MASTERCLASS ARCOTHOVA

INSUFFISANCE CARDIAQUE AIGUË: DE LA PHYSIOPATHOLOGIE AU TRAITEMENT

BORDEAUX, 4-5 FÉVRIER 2019

ARCOTHOVA
Anesthésistes Réanimateurs
Cœur - Thorax - Vaisseaux

Stratégie de sevrage des assistances et des inotropes

Dr Philippe GAUDARD

Réanimation DAR ADV

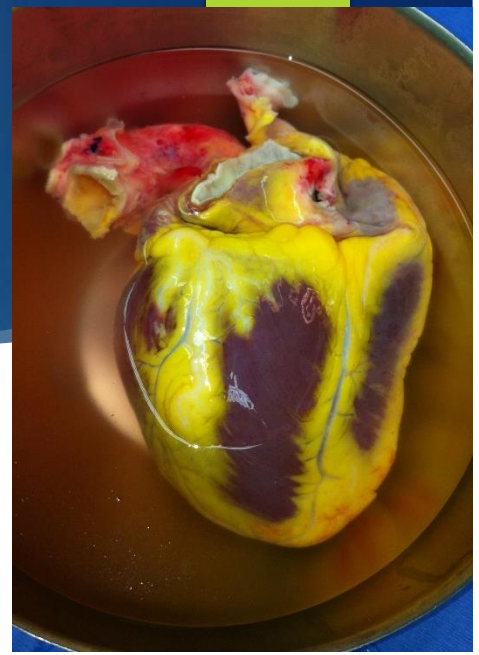
CHU de MONTPELLIER

DAR ADV

COEUR & POUMONS
CHU
MONTPELLIER
CENTRE HOSPITALIER
UNIVERSITAIRE

UNIVERSITÉ DE MONTPELLIER

Choc cardiogénique: Projet thérapeutique ?



- Récupération rapide
- Bridge à la transplantation cardiaque
- Bridge à l'assistance cardiaque de longue durée
  - En bridge to bridge: vers la transplantation
  - En « destination therapy »: LVAD implantables uniquement actuellement
  - En attente de récupération (rare)
- Aucune possibilité: palliatif

Objectif:
Réduire la durée de support temporaire ?

- Risques ↗ en cas de traitement prolongé
  - Inotropes: le moins longtemps possible (catécholamines+++)
  - Assistances de courtes durées
    - ECLS: 15 j
    - Impella CP: 7 j / 5.0: 15 j
- Diminuer la dose de suppléance dès que possible
  - Inotropes: effets indésirables, consommation en O2, tachyphylaxie
  - ECLS: risque de surcharge VG, circulation pulmonaire, thrombose cavités cardiaques ou culot aortique, hémolyse …
  - Impella: Hémolyse, déplacement
- Déterminer rapidement la possibilité de récupération
  - Oui: organiser le sevrage
  - Non: Prévoir le bridge sans délai

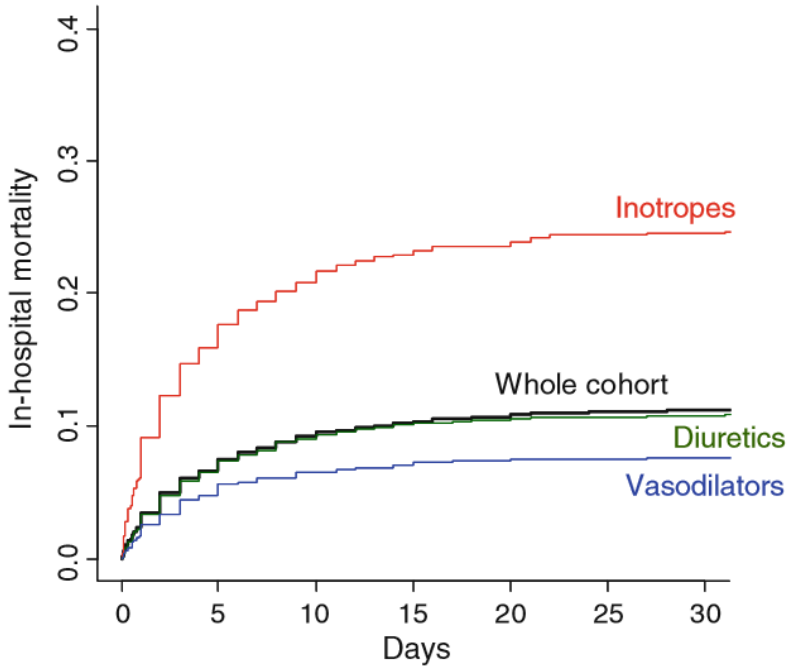
Toxicité des catécholamines

Intensive Care Med (2011) 37:290–301
DOI 10.1007/s00134-010-2073-4

ORIGINAL

Alexandre Mebazaa
John Parissis
Raphael Porcher
Etienne Gayat
Maria Nikolaou
Fabio Vilas Boas
J. F. Delgado
Ferenc Follath

Short-term survival by treatment among patients hospitalized with acute heart failure: the global ALARM-HF registry using propensity scoring methods



- Etude cohorte n=4953
- Multicentrique, 9 pays
- Hospitalisation pour AHF
- Impact des traitements sur outcome
- Ajustement / Propensity score

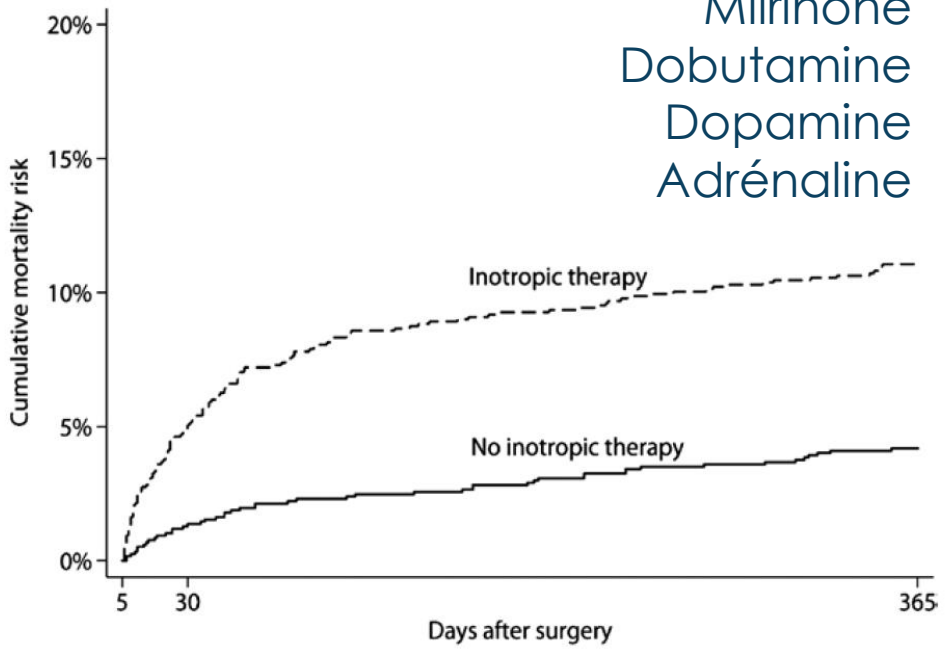
Health Outcomes with and without Use of Inotropic Therapy in Cardiac Surgery

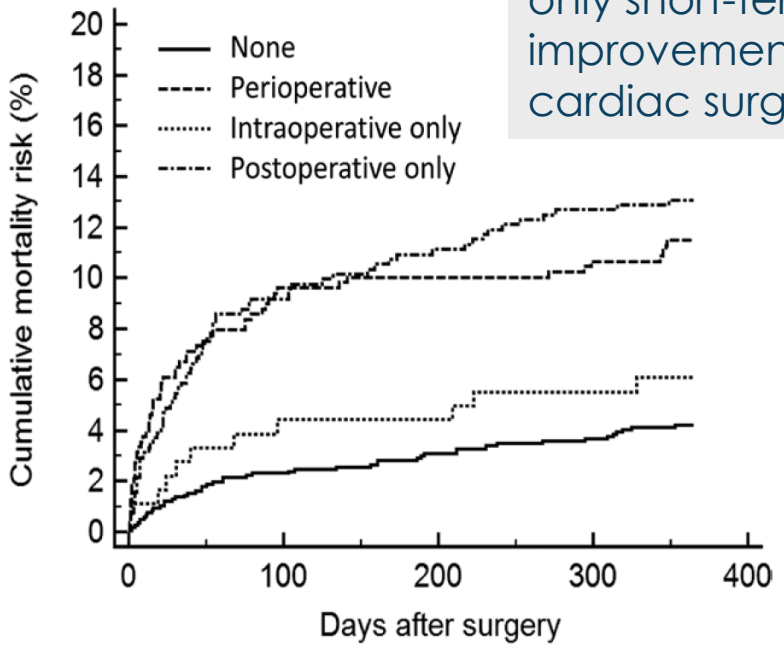
Results of a Propensity Score–matched Analysis

Dorthe Viemose Nielsen, M.D., Malene Kærslund Hansen, M.B.B.S., Søren Paaske Johnsen, M.D., Ph.D., Mads Hansen, M.D., Karsten Hindsholm, M.D., H.D., Carl-Johan Jakobsen, M.D.

"The results indicate that the beneficial effects of current inotropic drugs may be limited to only short-term hemodynamic improvement in patients after cardiac surgery."

TT inotrope 35%:
Milrinone
Dobutamine
Dopamine
Adrénaline



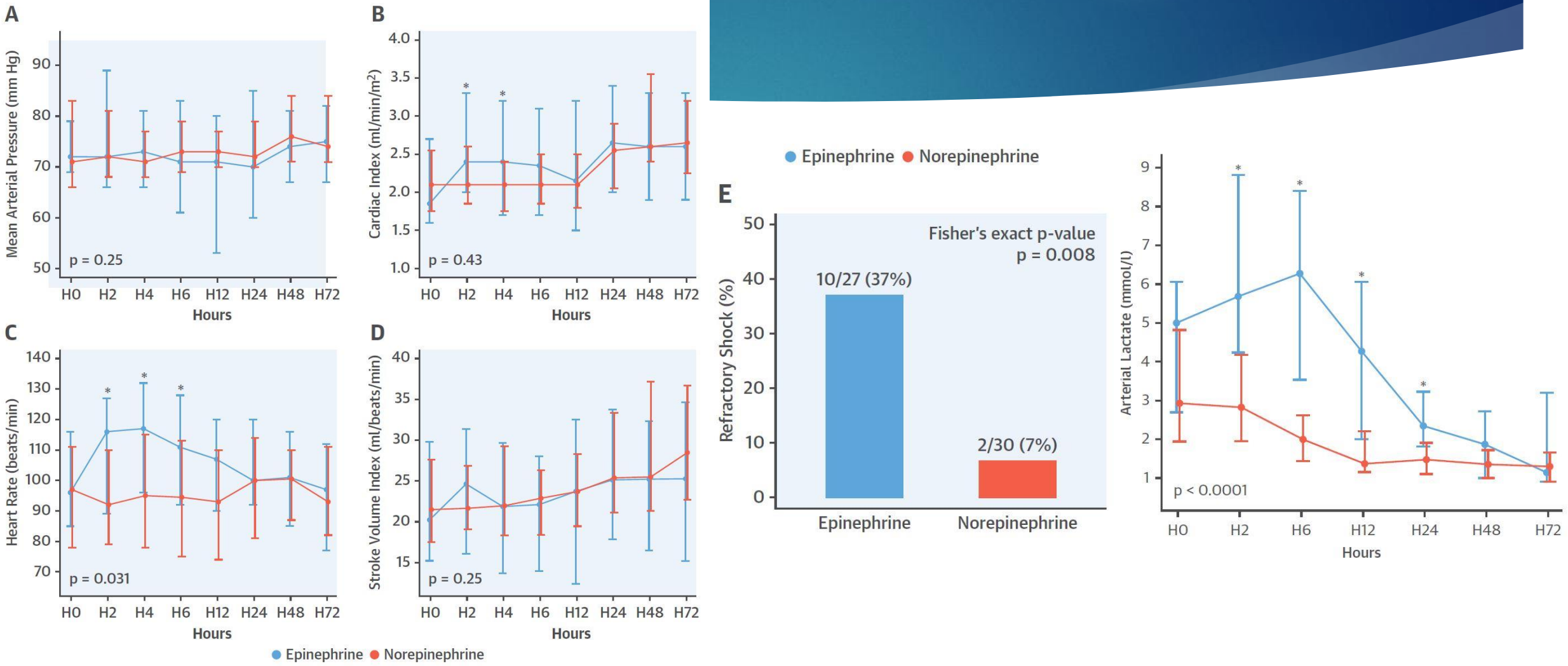


Nielsen, Anestheiology 2014

Noradrénaline vs adrénaline ?

Epinephrine Versus Norepinephrine for Cardiogenic Shock After Acute Myocardial Infarction

Levy, B. et al. J Am Coll Cardiol. 2018;72(2):173-82.



