

# Myocardiopathie du péripartum



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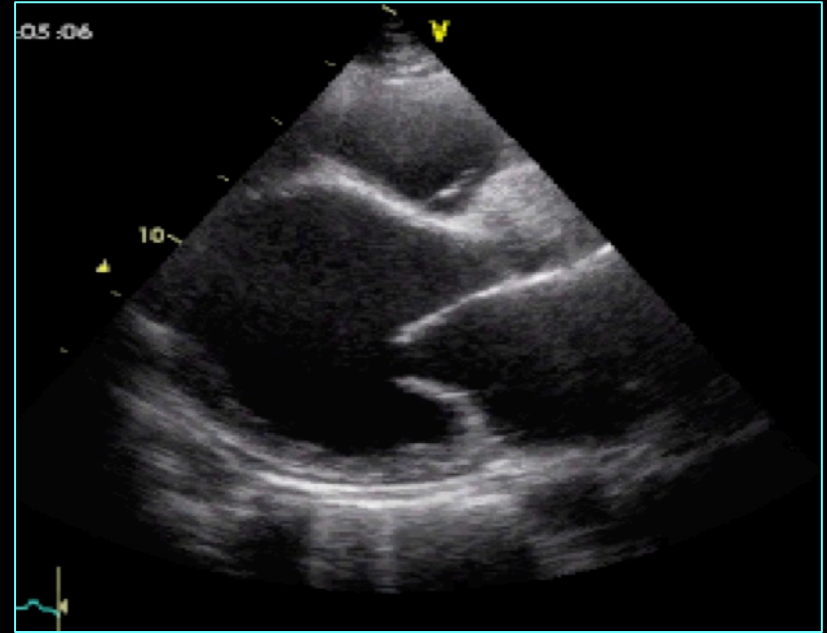
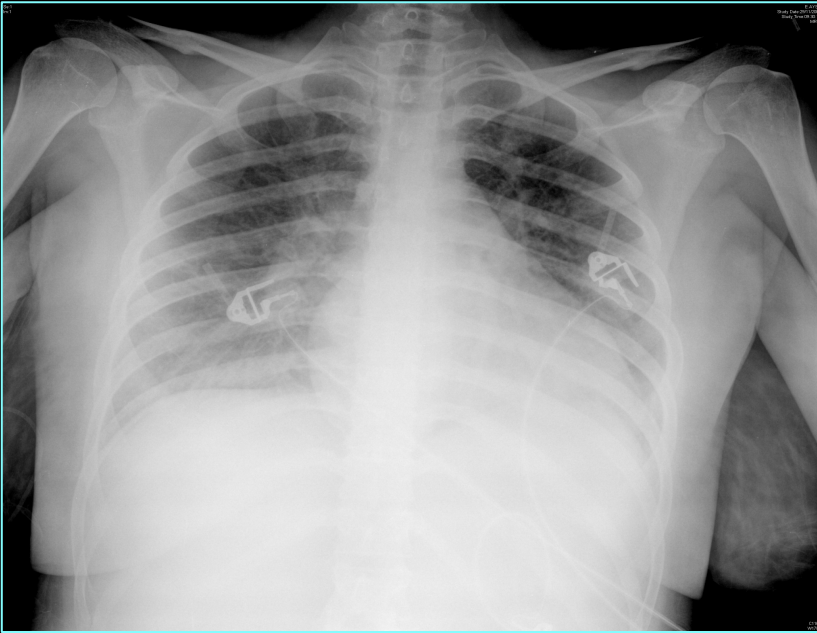
# Conflict of Interest Disclosure

	Employment	Stockholder	Owner	Consulting Fees	Lecture Fees	Invitations to congress	Educational / research grants
<i>Abott Cardiovascular</i>							<b>X</b>
<i>Astra Zeneca</i>				<b>X</b>	<b>X</b>	<b>X</b>	<b>X</b>
<i>Bayer</i>						<b>X</b>	
<i>Biopharma</i>					<b>X</b>	<b>X</b>	<b>X</b>
<i>Bristol Meyer Squibb</i>						<b>X</b>	
<i>Boston Scientific</i>							<b>X</b>
<i>Daichi-Sankyo</i>				<b>X</b>	<b>X</b>	<b>X</b>	<b>X</b>
<i>Edwards</i>					<b>X</b>	<b>X</b>	
<i>Hexacath</i>						<b>X</b>	<b>X</b>
<i>Johnson &amp; Johnson</i>						<b>X</b>	<b>X</b>
<i>Lilly</i>				<b>X</b>	<b>X</b>	<b>X</b>	<b>X</b>
<i>Medtronic</i>					<b>X</b>		<b>X</b>
<i>Sanofi-Aventis</i>					<b>X</b>	<b>X</b>	<b>X</b>
<i>The Médecine Co</i>					<b>X</b>	<b>X</b>	<b>X</b>

# Case report

- 29 yr old woman without past medical history
- 30/10 3<sup>rd</sup> normal pregnancy – 3<sup>rd</sup> delivery at 39 w.o.a  
Caesarean section because of umbilical cord precedence  
Healthy 2.9 kg female baby
- 06/11 Discharge – LMWH prophylaxis
- 08/11 Onset of dyspnoea and atypical chest pain
- 09/11 Admission to ER
  - Pulmonary embolism ruled out
  - Final diagnosis : pneumonia - Amoxycilline + clavulanic Ac.
- 18/11 Back to ER
  - Intense fatigue and abdominal chest pain
  - Patent congestive heart failure, BP 84/68 mmHg, HR 105 bpm, Normal EKG

# Case report



- LV dilation 55 mm (i.e., 33 mm/m<sup>2</sup>), LVEF 32%, restrictive mitral flow
- CO: 2.5 l/min
- Mild mitral regurgitation
- Mild pericardial effusion

# Case report

- 19/11 Furosemide, Heparin Dobutamine
- 20/11 CO 2l/min, worsening EF (20% ) IABP
- 22/11 Declining hemodynamic status  
Multiple organ failure ECLS
- 27/11 Hemodynamic stabilisation  
Regression of MOF  
Complete LV akynesia with apical thrombus  
Cardiac transplantation "SU" listing
- 28/11 Cardiac transplantation
- 3 yr follow-up: Mother and child are fine

# Definition : NHBLY 1997

1. Congestive heart failure occurring during
  - last month\* of pregnancy    \* Or last trimester : « early peri-partum CMP »
  - or within 5 months after delivery
2. Absence of found aetiology despite exhaustive testing (“elimination diagnosis”)
3. Absence of previously know heart disease
4. TEE evidences of LV dysfunction
  - LVEF < 45% ou LVSF < 30%
  - LV dilation with EDD > 2.7 cm/m<sup>2</sup>



