

# HeFSSA Practitioners Program 2015

## Theme - Women and Heart Failure

08:00 - 08:20	Registration & Breakfast
08:20 - 08:25	Welcome and Thank You to Sponsors
08:25 - 08:30	HeFSSA smartphone patient app (video)
08:30 - 09:15	Implantable devices, women and heart failure
09:15 - 10:00	<b>Peri-partum cardiomyopathy</b>
10:00 - 10:30	Tea Break
10:30 - 11:15	Hypertension in pregnancy
11:15 - 11:45	Elderly women with Heart Failure
11:45 - 12:00	Questionnaire
12:00	Departure



# CASE STUDY: Peri-partum cardiomyopathy

**A young women presenting with  
shortness of breath post partum**

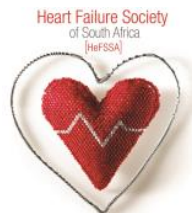
**NOVEL FINDINGS IN  
PERIPARTUM CARDIOMYOPATHY**



# **CASE STUDY:**

## **Peri-partum cardiomyopathy**

- **25 year old woman**
- **Sudden onset of shortness of breath**
- **Medical History: What would you ask?**



# CASE

## **Medical Hx:**

- **Symptoms started 6 weeks after delivery,**
- **SOB gradually increasing over 3 days**

**Has 2 children, 3 & 4 years old**

**No cardiovascular risk factors such as: No HT, no diabetes, non-smoker**

**No FHx**

**Examination: - what would you expect?**

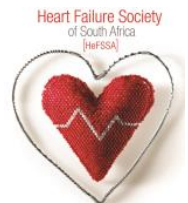


# CASE

## Examination:

- **HR 120 bpm**
- **Pulse: small volume**
- **BP 95/65**
- **JVP raised**
- **Apex: displaced, hypokinetic**
- **Auscultation: 2/6 pan systolic murmur, gallop sounds**
- **2 + pedal oedema, minimal ascites**
- **Crackles up to mid-zone both lungs**

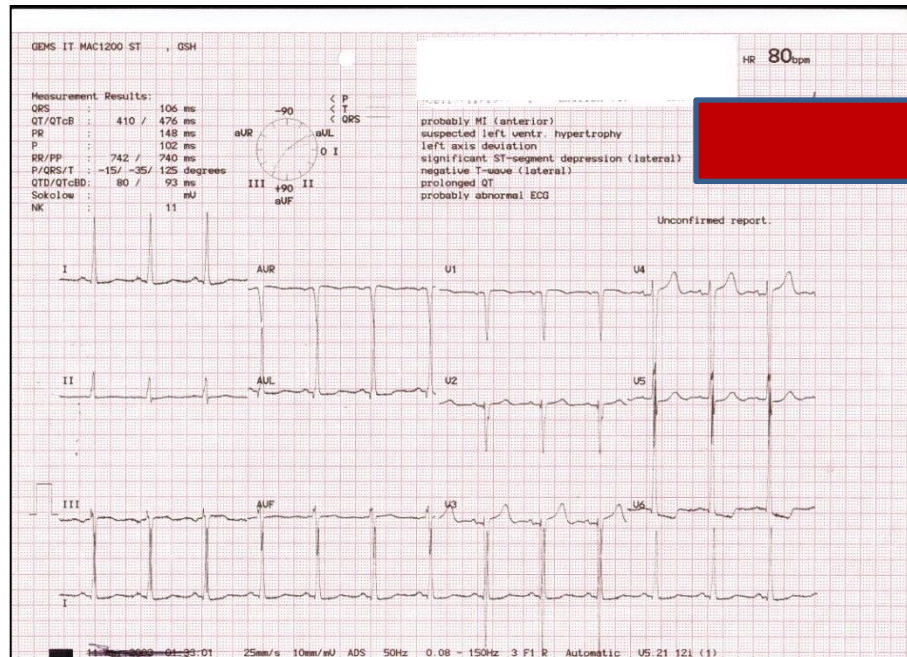
**Differential diagnosis ?**



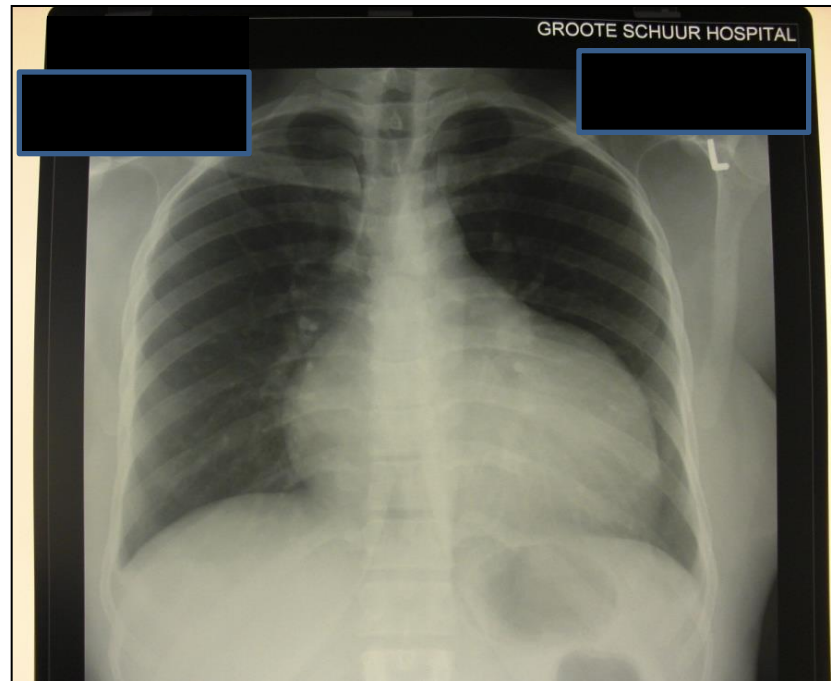
# CASE

- **Differential diagnosis:**
  - 1. Cardiomyopathy?**
    - 1. Peripartum?**
    - 2. HIV-associated?**
    - 3. Familial?**
    - 4. Idiopathic?**
  - 2. Rheumatic heart disease?**
  - 3. Pulmonary embolus?**
  - 4. Pericardial disease?**