Adrénaline: surmortalité dans le choc cardiogénique

SYSTEMATIC REVIEW

Epinephrine and short-term survival in cardiogenic shock: an individual data meta-analysis of 2583 patients

	No. of patients	No. of patients receiving epinephrine	OR for short-term mortality [95% CI]
Adler, 2012	40	10	4.00 [0.87 - 18.45]
Adler,unpublished	47	9	4.27 [0.88 - 20.67]
AHEAD, 2011	674	304	15.08 [9.08 - 25.05]
ALARM, 2011	520	86	2.14 [1.34 - 3.42]
Chua, 2011	105	80	0.99 [0.40 - 2.45]
CARDSHOCK, 2016	219	46	6.64 [3.22 - 13.71]
Champion, 2014	192	130	7.27 [2.85 - 18.54]
EFICA, 2006	158	75	3.10 [1.61 - 5.98]
Gaudard, 2015	40	11	3.15 [0.75 - 13.29]
IMPRESS in Severe Shock, 2017	48	14	12.55 [2.38 - 66.01]
OPTIMA CC, 2018	57	27	2.55 [0.84 - 7.72]
Basir, unpublished	45	8	0.96 [0.16 - 5.73]
Popovic, 2011	86	47	1.11 [0.47 - 2.63]
Simonis, 2012	89	25	1.37 [0.53 - 3.55]
SMASH, 1998	111	41	0.62 [0.26 - 1.47]
Valente, 2011	152	34	2.40 [0.38 - 14.96]
All studies	2583	947	3.33 [2.81 - 3.94]

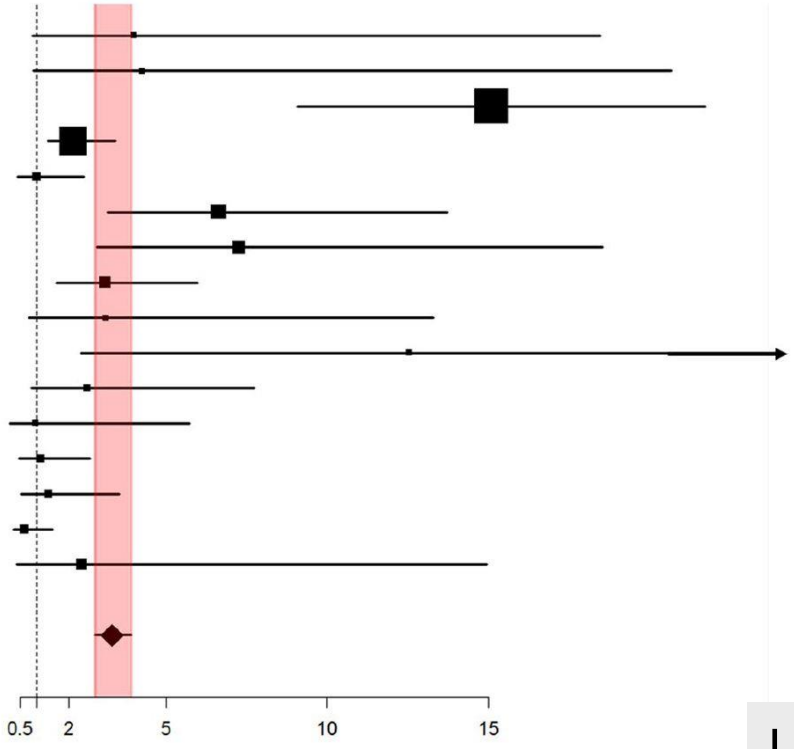


Fig. 3 Forest plot of the meta-analysis of short-term mortality

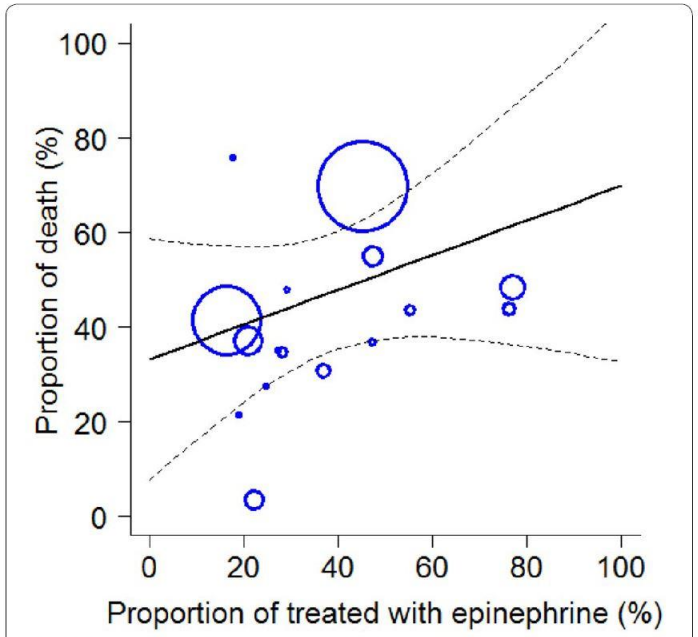


Fig. 2 Association between short-term mortality and the proportion of patients receiving epinephrine. Each circle represents one study. The radius of the circle is proportional to the cohort size

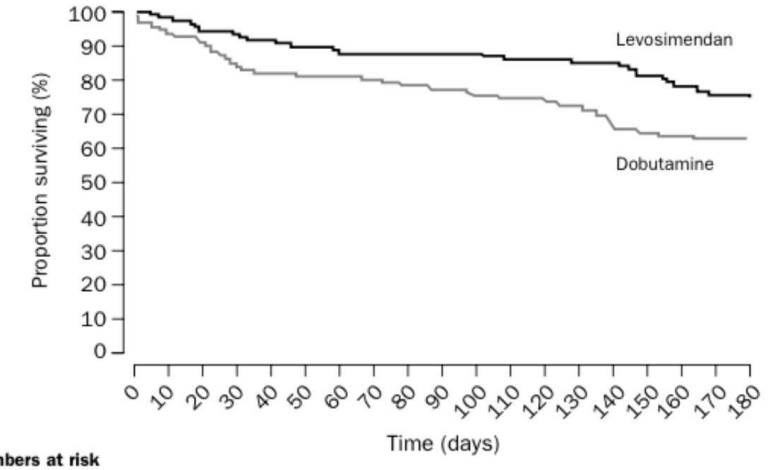
Léopold et al, ICM 2018

Lévosimendan et AHF

Efficacy and safety of intravenous levosimendan compared with dobutamine in severe low-output heart failure (the LIDO study): a randomised double-blind trial

THE LANCET • Vol 360 • July 20, 2002

*F Follath, J G F Cleland, H Just, J G Y Papp, H Scholz, K Peuhkurinen, V P Harjola, V Mitrovic, M Abdalla, E-P Sandell, L Lehtonen, for the Steering Committee and Investigators of the Levosimendan Infusion versus Dobutamine (LIDO) Study**



Numbers at risk

Dobutamine	100	94	91	85	82	81	81	80	78	77	75	74	74	72	67	64	63	62	62
Levosimendan	103	101	97	96	94	92	91	90	90	90	90	88	88	87	87	83	80	77	76

Figure 4: **Kaplan-Meier estimates (analysis of time to first event) of risk of death during first 180 days after randomisation (based on the intention-to-treat analysis)**

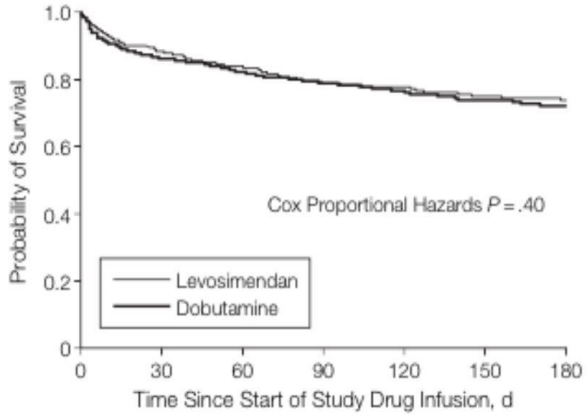
203 patients

Levosimendan vs Dobutamine for Patients With Acute Decompensated Heart Failure

The SURVIVE Randomized Trial

JAMA, May 2, 2007—Vol 297, No. 17

Figure 2. Effect of Dobutamine and Levosimendan Treatment on All-Cause Mortality During 180 Days Following the Start of Study Drug Infusion



No. at Risk

Levosimendan	664	608	586	525	462
Dobutamine	663	596	568	519	454

-1328 patients
-Non en choc

Lévosimendan et AHF

Levosimendan is superior to enoximone in refractory cardiogenic shock complicating acute myocardial infarction*

Joerg T. Fuhrmann, MD; Alexander Schmeisser, MD; Matthias R. Schulze, MD; Carsten Wunderlich, MD; Steffen P. Schoen, MD; Thomas Rauwolf, PhD; Christof Weinbrenner, MD; Ruth H. Strasser, MD

Crit Care Med 2008 Vol. 36, No. 8

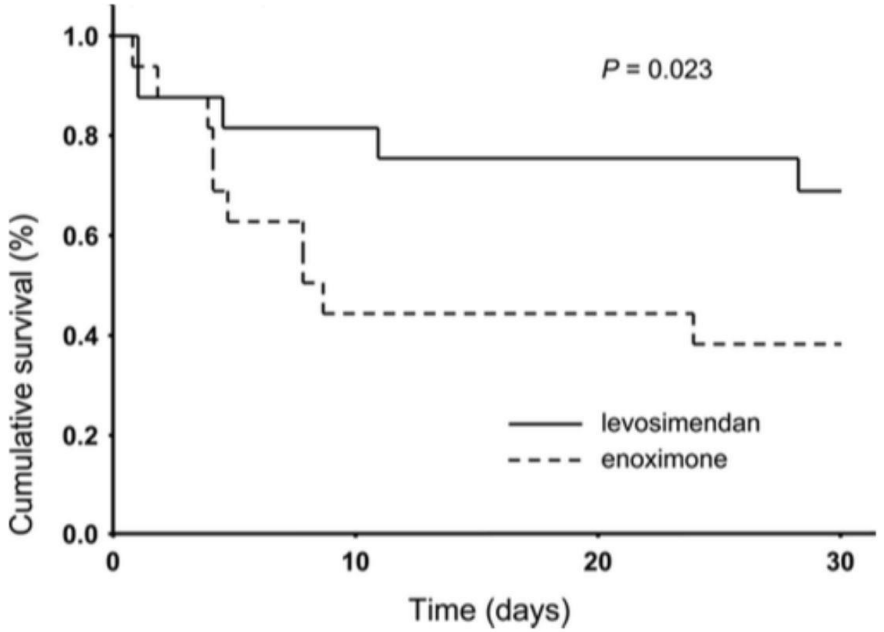
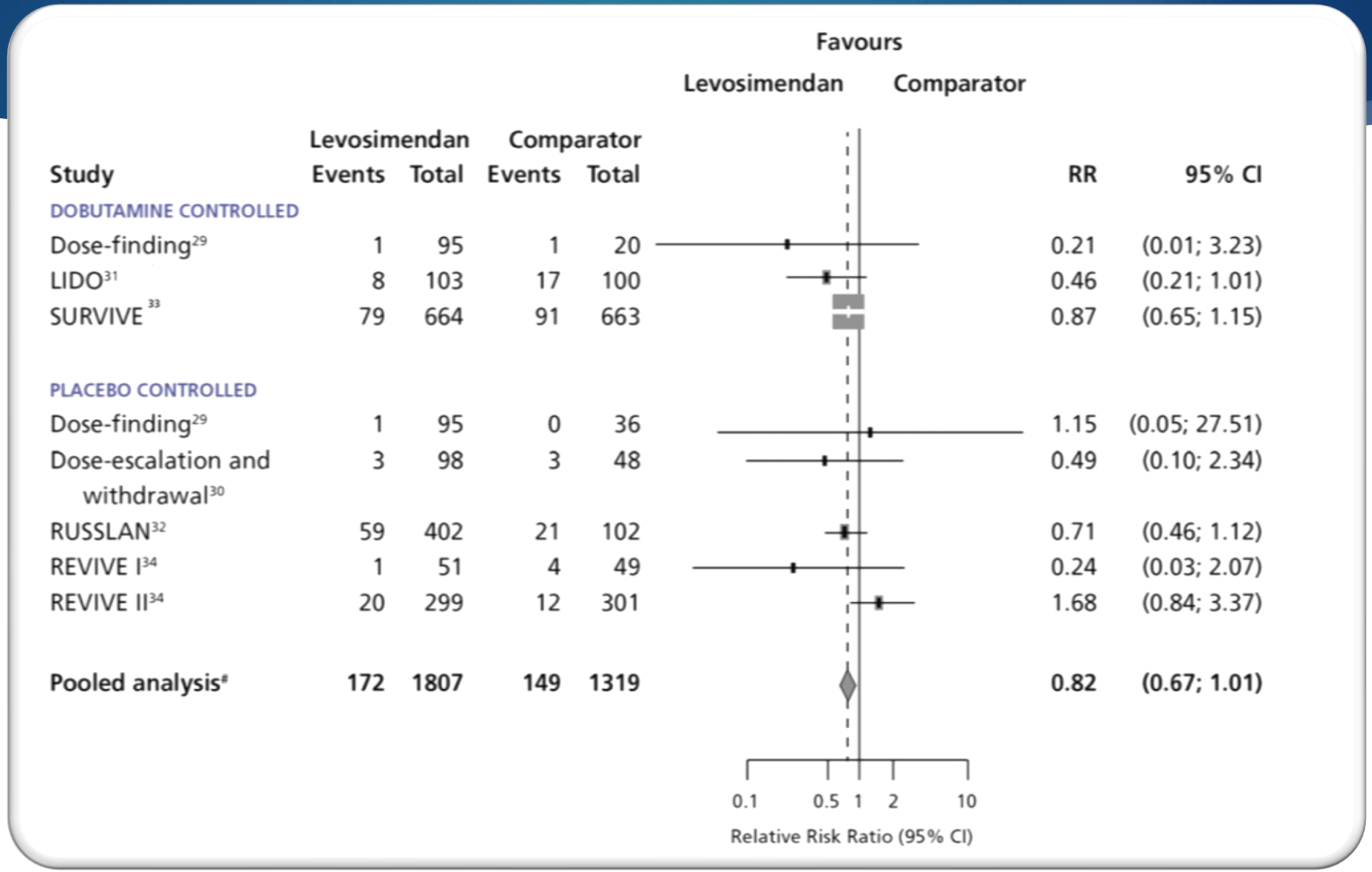
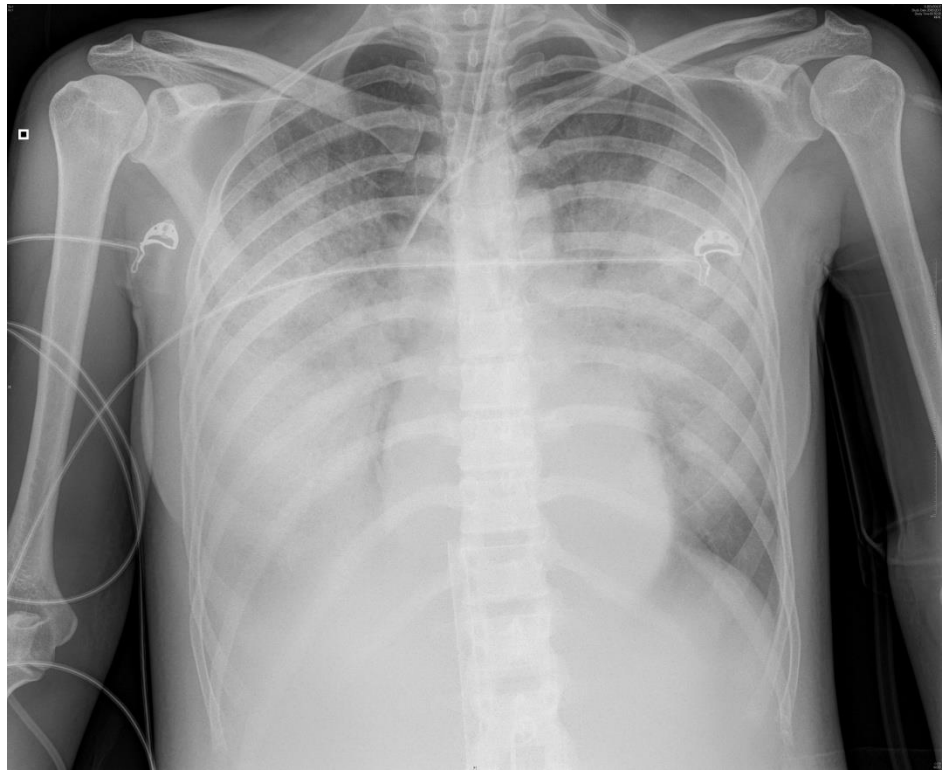


