

# Doit on encore utiliser l'adrénaline pour la réanimation des arrêts cardiaques ?

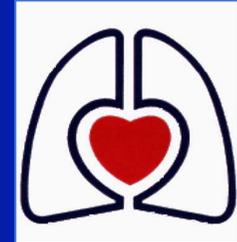
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# Algorithme de la RCP médicalisée 2010



Pas de réaction  
Pas de ventilation  
ou gags occasionnels

Appeler  
l'équipe de réanimation

RCO 30:2  
Brancher le défibrillateur / moniteur  
limiter les interruptions du MCE

Analyse  
du Ry thme

Chocable  
FV, TV sans pouls

NON Chocable  
Asystole, R sans pouls

1 Choc

Retour à une  
circulation spontanée

Reprendre immédiatement  
la RCP pendant 2 min  
Limiter les interruptions du MCE

Reprendre immédiatement  
la RCP pendant 2 min  
Limiter les interruptions du MCE

Réanimation immédiate post ACR

- Examen clinique « ABCDE »
- Oxygénation et ventilation contrôlée
- ECG 12 dérivations
- Traitement des causes déclenchantes
- Contrôle de la température et hypothermie thérapeutique

Pendant la RCP

- Assurer un MCE de qualité:
  - Fréquence , profondeur, relaxation
- Préparer les interventions avant d'interrompre le MCE
- Oxygénation
- Envisager le contrôle spécialisé des voies aériennes et la capnographie
- Compression thoracique en continu après contrôle des voies aériennes
- Accès vasculaire (IV ou intra-osseux)
- **Adrénaline toutes les 3-5 min**
- Traitement des causes curables

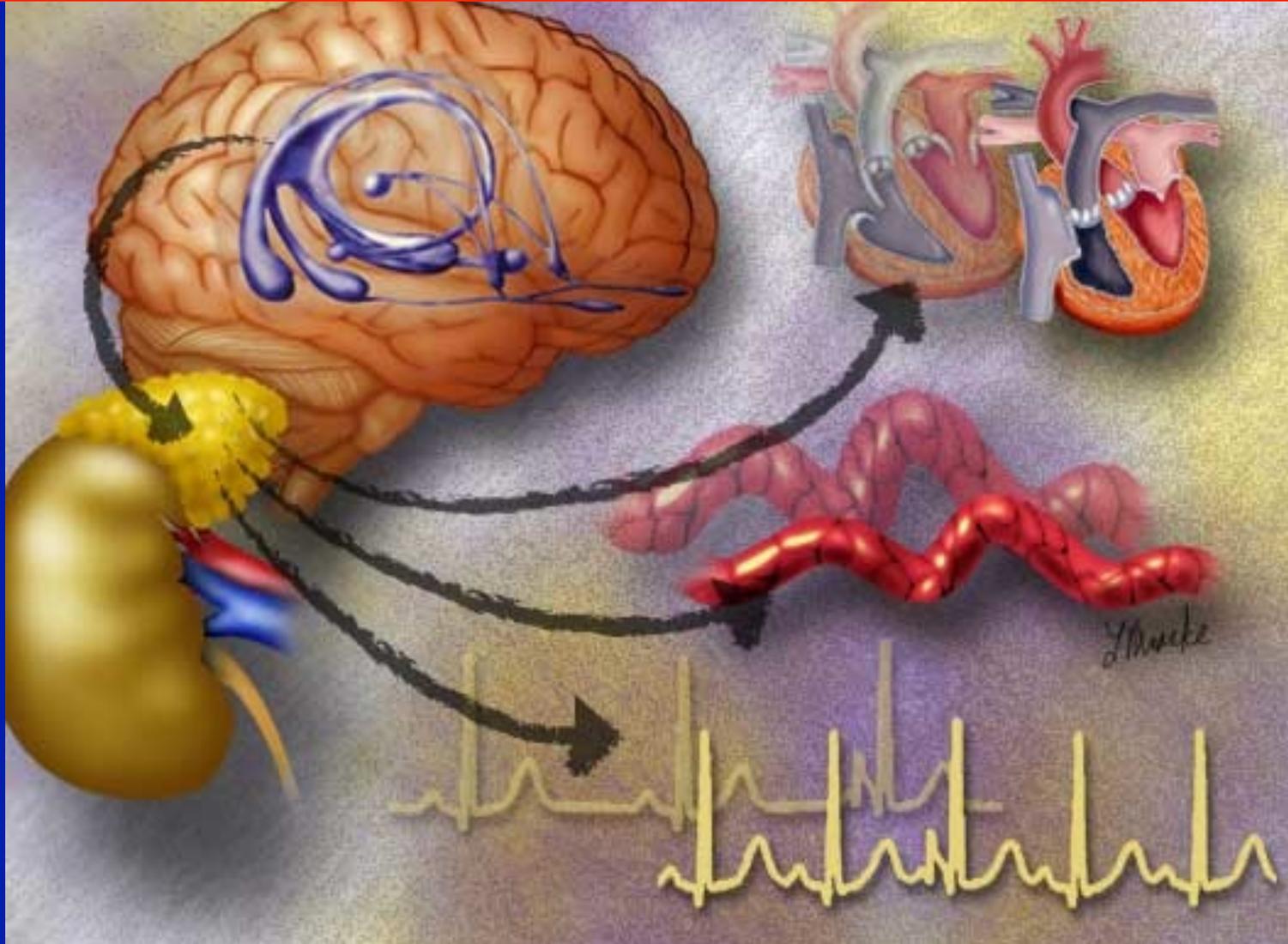
Les causes « curables »

- Hypoxie
- Hypovolémie
- Hypo - hyper kaliémie / causes métaboliques
- Hypothermie
- Thrombose
- Tamponnade
- Toxique
- Pneumothorax suffocant

# Adrénaline en 2010

- **Pour la FV et la TV sans pouls**
  - 1mg d'adrénaline IV si elle persiste après un 3ème choc et avant l'amiodarone
  - 1 mg toutes les 3 à 5 minutes ensuite si le trouble du rythme persiste.
- **Rythme sans pouls et asystole :**
  - 1 mg d'Adrénaline IV dès qu'une voie veineuse (ou IO) est obtenue
  - réinjecter toutes les 3 à 5 minutes jusqu'à ce qu'il y est le retour à une circulation spontanée.