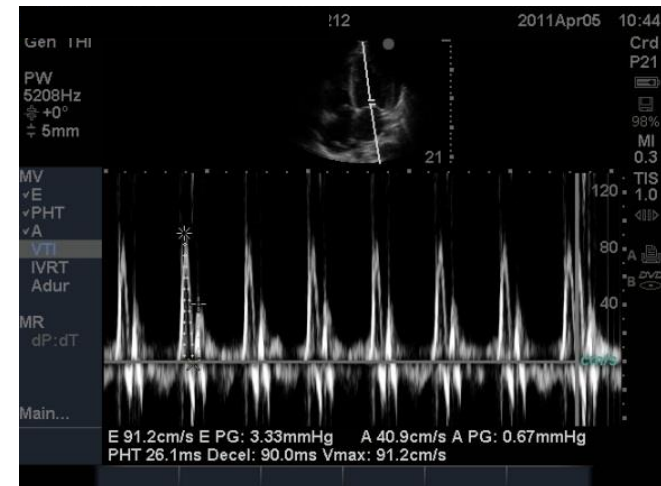
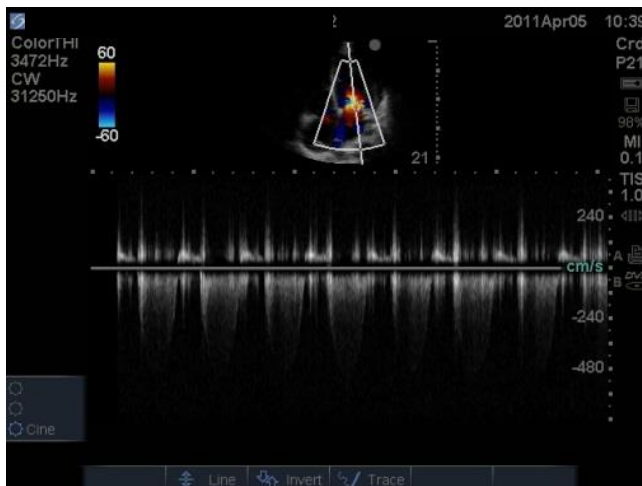
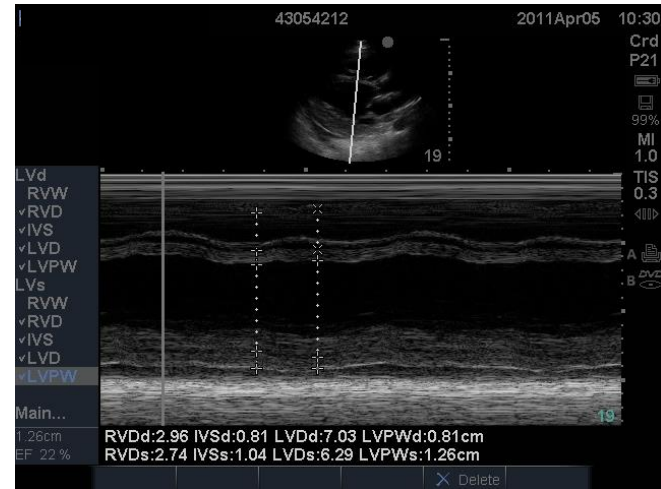
# Investigations



# Investigations



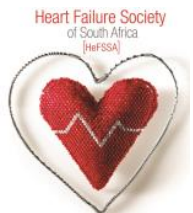
# Case Echocardiography



# Case

## Blood tests:

**HIV negative, d-dimers negative, normal renal function, CRP in normal range**

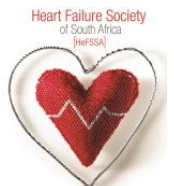


# Case

## Diagnosis:

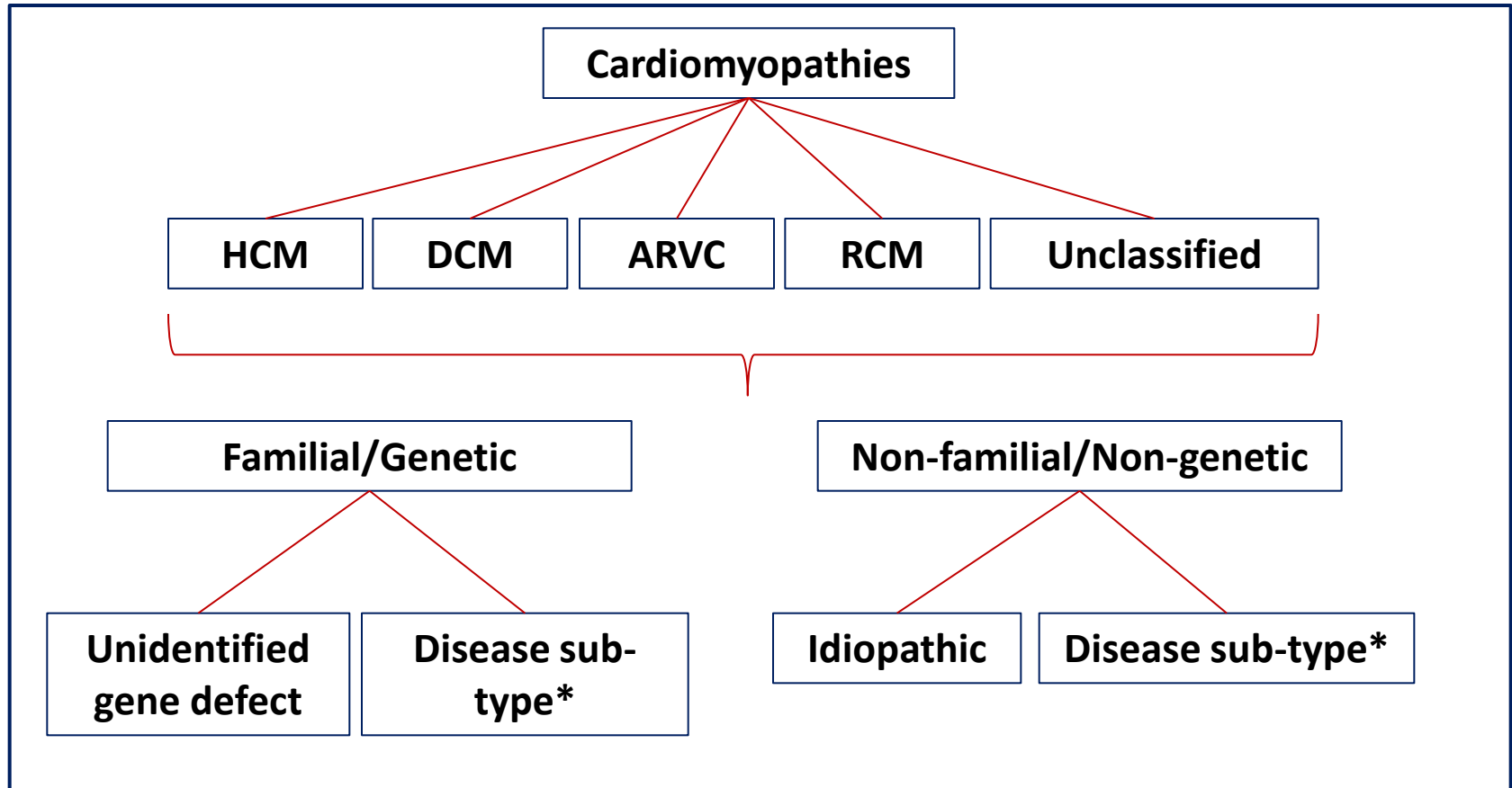
**Peripartum Cardiomyopathy (PPCM) with features of poor prognosis :**

