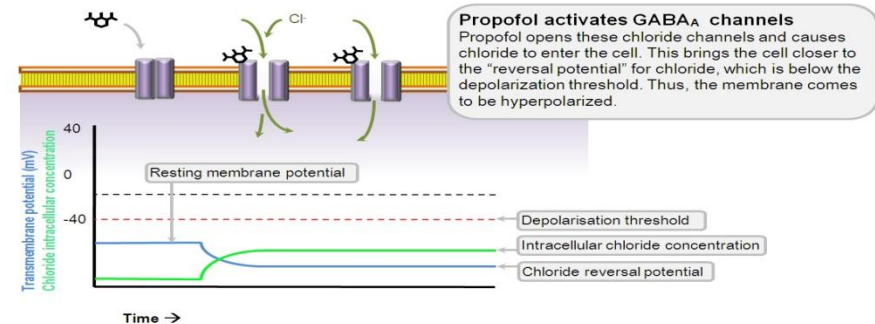
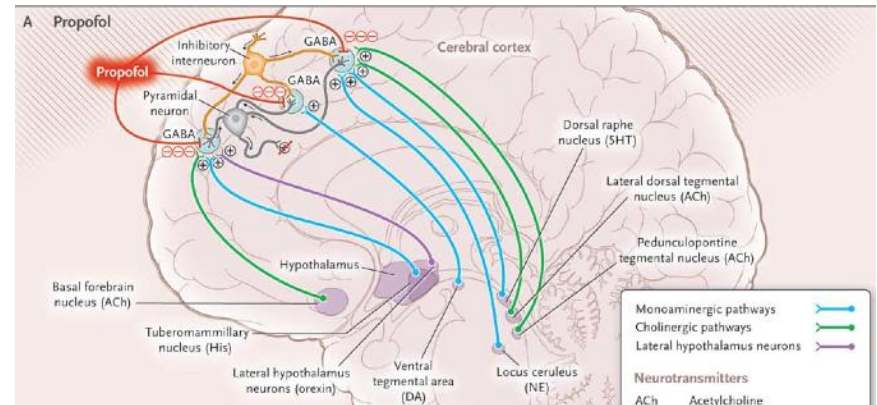
<sup>1</sup> Department of Biofunctional Evaluation, Molecular Pharmacology, Gifu Pharmaceutical University, Gifu 502-8585, Japan

<sup>2</sup> Department of Neurosurgery, Gifu University Graduate School of Medicine, Gifu 501-1194, Japan

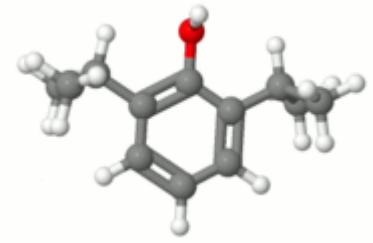
CNS Neuroscience & Therapeutics 14 (2008) 95–106 © 2008 The Authors. Journal compilation © 2008 Blackwell Publishing Ltd

- anestetikum/sedativum/hypnotikum/antiepileptikum
  - slabé analgetikum/anxiolytikum
  - neuroprotektivum?
  - imunomodulans?
- aktivace GABA<sub>A</sub>
- inhibice NMDA
- rychlý nástup účinku
  - vazba na plazmat. proteiny (97-98%)
  - clearance 23-50ml/kg/h (játra→ledviny)

- **prolong. aplikace: biol. poločas až 1-3dny!!!**



# PROPOFOL



Annals of Intensive Care 2013, 3:24  
<http://www.annalsofintensivecare.com/content/3/1/24>

Annals of Intensive Care  
 a SpringerOpen Journal

RESEARCH

Open Access

## Sedation in French intensive care units: a survey of clinical practice

The SRLF Trial Group

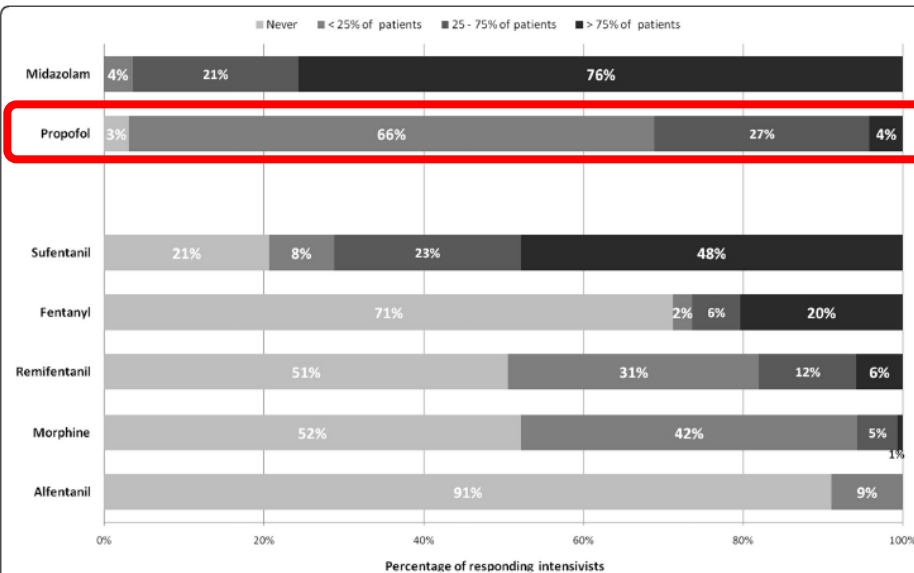


Figure 1 Use of IV continuous infusions of hypnotics and opioids.

**AJCC** American Journal of  
 Critical Care

Evidence-based interdisciplinary knowledge for high acuity and critical care

## Sedation Management in Australian and New Zealand Intensive Care Units: Doctors' and Nurses' Practices and Opinions

Mark O'Connor, Tracey Bucknall and Elizabeth Manias

Am J Crit Care 2010;19:285-295 doi: 10.4037/ajcc2009541  
 © 2010 American Association of Critical-Care Nurses  
 Published online <http://www.ajconline.org>

**Table 2**  
 Respondents' Indications of how frequently they used individual analgesics, sedatives, and inhalant medicines in their intensive care units (n = 267-279)

