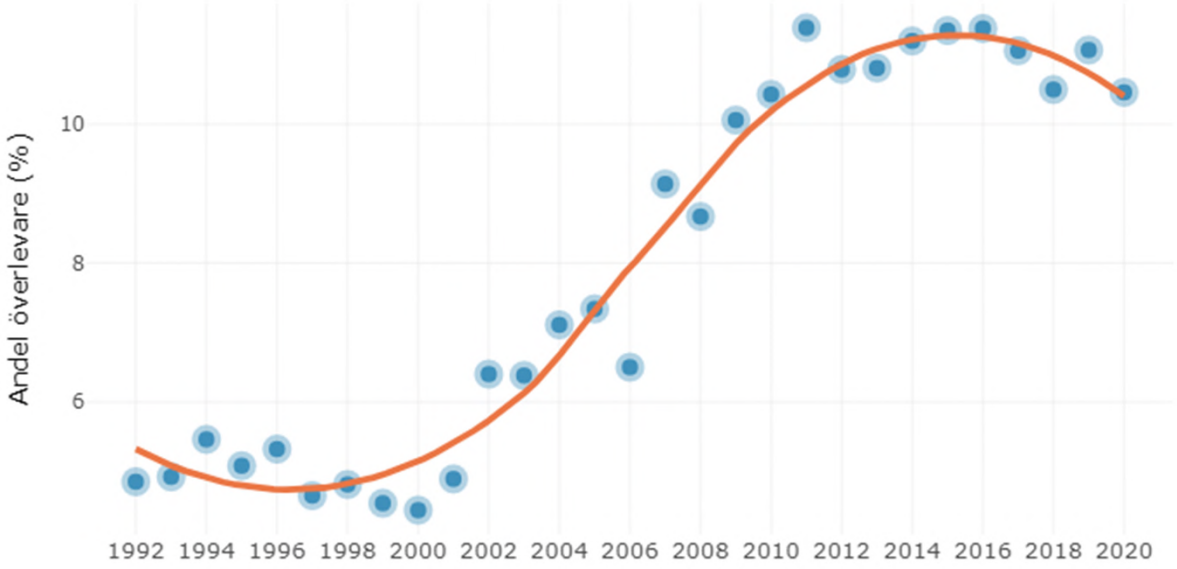
Läkemedelsbehandling vid hjärtstopp

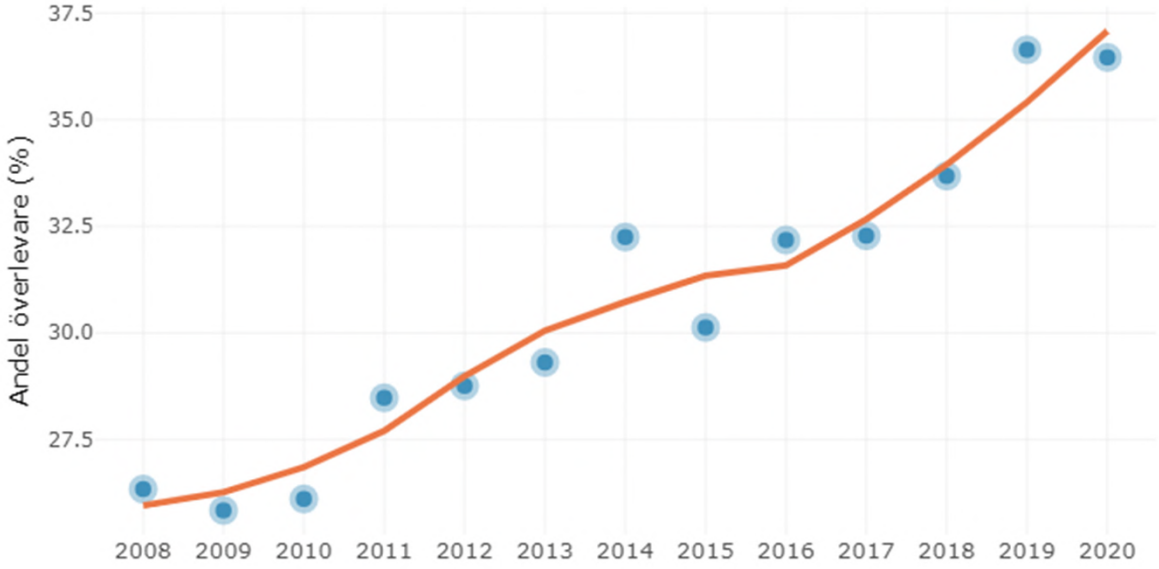
Sune Forsberg
Norrtälje

Vi har gjort framsteg genom åren!