EUROPEAN  
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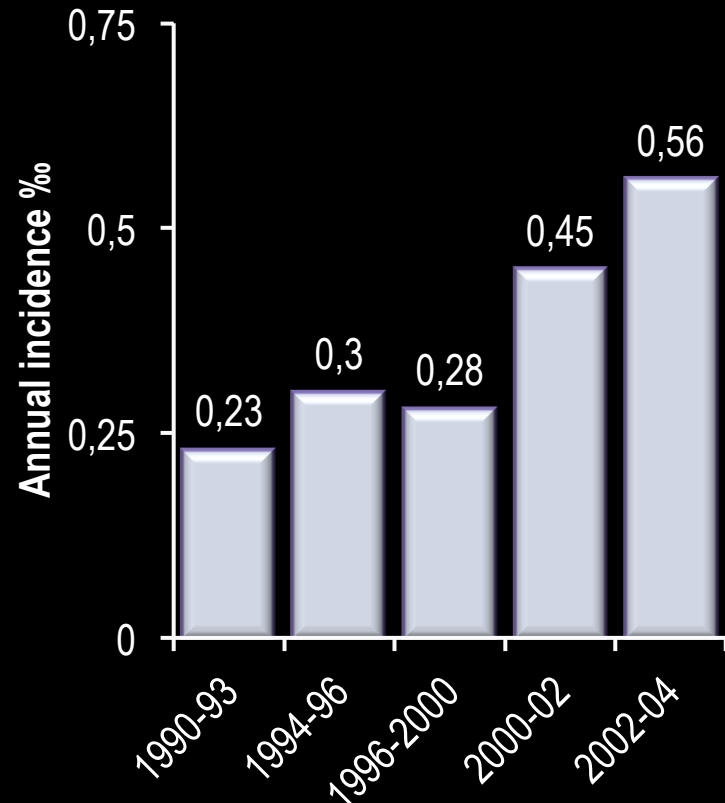
# Definition : ESC 2011

- « PPCM is an idiopathic cardiomyopathy presenting with heart failure secondary to LV systolic dysfunction towards the end of pregnancy or in the months following delivery, in a previously healthy woman
- It is a diagnosis of exclusion when no other cause of heart failure is found.
- The LV may not be dilated, but the EF is nearly always reduced below 45%. »