- 1. Mitral regurgitation**
- 2. Pulmonary hypertension**



# Cardiomyopathy

## Classification – Structure, Function and Aetiology



HCM = hypertrophic cardiomyopathy; DCM = dilated cardiomyopathy; ARVC = arrhythmogenic right ventricular cardiomyopathy; RCM = right ventricular cardiomyopathy



# Definition/classification of PPCM

European Society of Cardiology on the classification of cardiomyopathies (Dickstein 2008, Eur J Heart Failure)	A non-familial, non-genetic form of dilated cardiomyopathy associated with pregnancy.
AHA Scientific Statement on contemporary definitions and classifications of the cardiomyopathies (Maron 2006, Circulation)	A rare and dilated acquired primary cardiomyopathy, associated with LV dysfunction and heart failure.
Workshop held by the National Heart Lung and Blood Institute and the Office of Rare Diseases (Pearson 2000, JAMA)	<ol style="list-style-type: none"> <li>1) The development of heart failure in the last month of pregnancy, or within 5 months post partum.</li> <li>2) The absence of an identifiable cause of heart failure.</li> <li>3) The absence of recognizable heart disease prior to the last month of pregnancy; LV systolic dysfunction demonstrated by classical echocardiographic criteria. The latter may be characterized by an LV ejection fraction &lt;45%, fractional shortening &lt;30% , or both, with or without an LV end-diastolic dimension &gt;2.7 cm/m<sup>2</sup> body surface area.</li> </ol>
<p>Heart Failure Association of the European Society of Cardiology Working Group on PPCM 2010</p> <p>Sliwa et al. European Journal Heart Failure 2010</p>	<p>PPCM is an idiopathic form of cardiomyopathy, presenting with heart failure secondary to left ventricular systolic dysfunction towards the end of pregnancy, or in the months following delivery, where no other causes of heart failure are found. It is a diagnosis of exclusion. The left ventricle is not necessarily dilated, but the ejection fraction is usually below 45%.</p>



# Epidemiology

1: 3500 - 1:15000 USA\*

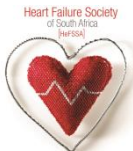
1:1000 in South Africa<sup>#</sup>

\*Lampert M, Lang RM. *Am Heart J* 1995

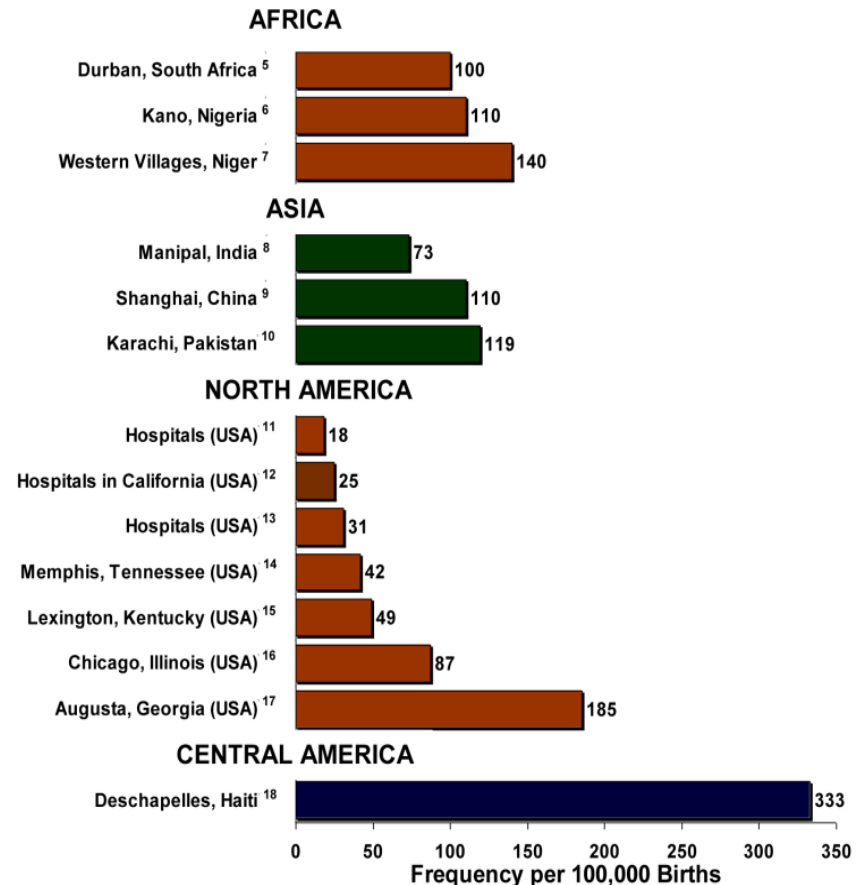
<sup>#</sup> Sliwa et al. *The Lancet* 2006

No prospective data from Australia or Europe

*Deneux-Tharaux C et al. Obstet Gynecol* 2005: Underreporting of pregnancy related mortality in the United States and Europe



## Incidence of PPCM



# Mode of Presentation: PPCM – Symptoms and Signs

## Most common

Dyspnoea (NYHA class III-IV)  
Cough  
Fatigue

## Common

Lower extremity edema  
Orthopnoea  
Paroxysmal nocturnal dyspnoea  
Palpitations  
Dizziness