**Adrénaline :  
une thérapeutique utilisée dans l'arrêt cardiaque depuis 1906**



**Sans réelle évaluation  
mais une nécessité de limitation des Effets Indésirables**

# L'adrénaline : Pourquoi ?

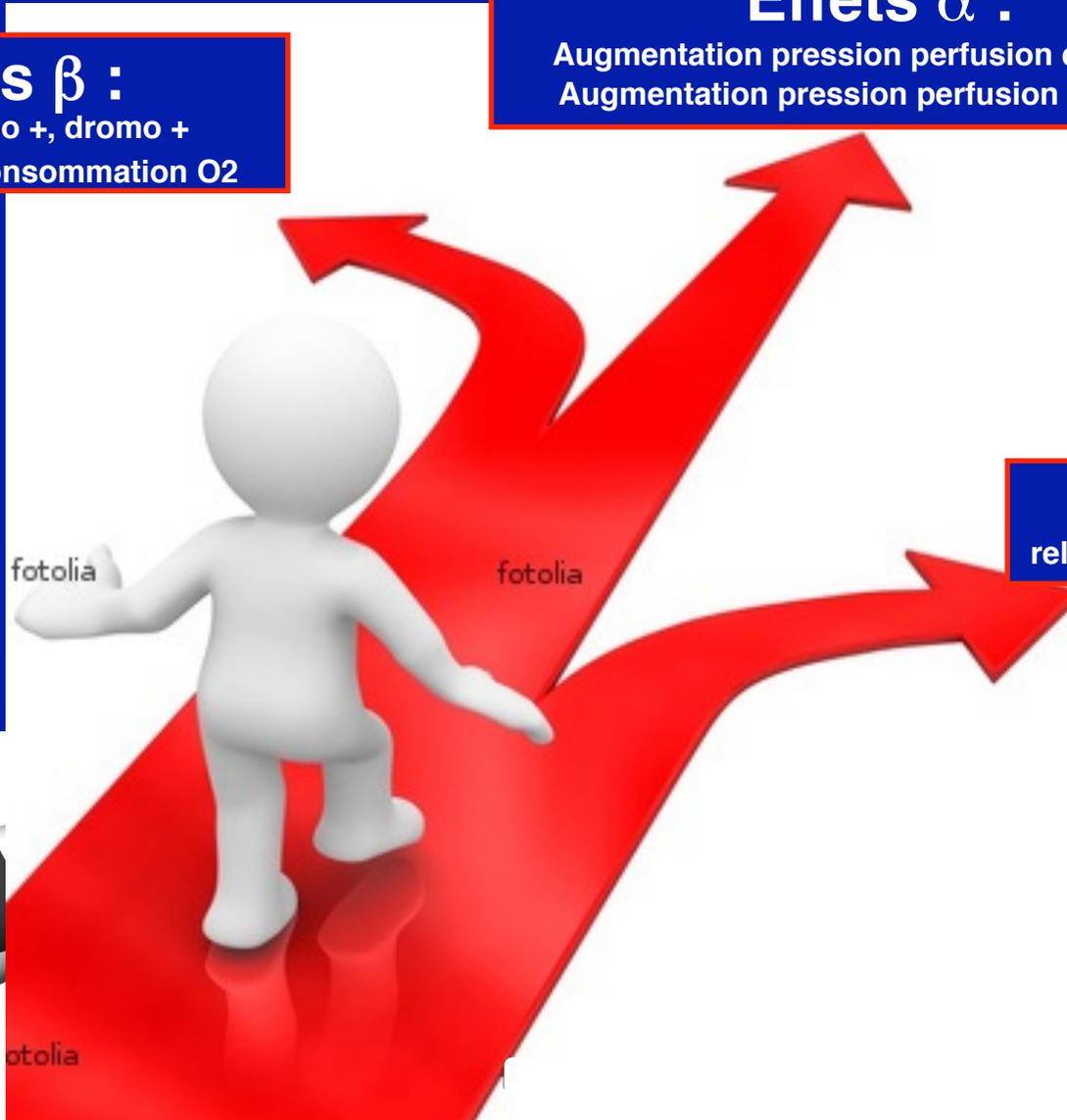
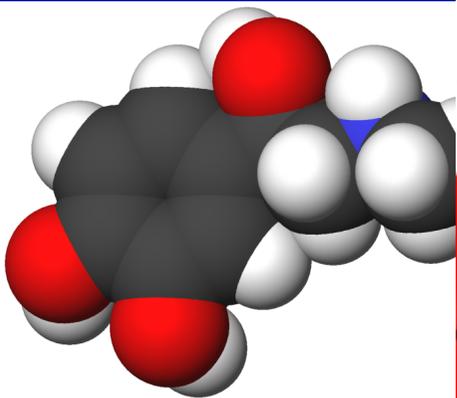
## Effets $\beta$ :

Bath +, chrono +, dromo +  
Augmentation consommation O<sub>2</sub>

## Effets $\alpha$ :

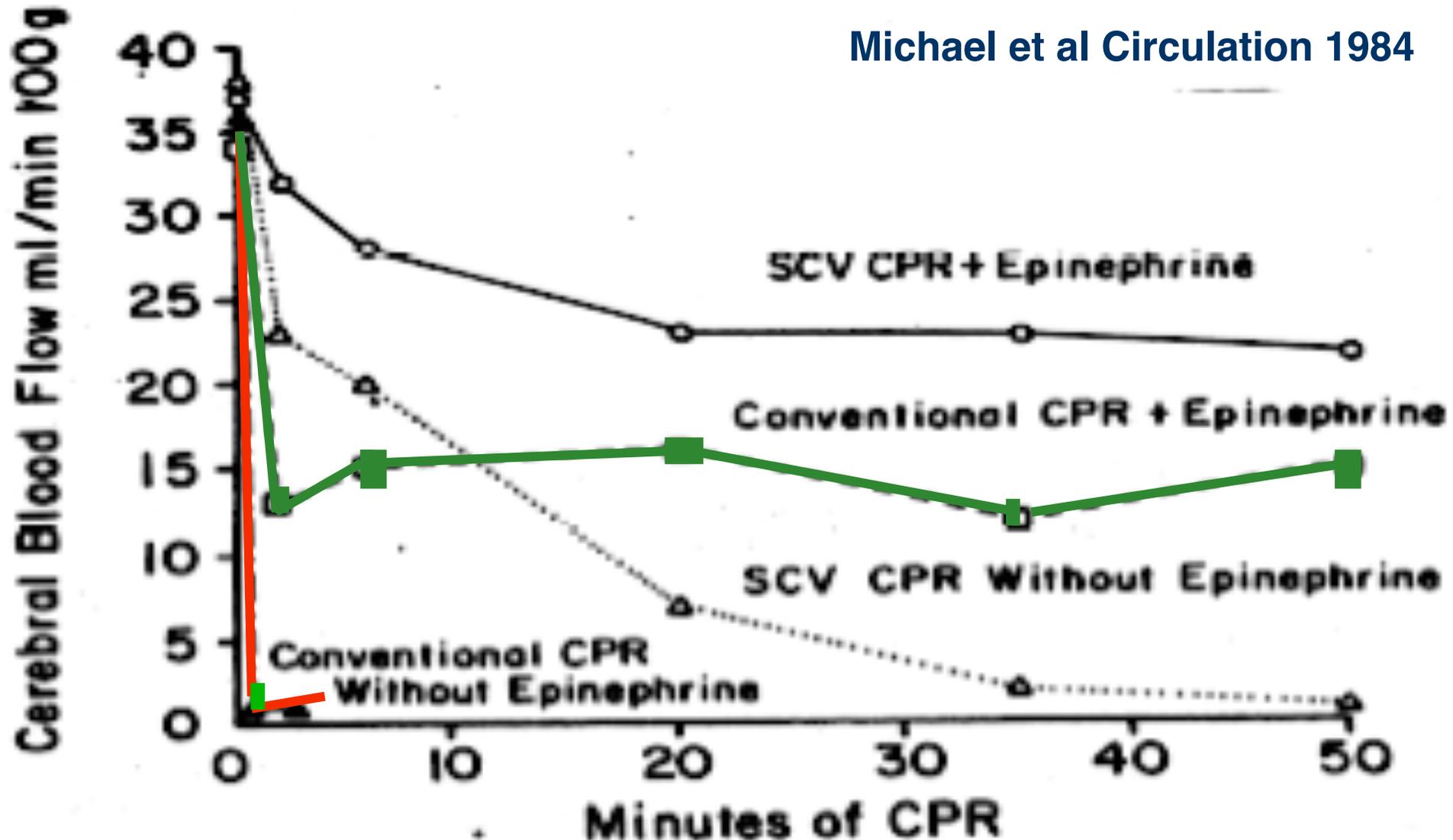
Augmentation pression perfusion coronaire  
Augmentation pression perfusion cérébrale