Figur 1A. Andel som överlever 30 dagar, hjärtstopp utanför sjukhus



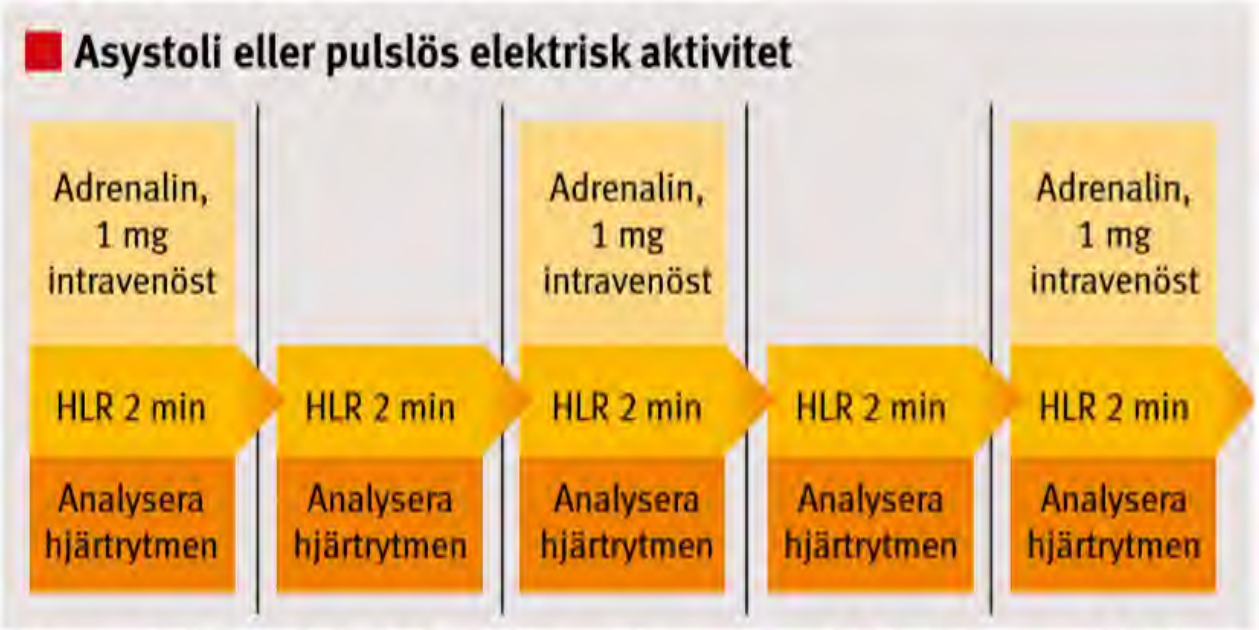
Figur 1B. Andel som överlever 30 dagar, hjärtstopp på sjukhus



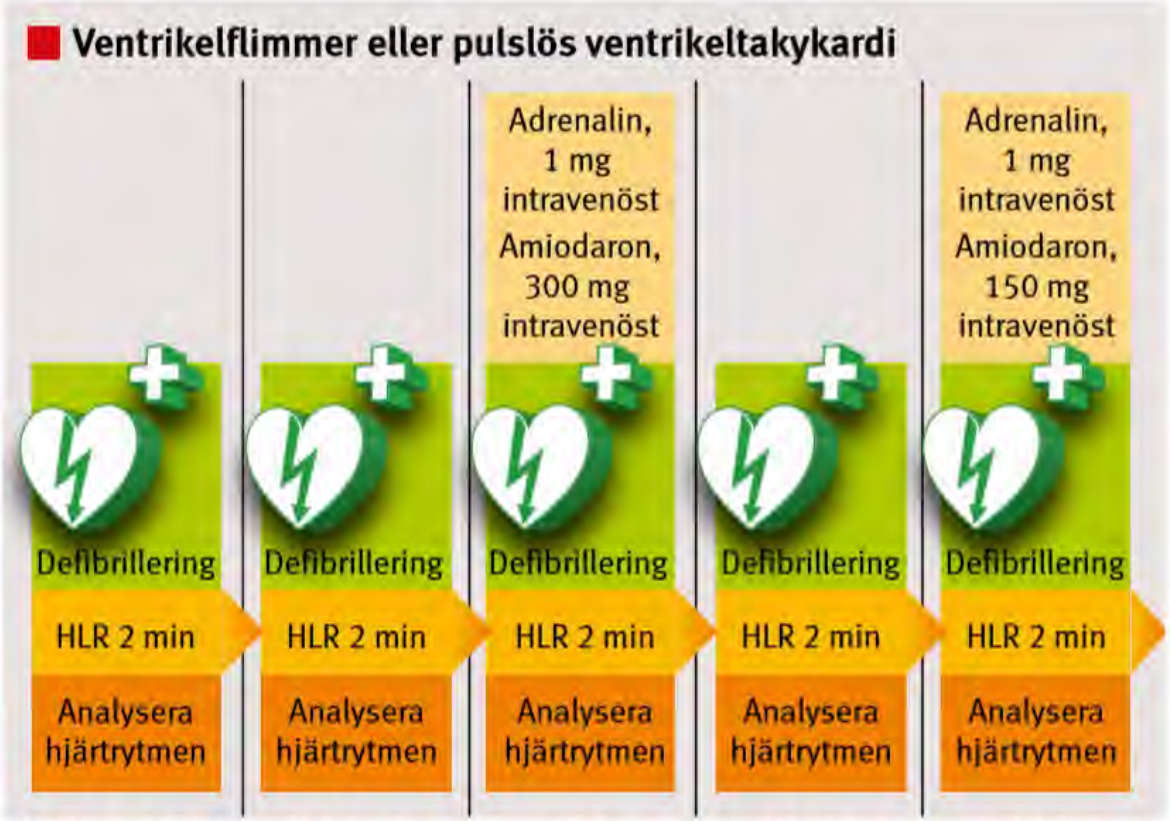
Svenska Hjärt-Lungräddningsregistret 2020

Standardbehandling

When adrenaline is used it should be used as soon as possible when the cardiac arrest rhythm is non-shockable cardiac arrest, and after 3 defibrillation attempts for a shockable cardiac arrest rhythm



Figur 1. Läkemedelsbehandling vid avancerad hjärt–lungräddning (A-HLR) vid asystoli eller pulslös elektrisk aktivitet enligt 2010 års internationella riktlinjer.