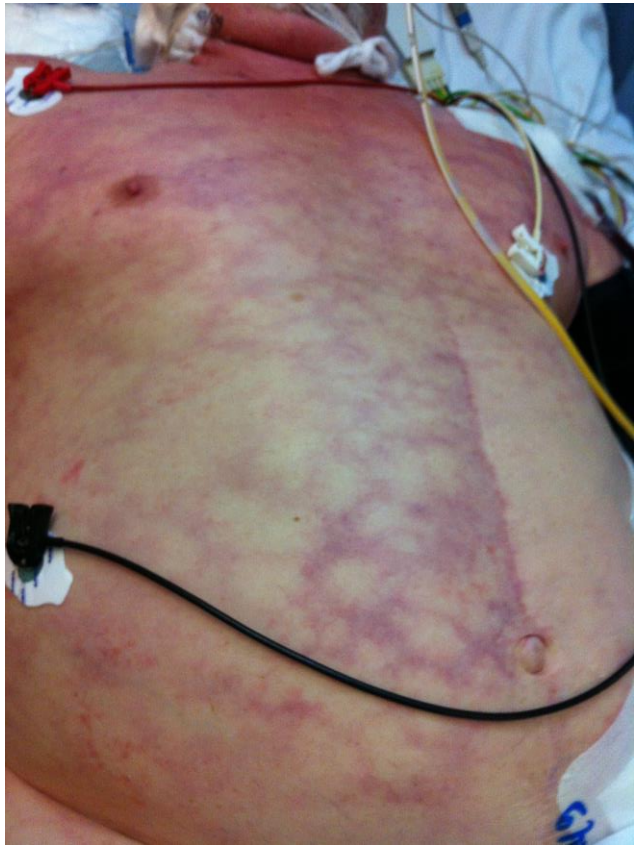
Figure 2. Kaplan-Meier analysis of the 30-day all-cause mortality rate in the levosimendan (*solid line*) and enoximone-treated groups (*broken line*), $p = 0.023$ (log-rank test).

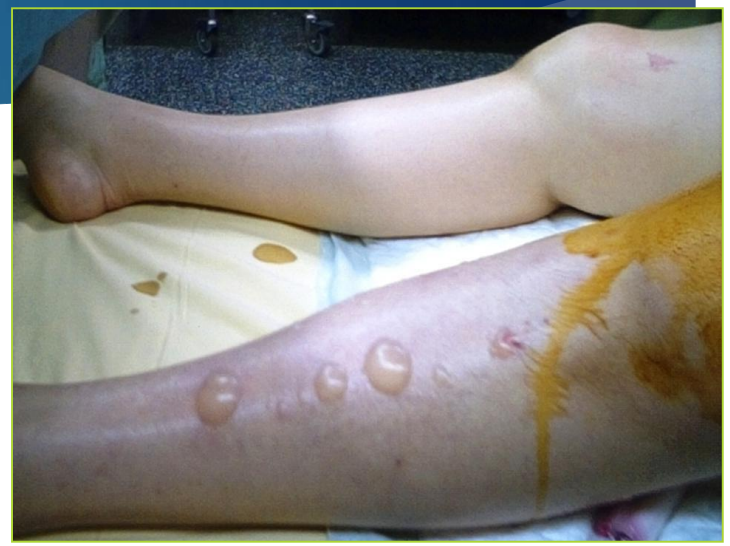
Lévosimendan et AHF



Les dangers de l'assistance circulatoire





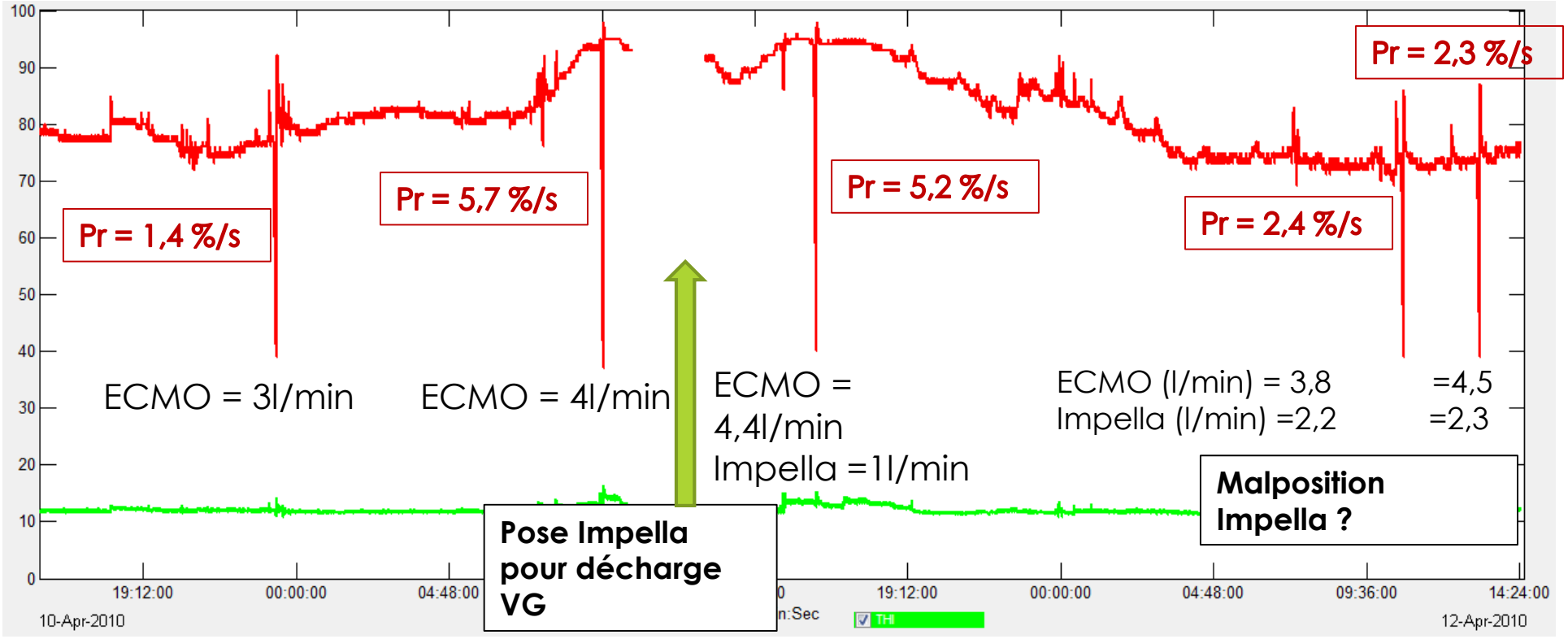


Timing du sevrage ?

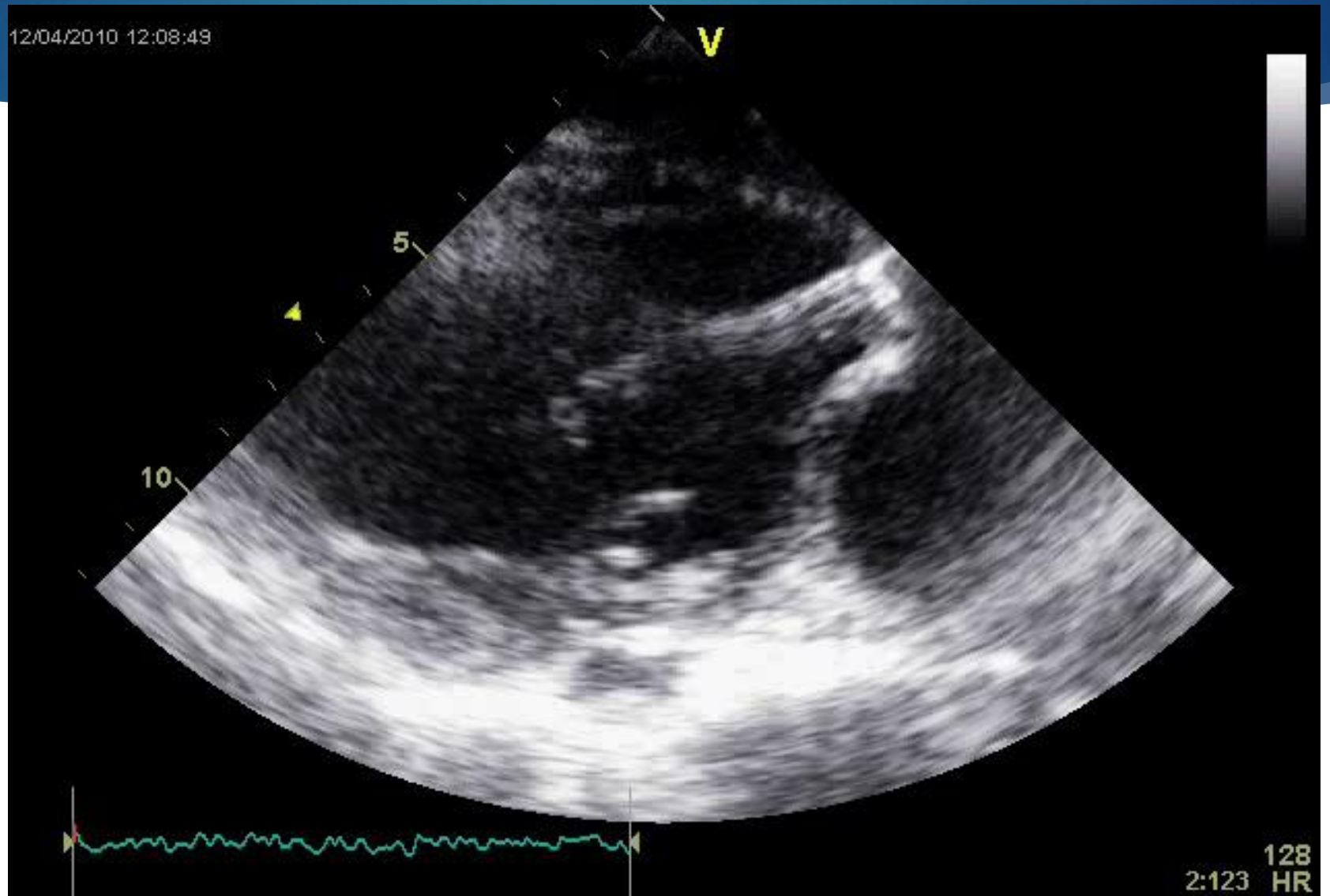
- LE PLUS TÔT POSSIBLE !
- Réduire les doses d'inotropes en priorité
- Réduire les débits de suppléance: le minimum nécessaire
  - Perfusion d'organes adaptée: SvO2, lactate, diurèse, NIRS, microcirculation
- Envisager le sevrage
  - Stabilisation ou régression des défaillances d'organe
  - Stabilisation HD: doses de vasopresseurs, fuite capillaire
  - Consommation en O2 équilibrée
  - Stigmates de récupération myocardique: Pression pulsée, écho