Effets endocriniens,  
bronchodilatateurs,  
relaxation des muscles lisses



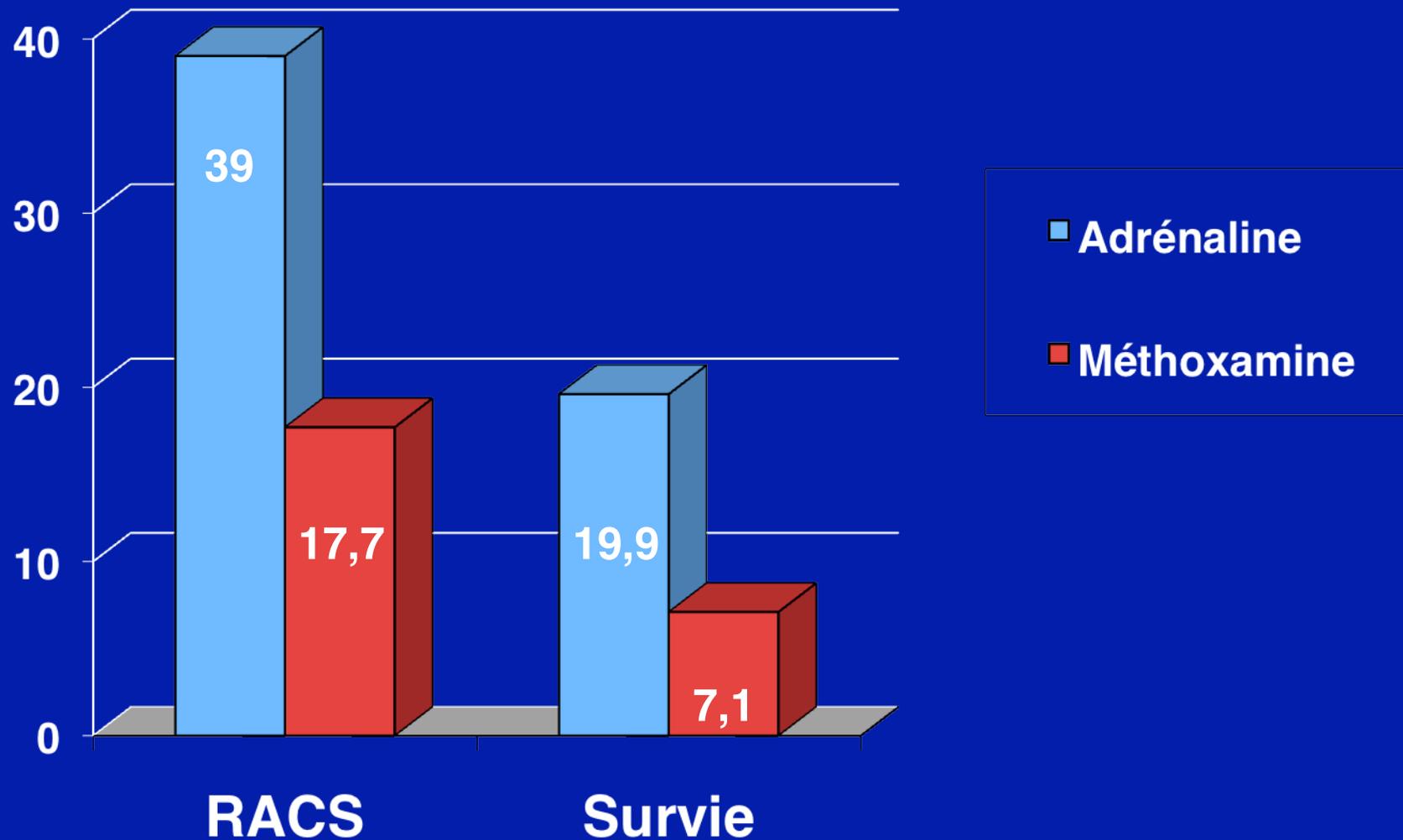
# Perfusion cérébrale et adrénaline

Michael et al Circulation 1984



# Adrénaline ou $\alpha$ 2 agoniste pur ?

Olson et al. Ann Emerg Med 1989



# Adrénaline, noradrénaline ou dopamine

## ▶ **Noradrénaline**

- ▶ Callaham JAMA 1992
- ▶ Noradrenaline vs adrenaline standard vs adrénaline forte dose : pas de différence significative