Figur 2. Läkemedelsbehandling vid avancerad hjärt–lungräddning (A-HLR) vid ventrikelflimmer eller pulslös ventrikeltakykardi enligt 2010 års internationella riktlinjer.

Evidens för standardbehandling

- **Adrenalin**

Ökad ROSC och korttidsöverlevnad.

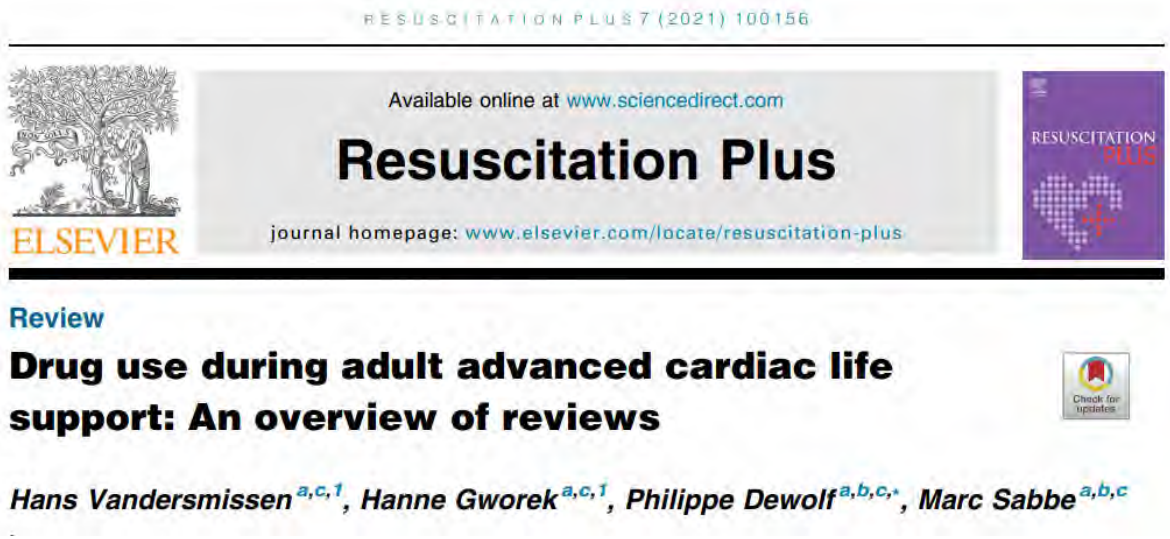
Jacobs et al. Resuscitation. 2011;82:1138–1143
Perkins et al N Engl J Med. 2018;379:711–721.
Andersen et al BMJ 2016;353:i1577

- **Amiodarone**

Tidigare visat en ökad andel överlevnad till sjukhusinläggning jämfört med placebo eller Lidocain. Men nyare studier kan inte påvisa någon skillnad.

Kudenchuk. Amiodarone, Lidocaine, or Placebo in Out-of-Hospital Cardiac Arrest. N Engl J Med 2016;374:171122

Ingen nuvarande känd läkemedelsbehandling som bevisligen ökar långtidsöverlevnad med god neurologisk funktion efter hjärtstopp så till den grad att det påverkat riktlinjer.


RESUSCITATION PLUS 7 (2021) 100156

Available online at www.sciencedirect.com

Resuscitation Plus

journal homepage: www.elsevier.com/locate/resuscitation-plus

ELSEVIER

Review

Drug use during adult advanced cardiac life support: An overview of reviews

Hans Vandersmissen[a,c,1], Hanne Gworek[a,c,1], Philippe Dewolf[a,b,c,], Marc Sabbe[a,b,c]*

Adrenalin
Vasopressin
Kortison
Lidocain
Amidarone
Betablocklad
Magnesium
Trombolys etc

RESUSCITATION 161 (2021) 115–151

Available online at www.sciencedirect.com

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

ELSEVIER

EUROPEAN RESUSCITATION COUNCIL

European Resuscitation Council Guidelines 2021: Adult advanced life support

Jasmeet Soar[a,], Bernd W. Böttiger[b], Pierre Carli[c], Keith Couper[d], Charles D. Deakin[e], Therese Djärv[f], Carsten Lott[g], Theresa Olasveengen[h], Peter Paal[i], Tommaso Pellis[j], Gavin D. Perkins[k], Claudio Sandroni[l,m], Jerry P. Nolan[n]*

Rekommendationen lutar sig mot 14 randomiserade och 17 observationsstudier:

- **lidocain**
- **amiodarone**
- magnesium
- bretylium
- nifekalant
- procainamid

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Vasopressor drugs

- Give adrenaline 1 mg IV (IO) as soon as possible for adult patients in cardiac arrest with a non-shockable rhythm.
- Give adrenaline 1 mg IV (IO) after the 3rd shock for adult patients in cardiac arrest with a shockable rhythm.
- Repeat adrenaline 1 mg IV (IO) every 3–5 min whilst ALS continues.