Microcirculation et ECMO

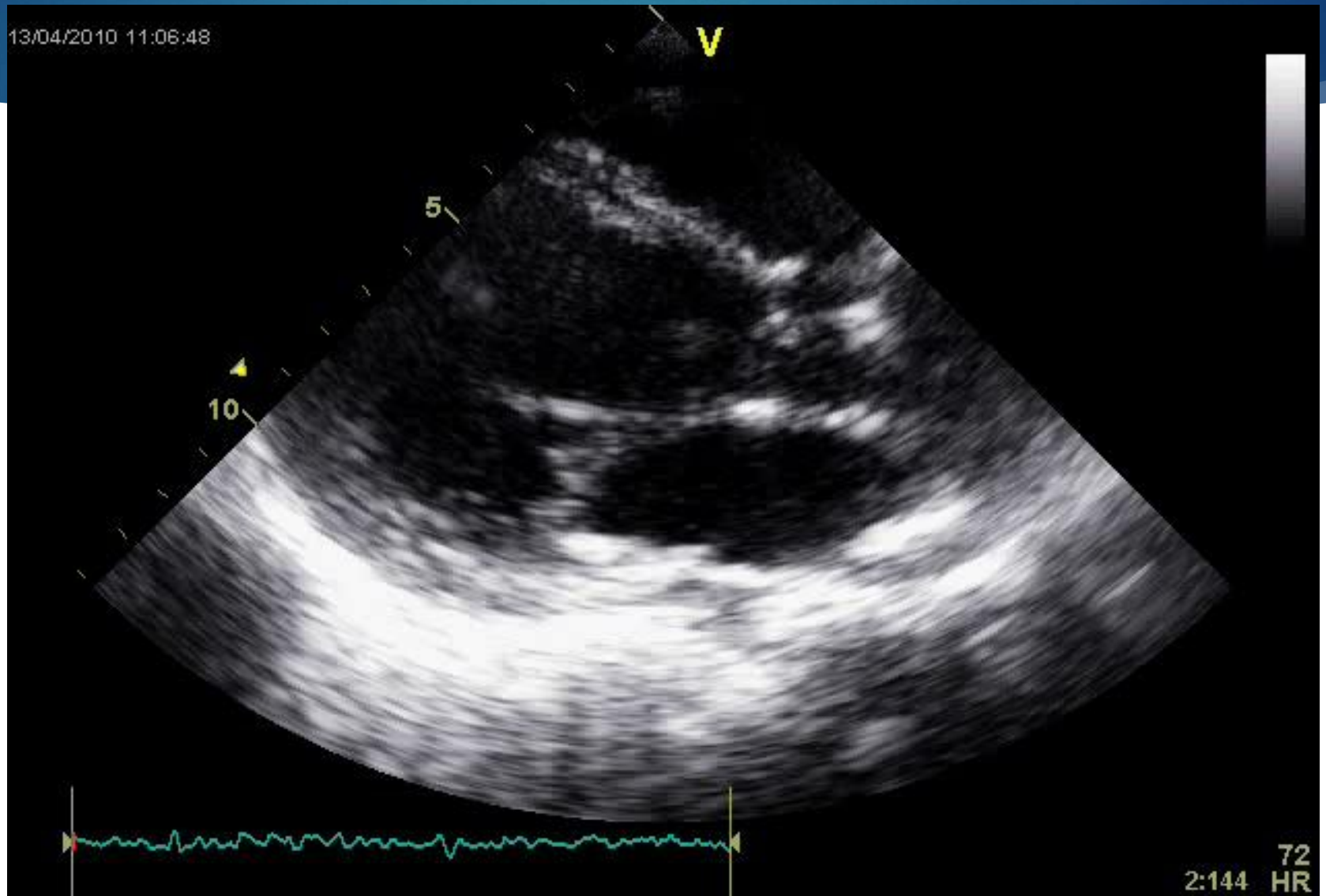
- Patient 17 ans, choc cardiogénique sur CMD, sous ECMO depuis 48h. Absence d'éjection cœur natif.



ETT



ETT: repositionnement Impella



Intensive Care Med (2011) 37:1738–1745
DOI 10.1007/s00134-011-2358-2

ORIGINAL

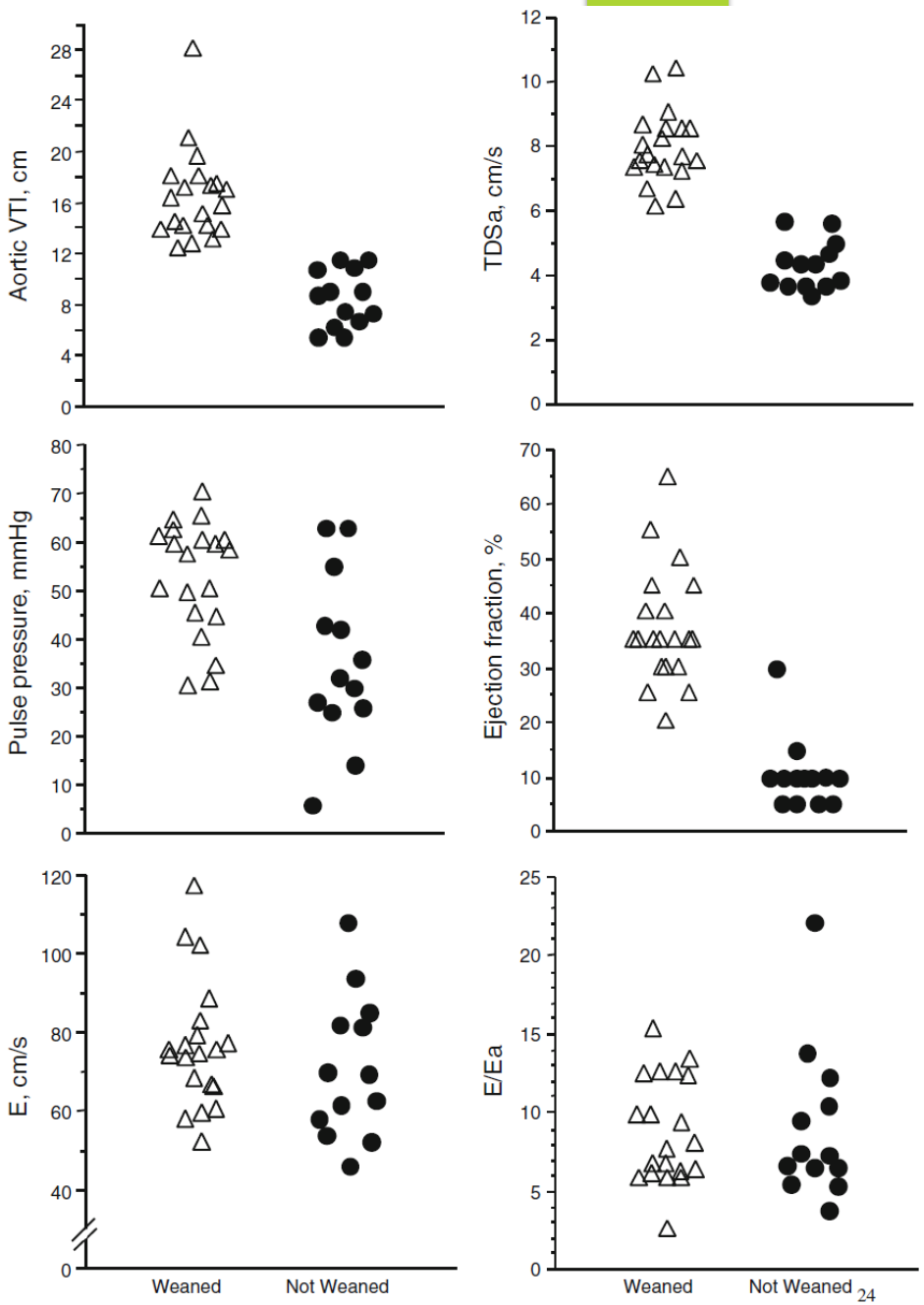
Nadia Aissaoui
Charles-Edouard Luyt
Pascal Leprince
Jean-Louis Trouillet
Philippe Léger
Alain Pavie
Benoit Diebold
Jean Chastre
Alain Combes

Predictors of successful extracorporeal membrane oxygenation (ECMO) weaning after assistance for refractory cardiogenic shock

Parameter	Tolerated weaning trial ($n = 38$)	Did not undergo/ tolerate weaning trial ($n = 13$)
ECMO duration (days)		
Mean ± SD	8 ± 6	4 ± 2
Median (IQR)	7 (3–10)	3 (2–4)
Serious complications under ECMO	16 (42)	7 (54)
Major bleeding	7 (18)	6 (46)
Arterial ischemia	1 (3)	1 (8)
Surgical wound infection	2 (5)	1 (8)
Pulmonary edema	7 (18)	0
Stroke	2 (5)	1 (8)
Need for renal replacement therapy	12 (32)	4 (31)
ICU length of stay, days	19 (9–33)	3 (2–5)
30-Day survivors	28 (74)	1 (8)

Characteristic	Weaned ($n = 20$)	Nonweaned ($n = 13$)
ECMO duration (days)		
Mean ± SD	7 ± 4	11 ± 7
Median (interquartile range)	6 (3–8)	7 (5–17)
Pulse pressure (mmHg)	52 ± 12	39 ± 15
Heart rate (b/min)	95 ± 16	115 ± 19
Echocardiographic parameters		
Aortic VTI (cm)	16.4 ± 3.6	8.5 ± 2.3
LVEF (%)	37 ± 11	10 ± 7
TDSa (cm/s)	7.9 ± 1.2	4.3 ± 0.7
E (cm/s)	76 ± 16	71 ± 18
TDI Ea (cm/s)	10.1 ± 4.9	8.5 ± 3.0
E/Ea	8.7 ± 3.4	9.4 ± 4.6

Critères de sevrage (débit minimal ECMO)
- ITV > 10
- FEVG > 20-25%
- Onde S > 6 cm/s



LETTER

Right–left ventricular interdependence: a promising predictor of successful extracorporeal membrane oxygenation (ECMO) weaning after assistance for refractory cardiogenic shock

Intensive Care Med
DOI 10.1007/s00134-016-4657-0

Nadia Aissaoui[1*], Julia Caudron[2], Pascal Leprince[3], Jean-Yves Fagon[1], Guillaume Lebreton[3], Alain Combes[4] and Benoit Diebold[2]

	D_1		D_L	
	Dep−	Dep+	Dep−	Dep+
Number of patients (%)	19 (58)	14 (42)	17 (51)	16 (48)
Number of weaned patients (%)	14 (74)	2 (14)*	16 (94)	0*
Maximal ECMO flow (L/min)	4.3 ± 1.2	4.8 ± 1.0	2.8 ± 0.5	4.3 ± 0.9
LVEDV				
At maximal ECMO flow	109 ± 62	98 ± 40	93 ± 60	119 ± 67
Variation between maximum and minimum ECMO flow	28 ± 26	−13 ± 9*	+20 ± 16	−31 ± 20*
RV EDV				
At maximal ECMO flow	20 ± 11	28 ± 19	24 ± 14	21 ± 23
Variation between maximum and minimum ECMO flow	+23 ± 19	+14 ± 15	+11 ± 11	+11 ± 11
MBP (mmHg)	95 ± 15	81 ± 14*	91 ± 16	74 ± 12*
LVEF (%)	16 ± 11	15 ± 15	28 ± 15	16 ± 13*
RVEF (%)	23 ± 17	28 ± 15	35 ± 10	20 ± 12*
Aortic VTI	5.0 ± 3.7	4.4 ± 5.7	11 ± 5.0	7.6 ± 5.0*
E wave (cm/s)	33 ± 21	40 ± 25	55 ± 21	50 ± 28
Ea (cm/s)	7.2 ± 4.1	6.5 ± 3.0	8.7 ± 3.0	8.2 ± 5.0
Sa (cm/s)	4.8 ± 1.4	4.7 ± 1.7	7.1 ± 1.1	5.4 ± 0.8*

Optimiser la réponse au sevrage

- Réponse immédiate: Faciliter le sevrage
  - Transport en oxygène
  - Consommation en oxygène systémique
  - Volémie optimisée
- Réponse soutenue: Favoriser la récupération myocardique
  - Réduire la consommation en O2 du myocarde
  - Optimiser la revascularisation myocardique
  - Contrôle des arythmies, et troubles conductifs
  - Place du Lévosimendan ?