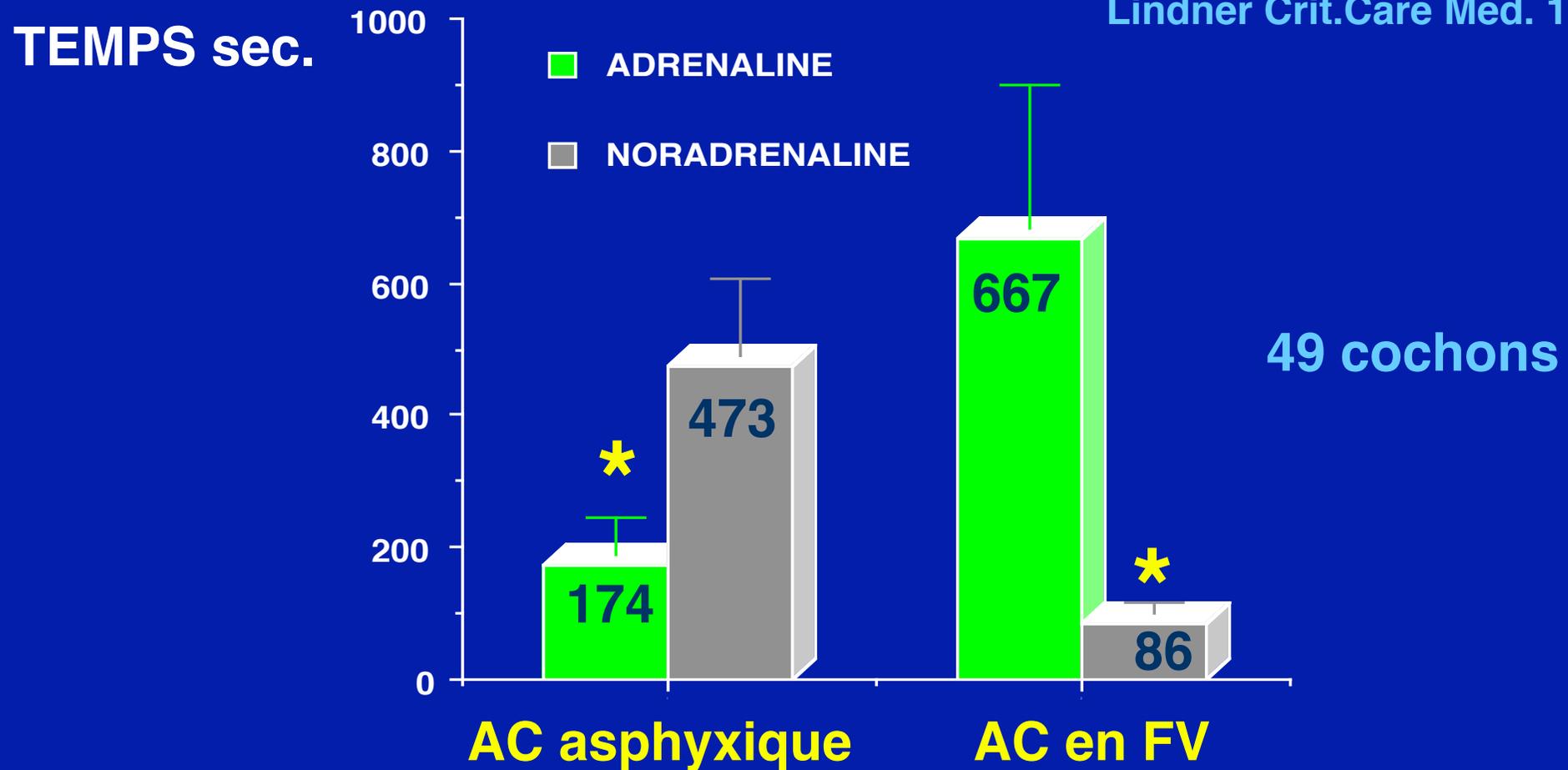
## ▶ **Dopamine**

- ▶ Des études animales incertaines
- ▶ Aucune étude clinique

# Adrénaline ou noradrénaline ?

## Temps de récupération de l' AC

Lindner Crit.Care Med. 1989



# **A comparison of repeated high doses and repeated standard doses of epinephrine for cardiac arrest outside the hospital**

P.Y Gueugniaud NEJM 1998

**Etude multicentrique randomisée (12 centres)**

**Adrénaline 1 mg versus 5 mg**

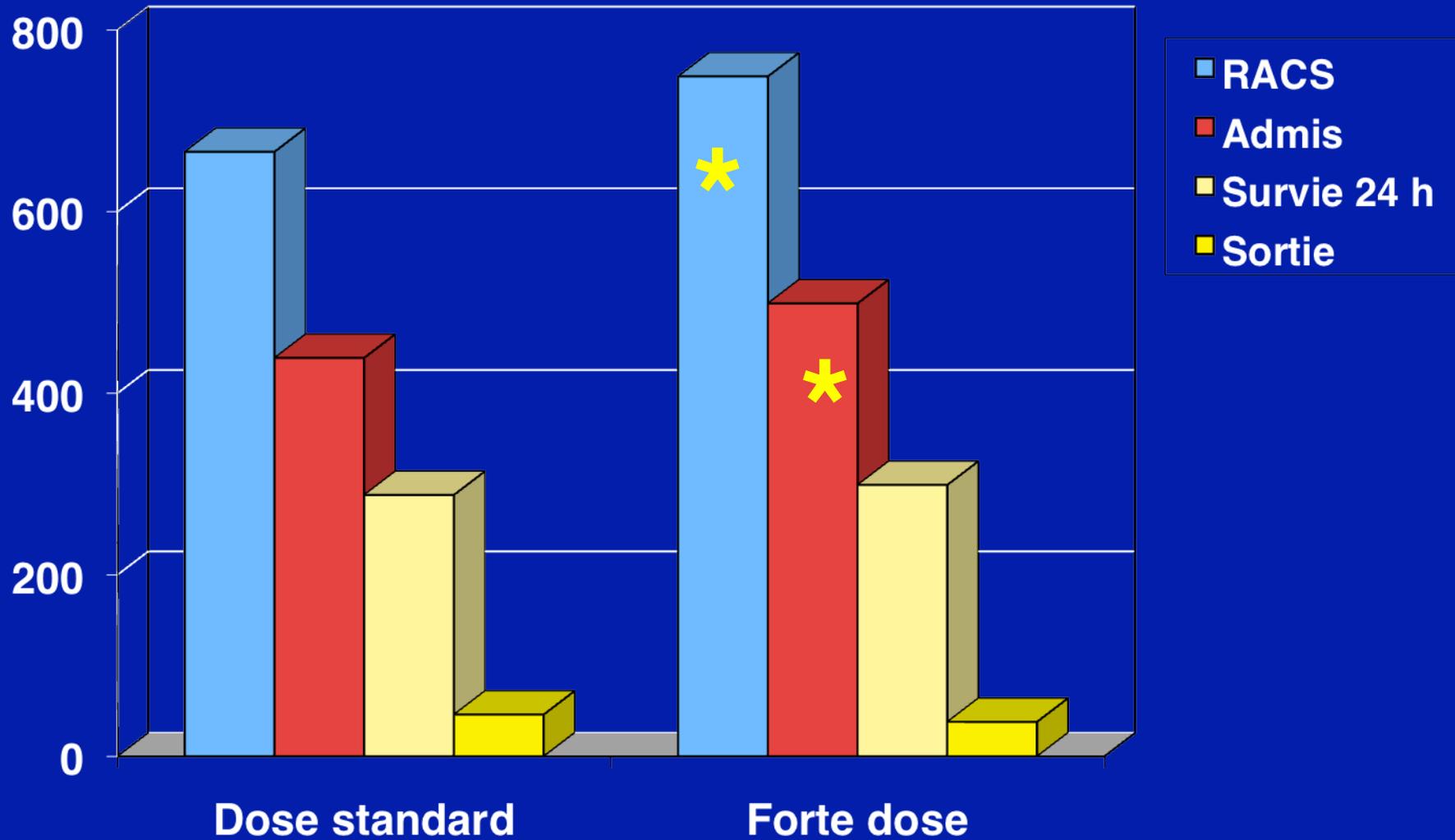
**Réanimation / recommandations internationales**