# Epidemiology

- Incidence in western countries  
1 / 3000 live births, and increasing

In France :  $\pm$  800 000 births  
Estimated incidence 250-300 / yr

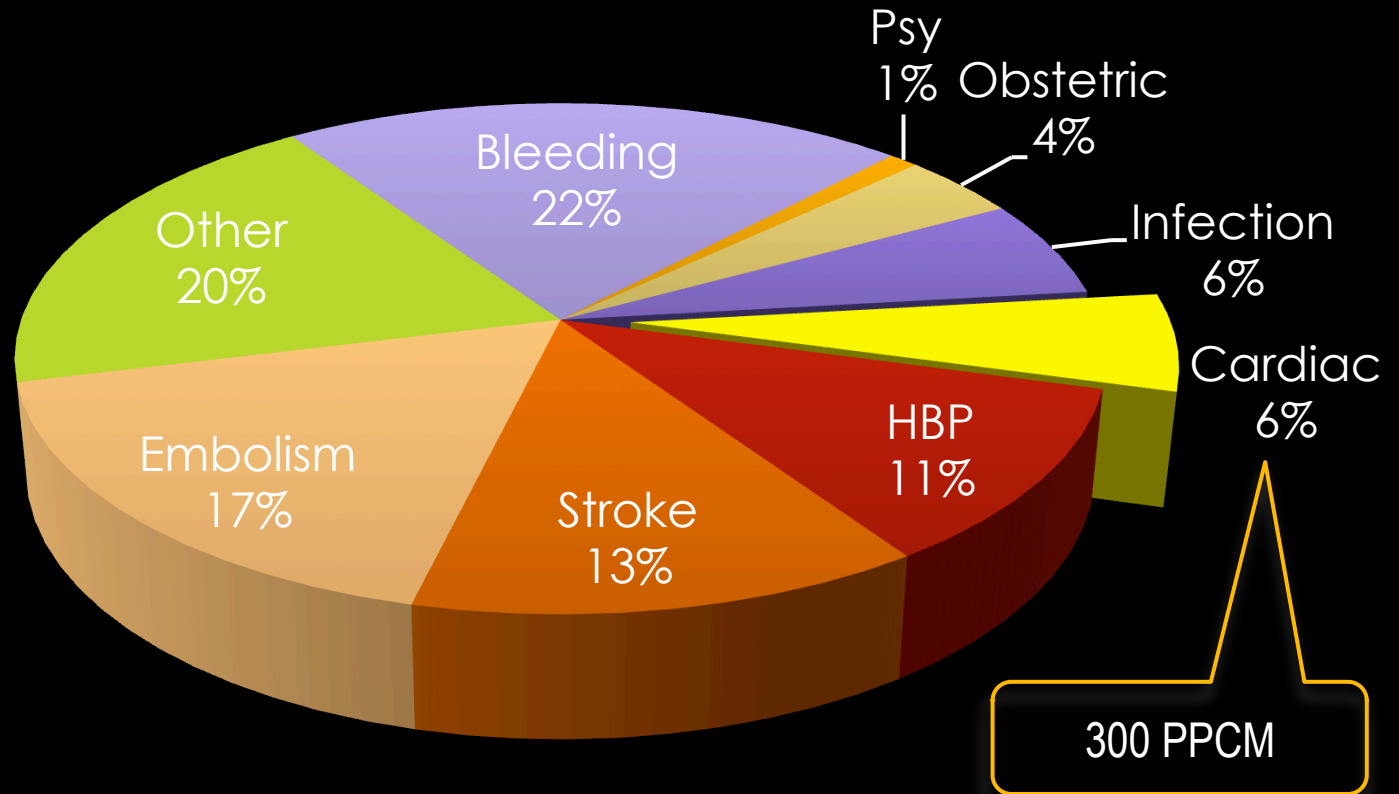


- Wide geographic variations +++

Nigéria	1/100
South Africa	1/1000
Haiti	1/300
Côte d'Ivoire	1/2500

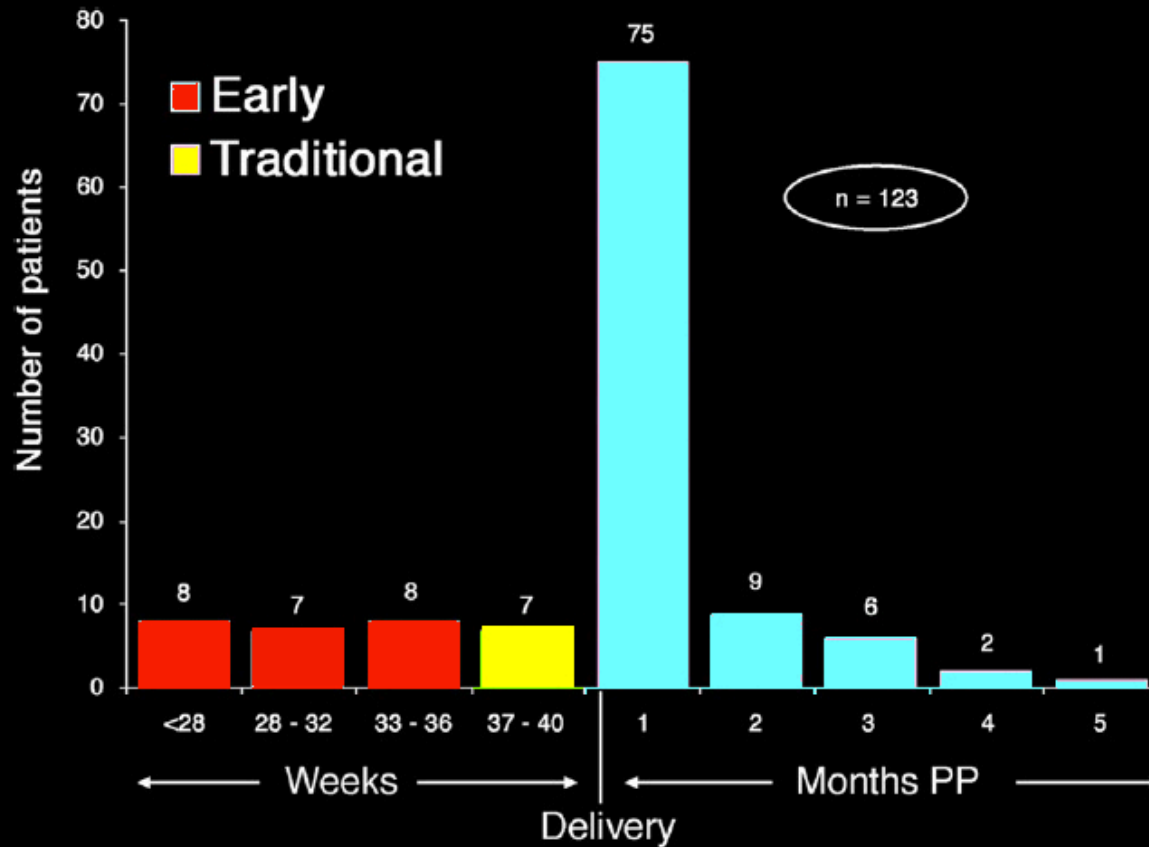


# Peripartum complications



# Epidemiology

- Incidence peak : 2<sup>nd</sup> week after delivery



# Risk factors

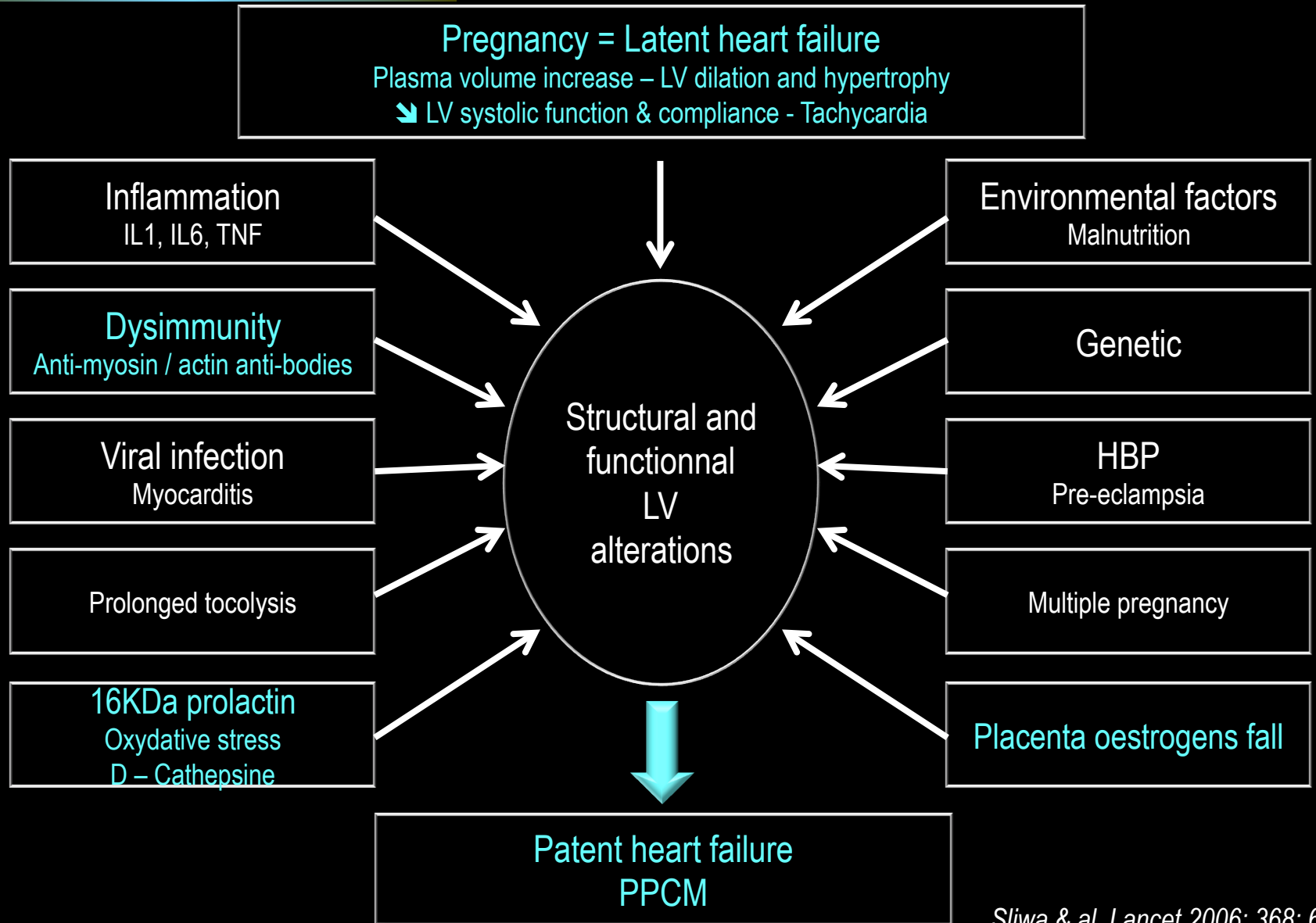
- Family (?) or personal history of PPCM
- Age > 30 years - Teenagers
- HBP & pre-eclampsia
- Multiparity (in northern countries)
- Multiple pregnancy
- Obesity, diabetes, active smoking
- South- African origin, low socio-economical level, tropical regions
- 24-37% of women presenting with PPCM have no RF

# Risk factors

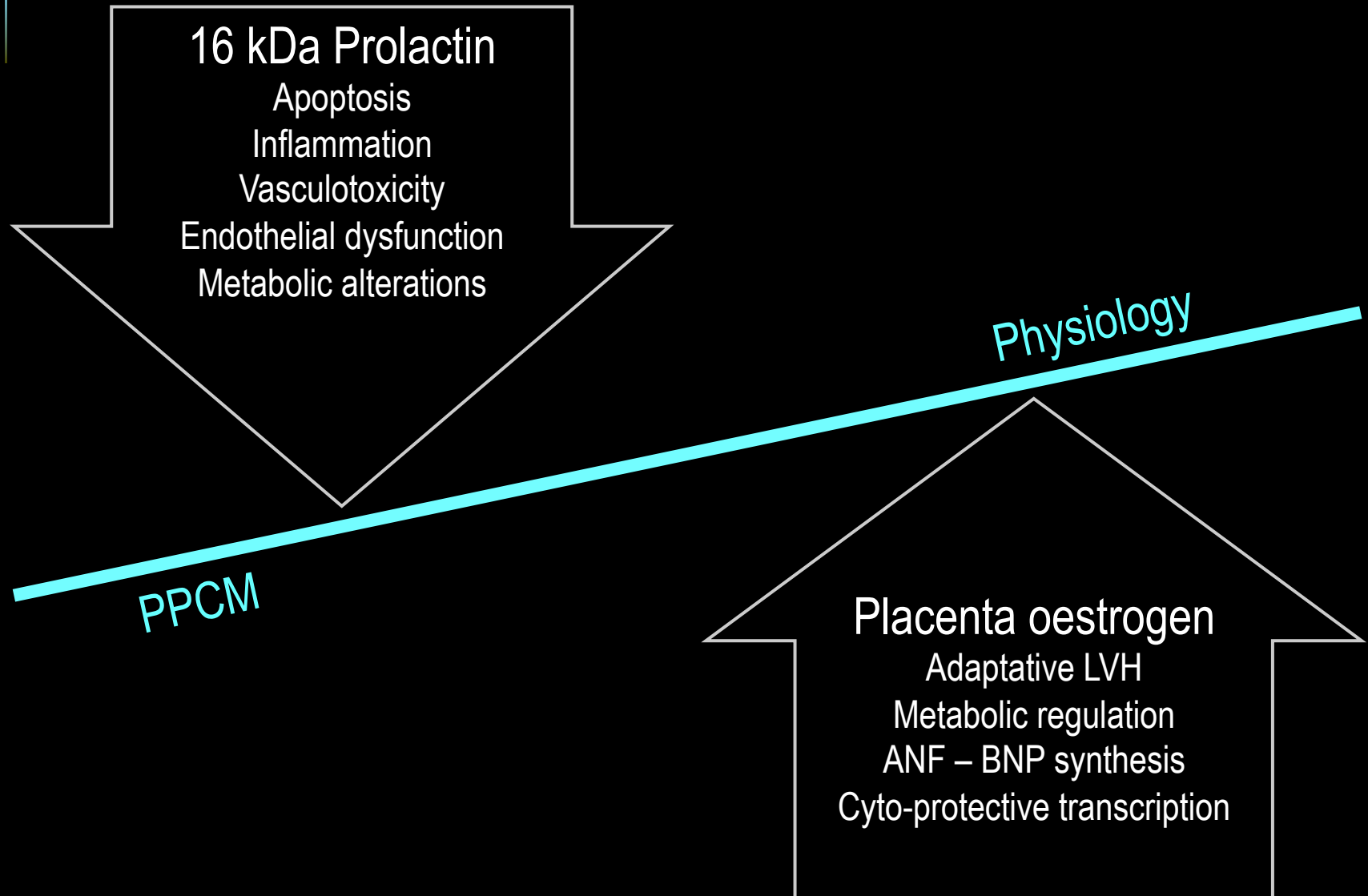
8 severe PPCM ( 2008 - 2010)