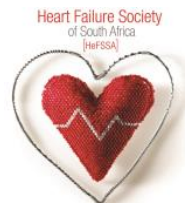
## Less common

Nocturia  
Right upper quadrant pain  
(hepatic congestion)  
Chest pain  
Postural hypotension  
Syncope

Symptoms can  
be subtle to  
dramatic

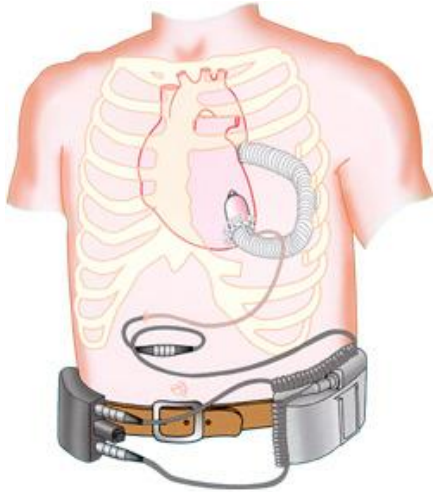
Highly variable  
presentation

Often ignored  
by patients,  
nurses and  
doctors



# Mode of Presentation:

## Acute, dramatic presentation needing circulatory support



- Prognosis in e.g. PPCM is different from DCM, with a significant proportion of patients normalizing their LV function within the first six months postpartum.
- Left ventricular assisted device (LVAD) may be considered before listing the patient for cardiac transplantation.
- Optimum strategy is not known and discussion between experts on a case-by-case basis may be helpful.
- Thrombotic complications possibly more often because PPCM is a pro-thrombotic condition.
- Size of device also remains a limiting factor as not all fully implantable devices will fit into a small woman.

# Algorithm Diagnosing PPCM

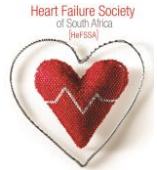


European Journal of Heart Failure (2010) 12, 767–778  
doi:10.1093/eurjhf/hfq120

## POSITION STATEMENT

**Current state of knowledge on aetiology, diagnosis, management, and therapy of peripartum cardiomyopathy: a position statement from the Heart Failure Association of the European Society of Cardiology Working Group on peripartum cardiomyopathy**

Karen Sliwa<sup>1\*</sup>, Denise Hilfiker-Kleiner<sup>2</sup>, Mark C. Petrie<sup>3</sup>, Alexandre Mebazaa<sup>4</sup>, Burkert Pieske<sup>5</sup>, Eckhart Buchmann<sup>6</sup>, Vera Regitz-Zagrosek<sup>7</sup>, Maria Schaufelberger<sup>8</sup>, Luigi Tavazzi<sup>9</sup>, Dirk J. van Veldhuisen<sup>10</sup>, Hugh Watkins<sup>11</sup>, Ajay J. Shah<sup>12</sup>, Petar M. Seferovic<sup>13</sup>, Uri Elkayam<sup>14</sup>, Sabine Pankuweit<sup>15</sup>, Zoltan Papp<sup>16</sup>, Frederic Mouquet<sup>17</sup>, and John J.V. McMurray<sup>18</sup>



Breathless woman  
towards the end of  
pregnancy/early post  
partum

ECG or Natriuretic  
peptides AND  
echocardiography

Any abnormalities

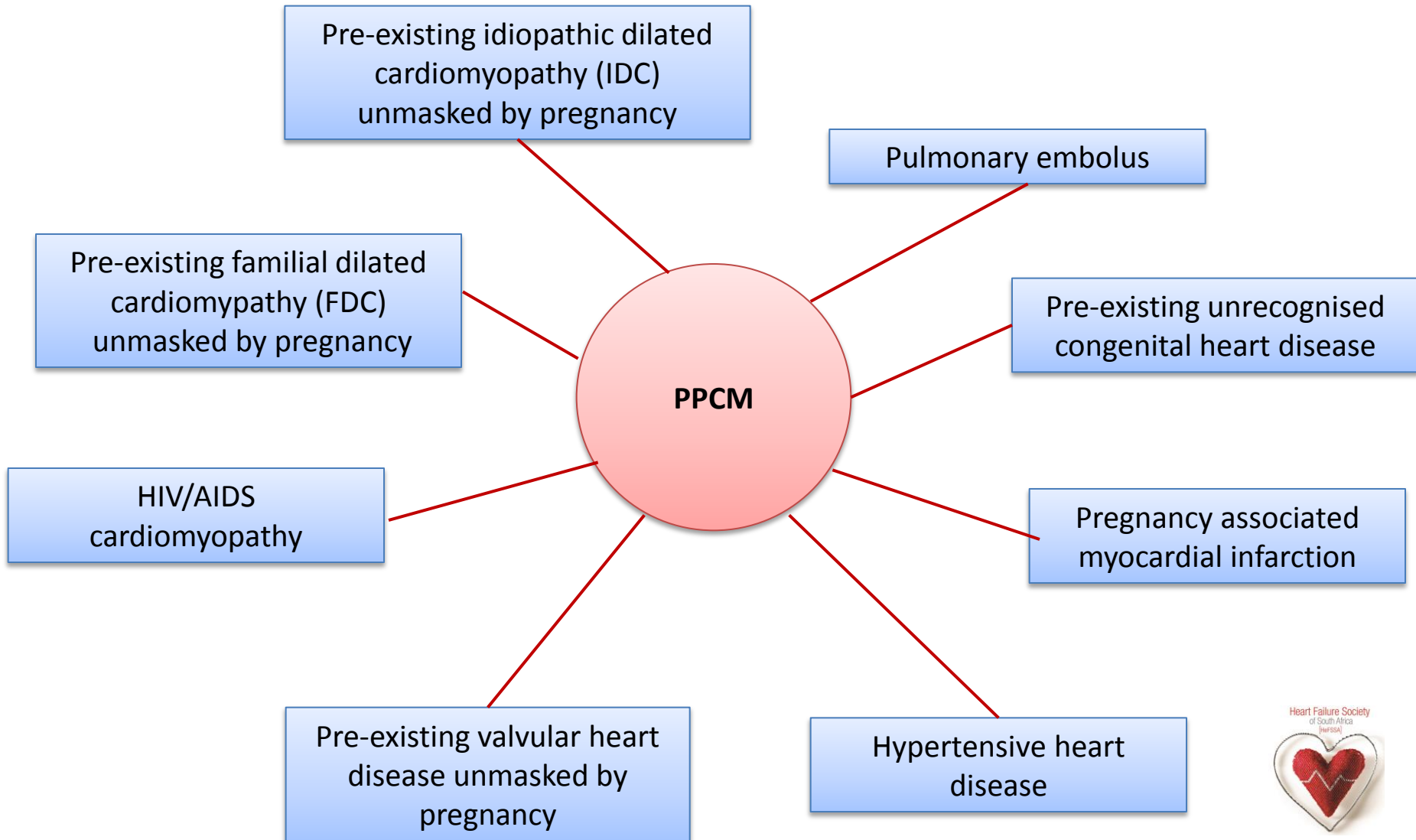
All normal

Cardiology review (consider  
differential cardiovascular  
diagnoses of PPCM – table)