| Medication   | Frequency of use, <sup>a</sup> % |       |                            |                                   |                             |                                  | No. of respondents |                              |
|--|----------------------------------|-------|----------------------------|-----------------------------------|-----------------------------|----------------------------------|--------------------|------------------------------|
|  | Do not know this medicine        | Never | Rarely (1%-5% of patients) | Occasionally (6%-25% of patients) | Often (26%-50% of patients) | Frequently (51%-75% of patients) |                    | Primarily (>75% of patients) |
| <b>Analgesics</b>                                  |                                  |       |                            |                                   |                             |                                  |                    |                              |
| Morphine   | 0.0                              | 0.0   | 1.8                        | 3.3                               | 10.5                        | 17.0                             | 67.4               | 276                          |
| Fentanyl   | 0.0                              | 0.7   | 15.6                       | 35.1                              | 19.6                        | 15.9                             | 13.0               | 276                          |
| Remifentanyl                                       | 7.4                              | 48.0  | 31.9                       | 6.3                               | 2.6                         | 1.5                              | 2.2                | 270                          |
| Tramadol   | 0.0                              | 18.0  | 25.0                       | 27.9                              | 16.9                        | 10.7                             | 1.5                | 272                          |
| Ketamine   | 0.0                              | 10.6  | 42.7                       | 38.0                              | 6.6                         | 1.8                              | 0.4                | 274                          |
| Pethidine (meperidine)                             | 0.0                              | 41.7  | 38.4                       | 14.8                              | 3.7                         | 1.5                              | 0.0                | 271                          |
| Codeine  | 0.0                              | 42.6  | 41.9                       | 13.3                              | 2.2                         | 0.0                              | 0.0                | 270                          |
| Alfentanil   | 11.1                             | 63.8  | 21.4                       | 1.1                               | 1.1                         | 1.1                              | 0.4                | 271                          |
| <b>Sedatives</b>                                   |                                  |       |                            |                                   |                             |                                  |                    |                              |
| Midazolam  | 0.0                              | 1.1   | 1.1                        | 0.0                               | 13.1                        | 28.8                             | 51.5               | 274                          |
| <b>Propofol</b>                                    | 0.0                              | 0.4   | 3.3                        | 9.2                               | 9.5                         | 28.2                             | 49.5               | 273                          |
| Diazepam   | 0.0                              | 19.3  | 36.9                       | 23.1                              | 10.1                        | 4.3                              | 3.7                | 268                          |
| Chloral hydrate                                    | 5.9                              | 54.6  | 20.8                       | 9.3                               | 3.0                         | 2.6                              | 3.7                | 269                          |
| Clonidine  | 0.4                              | 14.4  | 35.9                       | 32.2                              | 15.2                        | 1.5                              | 0.4                | 270                          |
| Lorazepam  | 0.0                              | 48.3  | 39.0                       | 10.1                              | 1.5                         | 1.1                              | 0.0                | 267                          |
| Clonazepam   | 0.4                              | 27.5  | 52.4                       | 16.0                              | 1.9                         | 1.9                              | 0.0                | 269                          |
| Dexmedetomidine                                    | 14.1                             | 36.0  | 28.6                       | 14.9                              | 3.7                         | 2.2                              | 0.0                | 269                          |
| <b>Inhalants</b>                                   |                                  |       |                            |                                   |                             |                                  |                    |                              |
| Nitrous oxide/50% nitrous oxide plus 50% oxygen    | 0.0                              | 79.6  | 13.6                       | 4.3                               | 0.7                         | 1.1                              | 0.7                | 279                          |
| Isflurane  | 1.4                              | 80.3  | 16.5                       | 1.1                               | 0.4                         | 0.4                              | 0.0                | 279                          |
| Other volatile anesthetic agents (eg, sevoflurane) | 0.7                              | 82.1  | 15.4                       | 1.1                               | 0.4                         | 0.4                              | 0.0                | 279                          |

<sup>a</sup>Because of rounding, not all percentages total 100.



# KAZUISTIKA



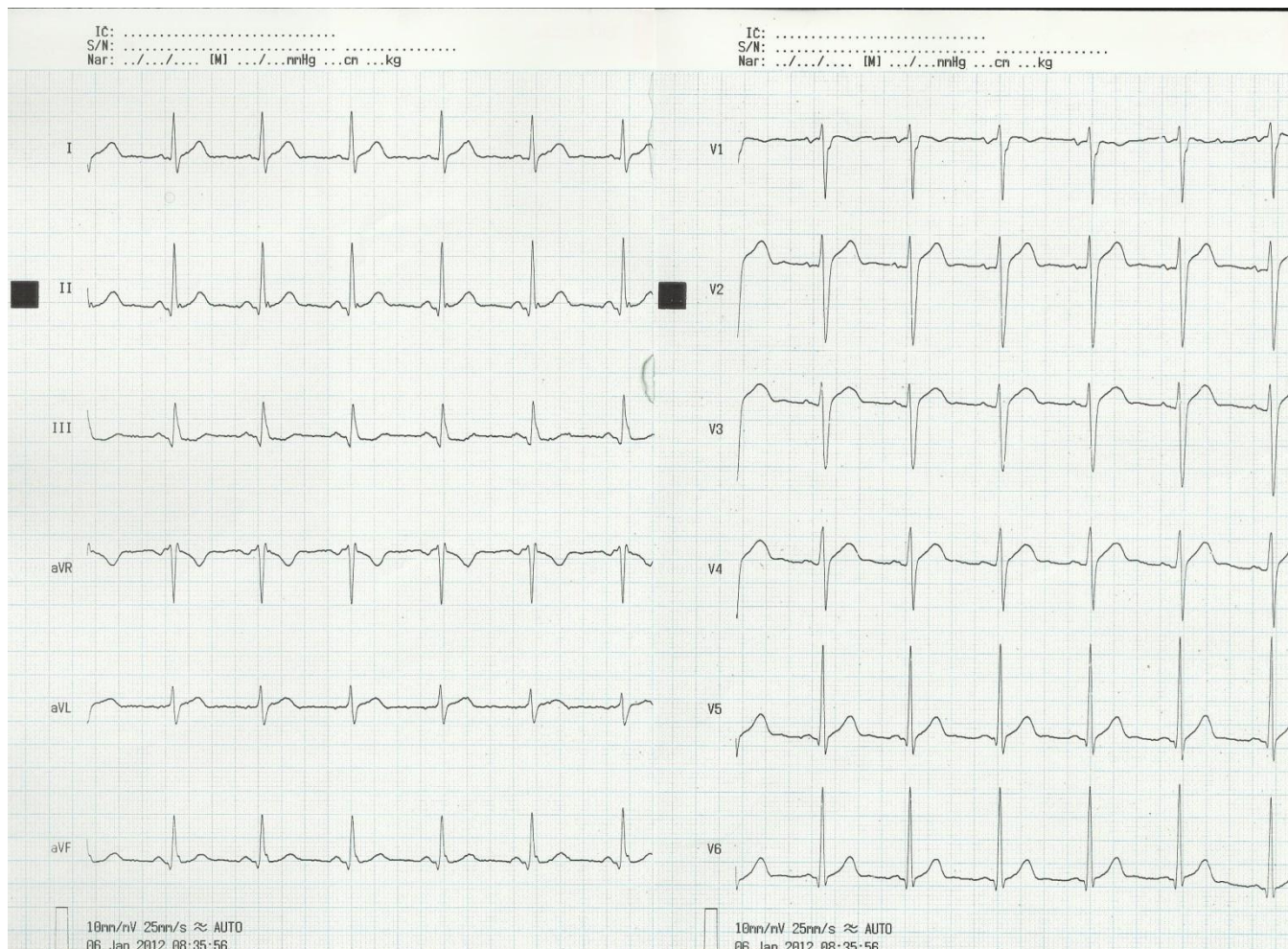
- 1/2012
- muž, 19 let
  
- intoxikace CO (COHb 29.4%) → koma → UPV → JIP
- normobarická hyperoxie → clearance CO (4hod.)
- posthypoxické postižení CNS: MR vs. EP
- sedace: **propofol (4 dny, 100-400mg/h = 1.3-5.2mg/kg/h)**
  