Age (year)	33 $\pm$ 8	20 – 43
> 30 years (N)	6	75%
BMI (kg/m <sup>2</sup> )	22.6 $\pm$ 6.9	17.1 – 39.2
Parity (n)	4.1 $\pm$ 2.6	G2P2 – G10P7
Multiple pregnancy	3 (38%)	
Term (W.o.A)	37 $\pm$ 2	33 – 39
Caesarean section	4 (50%)	
Median delay of onset > delivery (J)	+ 13	+2 à + 60
Clinical presentation		
Dyspnea NHYA III-IV	5	
Acute pulmonary oedema	2	
ACS	1	
LV EDD(cm/m <sup>2</sup> )	3.8 $\pm$ 6	29 – 40
LVEF (%)	23 $\pm$ 9	10 – 40

# Pathophysiology



# 16 kDa prolactin / Placenta oestrogens



# Diagnosis

- Clinical presentation
  - Rapidly worsening dyspnoea
  - Cough (increased with decubitus)
  - Chest pain = 50% of the cases
  - Fatigue, LL oedema
- Physical examination, blood testing and X rays = Non specific
- EKG
  - Sinus tachycardia, possible VPB or VT
  - Non specific ST-T abnormalities (myocarditis? ACS?)

# Differential diagnosis

- May cause delay in Dc and therapeutic management
  - Pulmonary embolism
  - Pneumonia
  - Acute coronary syndrom
    - Spontaneous coronary dissection
    - Sulprostone (Nalador®)
  - Other causes of heart failure
    - Previously unknown CMP (3<sup>rd</sup> trimester)
    - Prolonged tocolysis with  $\beta$ -analogues (stress CMP)



# Testing

- TEE +++
  - Moderate LV dilation
  - Decreased LVEF < 45%
  - RV associated dysfunction ( 56% TAPSE < 14) → prognosis
  - LV thrombus
  - Differential diagnosis with previous CMP
- MRI
  - Myocarditis
  - Prognostic value ?

# Testing

- Invasive testing
  - Unnecessary
  - Emergent coronary angiography when ACS suspected
  - Hemodynamic monitoring in fulminant types (ECLS ?)
- Endomyocardic biopsy
  - No consensus (fulminant type ?)
  - Non specific myocarditis
  - Possible therapeutic impact ?
    - Inflammation / lymphocytes
    - Tegelin / immunosuppressive Rx ?

# Evolution : Rapid and unpredictable

- Hemodynamic
  - Refractory cardiogenic choc (10-15%)
- Arrhythmias
  - Rhythmic storm, VT, VF
- Embolism
  - High risk of cardiac thrombus (10 – 17%)
- Fatality
  - 0 to 19% in US series

# Therapeutic management

- Consider admission in tertiary ICCU with life support capability and cardiac surgery
- Non specific medical regiment

## During pregnancy

- ◆ Rest, HSR
- ◆ **ACEi/ARB Nitrates + Hydralazin**
- ◆  $\beta$ -blockers (metoprolol)
- ◆ **Loop diuretics (!)**
- ◆ Digoxin
- ◆ **Anticoagulation** if LVEF < 35-40%

Delivery asap

## After delivery

- ◆ Rest, HSR
- ◆ ACEi/ARB  $\pm$  spironolactone
- ◆  $\beta$ -blockers
- ◆ Loop diuretics
- ◆ Digoxin
- ◆ **Anticoagulation** if LVEF < 35-40%

Contraception  $\rightarrow$  LVEF > 50%

- ◆ Inotropic drugs
- ◆ Non invasive / invasive ventilation
- ◆ Life support (IABP to ECLS)

# Therapeutic management

- If a patient is dependent on inotropes despite optimal medical therapy, she should be transferred to a facility where intra-aortic balloon pump counterpulsation, ventricular assist devices, and transplant consult teams are available.

# Specific therapy ?

- Immunologic

- Empiric
- Biopsy = myocarditis (inflammations / lymphocytes +++)
- Azathiopyrin  $\pm$  corticoids  $\pm$  IV immunoglobulins

*Murali & al. Crit Care Med 2007 ; 33 : S340–6*

- Bromocriptine

- Hypothesis : oxydative stress – D cathepsin D – 16kDa prolactin
- Dopaminergic agonists
- Inhibition of 23kDa prolactin by HHS

*Sliwa & al. Circulation. 2010 ; 121 : 1465-73*

# Bromocriptine

**Circulation**  
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart  
Association  
*Learn and Live™*

(*Circulation*. 2010;121:1465-1473.)