Consider non-cardiovascular causes  
of breathlessness

# Differential diagnoses of PPCM:

## 2 conditions can co-exists!

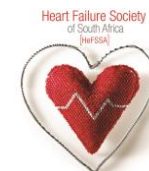


## The 12-lead ECG in peripartum cardiomyopathy

KEMI TIBAZARWA, GERALDINE LEE, BONGANI MAYOSI, MELINDA CARRINGTON, SIMON STEWART,  
KAREN SLIWA

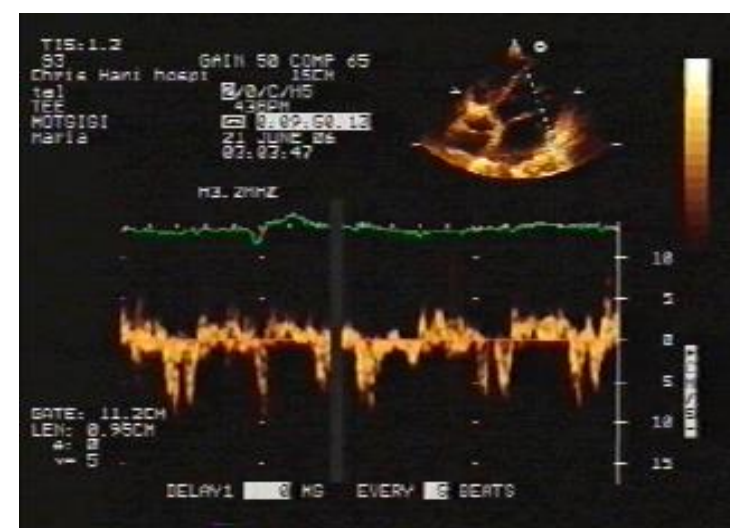
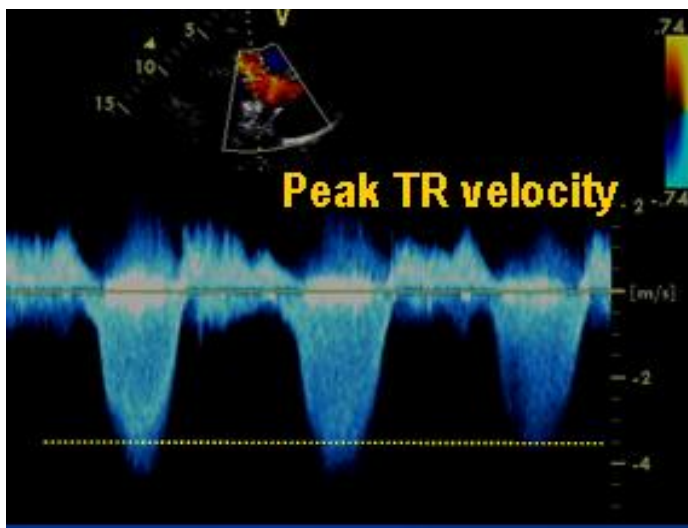
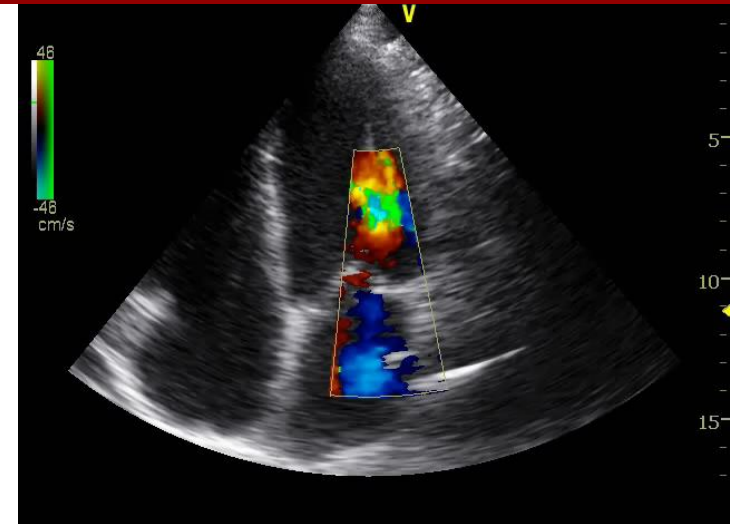
**Conclusions:** Almost all women suffering from PPCM had an 'abnormal' 12-lead ECG. Pending more definitive studies, the ECG appears to be a useful adjunctive tool in both screening and monitoring.

Patients with e.g. shortness of breath due to asthma would not have e.g. LBBB, broad QRS, T-wave inversion