- → **ΔEKG: LQT (QTc>680ms, TF 102/min), bez L-MAC**
- → 32hod.: QTc 432ms
  
- **JIP-LOS: 21 dní** → DIP → DIP-LOS: 30 dní → LDN

# KAZUISTIKA



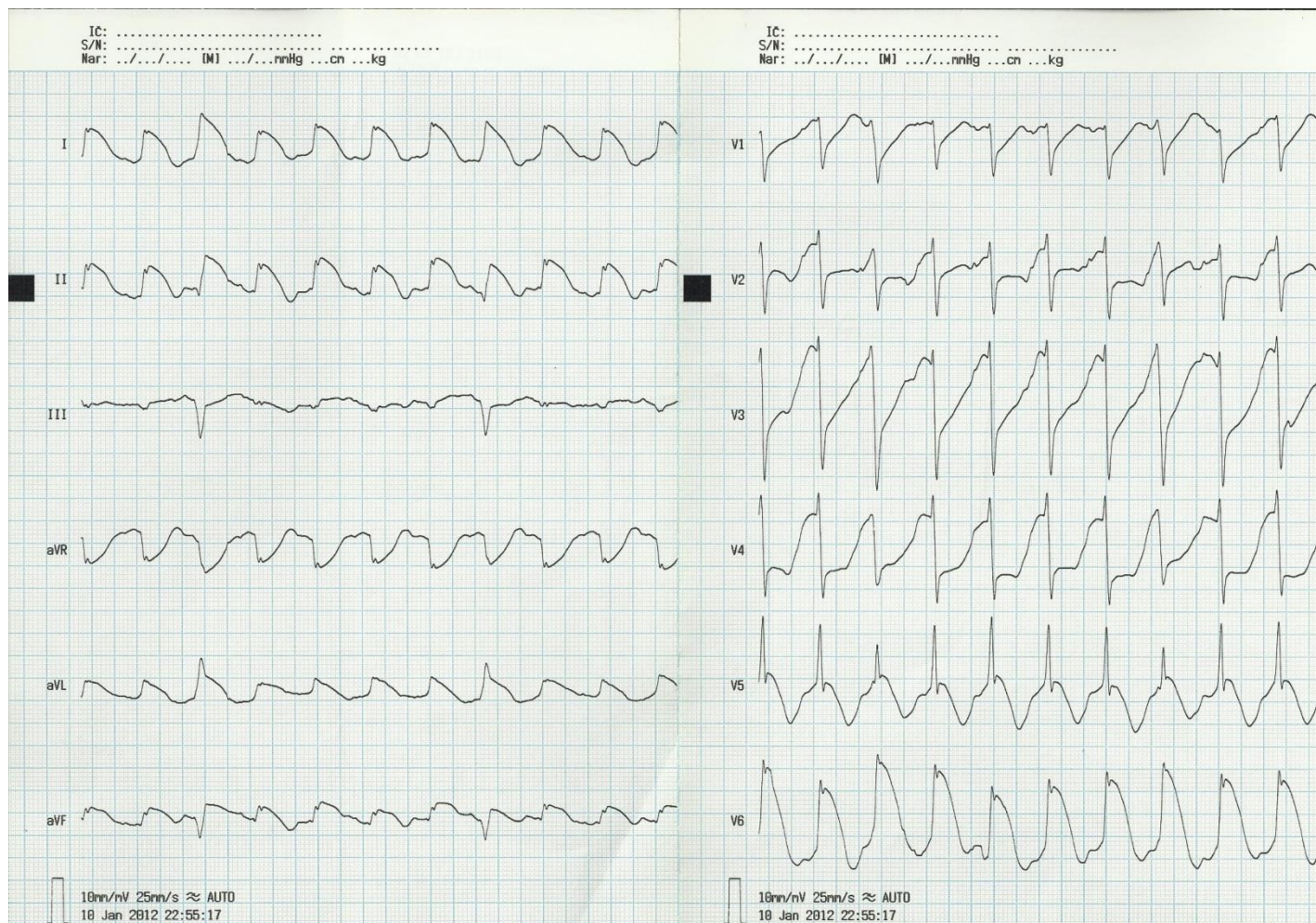
| parametr                            | 10.1.2012   | 10.1.2012  | 11.1.2012   | 12.1.2012   |
|-------------------------------------|-------------|------------|-------------|-------------|
|                                     | 4:59        | 23:45      | 5:03        | 4:58        |
| leukocyty ( $\times 10^9/l$ )       | 8,5         | N/A        | 7,9         | 13,4        |
| trombocyty ( $\times 10^9/l$ )      | 97          | N/A        | 114         | 154         |
| bilirubin ( $\mu\text{mol/l}$ )     | 14          | N/A        | 7           | 15          |
| urea (mmol/l)                       | 2,8         | N/A        | 3,3         | 4,8         |
| kreatinin ( $\mu\text{mol/l}$ )     | 94          | N/A        | 87          | 75          |
| troponin I ( $\mu\text{g/l}$ )      | <b>0,74</b> | N/A        | <b>0,36</b> | <b>0,19</b> |
| myoglobin ( $\mu\text{g/l}$ )       | <b>208</b>  | N/A        | <b>131</b>  | <b>120</b>  |
| kreatinkináza ( $\mu\text{kat/l}$ ) | <b>6,9</b>  | N/A        | <b>3,1</b>  | <b>2,3</b>  |
| CRP (mg/l)                          | 326         | N/A        | 182         | 96          |
| aPTT (s)                            | N/A         | N/A        | 39,9        | N/A         |
| INR                                 | N/A         | N/A        | 1,1         | N/A         |
| pH                                  | 7,34        | 7,37       | 7,36        | 7,34        |
| pO <sub>2</sub> (kPa)               | 7,9         | 18,3       | 16,4        | 15,8        |
| pCO <sub>2</sub> (kPa)              | 6,4         | 6,0        | 6,0         | 5,6         |
| BE                                  | 0,1         | 1,0        | 0,6         | 0,1         |
| a-laktát (mmol/l)                   | <b>1,1</b>  | <b>0,8</b> | <b>0,7</b>  | <b>0,7</b>  |
| Mg <sup>2+</sup> (mmol/l)           | 1,26        | 1,13       | 1,15        | 1,10        |