Antiarrhythmic drugs

- Give amiodarone 300 mg IV(IO) for adult patients in cardiac arrest who are in VF/pVT after three shocks have been administered.
- Give a further dose of amiodarone 150 mg IV (IO) for adult patients in cardiac arrest who are in VF/pVT after five shocks have been administered.
- Lidocaine 100 mg IV (IO) may be used as an alternative if amiodarone is not available or a local decision has been made to use lidocaine instead of amiodarone. An additional bolus of lidocaine 50 mg can also be given after five defibrillation attempts.

Thrombolytic drugs

- Consider thrombolytic drug therapy when pulmonary embolus is the suspected or confirmed cause of cardiac arrest.
- Consider CPR for 60–90 min after administration of thrombolytic drugs.

Fluids

- Give IV (IO) fluids only where the cardiac arrest is caused by or possibly caused by hypovolaemia.

Om vi backar 5 år

Part 7: Adult Advanced Cardiovascular Life Support

2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

Mark S. Link, Chair; Lauren C. Berkow; Peter J. Kudenchuk; Henry R. Halperin; Erik P. Hess; Vivek K. Moitra; Robert W. Neumar; Brian J. O'Neil; James H. Paxton; Scott M. Silvers; Roger D. White; Demetris Yannopoulos; Michael W. Donnino

Vad säger guidelines?

AHA

2015 Recommendations—New

There are no data to recommend for or against the routine use of steroids alone for IHCA patients.

In IHCA, the combination of intra-arrest vasopressin, epinephrine, and methylprednisolone and post-arrest hydrocortisone as described by Mentzelopoulos et al[139] may be considered; however, further studies are needed before recommending the routine use of this therapeutic strategy (Class IIb, LOE C-LD).

For patients with OHCA, use of steroids during CPR is of uncertain benefit (Class IIb, LOE C-LD).

CLASS IIb (WEAK) **Benefit ≥ Risk**

Suggested phrases for writing recommendations:

- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well established

ERC

Steroids

Two studies suggest that a bundled regimen of adrenaline, vasopressin and methylprednisolone improved survival after in-hospital cardiac arrest. In a single-centre randomised, placebo-controlled trial in patients with in-hospital cardiac arrest, a combination of vasopressin 20 IU and adrenaline 1 mg per CPR cycle for the first 5 CPR cycles *plus* methylprednisolone 40 mg at the first CPR cycle *plus* hydrocortisone 300 mg in case of post-resuscitation shock was associated with significantly higher rates of ROSC (39/48 [81%] vs. 27 of 52 [52%]; $p = 0.003$) and survival to hospital discharge (9 [19%] vs. 2 [4%]; $p = 0.02$) than conventional treatment.[668] These results were confirmed by a subsequent three-centre trial including a total of 300 patients from the same group of investigators.[669] This last trial also showed significantly higher odds of survival with good neurological outcome (CPC = 1–2) (OR 3.28, 95% CI 1.17–9.20; $p = 0.02$).

The population in these studies had very rapid advanced life support, a high incidence of asystolic cardiac arrest and low baseline survival compared to other in-hospital studies. Thus the findings of these studies are not generalisable to all cardiac arrests and we suggest that steroids are not used routinely for cardiac arrest.[4]

ORIGINAL INVESTIGATION

Vasopressin, Epinephrine, and Corticosteroids for In-Hospital Cardiac Arrest

Spyros D. Mentzelopoulos, MD, PhD; Spyros G. Zakynthinos, MD, PhD; Maria Tzoufi, MD, PhD; Nikos Katsios, MD; Androula Papastylianou, MD; Sotiria Gkisioti, MD; Anastasios Stathopoulos, MD; Androniki Kollintza, PhD; Elissavet Stamataki, MD, PhD; Charis Roussos, MD, PhD

100 patienter

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Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Vasopressin, Steroids, and Epinephrine and Neurologically Favorable Survival After In-Hospital Cardiac Arrest