# Echocardiography:

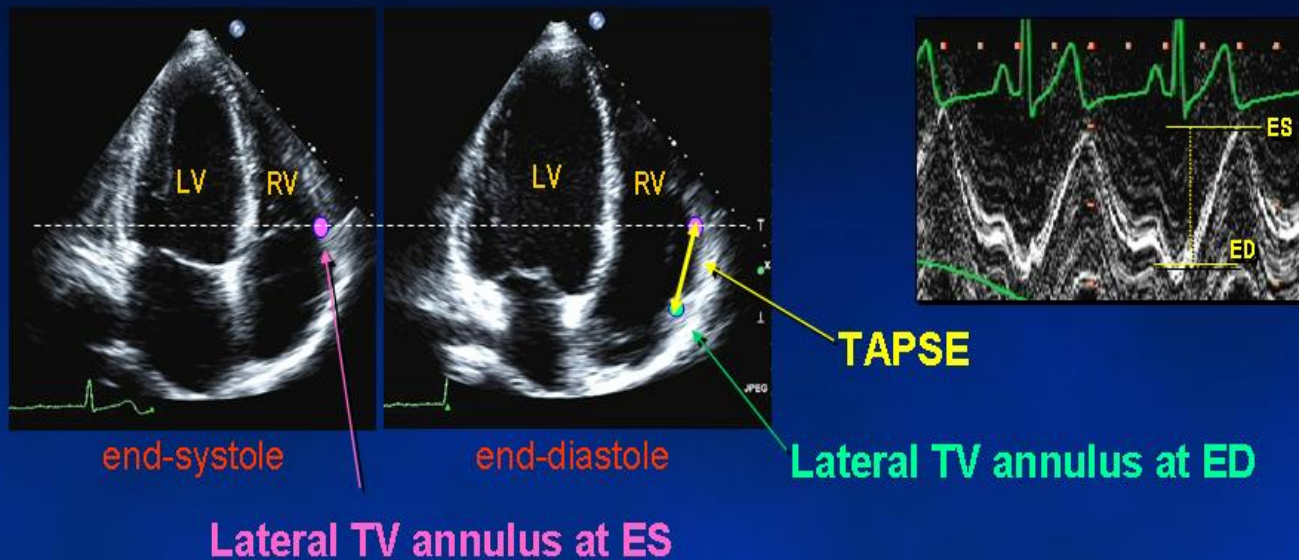
## Left Ventricular Dysfunction often with Mitral Regurgitation and Pulmonary Hypertension



# TAPSE : An index of RV function but also a predictor of mortality in cardiomyopathy!

## Tricuspid annular plane excursion (TAPSE)

reflects longitudinal systolic excursion of the lateral valve annulus towards apex



Reduced TAPSE, signifying RV systolic dysfunction, is defined as value of  $\leq 14$  mm



## Right ventricular systolic function in peripartum and dilated cardiomyopathies

Kamilu M. Karaye\*

Department of Medicine, Bayero University and Aminu Kano Teaching Hospital, PO Box 4445, Kano, Nigeria

Received 12 January 2011; accepted after revision 20 February 2011; online publish-ahead-of-print 17 March 2011

Comparison of 35 patients with DCM versus 55 patients with PPCM recruited over the 8 months period.

TAPSE  $\leq 14$  mm was found in 54.6% of PPCM patients and in 37.1% of DCM patients.

Mean TAPSE was significantly less in PPCM (12.58 $\pm$ 4.27 mm) compared to DCM patients (14.46 $\pm$ 3.21 mm), (P < 0.028)

**Table 1** Baseline and clinical characteristics

	DCM (n = 35)	PPCM (n = 55)	P-value
Age (years)	50.89 $\pm$ 19.33	24.53 $\pm$ 6.95	<0.001*
Females	16 (45.7%)	55 (100%)	—
NYHA 3–4	29 (82.9%)	46 (83.6%)	0.923
TAPSE (mm)	14.46 $\pm$ 3.21	12.58 $\pm$ 4.27	0.028*
TAPSE $\leq 14$ mm	13 (37.1%)	30 (54.6%)	0.107
RVOTd (mm)	33.52 $\pm$ 6.69	32.50 $\pm$ 5.17	0.419
HR (b/min)	106.4 $\pm$ 22.5	104.9 $\pm$ 15.3	0.737
BMI (kg/m <sup>2</sup> )	23.76 $\pm$ 4.65	20.24 $\pm$ 2.72	<0.001*
LA (mm)	44.97 $\pm$ 7.35	42.02 $\pm$ 7.52	0.070
LVEDD (mm)	66.51 $\pm$ 8.19	66.71 $\pm$ 7.80	0.910
LVEDV (ml)	252.03 $\pm$ 78.80	250.55 $\pm$ 69.80	0.927
LVSF (ml)	72.86 $\pm$ 36.09	68.35 $\pm$ 24.66	0.483
LVEF (%)	28.91 $\pm$ 8.81	27.27 $\pm$ 9.46	0.412
E:A ratio	2.63 $\pm$ 2.27	2.57 $\pm$ 2.52	0.932
PV AT (ms)	74.90 $\pm$ 19.03	85.19 $\pm$ 25.58	0.285

NYHA, New York Heart Association classification; TAPSE, tricuspid annular plane systolic excursion; RVOTd, right ventricular outflow tract dimension at end-diastole; HR, heart rate; BMI, body mass index; LA, left atrium; LVEDD and LVEDV, LV end-diastolic and end-systolic dimensions, respectively; LVSF, left ventricular stroke volume; LVEF, left ventricular ejection fraction; E:A, ratio of early to late mitral valve filling velocities; EDV, end-diastolic volume; SV, stroke volume; PV AT, pulmonary valve acceleration time; \*P-value statistically significant. All values are expressed as means  $\pm$  standard deviations, or as numbers with percentages in parentheses.