Indication du lévosimendan

- Avis commission transparence has: **« La commission donne un avis favorable à l'inscription sur la liste des spécialités agréées à l'usage des collectivités uniquement en traitement de dernier recours chez les patients adultes en situation d'urgence notamment en cas de décompensation réfractaire, en échec de sevrage aux inotropes ou à l'assistance circulatoire »**

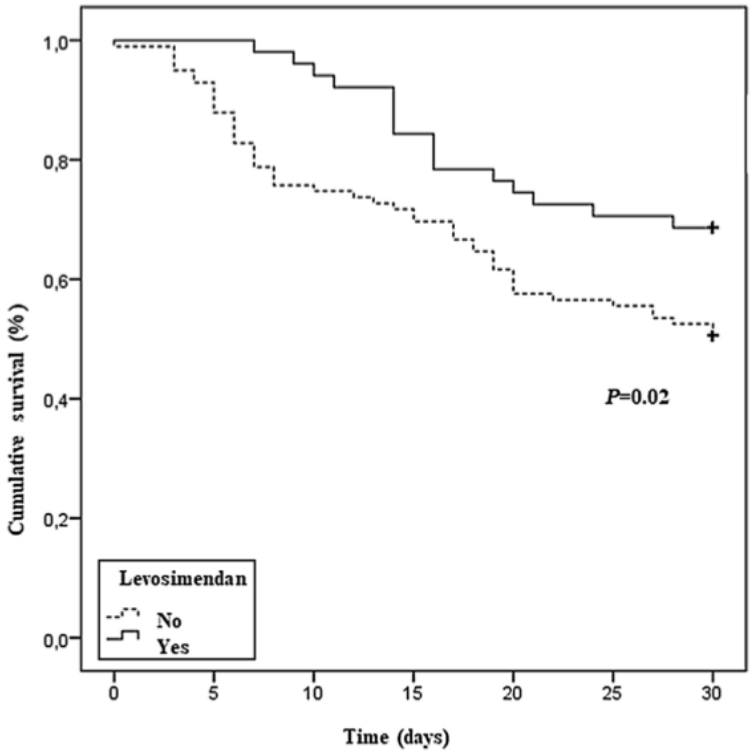
Vally *et al. Ann. Intensive Care* (2019) 9:24
https://doi.org/10.1186/s13613-019-0503-1

Annals of Intensive Care

RESEARCH Open Access

Impact of levosimendan on weaning from peripheral venoarterial extracorporeal membrane oxygenation in intensive care unit

Shamir Vally[1], Cyril Ferdynus[2,3], Romain Persichini[1], Bruno Bouchet[1], Eric Braunberger[4], Hugo Lo Pinto[1], Olivier Martinet[1], David Vandroux[1], Thomas Aujoulat[1], Jérôme Allyn[1] and Nicolas Allou[1,5*]

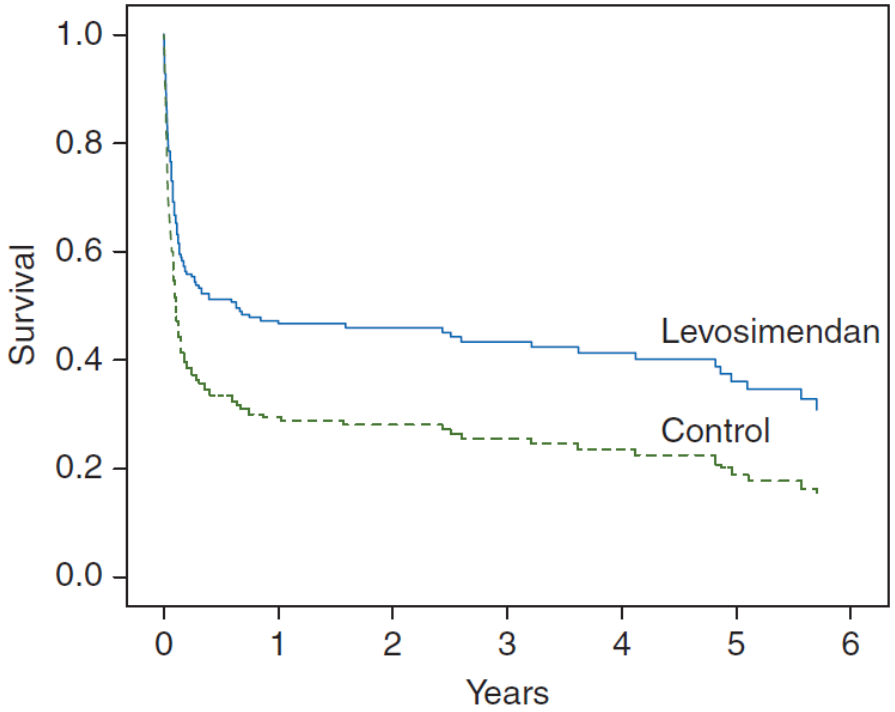


- Population matchée
  - LVS n=38
  - No LVS n=65
- Différence de mortalité à 30j = NS
  - HR = 0,55 (0,27-1,10) p=0,09
- Sevrage ECLS
  - Succès : 44% de LVS
  - Echec : 20% de LVS (p=0,01)
- Durée ECMO (12 vs 11j) NS

Sevrage de l'ECMO post-cardiotomie

Beneficial effects of levosimendan on survival in patients undergoing extracorporeal membrane oxygenation after cardiovascular surgery

K. Distelmaier[1], C. Roth[1], L. Schrutka[1], C. Binder[1], B. Steinlechner[2], G. Heinz[1], I. M. Lang[1], G. Maurer[1], H. Koinig[3], A. Niessner[1], M. Hülsmann[1], W. Speidl[1] and G. Goliasch[1,*]



British Journal of Anaesthesia, 117 (1): 52–8 (2016)

Early versus late treatment with levosimendan during temporary mechanical circulatory support

- Retrospective, monocentric
- All patients in ICU undergoing TCS
  - ECLS and/or
  - Impella CP or 5.0
- And receiving levosimendan during TCS
  - 24h of continuous infusion at 0.1 to 0.2 µg/kg/min
- From January 2015 to June 2017 (30 months)
- Comparison early (≤ Day 2) vs late (> Day 2) start of infusion
- Data: median [interquartile range]

Population description at baseline

	Early-LVS (N=10)	Late-LVS (N=22)	*p*
Age (y)	60.0 [57.5-66.8]	64.0 [59.0-68.5]	0.747
Weight (kg)	64.0 [60.4-68.8]	76.5 [62.0-80.8]	0.084
Male	4 (40%)	19 (86%)	**0.007**
Cardiac arrest	3 (30%)	10 (45%)	0.409
TCS under CPR	2 (20%)	6 (27%)	0.660
SAPS II ICU admission	52.5 [39.5-72.0]	62.5 [45.0-83.0]	0.328
SOFA at TCS start	8.5 [7.0-10.0]	10 [8.0-12.0]	0.175
Lactate at TCS start (mmol/l)	4.0 [2.6-6.1]	4.1 [2.9-10.3]	0.332
Encourage score	22.5 [15.8-30.0]	22.5 [18.0-25.5]	0.978
SAVE score	-5.0 [-12.3 to -0.3]	-8.5 [-12.0 to -4.0]	0.442
TCS flow at LVS start (l/min)	3.2 [2.9-4.5]	3.2 [2.7-3.8]	0.638

Hemodynamic results Day 0 vs Day 3 after LVS start

	Day 0 of LVS infusion (N=32)	Day 3 after LVS start (N=31)	*p*
TCS flow (l/min)	3.2 [2.8-4.5]	2.3 [0.0-4.2]	**<0.001**
Pulse pressure (mmHg)	30 [19-39]	37 [26-52]	**0.019**
Mean Arterial Pressure (mmHg)	72 [68-79]	73 [65-78]	0.420
LV-EF (%)	15 [7-21]	25 [11-36]	**0.004**
Vasoactive-inotropic score	18.2 [4.17-42.7]	17.8 [0.0-41.7]	0.768

- Hemodynamic changes = [Day 3 - Day 1]
  - No differences Early vs Late –LVS for all these parameters
  - Same hemodynamic response
  - TCS weaning at day 3 after LVS: 22 vs 32% (NS)