A Randomized Clinical Trial

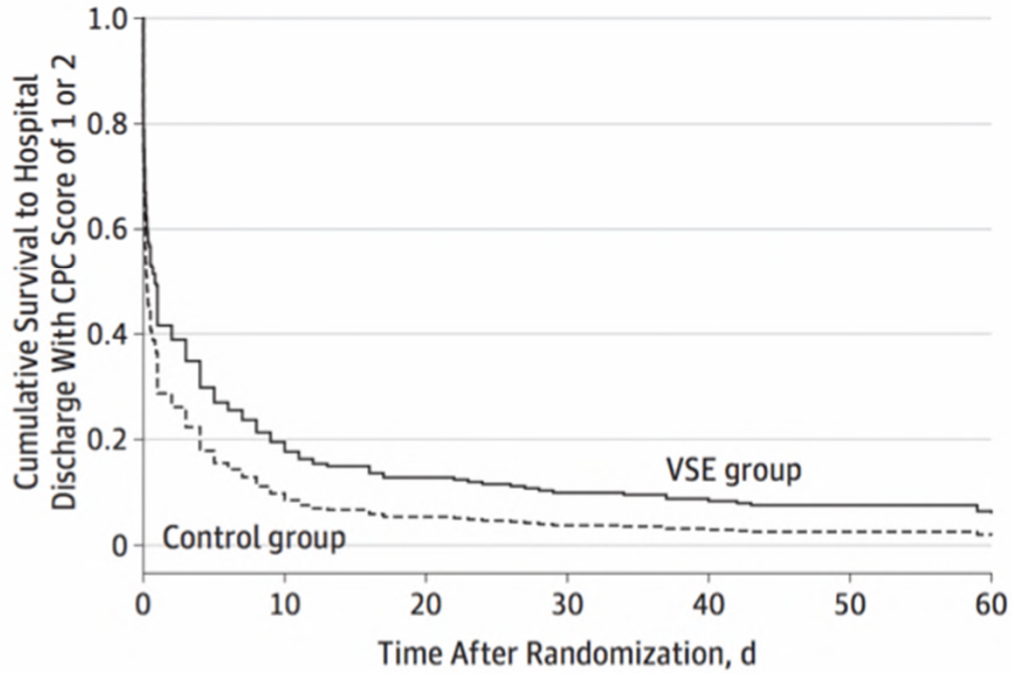
Spyros D. Mentzelopoulos, MD, PhD; Sotirios Malachias, MD; Christos Chamos, MD; Demetrios Konstantopoulos, MD; Theodora Ntaidou, MD; Androula Papastylianou, MD, PhD; Iosifinia Kolliantzaki, MD; Maria Theodoridi, MD; Helen Ischaki, MD, PhD; Demosthenes Makris, MD, PhD; Epaminondas Zakynthinos, MD, PhD; Elias Zintzaras, MD, PhD; Sotirios Sourlas, MD; Stavros Aloizos, MD; Spyros G. Zakynthinos, MD, PhD

JAMA 2013
3-center
268 patients

	ROSC	Survival
Intervention:	39/48 (81%)	9/48 (19%)
Placebo:	27/52 (52%)	2/52 (4%)

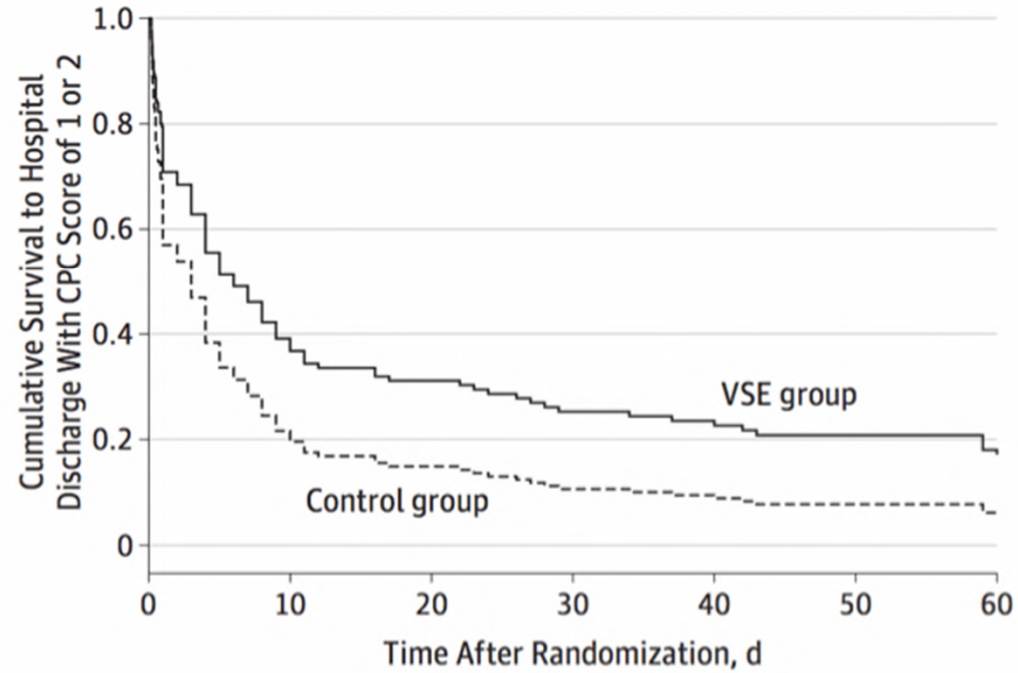
	ROSC	CPC 1-2
Intervention:	109/130 (84%)	18/130 (14%)
Placebo:	91/138 (66%)	7/138 (5%)

Figure 2. Results on Survival Analysis



No. at risk

VSE group	130	35	25	23	22	20	18
Control group	138	21	16	11	9	8	7



No. at risk

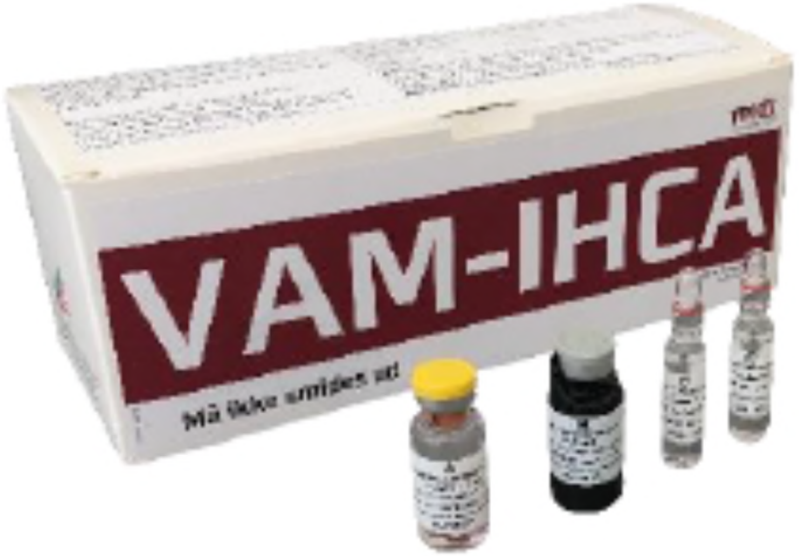
VSE group	76	29	23	22	20	18	16
Control group	73	18	14	9	8	7	6