**Scores neurologiques et survie**

**3327 patients (n = 1650 / 1 mg et n = 1677 / 5 mg)**

# Quelle dose d'adrénaline ?

Gueugniaud N Engl J Med 1998



ORIGINAL ARTICLE

## Vasopressin and Epinephrine vs. Epinephrine Alone in Cardiopulmonary Resuscitation

Pierre-Yves Gueugniaud, M.D., Ph.D., Jean-Stéphane David, M.D., Ph.D., Eric Chanzy, M.D., Hervé Hubert, Ph.D., Pierre-Yves Dubien, M.D., Patrick Mauriauourt, M.D., Coralie Bragança, M.D., Xavier Billères, M.D., Marie-Paule Clotteau-Lambert, M.D., Patrick Fuster, M.D., Didier Thiercelin, M.D., Guillaume Debaty, M.D., Agnès Ricard-Hibon, M.D., Patrick Roux, M.D., Catherine Espesson, M.D., Emgan Querellou, M.D., Laurent Ducros, M.D., Patrick Ecollan, M.D., Laurent Halbout, M.D., Dominique Savary, M.D., Frédéric Guillaumée, M.D., Régine Maupoint, M.D., Philippe Capelle, M.D., Cécile Bracq, M.D., Philippe Dreyfus, M.D., Philippe Nougier, M.D., Antoine Gache, M.D., Claude Meurisse, M.D., Bertrand Boulanger, M.D., Claude Lae, M.D., Jacques Metzger, M.D., Valérie Raphael, M.D., Arielle Beruben, M.D., Volker Wenzel, M.D., Comlavi Guinhouya, Ph.D., Christian Vilhelm, Ph.D., and Emmanuel Marret, M.D.

## Vasopressin and epinephrine VS epinephrine alone in cardiopulmonary resuscitation

Gueugniaud PY, NEJM, 2008, 359

**n = 2894**

	Adrenaline (n = 1452)	A + V (n = 1442)	P
ROSC	29.5 %	28.6 %	0.62
Hospital admission	21.3 %	20.7 %	0.69
Hospital discharge	2.3 %	1.7 %	0.24
1 Year survival	2.1 %	1.3 %	0.09

Pas de différence significative

# Intravenous Drug Administration During Out-of-Hospital Cardiac Arrest

## A Randomized Trial

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Theresa M. Olasveengen, MD

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Kjetil Sunde, MD, PhD

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Cathrine Brunborg, MSc

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Jon Thowsen

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Petter A. Steen, MD, PhD

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Lars Wik, MD, PhD

**Context** Intravenous access and drug administration are included in advanced cardiac life support (ACLS) guidelines despite a lack of evidence for improved outcomes. Epinephrine was an independent predictor of poor outcome in a large epidemiological study, possibly due to toxicity of the drug or cardiopulmonary resuscitation (CPR) interruptions secondary to establishing an intravenous line and drug administration.

**Objective** To determine whether removing intravenous drug administration from an ACLS protocol would improve survival to hospital discharge after out-of-hospital cardiac arrest.

## In-Hospital Treatment and Outcome

**Table 2.** In-Hospital Treatment and Outcome

	No Intravenous (n = 433)	Intravenous (n = 418)	P Value <sup>a</sup>
Any ROSC during resuscitation	107 (25)	165 (40)	<.001
Admitted to hospital	126 (29)	178 (43)	<.001
ROSC	89 (21)	133 (32)	<.001
Ongoing CPR	37 (9)	45 (11)	.33
Admitted to ICU <sup>b</sup>	88 (20)	125 (30)	.002
Awake at ICU admission	8 (9)	7 (6)	.48
Therapeutic hypothermia	62 (70)	90 (72)	.93
Angiography or PCI	43 (49)	50 (40)	.33
Time in ICU, median (range), d <sup>c</sup>	6 (1-31)	4 (1-44)	.05
Cause of death in ICU <sup>d</sup>			
Brain	29 (69)	52 (70)	>.99
Cardiac	8 (19)	12 (16)	.90
Multiorgan failure	5 (12)	10 (14)	>.99
Discharged alive	40 (9.2)	44 (10.5)	.61
Cerebral performance score at discharge			
1 (good cerebral performance)	30 (7.0)	37 (8.9)	.31
1-2 (good cerebral performance to moderate cerebral disability)	35 (8.1)	41 (9.8)	.45
2 (moderate cerebral disability)	5 (1.2)	4 (1.0)	>.99
3 (severe cerebral disability)	3 (1.0)	3 (1.0)	>.99
4 (coma or vegetative state)	2 (<1.0)	0	.50
Discharged from hospital if admitted to ICU	40 (45)	44 (35)	.17
Alive 1 y after cardiac arrest <sup>e</sup>	36 (8)	41 (10)	.53

Abbreviations: CPR, cardiopulmonary resuscitation; ICU, intensive care unit; PCI, percutaneous coronary intervention; ROSC, return of spontaneous circulation.

<sup>a</sup>The differences between groups were analyzed using the  $\chi^2$  test with continuity correction for categorical data and the Mann-Whitney test for number of days in the ICU.

<sup>b</sup>Includes patients admitted to the ICU only.

<sup>c</sup>Data are missing for 3 patients in each group.

<sup>d</sup>Includes patients who died in the ICU only. Data are missing for 6, leaving 42 as the denominator in the group with advanced life support without intravenous access or drug administration (no intravenous), and 7, leaving 74 as the denominator in the group with advanced cardiac life support and intravenous access and administration of drugs (intravenous).

<sup>e</sup>Two patients in the no intravenous group and 1 patient in the intravenous group were lost to 1-year follow-up.