Hemodynamic results Day 0 vs Day 3 after LVS start

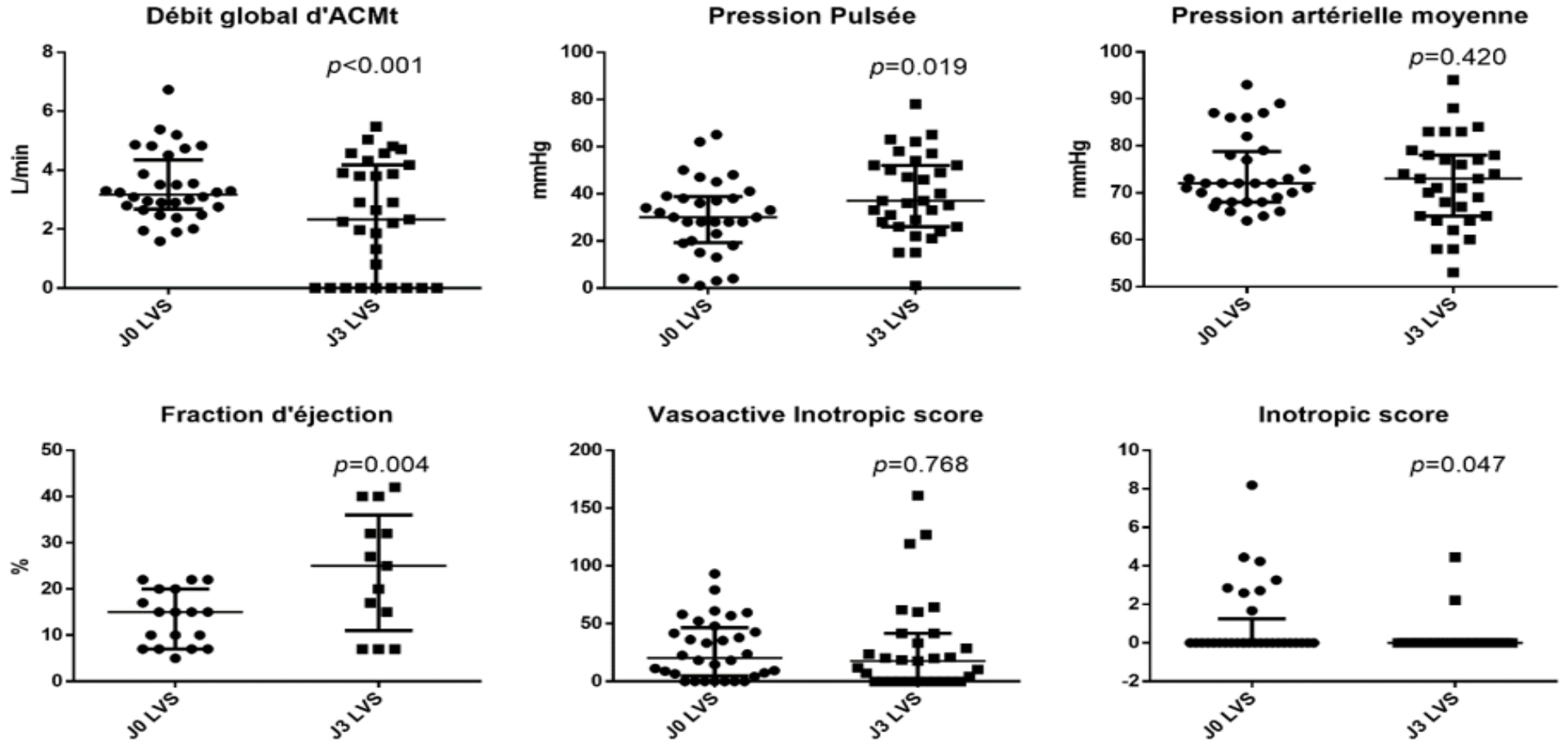
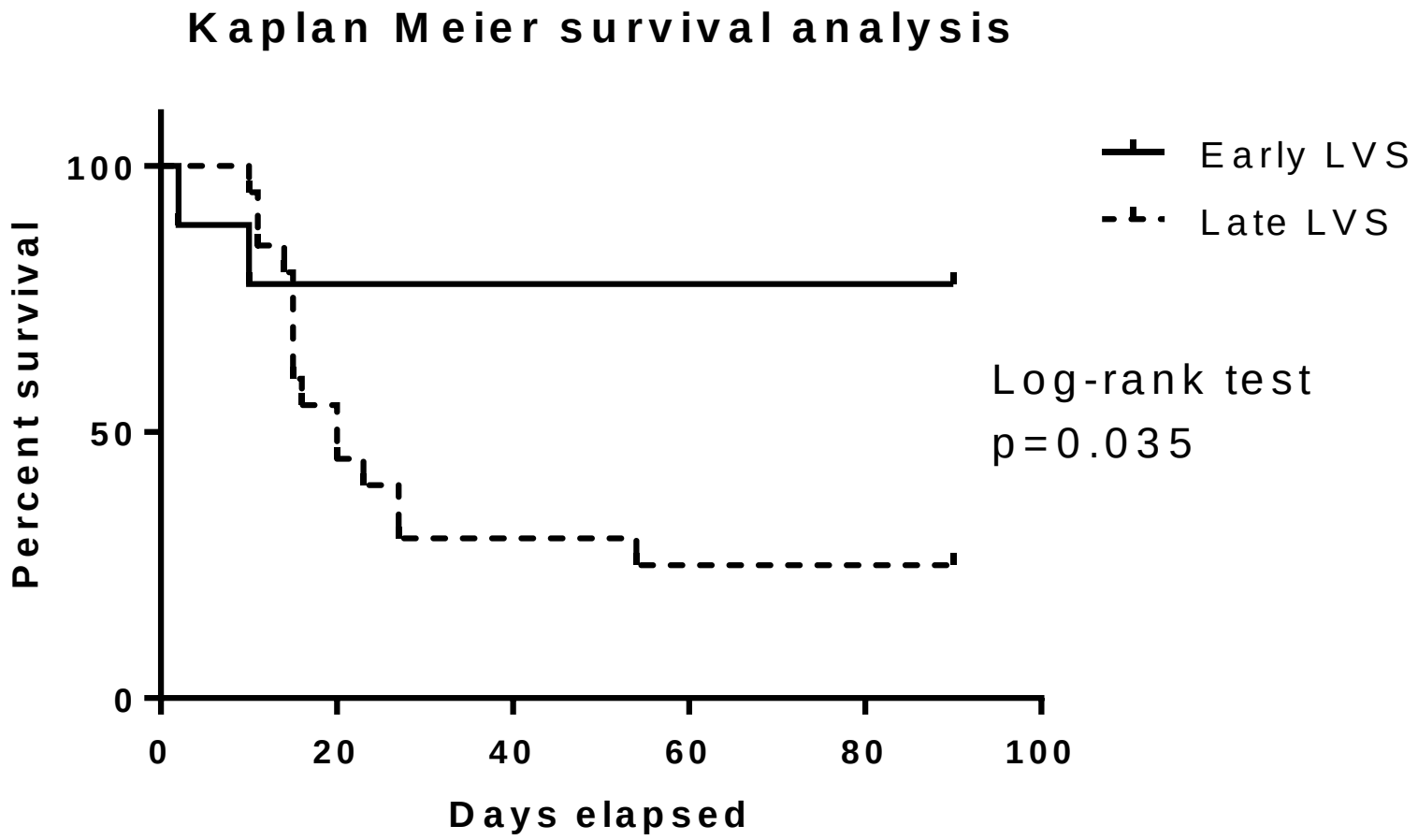


Figure 2 : Paramètres hémodynamiques à J0 et J3 d'administration de Lévosimendan chez des patients en choc cardiogénique sous assistances cardiaques mécaniques temporaires.

Outcome

	Early LVS (N=10)	Late LVS (N=22)	*p*
TCS duration (d)	9.0 [5.5-11.5]	11.5 [9.0-15.0]	**0.028**
SOFA after TCS stop	4 [1-6]	11 [6-15]	**0.008**
Days free of TCS at D28 (d)	18.5 [15.5-20.5]	15.5 [0.0-20.0]	0.173
ICU free days at D28 (d)	4.5 [0.5-11]	0.0 [0.0-2.8]	**0.029**
ICU stay after TCS (d)	13 [9-15]	16 [15-21]	**0.033**
ICU mortality	2 (20%)	13 (59%)	**0.04**
3-month mortality	2 (20%)	15 (68%)	**0.011**

Prognosis


Kaplan Meier survival analysis
Percent survival
100
50
0
0
20
40
60
80
100
Days elapsed
Early LVS
Late LVS
Log-rank test
p=0.035

Perspectives: PHRC-N

COMBES	Alain	PHRCN-17-0193	750712184	AP-HP

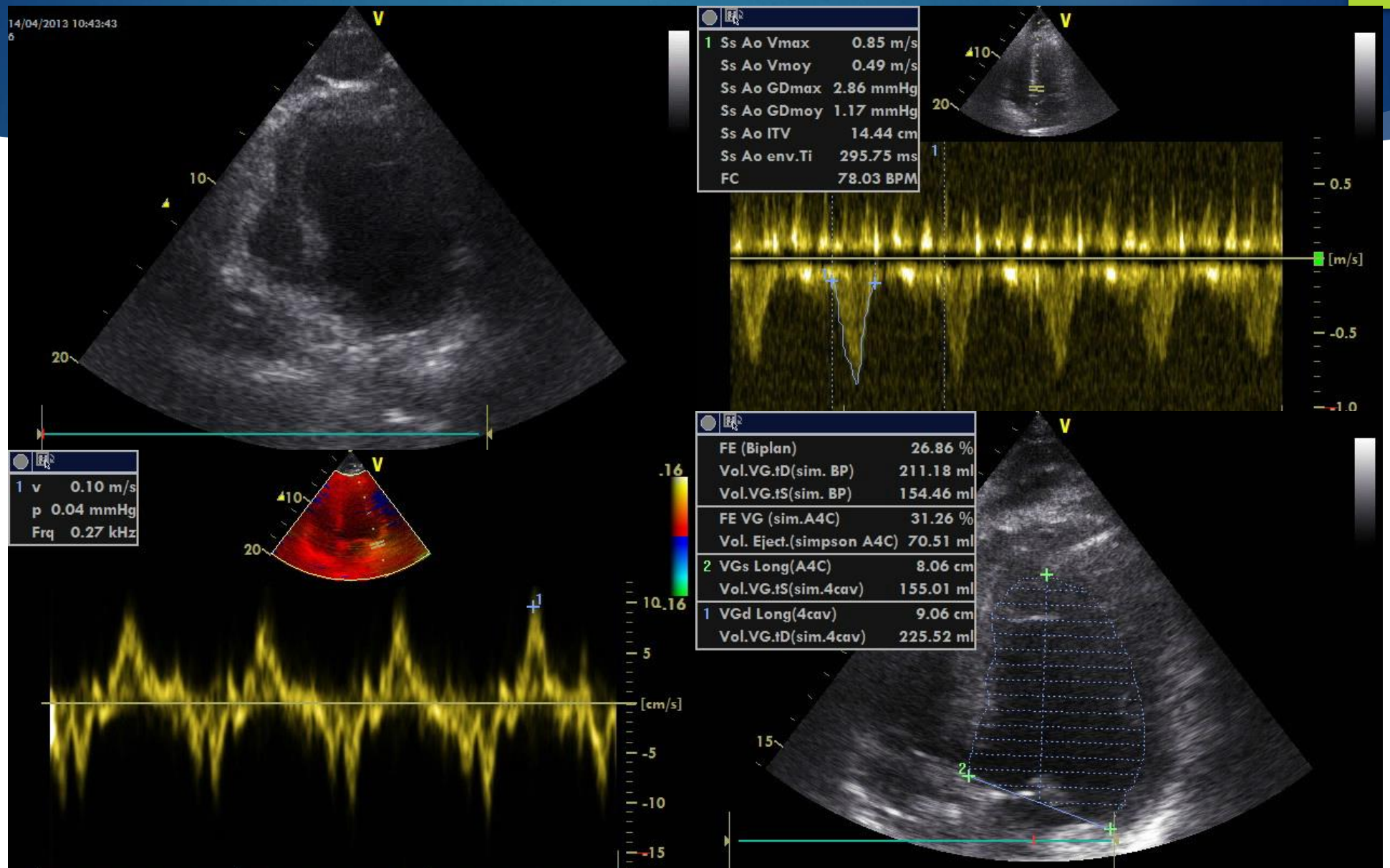
LEVOECMO	LEVOSIMENDAN to facilitate weaning from ECMO in refractory cardiogenic shock patients	558 838 €

Modalités de sevrage des ACM

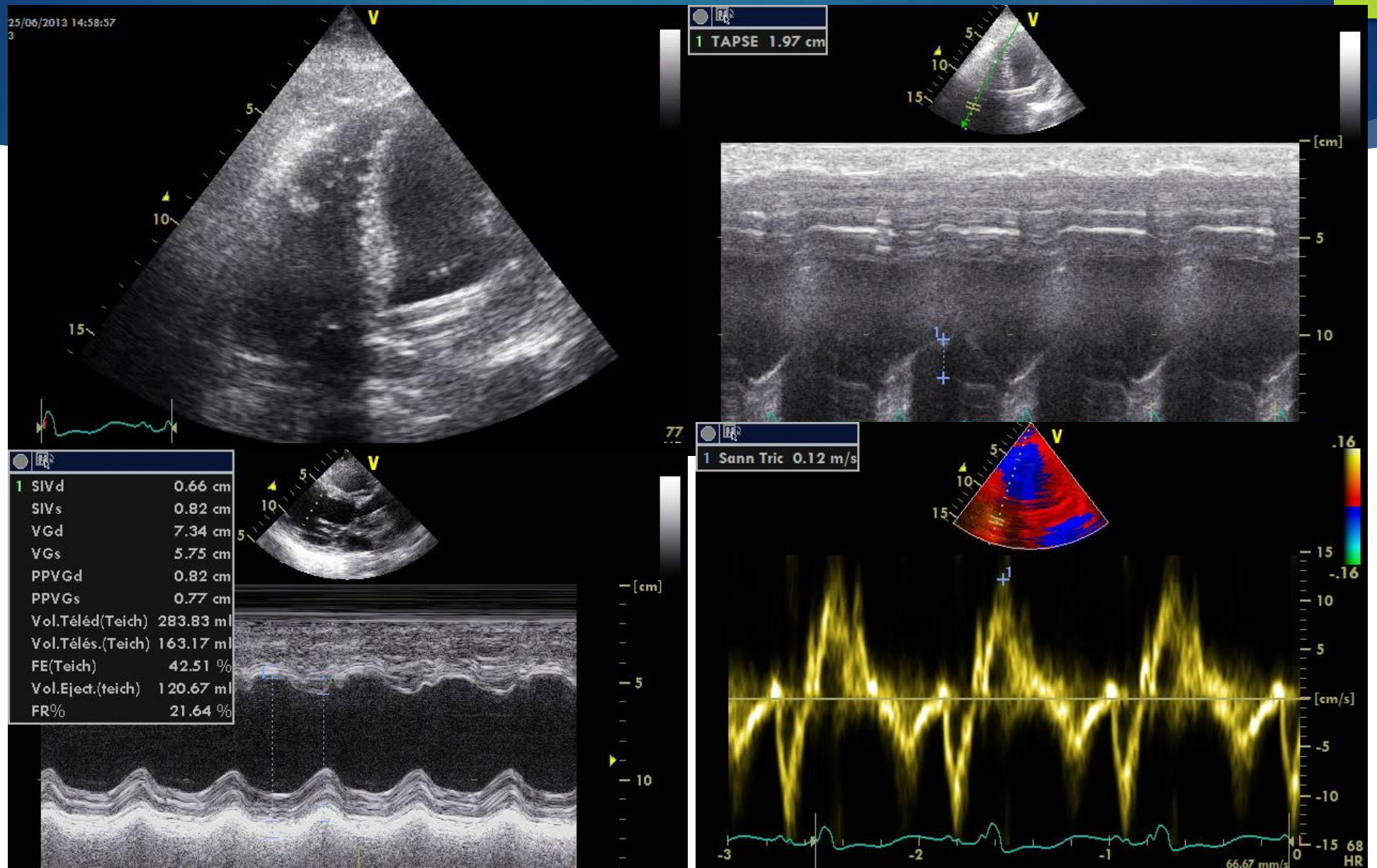
- Par paliers: transfert de débit
  - ↘ progressive débit ACM
  - Reprise parallèle du débit cardiaque natif
    - Débit transpulmonaire: Swan Ganz, EtCO2
    - VG: ITV sous-aortique, Pression Pulsée
- Transition:
  - Retour aux inotropes ?
  - Transfert vers ACM moins invasive: ECLS => Impella 5.0
- Précautions lors du sevrage
  - Majoration des cibles d'anticoagulation
- Test d'arrêt: controversé, toujours bref

- ECLS
  - Vitesse minimale: 1500 TPM
  - Débit minimal: 1,5 L/min
  - Test clampage: 15 min
    - Bolus HNF
    - Au bloc
- Impella
  - Vitesse minimale: P1
  - Pas d'arrêt complet mais correspond à la compensation de la fuite

Weaning ECMO or not ??