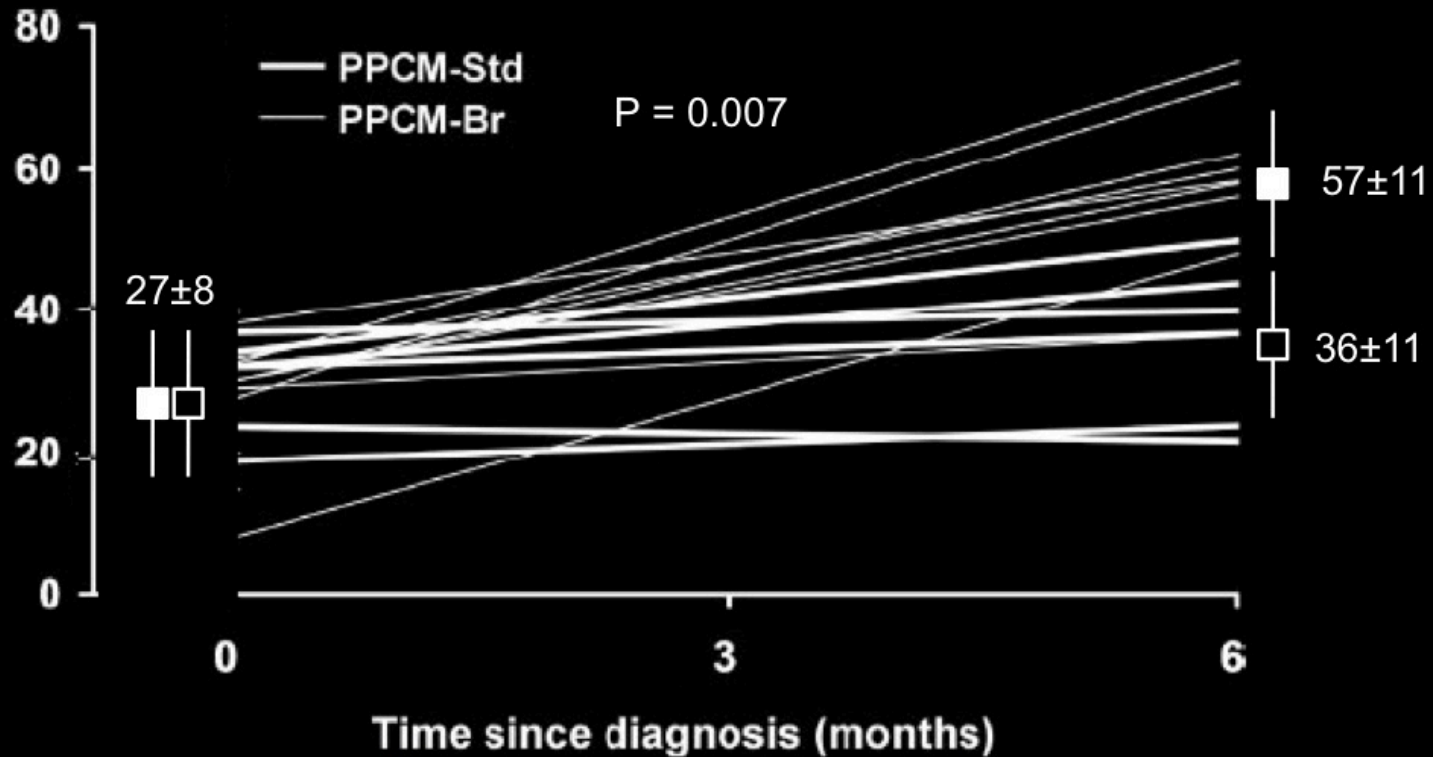
## **Evaluation of Bromocriptine in the Treatment of Acute Severe Peripartum Cardiomyopathy**

### **A Proof-of-Concept Pilot Study**

Karen Sliwa, MD, PhD; Lori Blauwet, MD; Kemi Tibazarwa, MD; Elena Libhaber, PhD; Jan-Peter Smedema, MD, MMed(Int); Anthony Becker, MD; John McMurray, MD, FESC; Hatice Yamac, MD; Saida Labidi, MSc; Ingrid Struman, PhD; Denise Hilfiker-Kleiner, PhD

- 20 pts with PPCM according to NHBLI criteria – NYHA class III-IV
- Averaged LVEF 27%
- Furosemide + Enalapril + Carvedilol + Vit-K antagonists if EF < 25%
- Randomised non blinded trial
  - Conventional Rx + Bromocriptin (2.5 mg bid for 15 days - 2.5 mg/j - 6 weeks)
  - vs. Conventional Rx alone

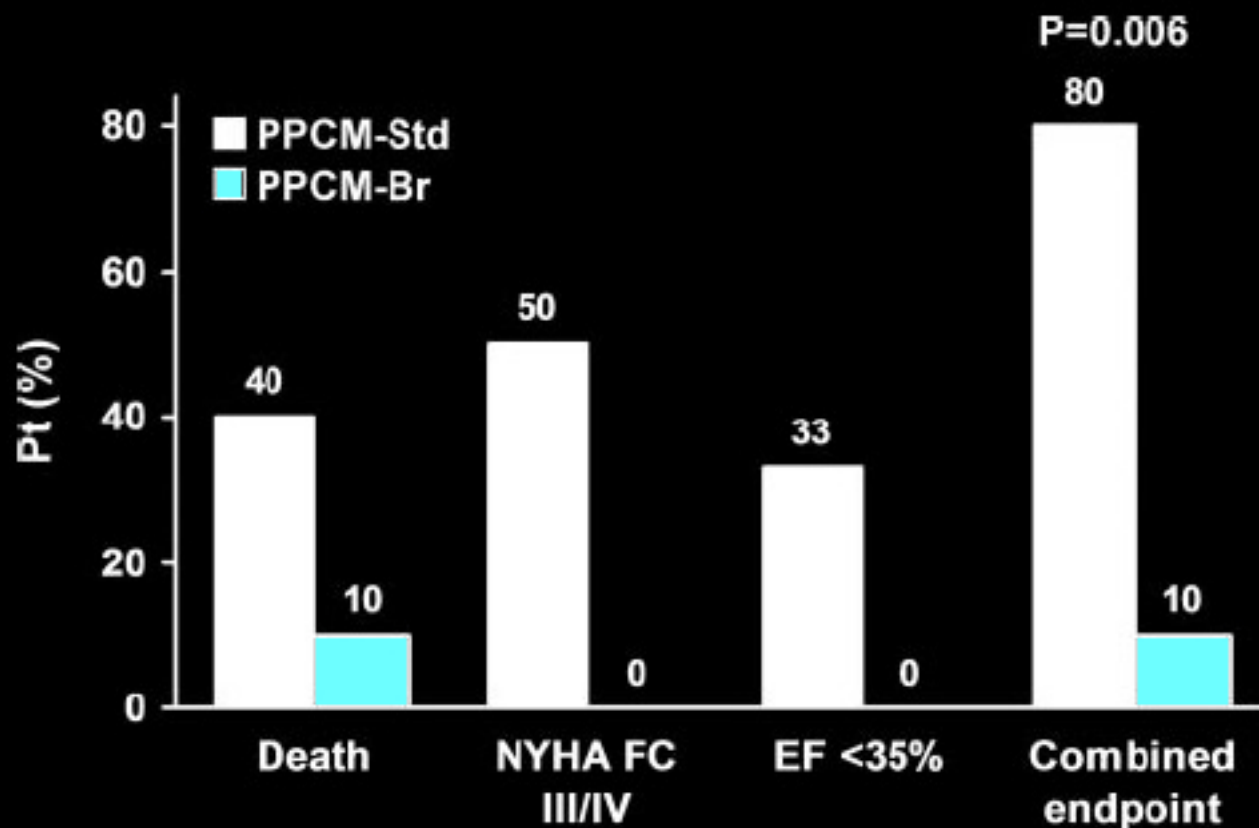
# Results – MRI LVEF



**Figure 2.** Change in LVEF from baseline to 6 months among survivors. Stars represent baseline LVEF for patients who died during the study period.