## Outcome for Subgroups With and Without Ventricular Fibrillation or Pulseless Ventricular Tachycardia Rhythms

Olasveengen, T. M. et al. JAMA 2009;302:2222-2229.

**Table 3.** Outcome for Subgroups With and Without Ventricular Fibrillation or Pulseless Ventricular Tachycardia Rhythms

	With Rhythms, No. (%)			Without Rhythms		
	No Intravenous (n = 142)	Intravenous (n = 144)	P Value <sup>a</sup>	No Intravenous (n = 291)	Intravenous (n = 274)	P Value <sup>a</sup>
Any ROSC during resuscitation	75 (53)	85 (59)	.35	32 (11)	80 (29)	<.001
Admitted to hospital	79 (56)	94 (65)	.12	47 (16)	84 (31)	<.001
Admitted to ICU	60 (42)	74 (51)	.15	28 (10)	51 (19)	.003
Discharged alive	32 (23)	39 (27)	.45	8 (3)	5 (2)	.65
Discharged with CPC score of 1-2	29 (20)	37 (26)	.36	6 (2)	4 (2)	.82
Discharged if admitted to ICU	32 (53)	39 (53)	>.99	8 (29)	5 (10)	.07

Abbreviations: CPC, cerebral performance score; ICU, intensive care unit; ROSC, return of spontaneous circulation.

<sup>a</sup>The differences between the groups were analyzed using the  $\chi^2$  test with continuity correction.

**Intérêt de l'adrénaline dans les asystoles**

## Intravenous drug administration during out-of-hospital cardiac arrest.

TM Olasveengen *et al* JAMA 2009; 302: 2222-9.

### Limites de l'étude

- Durée étude = 5 ans ...
- Monocentrique
- Tirage au sort mais pas d'aveugle
- Inclusion de certains patients par défaut (VVP impossible)
- Pas d'évaluation RCP
- ... Impossibilité à conclure / Pb population insuffisante ...

## Outcome when adrenaline (epinephrine) was actually given vs not given - post hoc analysis of a randomized clinical trial

Olasveengen T, Wik L Resuscitation 2011

- ▶ Reprise de l'étude : 851 patients tirage au sort exclusif

	Non adr� 481	Adr� 367	P
Admis H	128 (27)	<b>175 (48)</b>	< 0,001
Conscients � l'admission	<b>14 (13)</b>	1(1)	0,002
Sortis vivants	<b>60 (13)</b>	24 (7)	0,006
CPC 1-2	<b>57 (11)</b>	19 (5)	0,001
Vivants � 1 an	<b>56 (12)</b>	21 (6)	0,004

**Adr naline : Plus de RACS mais moins de survie**

# Outcome when adrenaline (epinephrine) was actually given vs not given - post hoc analysis of a randomized clinical trial

Olasveengen T, Wik L Resuscitation 2011

- **Régression logistique**

Facteurs confondants : FV/TV, AC dvt Témoin, délai de PEC, âge et intubation

	Survivants Odds Ratio	IC 95 %	P
FV ou TV initiale	15,6	7,75-31,41	<0,001
AC dvt témoin	2,33	1,08-5,01	0,031
Age	0,96	0,95-0,98	<0,001
Délai PEC / min	0,81	0,75-0,88	<0,001
Adrénaline	0,52	0,29-0,92	0,024
Intubation	0,38	0,20-0,72	0,003

**Patients du groupe Adrénaline ont une probabilité de survie diminuée de 48 % / patients sans adrénaline**

# Adrénaline ou placebo



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*Achieving International Excellence*



## *Placebo versus Adrenaline in Cardiac Arrest*

### *The PACA Trial*

**Professor Ian Jacobs**

Discipline of Emergency Medicine – University of Western Australia  
Clinical Services Director – WA Ambulance Service

**AHA - Nov 2010**

# Effect of adrenaline on survival in out of cardiac arrest : A randomised double blind placebo trial

Jacobs IG, Resuscitation 2011, 82 , 9 : 1138-43

- **1ère** Etude randomisée en double aveugle
- 2006 à 2009 ... monocentrique ...
- 4107 AC et 1586 RCP
- 602 inclusions / 535 analysés
- = 66 % exclusions !
- « Primary end point = survival to discharge hospital » !!
- « Secondary end point = ROSC and CPC »

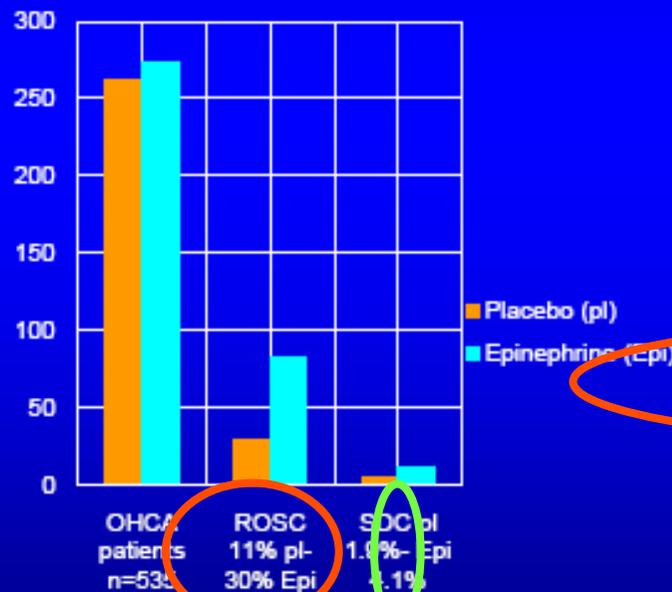
# A Randomised Placebo Controlled Trial of Adrenaline in Cardiac Arrest - The PACA Trial



**BACKGROUND:** Adrenaline (Epinephrine) remains the primary pharmacological agent in cardiac arrest. Despite a total absence of any experimental trials to establish efficacy, adrenaline is considered standard of care in resuscitation.

**PURPOSE:** To assess if Adrenaline (Epinephrine) is related to return of spontaneous circulation (ROSC), survival to hospital discharge (SDC) and neurological outcome (Cerebral Performance Category Score) at discharge.