# KAZUISTIKA



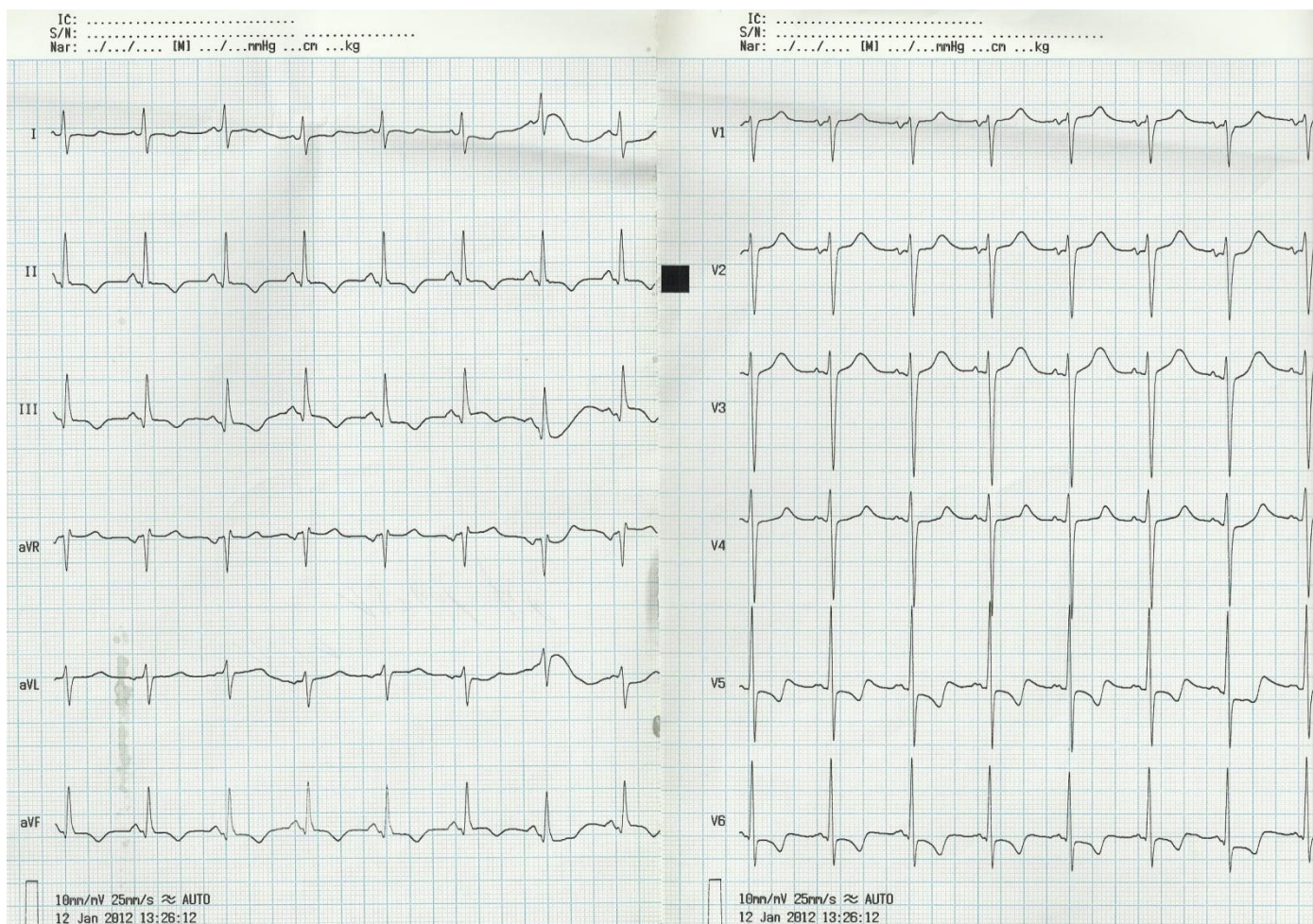


# KAZUISTIKA

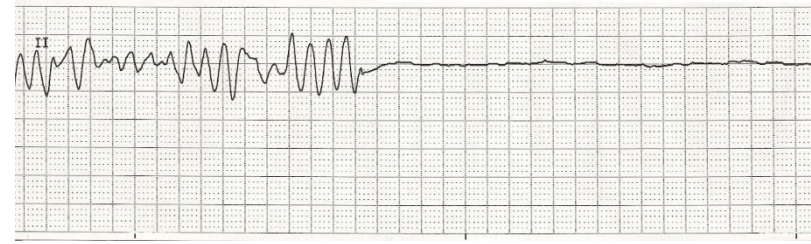




# KAZUISTIKA



# PRIS



## Metabolic acidosis and fatal myocardial failure after propofol infusion in children: five case reports

T J Parke, J E Stevens, A S C Rice, C L Greenaway, R J Bray, P J Smith, C S Waldmann, C Verghese

BMJ VOLUME 305 12 SEPTEMBER 1992

**Conclusion—Although the exact cause of death in these children could not be defined, propofol may have been a contributing factor.**

- akutní bradykardie rezistentní k léčbě
- progrese do asystolie
- steatóza jater, hyperlipidémie
- MAC, BE < -10mmol/l
- rabdomyolýza/myoglobinurie
- propofol >4mg/kg/h po dobu >48h

Paediatric Anaesthesia 1998 8: 491-499

## Propofol infusion syndrome in children

R.J. BRAY BA, MB BS, FRCA

Department of Anaesthesia, Royal Victoria Infirmary, Queen Victoria Road, Newcastle upon Tyne NE1 4LP, UK

### Summary

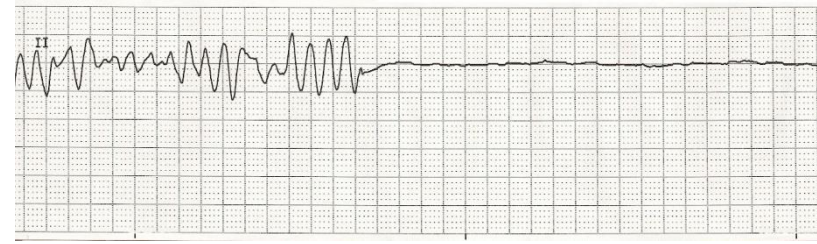
The use of propofol infusions to sedate children in intensive care units has decreased after reports of deaths from myocardial failure. More recently it has been suggested that propofol might have been

responsible for the death of about 18 children who had received serious unwanted effects. Three of the deaths occurred where propofol infusions had been administered during this period 44 children had been admitted to this unit and 10 had received long-term (>48 h), high-dose infusions and three had developed myocardial failure. There was a significant association between long-term, high-dose propofol

infusion and developing progressive myocardial failure (Fisher's Exact Test, two-tailed hypothesis,  $P=0.0128$ ) although a causative relationship could not be proved.



# PRIS



## Propofol infusion syndrome in anaesthesia and intensive care medicine

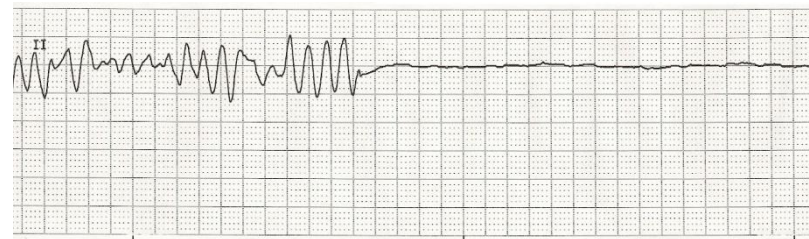
Axel Fudickar, Berthold Bein and Peter H. Tonner

Curr Opin Anaesthesiol 19:404–410. © 2006 Lippincott Williams & Wilkins.