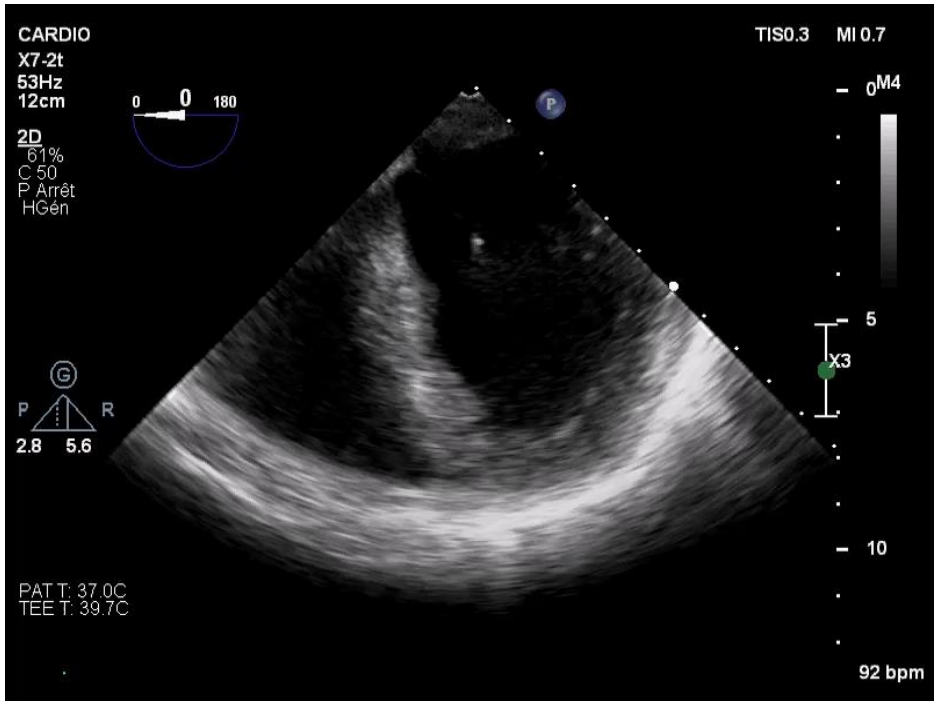


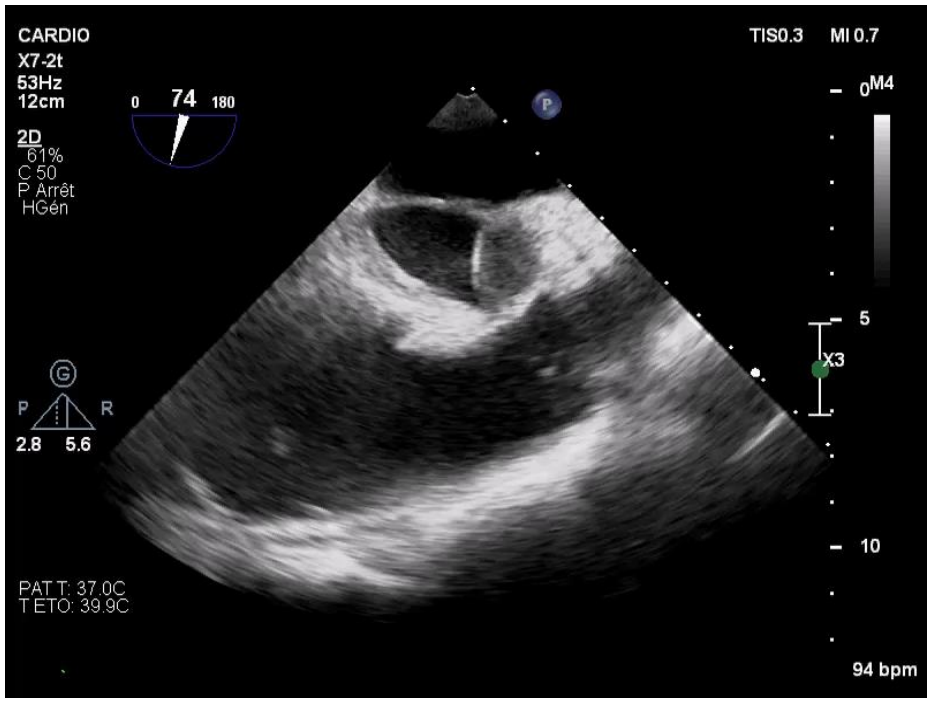
ECMO weaning on Impella®



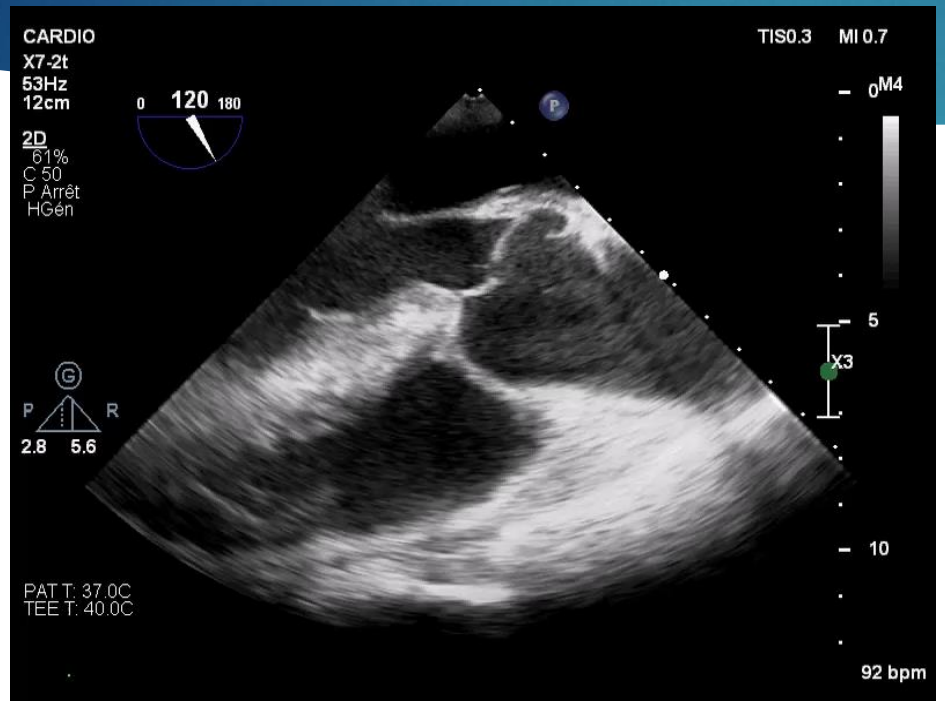
Sevrage ECLS ?

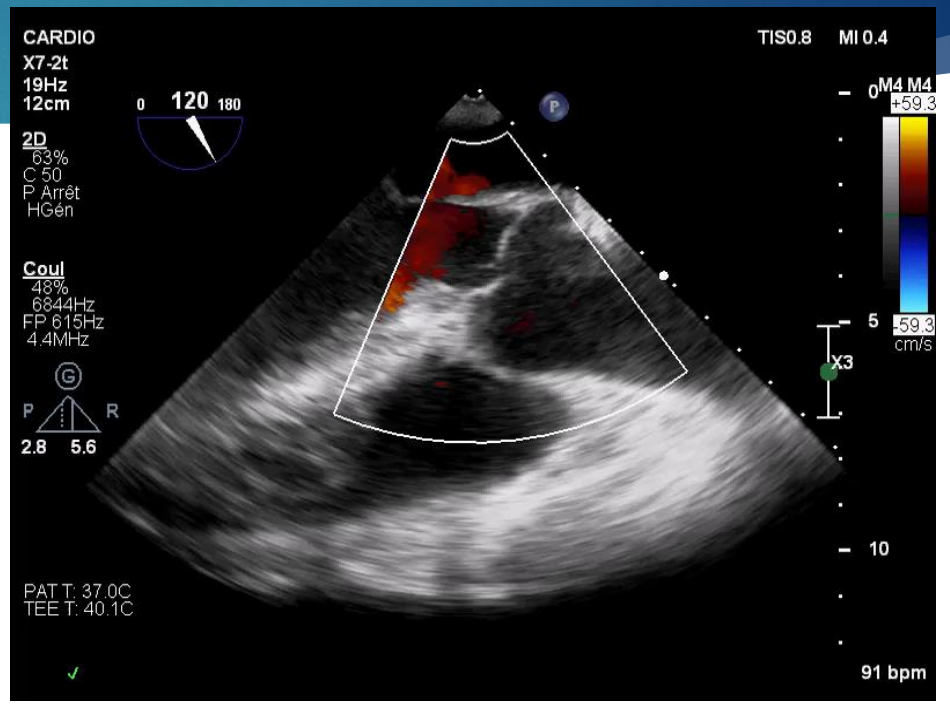
- Patient 55 ans sous ECMO-VA
- Après ACR sur SCA
- Evaluation fonction VG, récupération?