Potentiellt effektiva läkemedel

- **Vasopressin**
  - Kärlsammandragande effekt.
  - Ökar blodflödet i hjärtat och hjärnan.
  - Längre halveringstid jmf Adrenalin.
  - Har i studier ensamt inte visat förbättrad överlevnad jmf Adrenalin.
- **Kortison**
  - Minskar tiden till chock-återhämtning i sepsis.
  - Ökar effekten av Adrenalin.
  - Ökar ROSC i djurstudier
  - Högre S-koritsol associerat med bättre överlevnad i observationsstudier.

Design -Dansk studie

Lars W Andersen et al JAMA 2021



Investigator-initiated, multicenter, randomized, placebo-controlled, parallel group, double-blind, superiority trial

Intervention:

- **20 IE vasopressin** efter varje dos adrenalin (max 80 IE)
- **40 mg methylprednisolon** efter den första dosen adrenalin

10 centre, **512 (501)** patienter

Primary outcome: Egencirkulation (ROSC)
Sekundary: överlevnad & neurologisk outcome
Primärt utfall: ROSC

Research

JAMA | Original Investigation

Effect of Vasopressin and Methylprednisolone vs Placebo on Return of Spontaneous Circulation in Patients With In-Hospital Cardiac Arrest

A Randomized Clinical Trial

Lars W. Andersen, MD, MPH, PhD, DMSc; Dan Isbye, MD, PhD; Jesper Kjærgaard, MD, PhD, DMSc;

Published online September 29, 2021

	ROSC*	Survival 30-days	Pos. neurologisk outcome
Intervention	42 %	9,7 %	7,6 %
Placebo	33 %	12 %	7,6 %

* Endast ROSC kunde påvisa en signifikant skillnad mellan Intervention och Placebo