- **incidence** <1%
- **dávka:** 0.4-30mg/kg/h
- **doba:** 0.5-196h



# PRIS: features



## Predictors of mortality in patients with suspected propofol infusion syndrome

Jeffrey J. Fong, PharmD, BCPS; Lynne Sylvia, PharmD; Robin Ruthazer, MPH; Greg Schumaker, MD; Marisol Kcomt, PharmD; John W. Devlin, PharmD, BCPS, FCCM, FCCP  
 Crit Care Med 2008 Vol. 36, No. 8

Table 2. Frequency of clinical manifestations associated with propofol infusion syndrome and nonsurvivors (n [%])

|                      | All Cases<br>(n = 1139) | (n [%]) | (n [%]) | (n [%]) | (n [%]) |
|----------------------|-------------------------|---------|---------|---------|---------|
| Cardiac              | 498 (44)                | 2       |         |         |         |
| Cardiac arrest       | 231 (20)                | 1       |         |         |         |
| Bradycardia          | 195 (17)                |         |         |         |         |
| Vtach/Vfib           | 177 (16)                |         |         |         |         |
| Myocardial failure   | 116 (10)                |         |         |         |         |
| Bradyarrhythmia      | 60 (5)                  |         |         |         |         |
| Hypotension          | 387 (34)                | 1       |         |         |         |
| Rhabdomyolysis       | 307 (27)                | 1       |         |         |         |
| Hepatic              | 275 (24)                |         |         |         |         |
| Transaminitis        | 263 (23)                |         |         |         |         |
| Hepatic steatosis    | 51 (5)                  |         |         |         |         |
| Hepatomegaly         | 19 (2)                  |         |         |         |         |
| Renal                | 268 (24)                | 1       |         |         |         |
| Renal failure        | 253 (22)                | 1       |         |         |         |
| Oliguria/anuria      | 47 (4)                  |         |         |         |         |
| Hyperkalemia         | 78 (7)                  |         |         |         |         |
| Metabolic acidosis   | 229 (20)                | 1       |         |         |         |
| Hypoxia              | 199 (18)                |         |         |         |         |
| Hyperthermia         | 132 (12)                |         |         |         |         |
| Dyslipemia           | 60 (5)                  |         |         |         |         |
| Hypertriglyceridemia | 52 (5)                  | 20 (6)  | 32 (4)  | 0.174   |         |
| Lipemia              | 16 (1)                  | 12 (4)  | 4 (0.5) | <0.0001 |         |

<sup>a</sup>Died vs. survived.

PRIS, propofol infusion syndrome; Vtach, ventricular tachycardia; Vfib, ventricular fibrillation.

## Update on the propofol infusion syndrome in ICU management of patients with head injury

Luuk C. Otterspoor<sup>a</sup>, Cornelis J. Kalkman<sup>b</sup> and Olaf L. Cremer<sup>a</sup>

Current Opinion in Anaesthesiology 2008, 21:544-554

symptomy kardiální 44%  
 hypotenze 34%  
 rabdomyolýza 27%  
 akutní poškození ledvin 24%  
 metabolická acidóza 20%  
 hyperlipidémie 5%

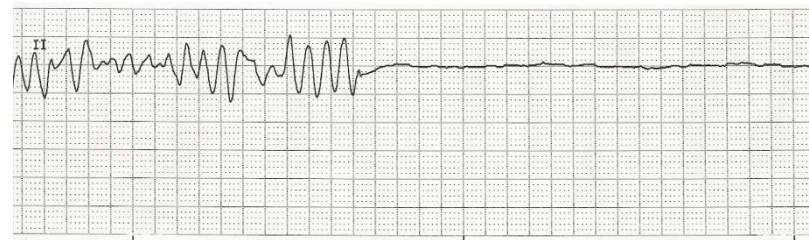
### Propofol infusion syndrome

#### Late signs

- Cardiovascular collapse
- Rhabdomyolysis
- Hyperkalemia
- Arrhythmia/heart block
- Renal failure

the right precordial leads

# PRIS: predictors



Predictors of mortality in patients with suspected propofol infusion syndrome

Jeffrey J. Fong, PharmD, BCPS  
 Marisol Kcomt, PharmD; John V  
 Crit Care Med 2008 Vol. 36, N

Table 3. Potential clinical and d

|                        | Mort     |                  |         |
|------------------------|----------|------------------|---------|
| Cardiac                |          |                  |         |
| Present (n = 498)      |          |                  |         |
| Not present (n = 641)  |          |                  |         |
| Hypotension            |          |                  |         |
| Present (n = 387)      |          |                  |         |
| Not present (n = 752)  |          |                  |         |
| Rhabdomyolysis         |          |                  |         |
| Present (n = 307)      |          |                  |         |
| Not present (n = 832)  |          |                  |         |
| Renal                  |          |                  |         |
| Present (n = 268)      |          |                  |         |
| Not present (n = 871)  |          |                  |         |
| Metabolic acidosis     |          |                  |         |
| Present (n = 229)      |          |                  |         |
| Not present (n = 910)  |          |                  |         |
| Dyslipidemia           |          |                  |         |
| Present (n = 60)       |          |                  |         |
| Not present (n = 1079) |          |                  |         |
| Use of catecholamines  |          |                  |         |
| Present (n = 169)      |          |                  |         |
| Not present (n = 970)  |          |                  |         |
| Gender                 |          |                  |         |
| Male (n = 584)         | 134 (35) | 1.34 (1.04-1.74) | 0.0234  |
| Female (n = 511)       | 138 (27) |                  |         |
| Age                    |          |                  |         |
| Under 18 (n = 199)     | 92 (46)  | 2.30 (1.68-3.17) | <0.0001 |
| 18 or older (n = 817)  | 817 (27) |                  |         |