# Is PPCM a genetic disease?

European Heart Journal Advance Access published February 20, 2014



European Heart Journal  
doi:10.1093/eurheartj/ehu050

CLINICAL RESEARCH

*Heart failure/cardiomyopathy*

## Titin gene mutations are common in families with both peripartum cardiomyopathy and dilated cardiomyopathy

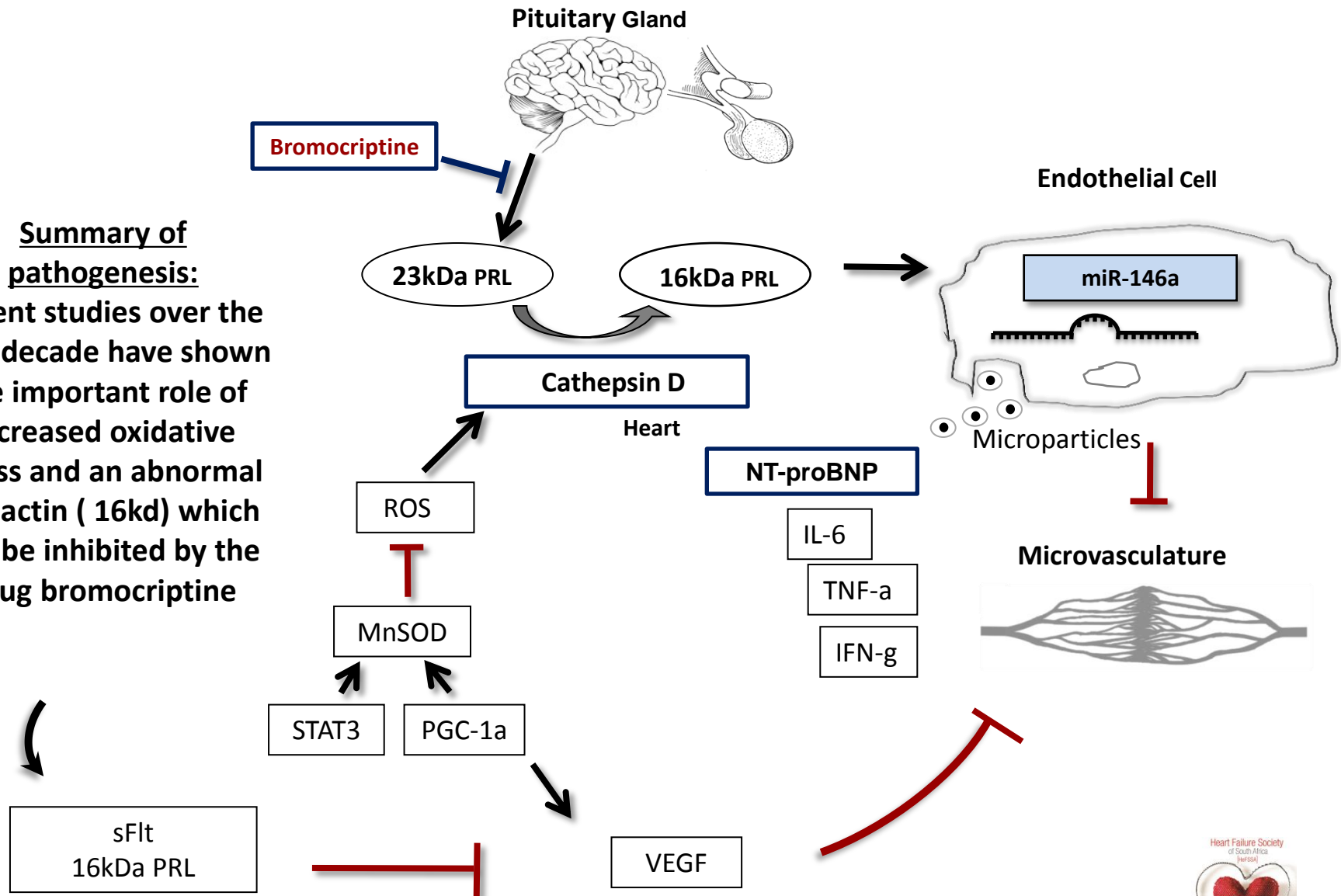
Karin Y. van Spaendonck-Zwarts<sup>1,2\*</sup>, Anna Posafalvi<sup>1</sup>, Maarten P. van den Berg<sup>3</sup>, Denise Hilfiker-Kleiner<sup>4</sup>, Ilse A.E. Bollen<sup>5</sup>, Karen Sliwa<sup>6</sup>, Mariëlle Alders<sup>2</sup>, Rowida Almomani<sup>1</sup>, Irene M. van Langen<sup>1</sup>, Peter van der Meer<sup>3</sup>, Richard J. Sinke<sup>1</sup>, Jolanda van der Velden<sup>5</sup>, Dirk J. Van Veldhuisen<sup>3</sup>, J. Peter van Tintelen<sup>1,7†</sup>, and Jan D.H. Jongbloed<sup>1†</sup>

**Conclusion:** Potentially causal mutations in cardiomyopathy-related genes are common in families with both PPCM and DCM. This supports the earlier finding that PPCM can be part of familial DCM. This cohort was particularly characterized by a high proportion of TTN mutations and a low recovery rate in PPCM cases.



# Proposed Pathogenesis of PPCM and Cardio-placental Syndrome

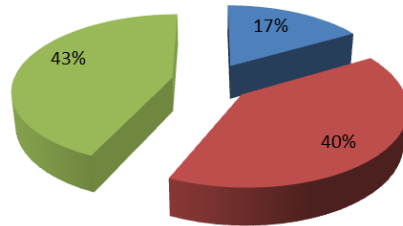
**Summary of pathogenesis:**  
Recent studies over the past decade have shown the important role of increased oxidative stress and an abnormal prolactin ( 16kd) which can be inhibited by the drug bromocriptine



# Management depending on time of presentation

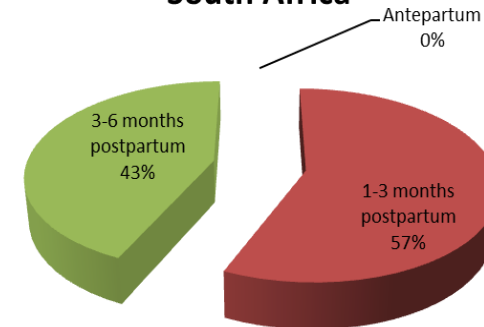
## Germany

■ Antepartum ■ 1-3 months postpartum ■ 3-6 months postpartum



*Haghikia A, et al. Phenotyping and outcome on contemporary management in a German cohort of patients with peripartum cardiomyopathy. Basic Research in Cardiology, 2013;108: 366*

## South Africa



*Sliwa K, Forster O, Libhaber E, et al. Peripartum cardiomyopathy: inflammatory markers as predictors of outcome in 100 prospective studied patients. Eur. Heart J. 2006*