# Results – Clinical end-points



# Bromocriptine

- « A recent small prospective randomized pilot study supports the hypothesis that the addition of bromocriptine to standard heart failure therapy has beneficial effects on ventricular EF and clinical outcome in women with acute severe PPCM
- Before this treatment can be recommended as a routine strategy, there is a need for larger trials, although some physician currently add bromocriptine to conventional therapy on an individual basis »

→ *CI if LV thrombus ?*

→ *Increased risk of VTE events ?*

# Evolution

- 3 modalities

- LV function recovery 50%
  - Residual CMP 30-40%
  - Refractory cardiogenic shock 10-20%
- Death, ECLS, rarely emergent cardiac transplantation*

*Chapa & al. Obstet Gynecol 2005;105:1303–8*

- Prognosis of heart transplantation = other CMP

*Rasmusson & al. J Heart Lung Transplant 2007 ; 26:1097–104*

- Long term prognosis factors

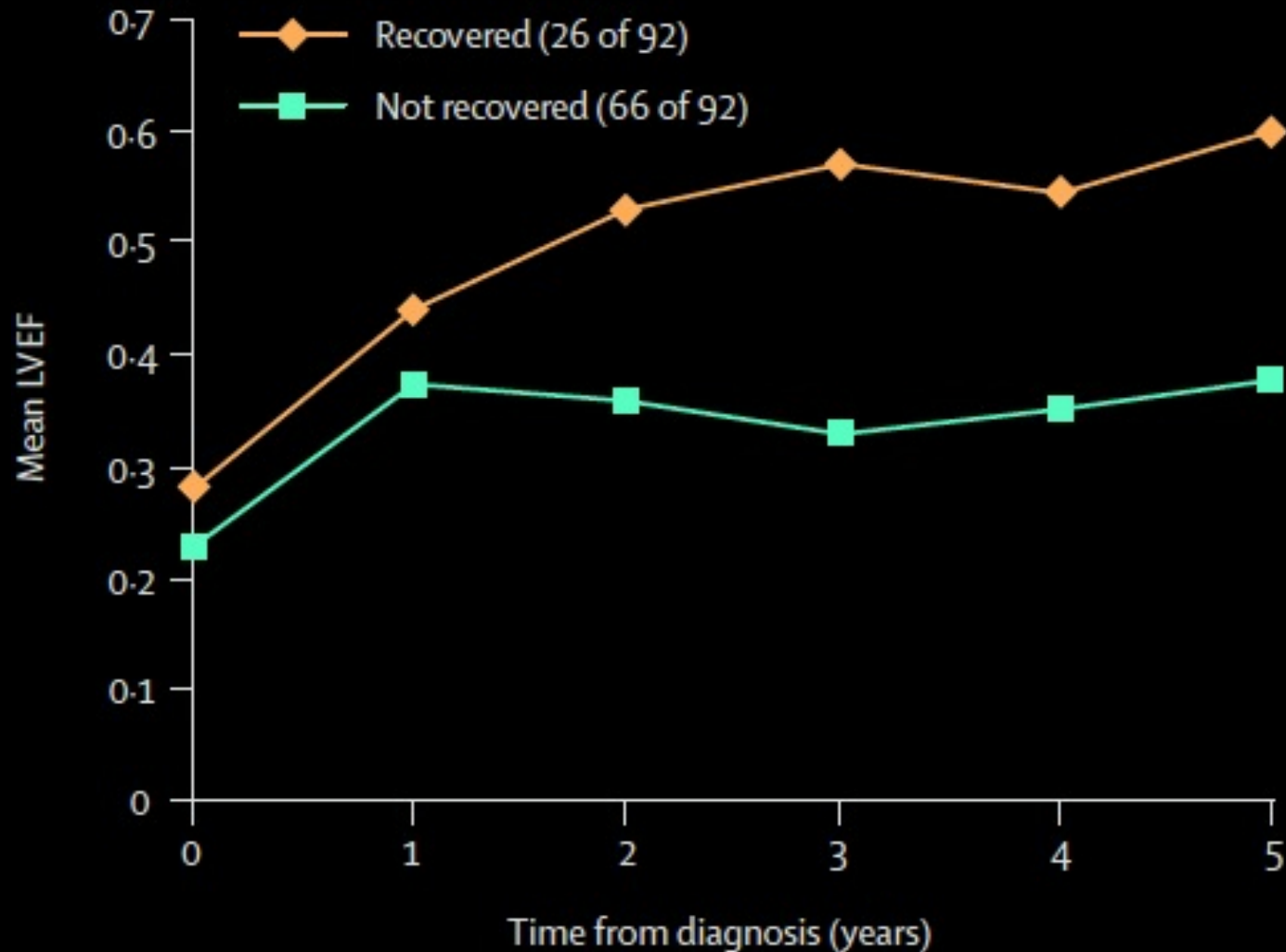
- Initial severity : LVEF < 25 - 30% - LVEDD > 55 - 60 mm - BNP (?)
- 3 month-LVEF < 45%