**vysoké dávky katecholaminů**

**nízký příjem sacharidů v dietě**

**vysoký příjem tuků v dietě**

**SIRS/sepse**

**steroidy?**

**polyneuromuskulopatie kriticky nemocných?**

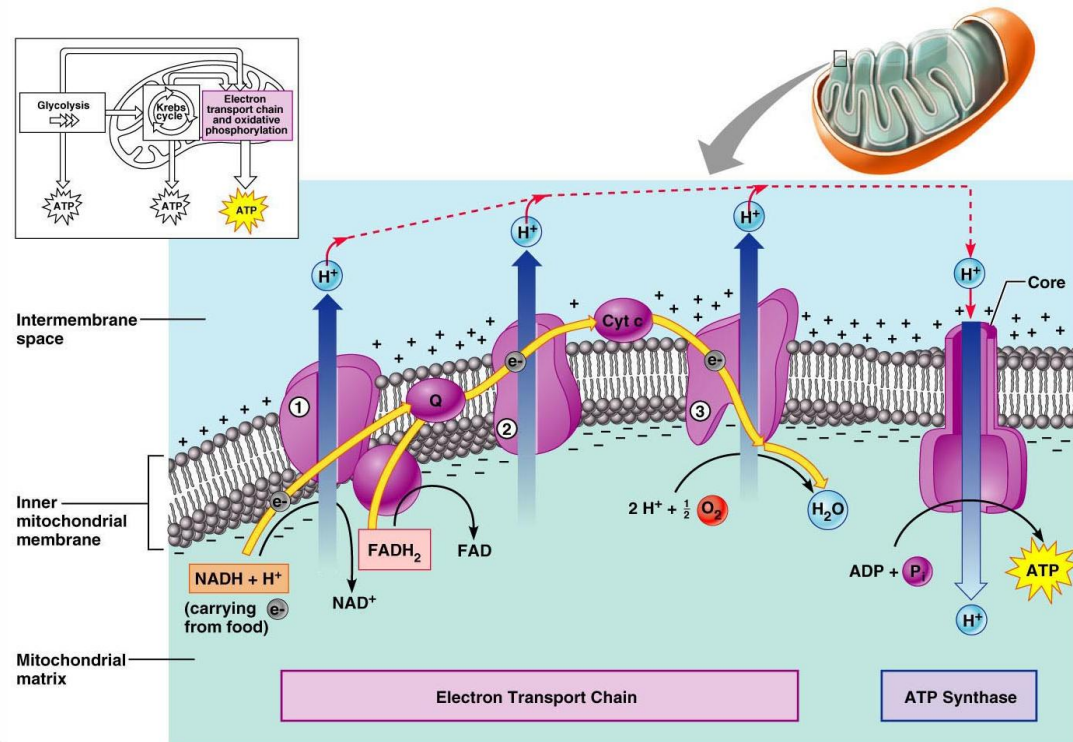
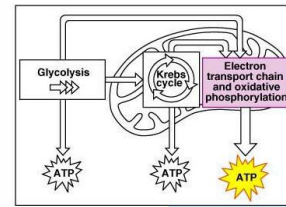
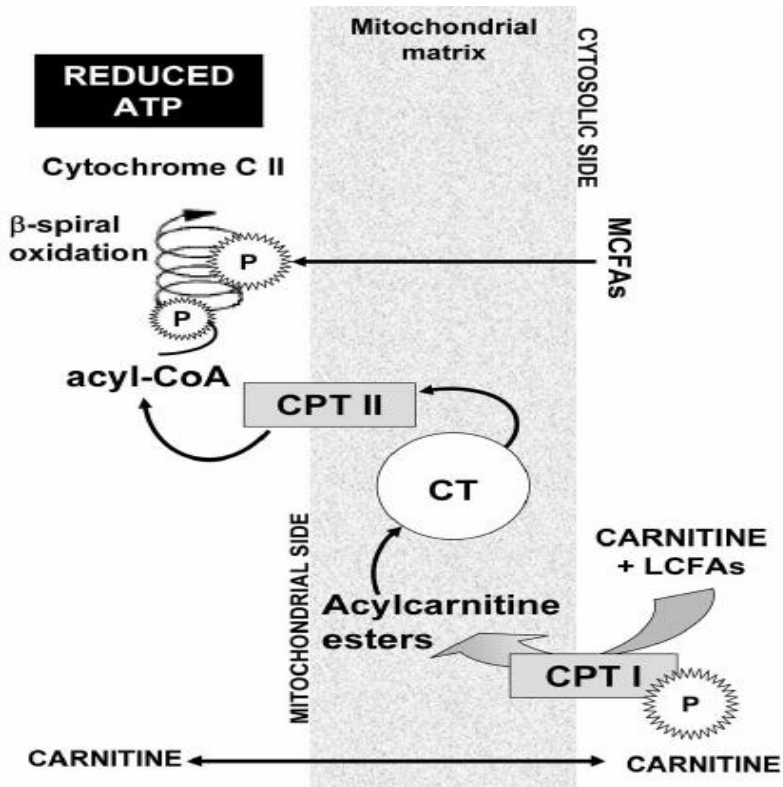
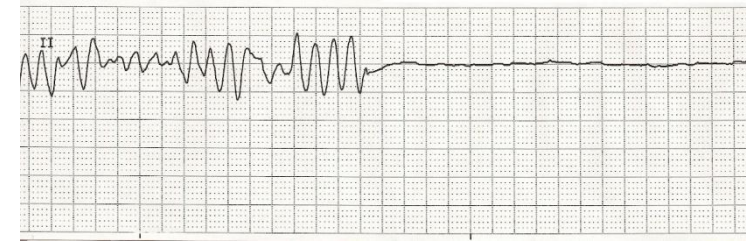
**vrozené defekty respiračního řetězce (MCADD)**

ology of propofol infusion  
 mple name for a complex

naesthesia and intensive

H. Tonner

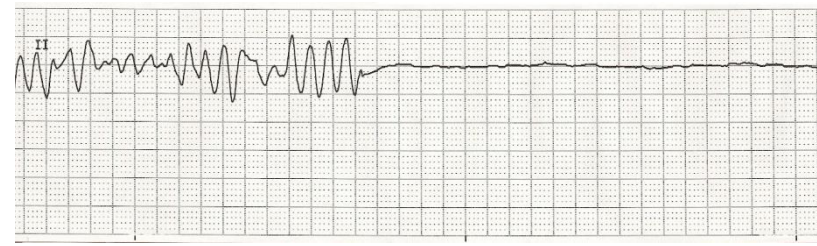
# PRIS: pathophysiology



- rozpojení oxidativní fosforylace a produkce energetických substrátů
- narušení toku elektronů
- antagonizace účinku katecholaminů na  $\beta$ -receptorech
- $\uparrow$  senzitivity acetylcholinových receptorů
- inhibice L-type Ca-kanálů  $\rightarrow$   $\downarrow$  kontraktilita myokardu



# PRIS: ECG pattern



*Heart Rhythm.* 2006 February ; 3(2): 131–137.