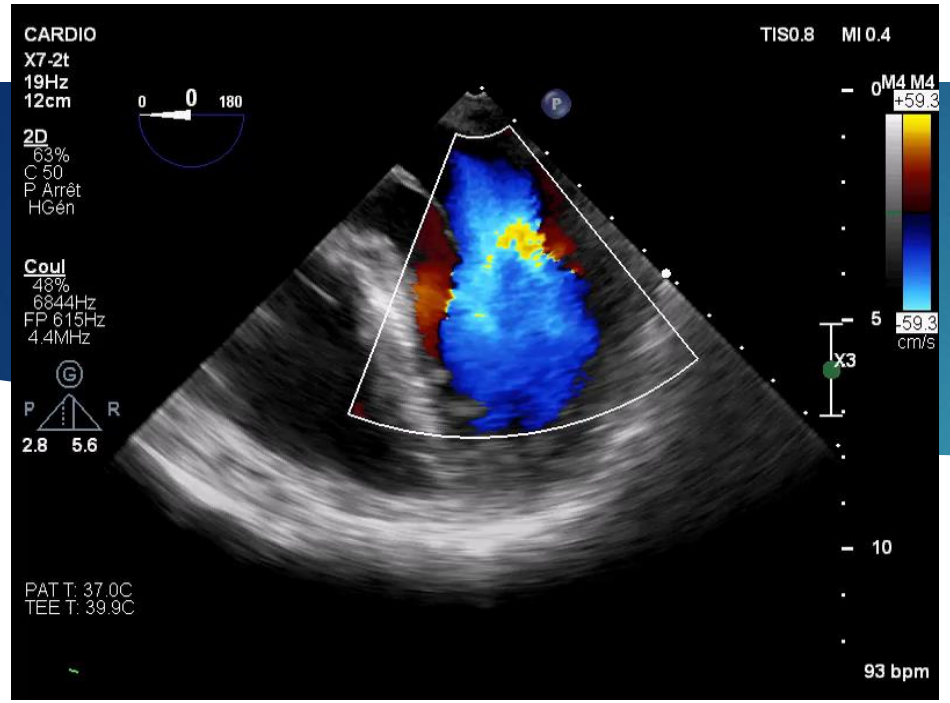


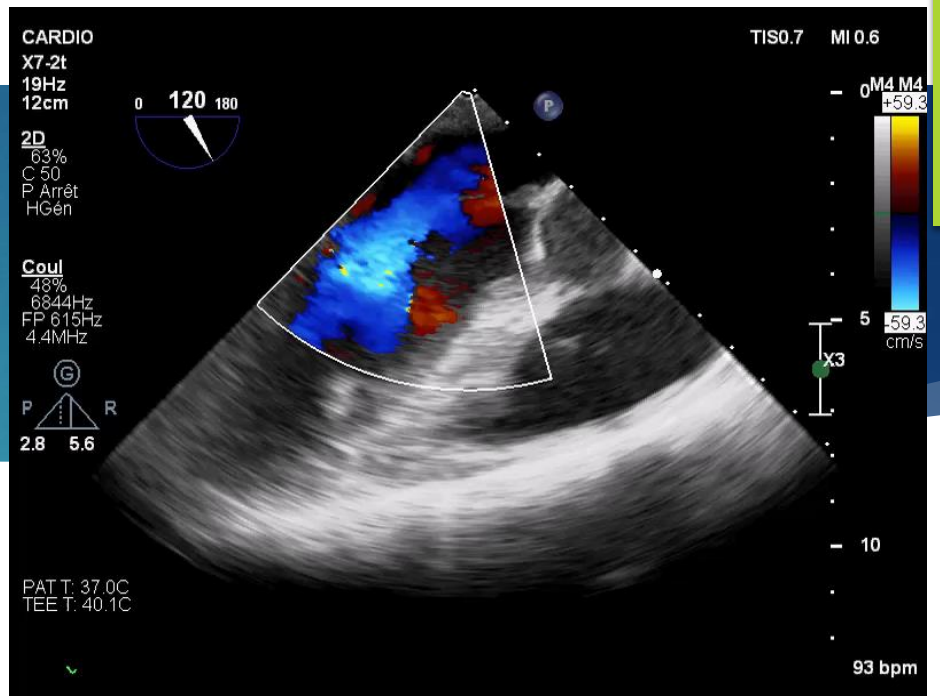


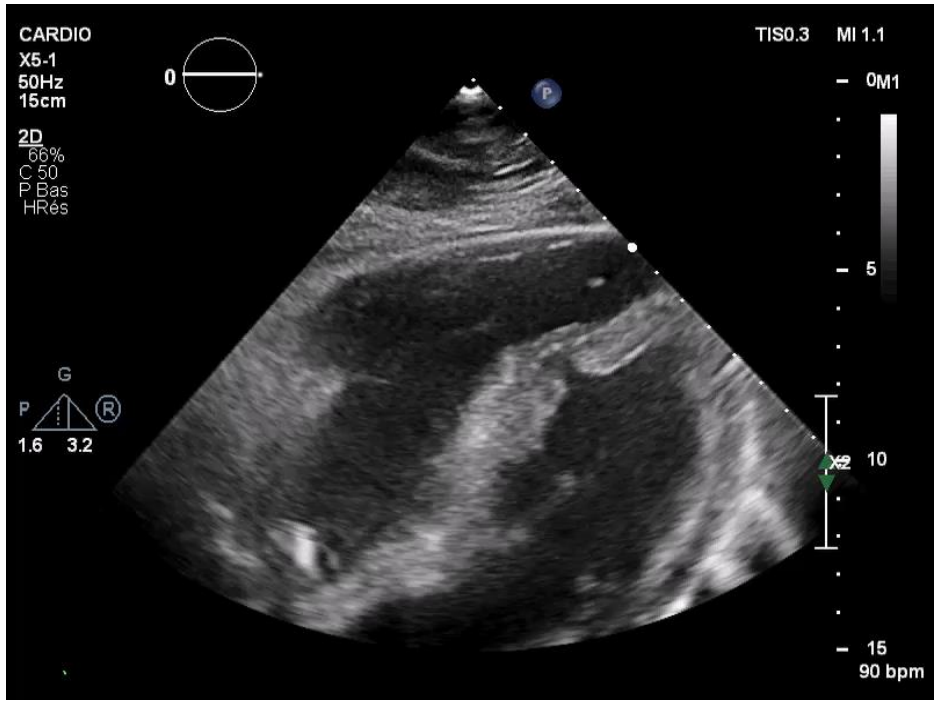
ITV sous-aortique ?

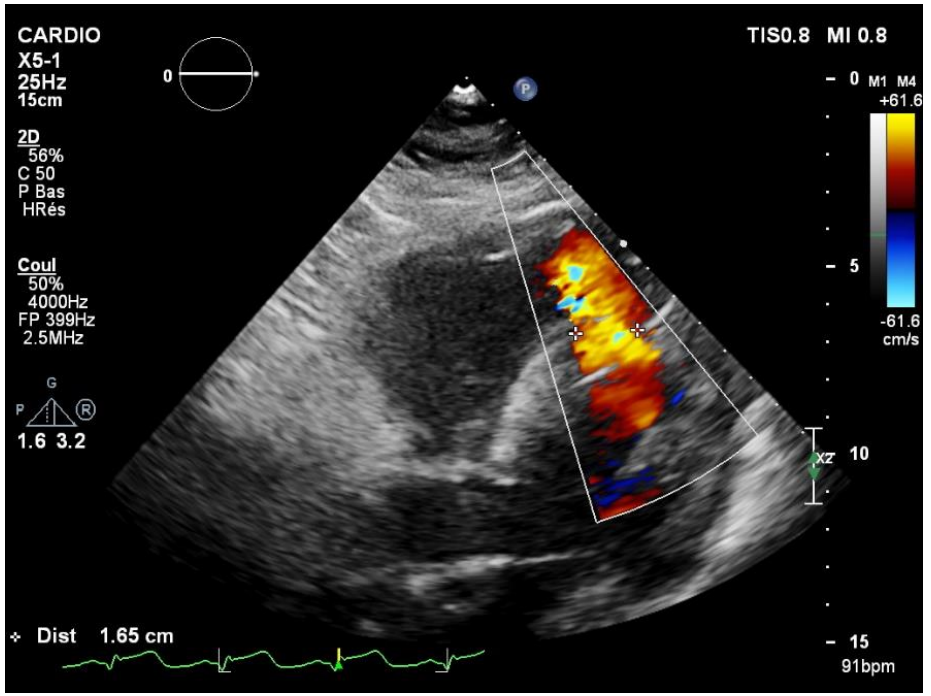





CARDIO
X7-2t
19Hz
12cm
2D
63%
C 50
P Arrêt
HGén
Coul
48%
6844Hz
FP 615Hz
4.4MHz
2.8 5.6
TIS0.8 MI 0.4
M4 M4
+59.3
-59.3
cm/s
PAT T: 37.0C
TEE T: 39.9C
93 bpm


CARDIO
X7-2t
19Hz
12cm
2D
63%
C 50
P Arrêt
HGén
Coul
48%
6844Hz
FP 615Hz
4.4MHz
2.8 5.6
TIS0.7 MI 0.6
M4 M4
+59.3
-59.3
cm/s
PAT T: 37.0C
TEE T: 40.1C
93 bpm


CARDIO
X5-1
50Hz
15cm
2D
66%
C 50
P Bas
HRés
1.6 3.2
TIS0.3 MI 1.1
M1
90 bpm


CARDIO
X5-1
25Hz
15cm
2D
56%
C 50
P Bas
HRés
Coul
50%
4000Hz
FP 399Hz
2.5MHz
1.6 3.2
TIS0.8 MI 0.8
M1 M4
+61.6
-61.6
cm/s
Dist 1.65 cm
91bpm

Evaluer la réponse au sevrage

- Tolérance du sevrage et du retrait de l'ACM
  - Hémodynamique
  - Perfusion tissulaire:
    - Lactate
    - SvO2 ou ScvO2
    - NIRS
  - Microcirculation
    - Sublinguale
    - Gap CO2
    - Réactivité microvasculaire
  - Fonctions d'organes
- Sevrage réussi
  - Absence de reprise d'inotropes ou d'assistance mécanique sur cœur natif à J2, 7 ou 15 ?

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DOI 10.1186/s13054-017-1855-2

Critical Care

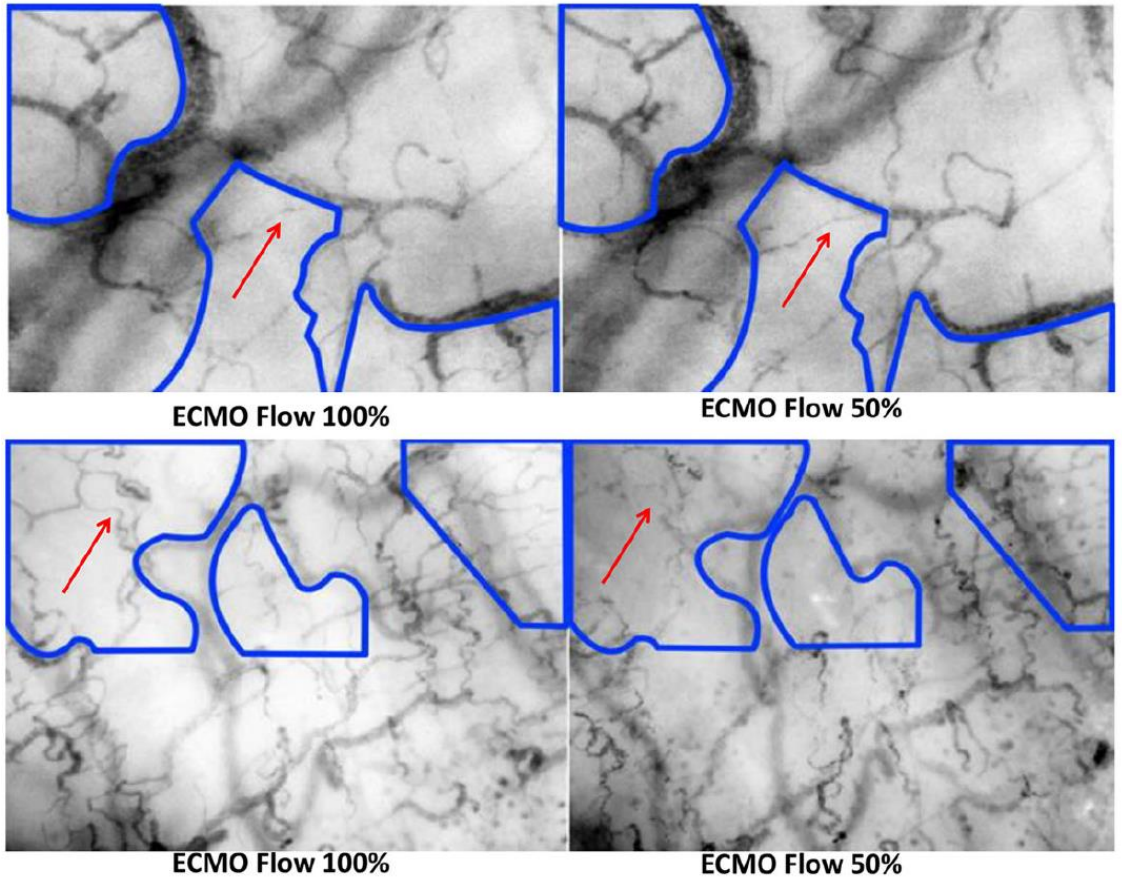
RESEARCH Open Access

Functional evaluation of sublingual microcirculation indicates successful weaning from VA-ECMO in cardiogenic shock

Sakir Akin[1,2*], Dinis dos Reis Miranda[1], Kadir Caliskan[2], Osama I. Soliman[2], Goksel Guven[1,2], Ard Struijs[1], Robert J. van Thiel[1], Lucia S. Jewbali[1,2], Alexandre Lima[1], Diederik Gommers[1], Felix Zijlstra[2] and Can Ince[1]

- F100: ECMO 6,1L/min; PAM 77mmHg
- Succès sevrage
- F50: ECMO 3L/min; PAM 64 mmHg

- F100: ECMO 4,7L/min; PAM 75mmHg
- F50: ECMO 2,7L/min; PAM 67 mmHg
- Echec sevrage



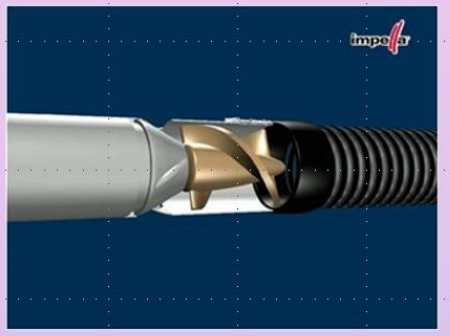
Gérer les échecs de sevrage

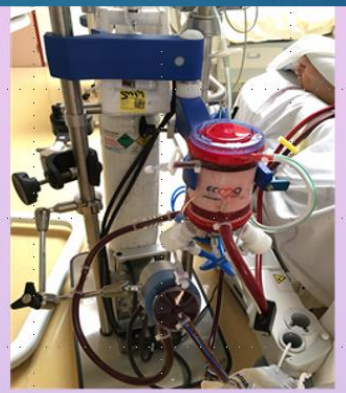
- Echec
  - Absence de critères positifs après un délai raisonnable d'ACM
  - Récidive du CC au retrait de l'ACM
- Facteurs favorisant l'échec ?
  - Critères de sevrage faussement positifs
  - Optimisation non optimale
  - Facteurs intercurrents: sepsis, hypoxémie
- Solutions alternatives en l'absence de récupération ?
  - Transplantation
  - LVAD, BiVAD, TAH
- Limitation thérapeutique ?

Conclusion

- Inotropes et ACM = traitements symptomatiques du choc cardiogénique
  - Vocation à être sevrés
  - Favoriser les moins délétères: Etudes à mener
- Définir une ou des stratégies d'ACM intégrant le sevrage
  - Priorité: restaurer les perfusions d'organe
  - Protéger le myocarde défaillant
  - Déterminer précocement la possibilité de récupération
  - Combiner les thérapeutiques
- Le sevrage aussi est un travail d'équipe: « Heart-Team »

HEART-TEAM





Cardiologue

Anesthésiste Réanimateur

Perfusioniste
IDE formées

Chirurgien cardiaque