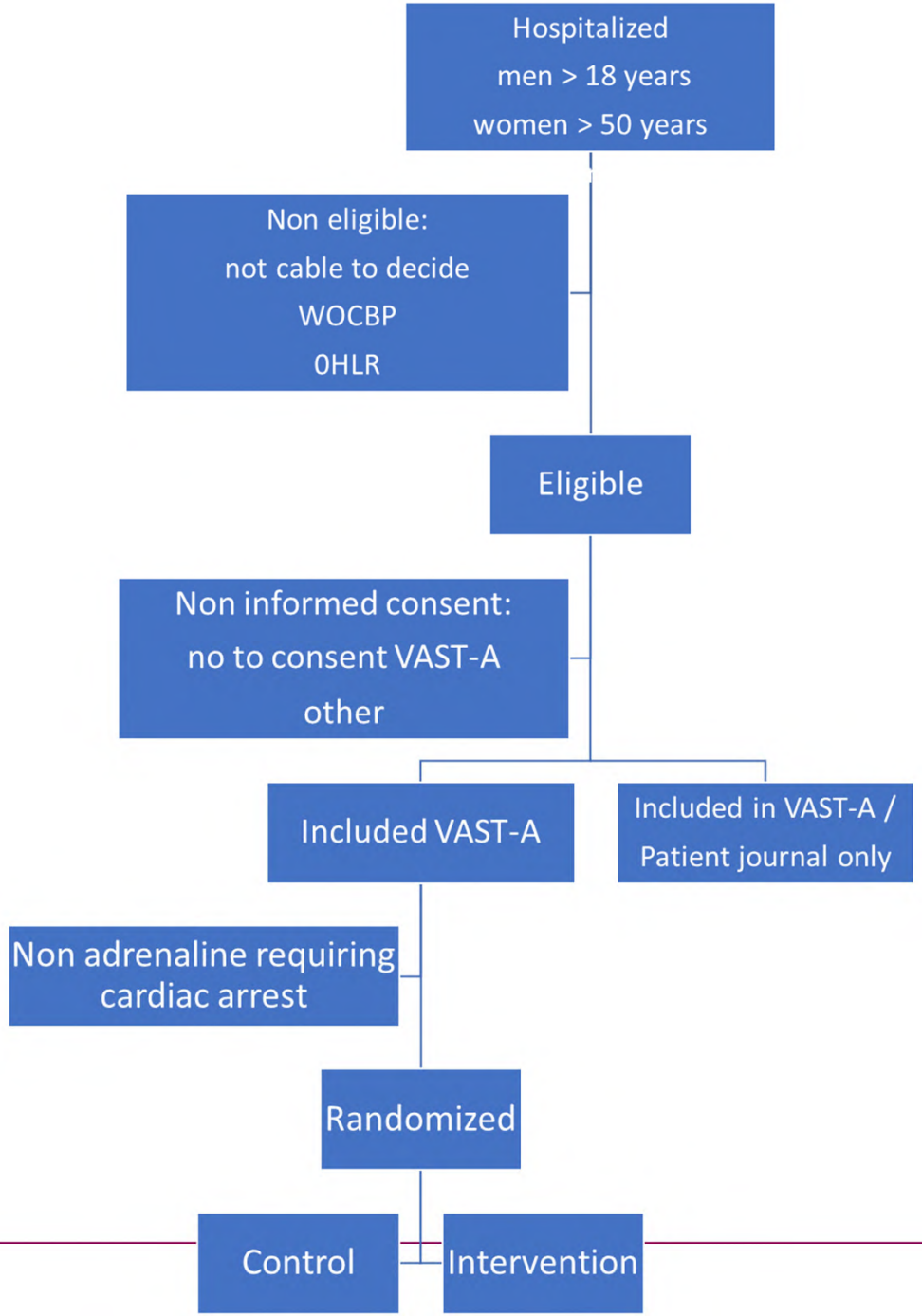
VASTA-studien

VAsopressin and **ST**eroids in addition to **A**drenaline in cardiac arrest

Primär endpoint: överlevnad 30 dagar

EU lagstiftning

- EU-direktivet för läkemedelsforskning, artikel 35 ger rätt att inkludera medvetslösa i LKM forskning.
- I övriga europeiska länder kan samtycke säkerställs i ett senare skede, genom samtycke från patientens lagliga representanter eller från patienten själv då han eller hon återfått medvetande.
- **Sverige har såsom enda EU-land valt att inte implementera detta EU-direktiv.**
  - → **LMV kräver informerat samtycke innan**



Inklusionskriterier

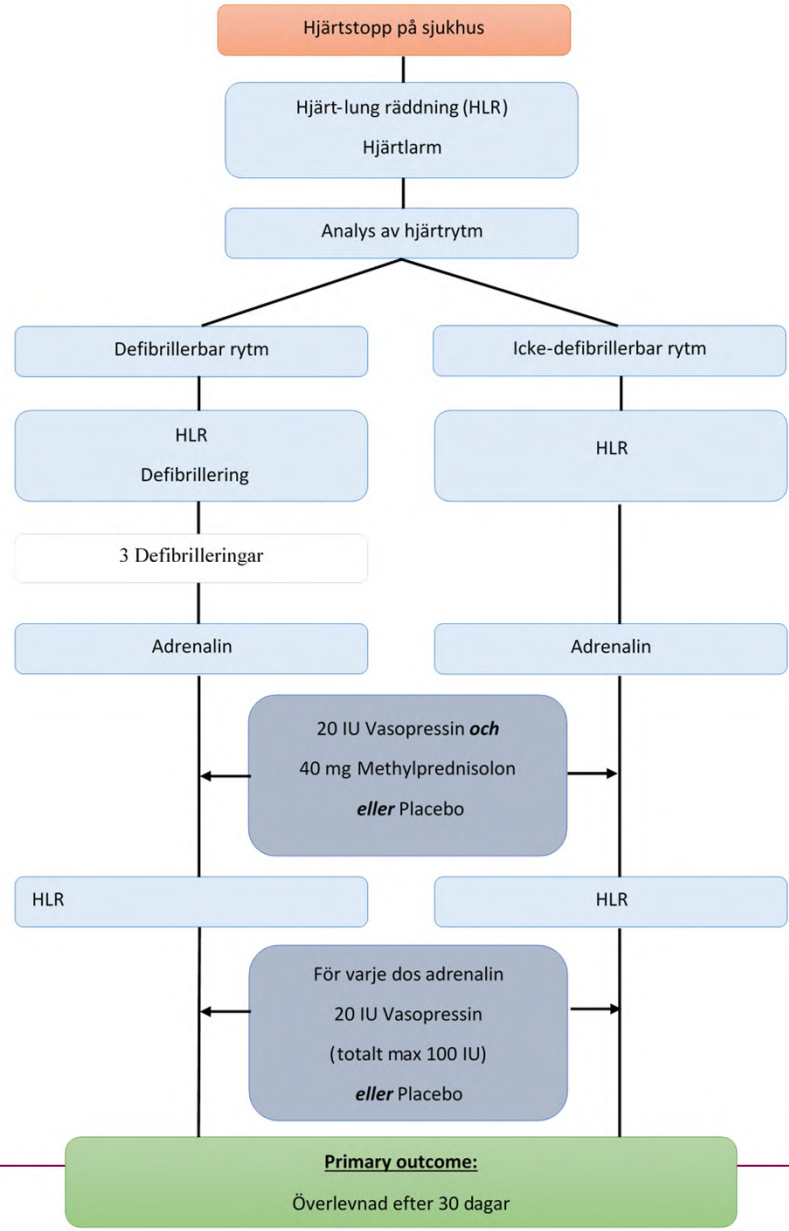
- Hjärtstopp på sjukhus där läkemedel ska ges
- Män från 18 år
- Icke fertila kvinnor >50 år