## A Randomized Placebo Controlled Trial of Epinephrine in Cardiac Arrest



**Primary Endpoints:** SDC

**Secondary Endpoints:** ROSC and neurological outcome at discharge

**Results:** During the study period paramedics attended 4107 cardiac arrests of which resuscitation was commenced in 1586 (38.6%) patients. Of these 602 (37.9%) were enrolled into the study with a further 67 (11.1%) being excluded after randomization. Of the remaining 535 patients 262 (48.9%) and 273 (51.0%) received placebo or adrenaline respectively. The percentage male (70.6% versus 74.8%); mean age (64.8 versus 65.4 years) and percentage of patients who received bystander CPR (55.7% versus 53.1%) were similar for the adrenaline and placebo groups respectively. ROSC was achieved in 83 (30.4%) patients receiving adrenaline and 29 (11.1%) receiving placebo - OR= 3.51 [95% CI 2.21 to 5.59]. Survival to hospital discharge occurred in 11 (4.1%) and 5 (1.9%) of the adrenaline and placebo patients OR= 2.16 [95% CI: 0.74 to 6.30]

**Primary Outcome:** SDC occurred in 11 (4.1%) and 5 (1.9%) of the adrenaline and placebo patients respectively

**Conclusion:** The use of adrenaline in cardiac arrest was associated with a significant increase in the proportion of patients achieving ROSC however this improvement did not extend to SDC.

**Implications:** The results are unable to rule out a clinically meaningful benefit of Epinephrine in terms of SDC, further investigation into the post resuscitation period for those achieving ROSC is required to identify management strategies to improve survival.

Ian Jacobs, PhD, American Heart Association ReSS

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**Adrénaline : RACS X 3,4**



***Placebo versus Adrenaline  
in Cardiac Arrest***

***The PACA Trial***

**Professor Ian Jacobs**

Discipline of Emergency Medicine – University of Western Australia  
Clinical Services Director – WA Ambulance Service

« Adrenaline in CA was associated with a significant increase in the proportion of patients achieving a ROSC however not survival to hospital discharge ... »

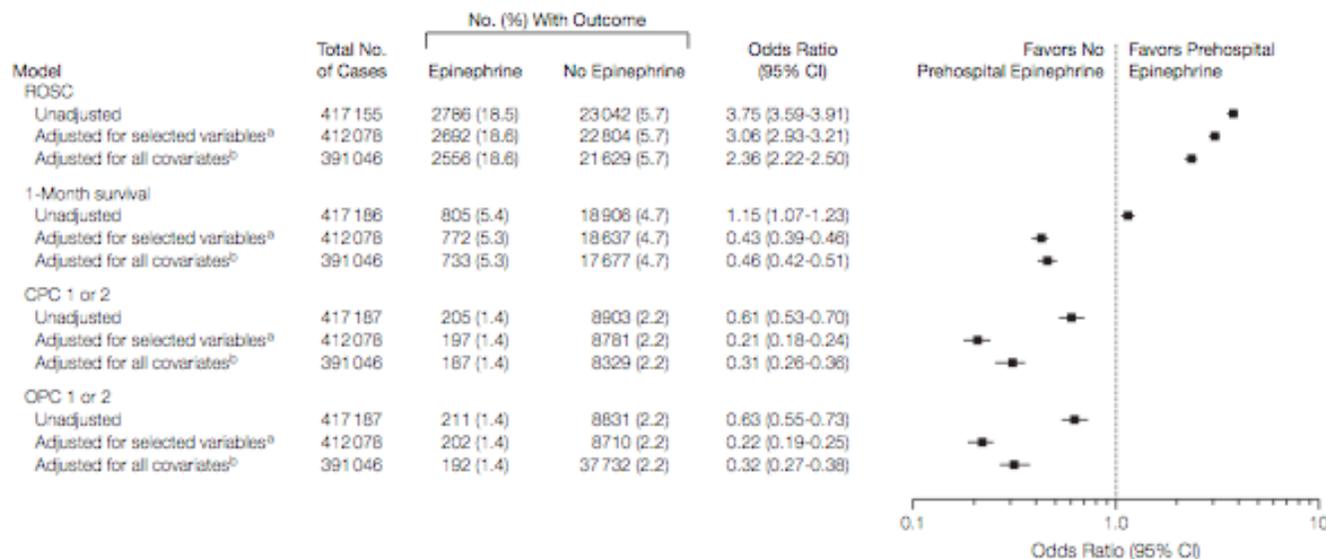
« Further investigation into the post resuscitation period is required to identify management strategies to improve survival ... »

# Prehospital epinephrine use and survival among patients with out of hospital cardiac arrest

Hagihara A, JAMA 2012, 307, 11 : 1161-8

- ▶ Etude prospective non randomisée entre 2005 et 2008
- ▶ 417188 AC préhospitaliers survenus au Japon

**Figure 2.** Results of Unconditional Logistic Regression Analyses Comparing Prehospital Epinephrine Use vs No Prehospital Epinephrine Use in Patients With Out-of-Hospital Cardiac Arrest



Utilisation préhospitalière d'adrénaline augmente le nombre de RACS mais diminue les chances de survie avec un bon score neurologique à 1 mois

## Rapid epinephrine administration improves early outcomes in out of hospital cardiac arrest

Koscik C, Resuscitation 2013 in press

- Etude rétrospective
- Adrénaline < ou > 10 min après l' appel au 911
- 686 patients : < 10 min : 155 / > 10 min : 531
- Tps moyen de l' EMS : 4,7 +/- 2,3 min
- Tps moyen d' injection : 14, 3 +/- 5,5 min

	RACS Odds ration / IC 95 %	Sortis vivants
Adré < 10 min	1,78 / 1,15 -2,74	0,91 / 0,35-2,37
FV/TV	1,82 / 1,19-2,79	4,6 / 1,94-10,88

Adrénaline précoce améliore la RACS mais pas les sortis vivants  
Meilleurs pronostics des FV / TV et devant témoins

# Association between timing of epinephrine administration and intact neurologic survival following out of cardiac arrest in Japan : a population based observational study