*Sliwa & al. J Am Coll Cardiol 2011; 58: 659-70*

*Frett & al. Mayo Proceed 2005; 80: 1602–06*

*Sliwa & al. Lancet 2006; 368: 687–93*

# Prognostic value of initial LVEF



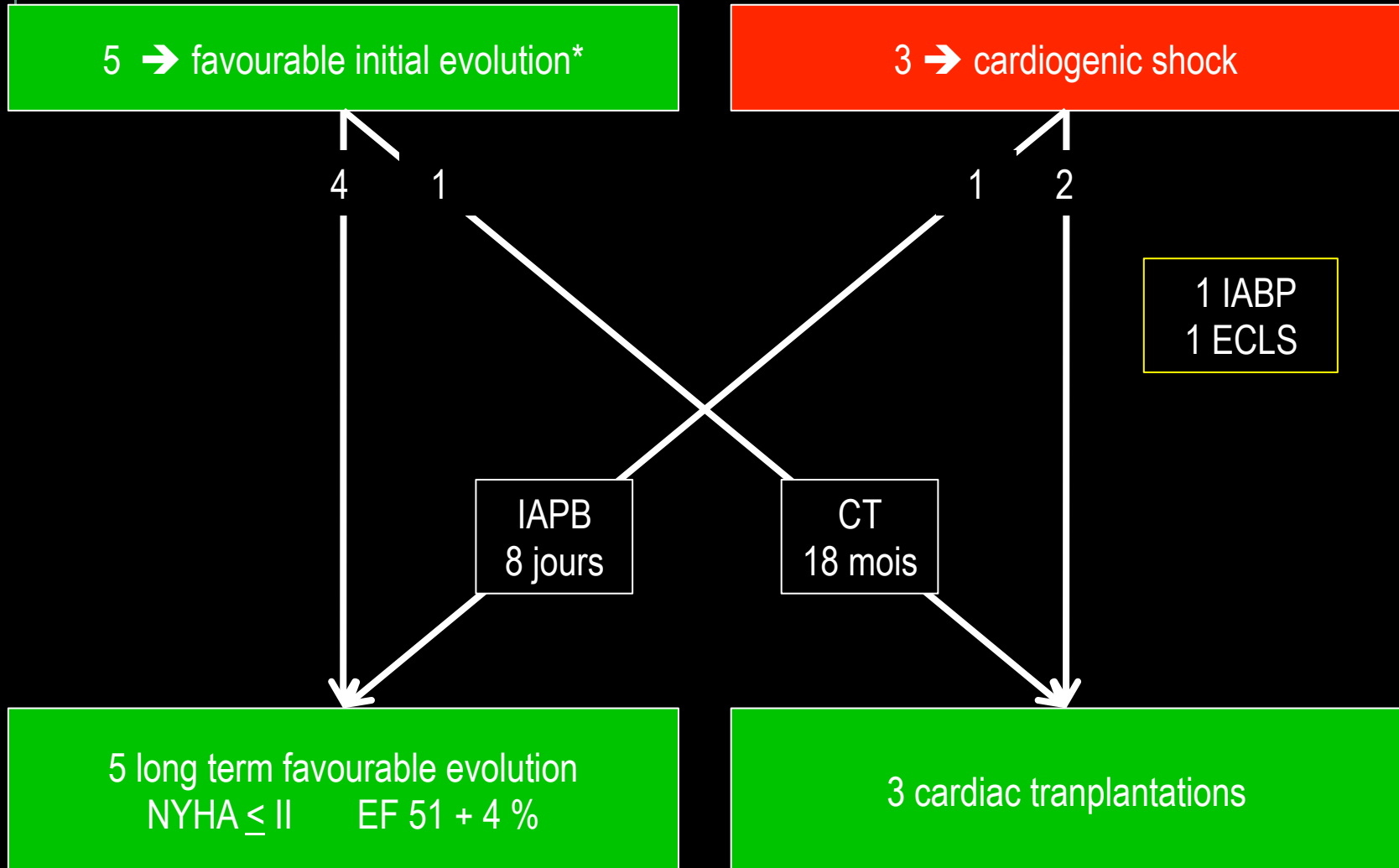
# Evolution

5 → favourable initial evolution\*

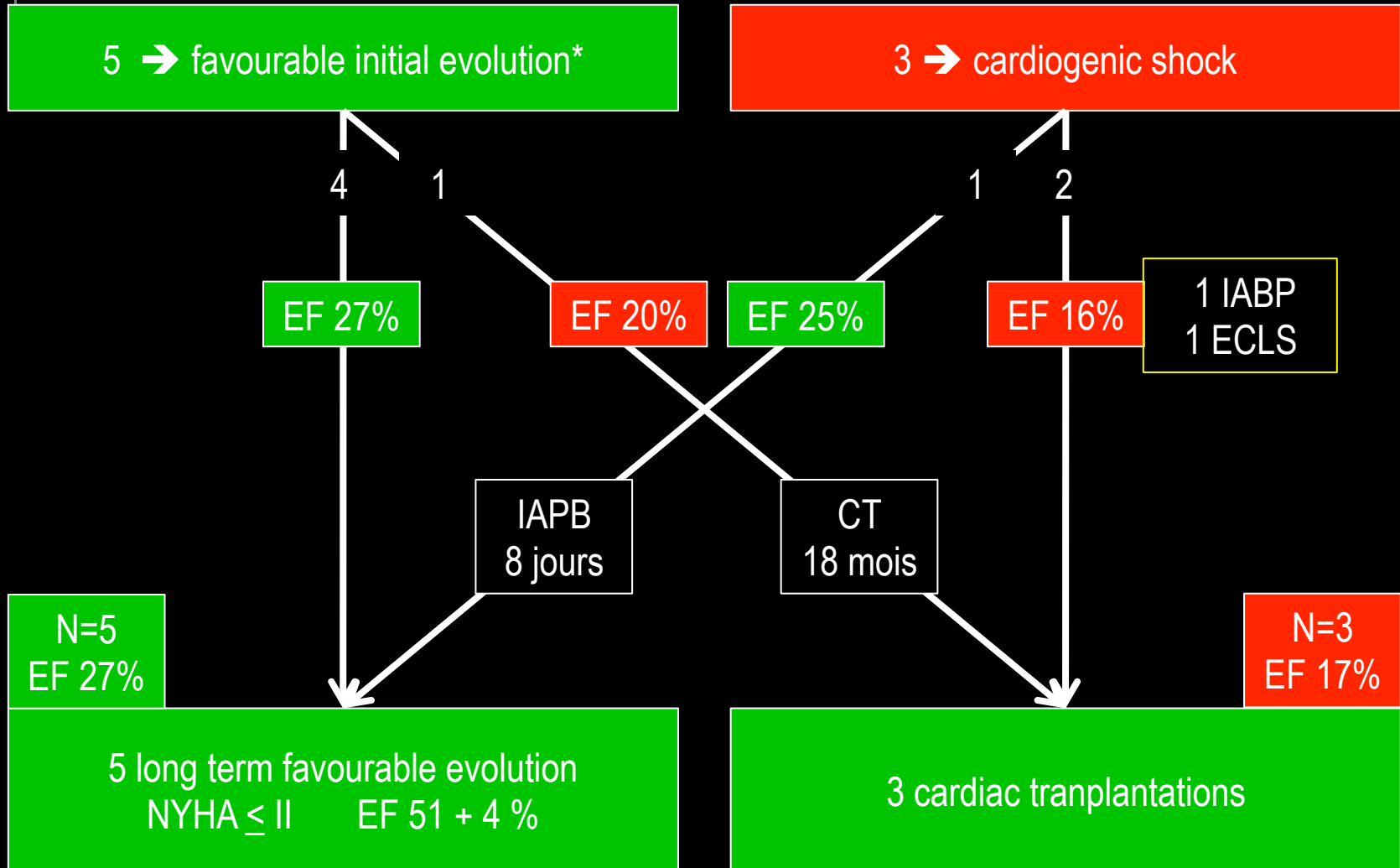
3 → cardiogenic shock

\*1 TIA

# Evolution



# Evolution

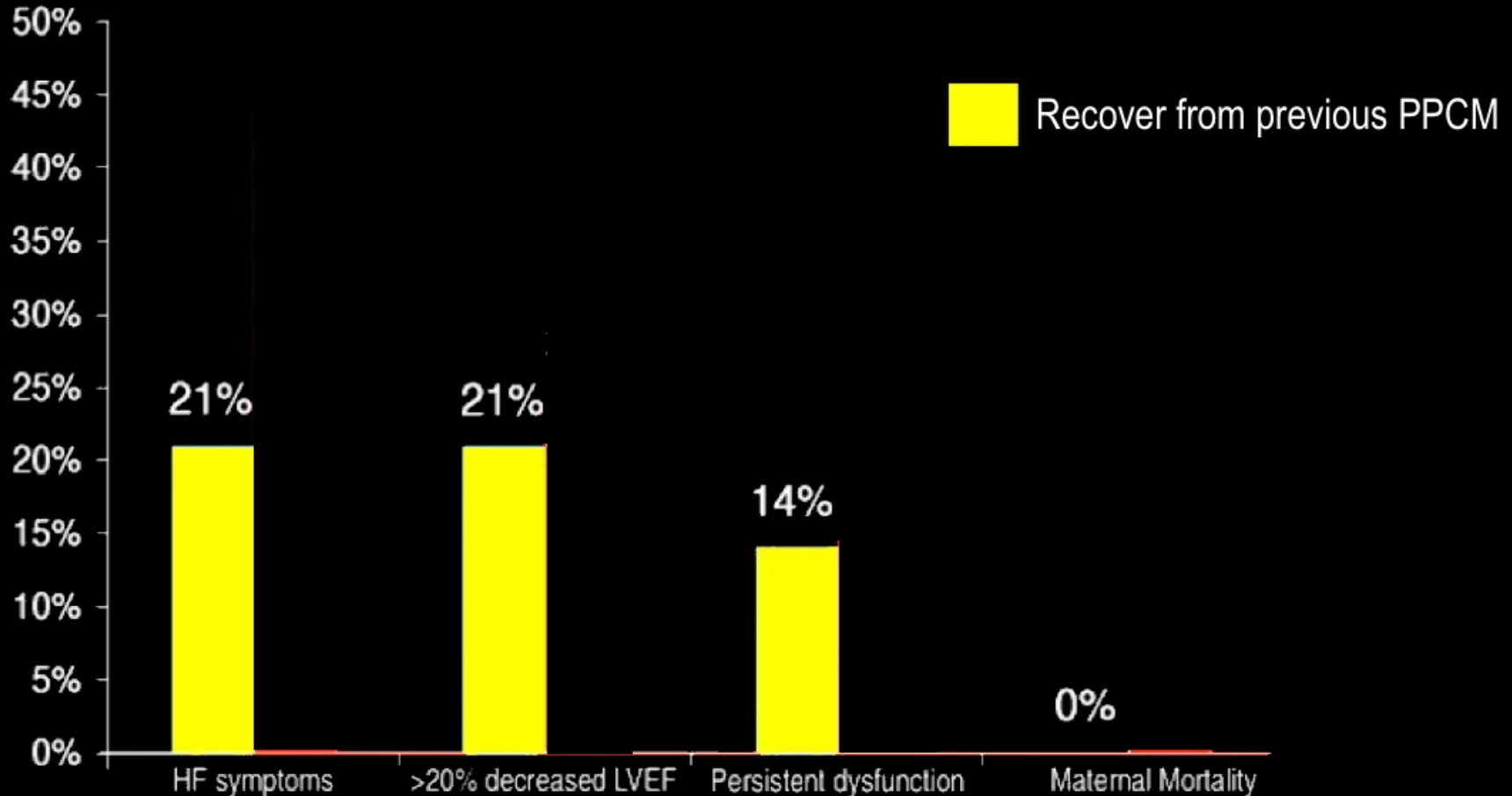


# Obstetrical management

- Vaginal delivery is always preferable (ASAP)
  - Patient haemodynamically stable
  - Favourable obstetric conditions (i.e., no other indications for caesarean)
  - Epidural analgesia preferred
  - Close hemodynamic monitoring
- Urgent delivery irrespective of gestation duration should be considered in women with advanced heart failure and haemodynamic instability / Rx
  - Caesarean section is recommended
  - Combined spinal and epidural anaesthesia.
  - In a center with ECLS facilities
- An experienced interdisciplinary team is required

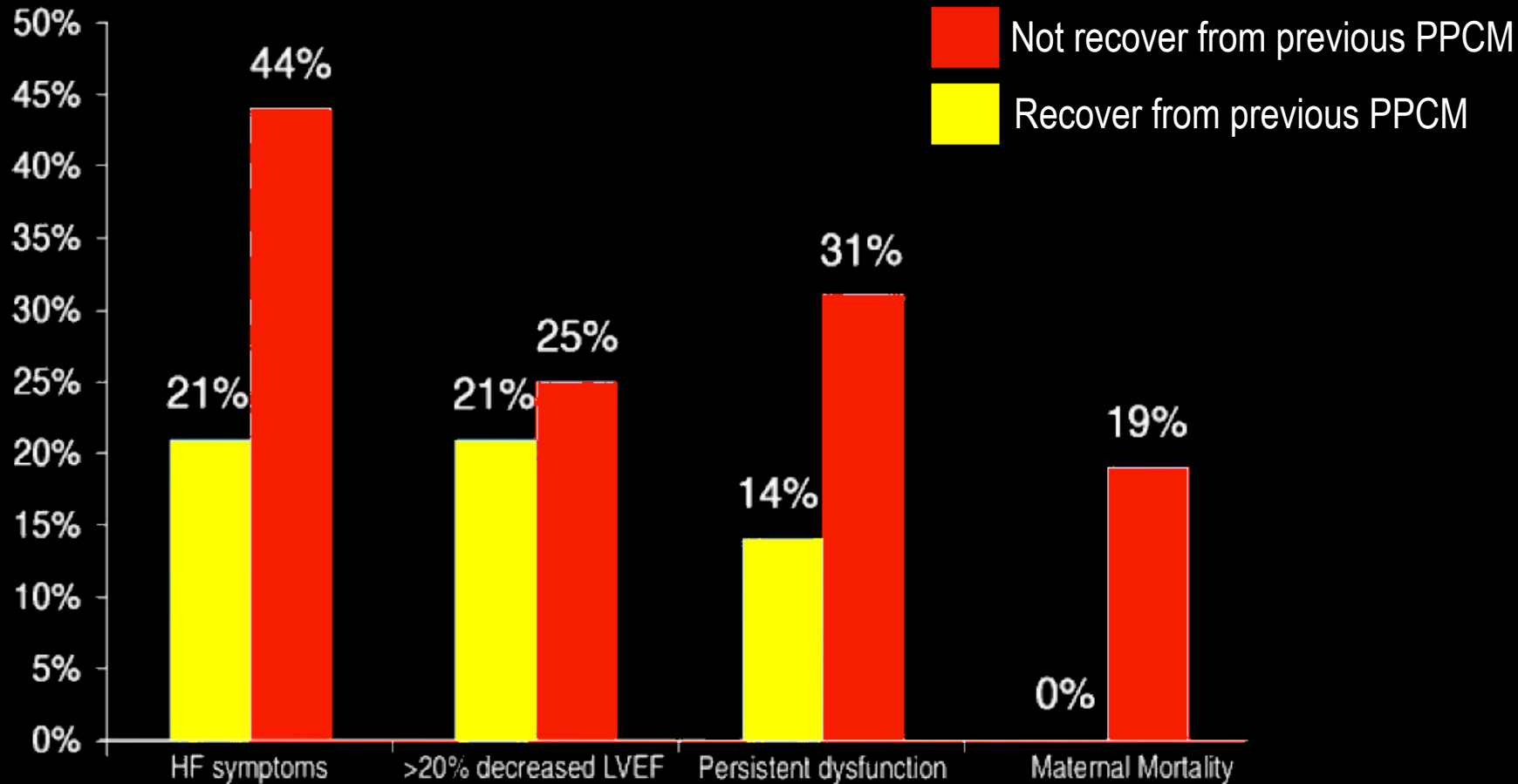


# Subsequent pregnancy?



**Incidence of Maternal Complications Associated With Subsequent Pregnancy in Women With PPCM**

# Subsequent pregnancy?



**Incidence of Maternal Complications Associated With Subsequent Pregnancy in Women With PPCM**

# Subsequent pregnancy?

- Deterioration in LV function is reported in up to 50% of cases despite optimal medical treatment and a subsequent pregnancy carries a recurrence risk for PPCM of 30–50%.
- When the EF has not normalized, a subsequent pregnancy should be discouraged.
- Even if the EF is normalized, there is still a need for counselling because of the risk of recurrence with a new pregnancy
  - Close clinic and TEE follow-up
  - Propose therapeutic pregnancy termination in case of LV worsening (<50%) due to a high risk of life-threatening heart failure during 2<sup>nd</sup> and 3<sup>rd</sup> trimester

# Take home messages

1. Think to PPCM !
  - Shortness of breath in the peri-partum period is not always normal nor embolism !
  - Especially when > 30 years, multiparity, multifoetal pregnancy
2. Perform emergent TEE for diagnosis and prognostication
  - Be aware if LVEF < 25% , major LV dilation, biventricular dysfunction
  - Carefully look for LV thrombus
3. Keep in mind that initial evolution is unpredictable and may be fulminant
  - Consider referring to tertiary ICCU with life support facility
4. Treat as soon as possible
  - Conventional Rx (except ACE-I/ARB/AA before delivery) + anticoagulation
  - Should we consider bromocriptin in severe PPCM ? (CI thrombosis & HBP)
5. Complete healing : 50% - Severe HF : 10%
6. Consider / avoid / prepare future pregnancy

# Selected bibliography

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