## Electrocardiographic changes predicting sudden death in propofol-related infusion syndrome

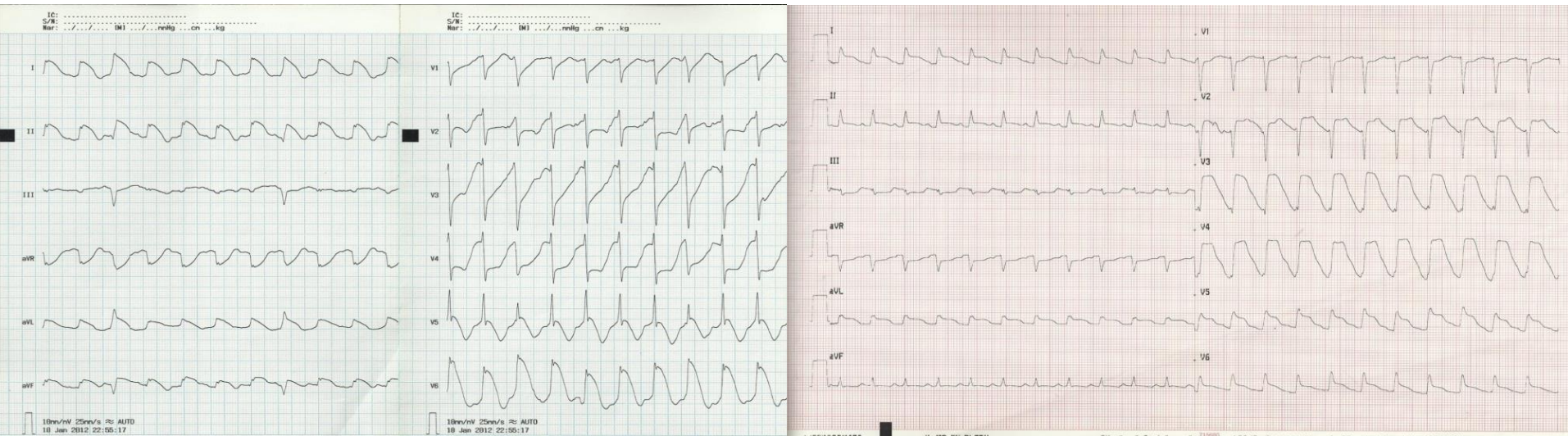
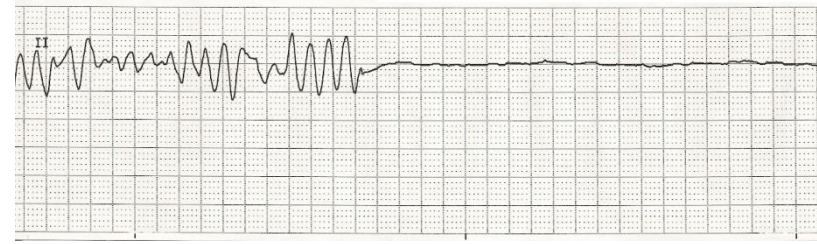
Kevin Vernoooy, MD<sup>a</sup>, Tammo Delhaas, MD, PhD<sup>a</sup>, Olaf L. Cremer, MD<sup>b</sup>, José M. Di Diego, MD<sup>c</sup>, Antonio Oliva, MD<sup>c</sup>, Carl Timmermans, MD, PhD<sup>a</sup>, Paul G. Volders, MD, PhD<sup>a</sup>, Frits W. Prinzen, PhD<sup>a</sup>, Harry J.G.M. Crijns, MD, PhD<sup>a</sup>, Charles Antzelevitch, PhD<sup>c</sup>, Cornelis J. Kalkman, MD, PhD<sup>b</sup>, Luz-Maria Rodriguez, MD, PhD<sup>a</sup>, and Ramon Brugada, MD<sup>d</sup>

## Conclusion

Our data indicate that development of the ECG pattern of ST-segment elevation in leads V<sub>1</sub> to V<sub>3</sub> is the first indicator of electrical instability and high risk for imminent sudden death. The data are based on a cohort of individuals with PRIS. Whether this finding applies to other patient cohorts is unclear, but the association of sudden death and the acquired ECG pattern has been observed in other disease states.<sup>18</sup>

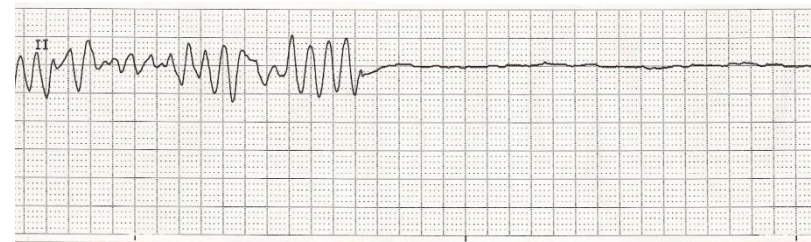
Our data suggest that ECG monitoring in patients receiving high-dose propofol can avert sudden cardiac death by alerting the physician to impending cardiac rhythm disturbances following the appearance of marked ST-segment elevation in the right precordial leads.

# PRIS: ECG pattern

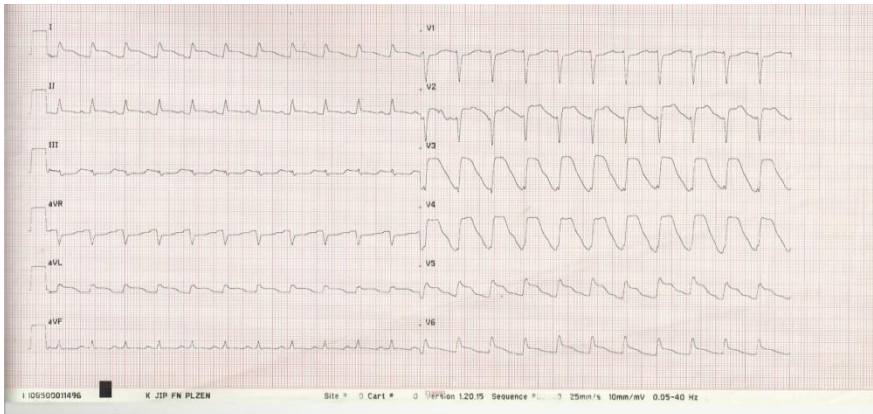




# PRIS: #01- #04



- věk: 27 (23;31)
- dávka propofolu: 1.3-7.2mg/kg/h
- doba podání: 2-5 dní
- poškození CNS: posthypoxické a/nebo epileptický status
- 1. varovný příznak:  $\Delta$ EKG vč. LQT



## MICHAEL JACKSON'S DEATH

Pop star Michael Jackson died from a lethal dose of the powerful anaesthetic Propofol given in a cocktail of drugs, leading authorities to suspect his doctor of manslaughter, court documents showed on Monday

**June 25**

11:30 a.m. (1830 GMT) Jackson reportedly received a range of medication from his personal physician, Dr. Conrad Murray, at his rental home in the Holmby Hills in L.A.

12:21 p.m. (1921 GMT) An unidentified man makes a 911 emergency call from the house, saying Jackson is unconscious and not breathing. Paramedics arrive a few minutes later, and treat him for 42 minutes. He is rushed to the nearby Ronald Reagan UCLA Medical Center

2:26 p.m. (2126 GMT) - Jackson is pronounced dead at the hospital. His body is flown by helicopter to the L.A. County Coroner's office, about 27 km away near downtown Los Angeles

4:35 p.m. (2335 GMT) The L.A. County Coroner confirms Jackson's death

**June 26**

2:20 p.m. (2120 GMT) - The L.A. County Coroner says an autopsy did not reveal any signs of foul play or external trauma, and orders toxicology tests that could take up to six weeks to complete

**June 27**

9:30 p.m. (Saturday/0430 GMT) Jackson's body is released to his family

11:47 a.m. (1847 GMT) - Celebrity gossip news site TMZ.com reports that Jackson's family has requested a second autopsy

4 p.m. (2300 GMT) The celebrity website TMZ.com reports that a second autopsy is underway in Los Angeles, on the orders of the Jackson family

7 p.m. (Sunday/0200 GMT) Dr. Conrad Murray, who was with the singer when he collapsed, is questioned again by L.A. police

### DRUGS REPORTED TO HAVE BEEN ADMINISTERED TO JACKSON

**DIPRIVAN (Propofol)**  
Short-acting sedative used for general anaesthesia, often on patients with a machine to help them breathe