Nakahara S, Society For Academic Emerg Med, 2012, 19 , 7 : 782- 92

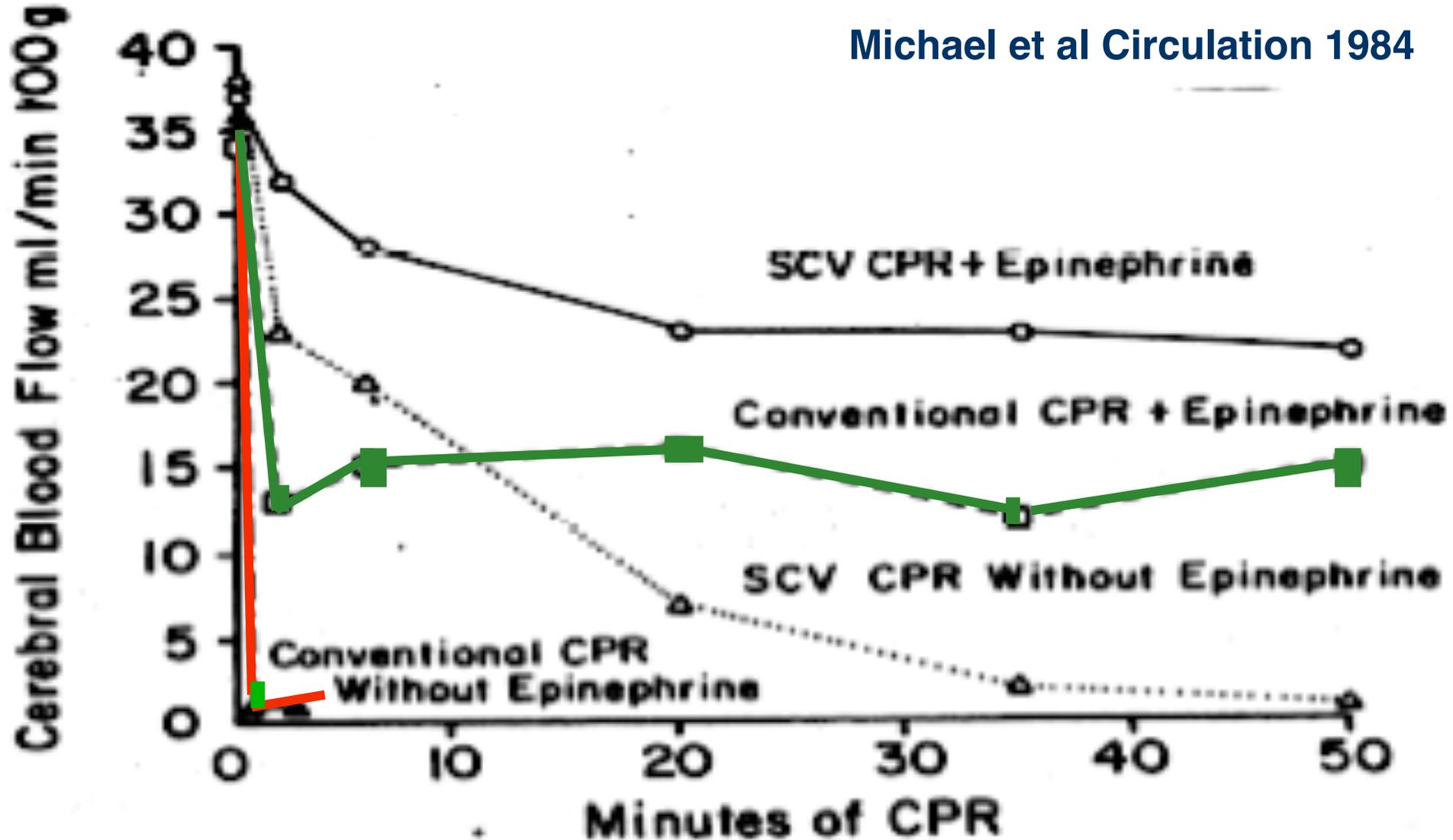
## De 2007 à 2008 : 49 165 patients

	Cardiac Origin (n = 33,163)			Noncardiac Origin (n = 16,002)		
	Total	CPC 1-2†	Survival†	Total	CPC 1-2†	Survival†
	n	n (%)	n (%)	n	n (%)	n (%)
<b>VF/VT</b>						
<b>With early epinephrine‡</b>						
By EMS	372	47 (12.6)	102 (27.4)	27	3 (11.1)	6 (22.2)
In-hospital	124	22 (17.7)	38 (30.6)	14	1 (7.1)	2 (14.3)
Subtotal	496	69 (13.9)	140 (28.2)	41	4 (9.8)	8 (19.5)
<b>Without early epinephrine‡</b>						
By EMS	722	40 (5.5)	108 (15.0)	61	1 (1.6)	3 (4.9)
In-hospital	5,188	216 (4.2)	546 (10.5)	657	11 (1.7)	33 (5.0)
ROSC before hospital	824	379 (46.0)	538 (65.3)	58	18 (31.0)	36 (62.1)
Subtotal	6,734	635 (9.4)	1,192 (17.7)	776	30 (3.9)	72 (9.3)
Chi-square§		10.6 (p = 0.001)	34.0 (p < 0.001)		3.4 (p = 0.07)	4.6 (p = 0.003)
<b>Non-VF/VT</b>						
<b>With early epinephrine‡</b>						
By EMS	781	5 (0.6)	34 (4.4)	350	2 (0.6)	20 (5.7)
In-hospital	485	6 (1.2)	25 (5.2)	248	2 (0.8)	16 (6.5)
Subtotal	1,266	11 (0.9)	59 (4.7)	598	4 (0.7)	36 (6.0)
<b>Without early epinephrine‡</b>						
By EMS	2,026	10 (0.5)	60 (3.0)	1,001	6 (0.6)	40 (4.0)
In-hospital	22,024	67 (0.3)	422 (1.9)	13,054	28 (0.2)	301 (2.3)
ROSC before hospital	617	100 (16.2)	283 (32.9)	532	29 (5.5)	148 (27.8)
Subtotal	24,667	177 (0.7)	685 (2.8)	14,587	63 (0.4)	499 (3.4)
Chi-square§		0.38 (p = 0.54)	15.3 (p < 0.001)		0.73 (p = 0.39)	12.2 (p < 0.001)

**Dans la FV/TV et dans l'asystole  
Intérêt de l'adrénaline injectée précocement < 10 min**

# Perfusion cérébrale et adrénaline

Michael et al Circulation 1984



## Potential negative effects of epinephrine on carotid blood flow and ETCO<sub>2</sub> during active compression-decompression CPR utilizing an impedance threshold

Burneet A, Resuscitation 2013 in press

- Etude expérimentale
- Arrêt cardiaque chez le cochon pdt 6 min
- Réanimation à 6 min en CDA
- Injection d'adrénaline à 10 min de RCP
- Augmentation de la pression de perfusion coronaire et cérébrale
- Chute de l'ETCO<sub>2</sub> (p= 0,04)

**Effet positif de l'adrénaline sur la macrocirculation  
mais négatif sur la microcirculation**

# Adrénaline en 2013

## Application des recommandations 2010

- ▶ Adrénaline en 2015 ????????
- ▶ Seule, encore
- ▶ En association avec CDP Choline ? Nitroprussiate ?
- ▶ Une nouvelle molécule innovante ????

**Aucune réponse actuellement MAIS UNE CERTITUDE**

10<sup>ème</sup> ÉDITION  
FORUM DE L'URGENCE  
2013

LILLE 2013  
4-5 DÉCEMBRE  
GRAND PALAIS



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# ARRET CARDIAQUE : 1 VIE = 3 GESTES

10<sup>ème</sup> ÉDITION  
FORUM DE L'URGENCE  
2013

LILLE 2013  
4-5 DÉCEMBRE  
GRAND PALAIS



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croix-rouge française