Exklusionskriterier

- i.v steroider
- Icke-bevittnat hjärtstopp
- 0 HLR-beslut

FLÖDESSCHEMA FÖR LÄKEMEDELSADMINISTRERING

VAST-A STUDIEN



Studiens storlek

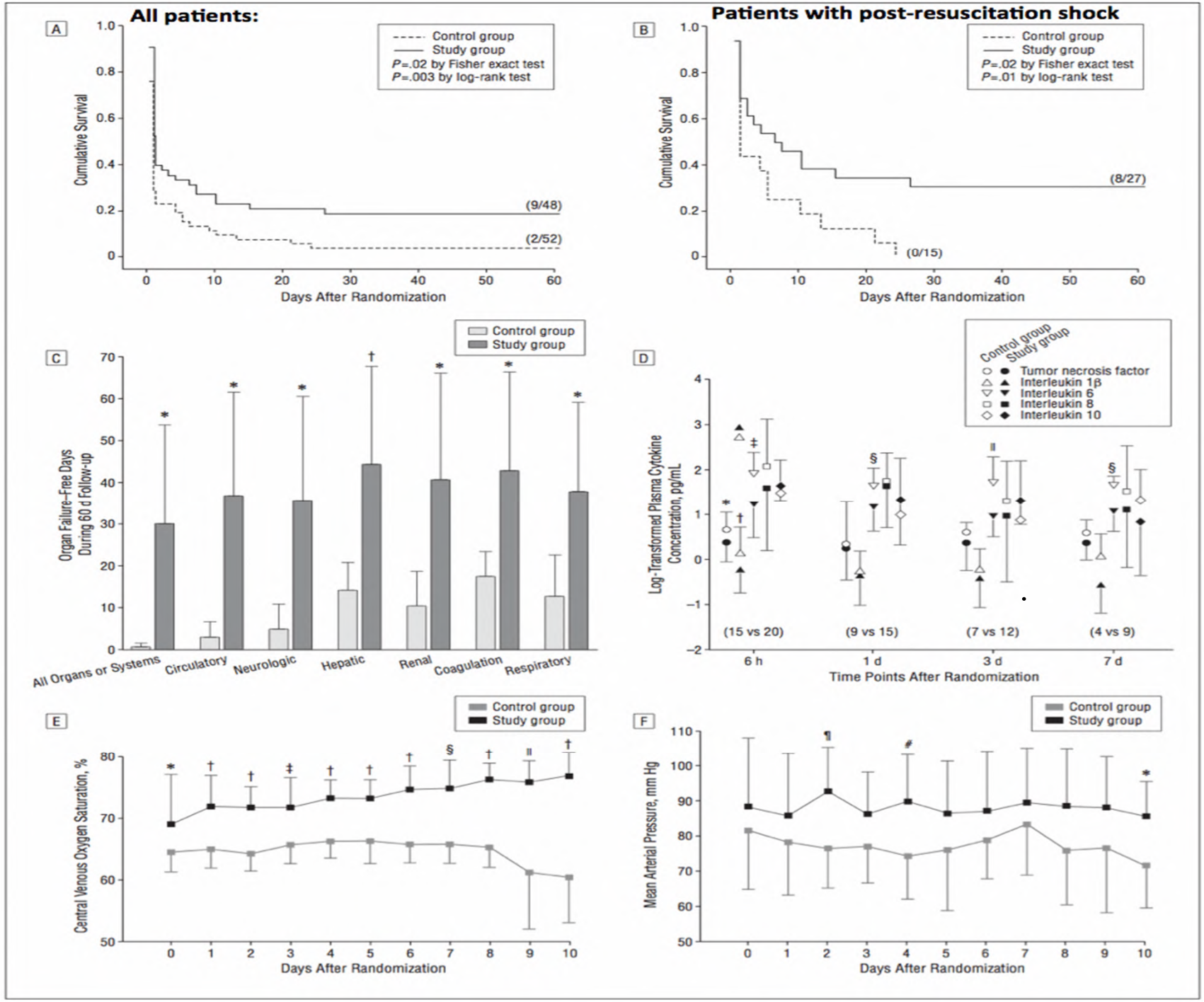
För att öka överlevnaden från 10% till 15 % behövs 1400 patienter inkluderade enligt nedan för att säkert kunna uttala sig.

.

	80%	90%
10% to 15%	700 + 700	900 + 900
10% to 13%	1800 + 1800	2400 + 2400
10% to 12%	3900 + 3900	5200 + 5200

Skillnader i studieupplägg VAM-IHCA/VAST-A

	VAM-IHCA	VAST-A
Methylprednisolone	1 dos, á 40 mg	1 dos, á 40 mg
Vasopressin	Max **4 doser**, á 20 IE	Max **5 doser**, á 20 IE
Solu-Cortef vid postchock	------	**Ja**



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Pilot

- Norrtälje
- SÖS
- Sahlgrenska

- 150 pat/1 år

- Säkerhet - genomförbarhet

Nuläge

Utbildningsinsatser

→ Film
→ Föreläsningar
→ Simulatorövningar

- **Startades 17 nov 2021**
  → Informationslapp om studie i samband med inskrivning
  → Informerat samtycke inhämtas dagligen på nyinlagda
    - De som sagt ja får ett blått armband
  → Randomisering sker centralt klumpvis (kluster)
  → Läkemedelssupporten fixar studieläkemedelsbox
    - Löpnummer, Läkemedelsinstruktion, Registreringsblad

Tack för uppmärksamheten