**VERSED (Midazolam)**  
Sedative used to calm patients before a surgical procedure.

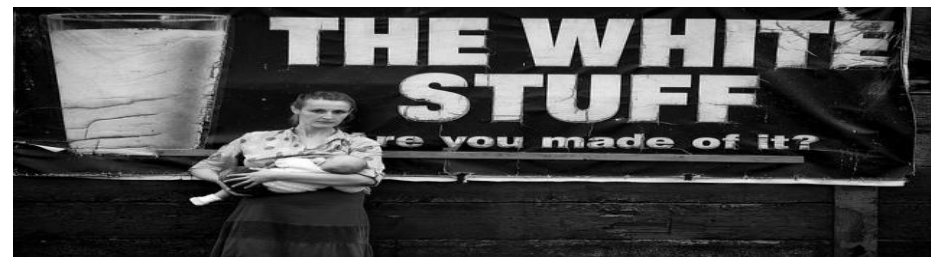
**LIDOCAINE (Xylocaine)**  
Used for anaesthesia, it can cause loss of consciousness

**VALIUM (Diazepam)**  
Anti-anxiety drug that can be habit-forming

**ATIVAN (Lorazepam)**  
Used for general anxiety disorder and sleeping problems

REUTERS

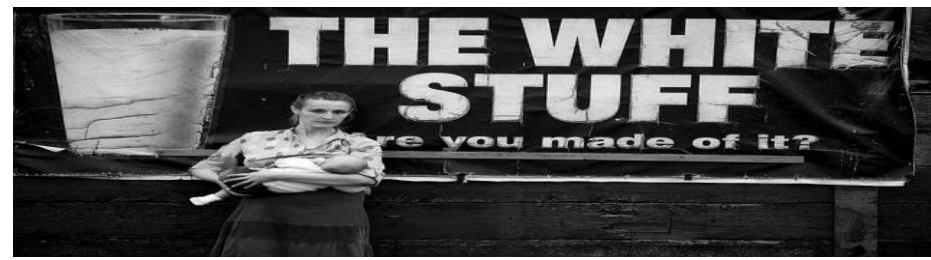
# PRIS: summary



- minimalizovat dávku propofolu („protokolizovaná sedace“):  $\leq 4\text{mg/kg/h}$
- minimalizovat dobu podání („protokolizovaná sedace“):  $< 7$  dní
- monitorace EKG vč. **morfologie (QRS + QT)**
- predisponující faktory
- aktivní přístup – myslet na komplikace/PRIS



# PRIS: summary



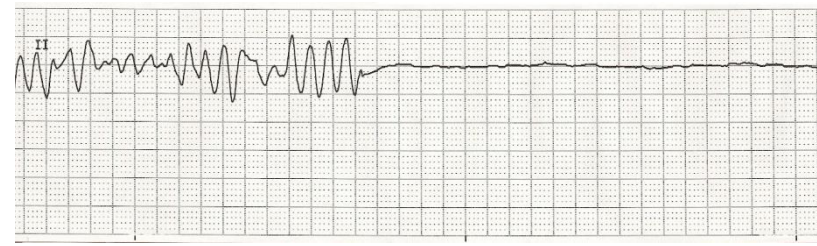
## Při podezření na rozvoj/probíhající PRIS:

- okamžitě ukončit aplikaci propofolu
- aplikovat glukózu 6-8mg/kg/min
- kontrola EKG (12-svod) + ABR + laktátu + kardiomarkerů + triglyceridů
- komplexní podpůrná léčba
- CRRT
- ECMO

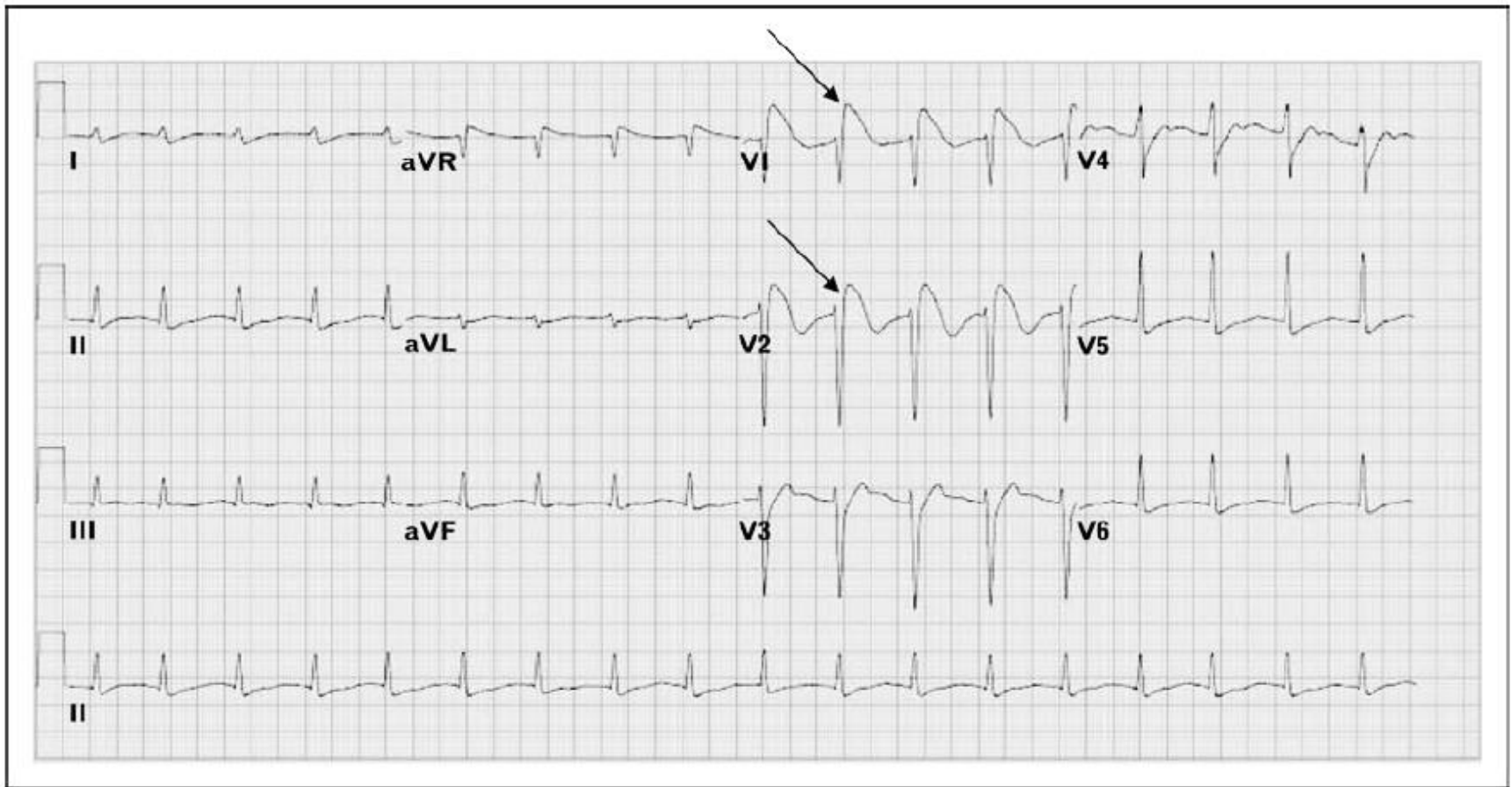




# PRIS: ECG pattern



## BRUGADA-LIKE PATTERN



DĚKUJI ZA POZORNOST...