# Treatment of Heart Failure in women with PPCM (new onset or with previously diagnosed PPCM)



Non Pregnant

According to  
standard heart  
failure guidelines



Early  
Pregnancy

Diuretics  
Hydralazine  
Beta Blocker



Late  
Pregnancy

Diuretics  
Hydralazine  
Beta Blocker



Postpartum

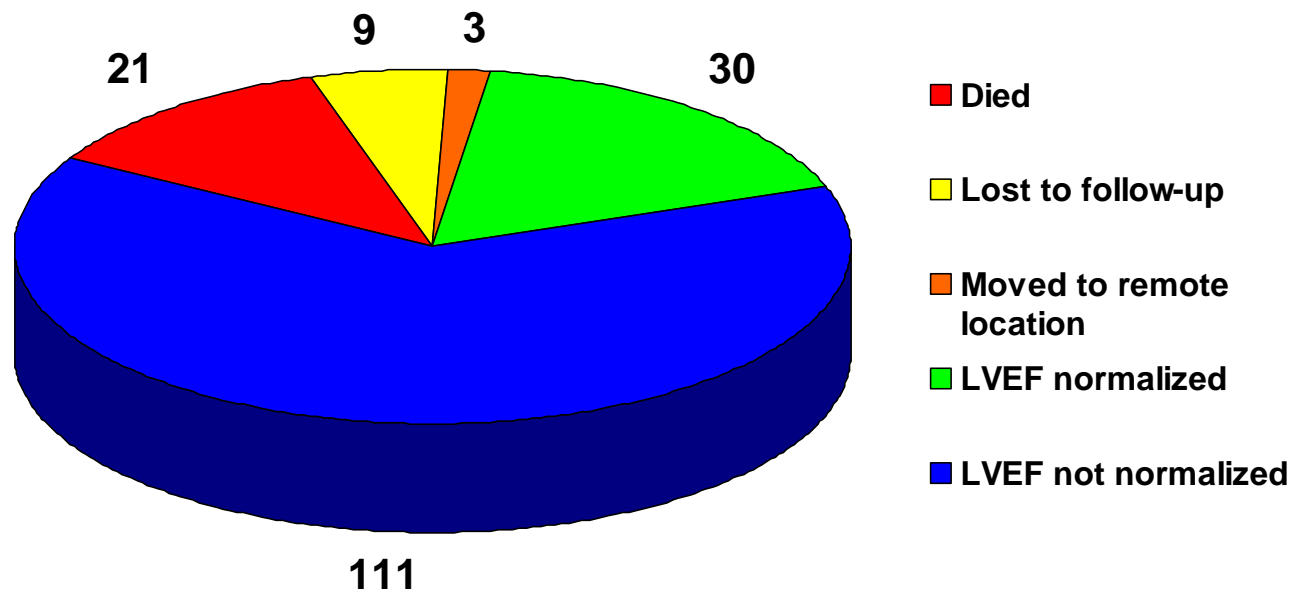
Diuretics  
Ace-inhibitor  
Beta blocker

## Predictors of outcome in 176 South African patients with peripartum cardiomyopathy

Lori A Blauwet,<sup>1</sup> Elena Libhaber,<sup>2,3</sup> Olaf Forster,<sup>4</sup> Kemi Tibazarwa,<sup>2,5</sup> Alex Mebazaa,<sup>6</sup> Denise Hilfiker-Kleiner,<sup>7</sup> Karen Sliwa<sup>2</sup>

All patients received diuretic, ACE-inhibitors and Carvedilol

### Outcome at 6 Months



12%

63%

Evaluation of Bromocriptine in the Treatment of Acute Severe Peripartum  
Cardiomyopathy : A Proof-of-Concept Pilot Study  
Karen Sliwa, Lori Blauwet, Kemi Tibazarwa, Elena Libhaber, Jan-Peter Smedema,  
Anthony Becker, John McMurray, Hatice Yamac, Saida Labidi, Ingrid Struman and  
Denise Hilfiker-Kleiner

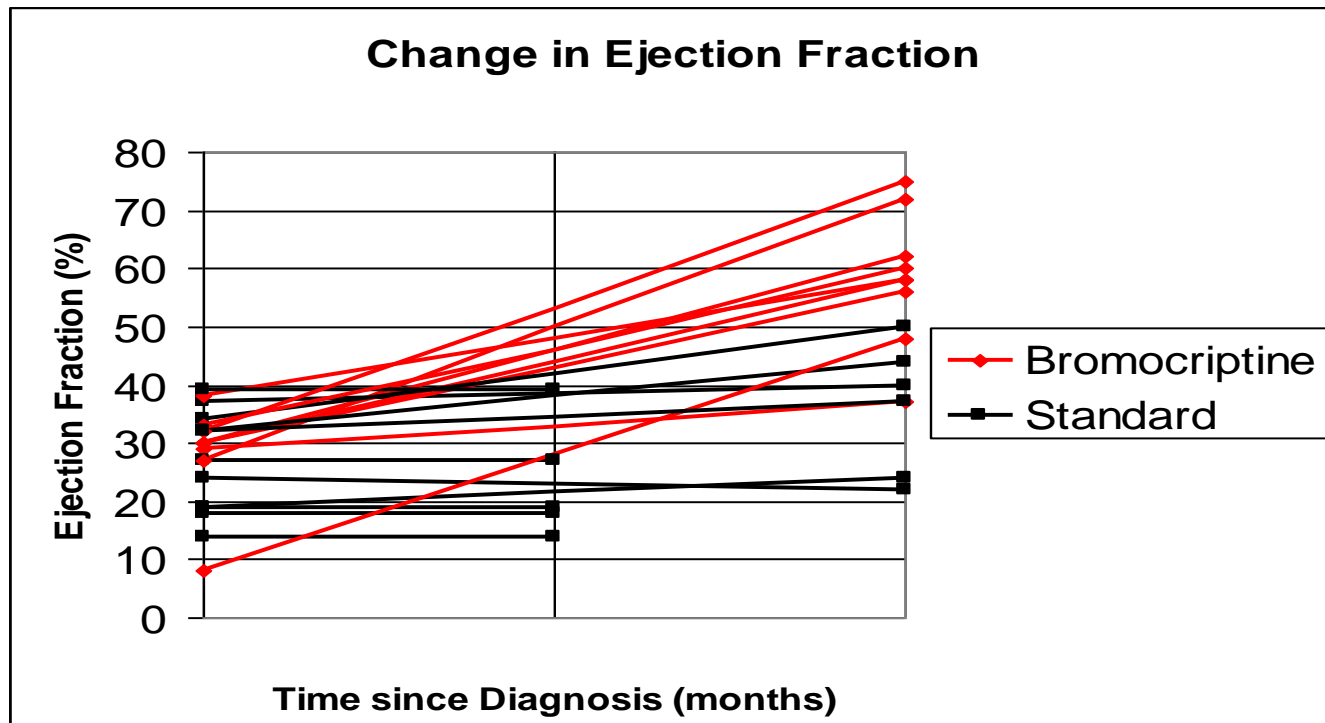
*Circulation* 2010, 121:1465-1473; originally published online March 22, 2010  
doi: 10.1161/CIRCULATIONAHA.109.901496

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX  
72514  
Copyright © 2010 American Heart Association. All rights reserved. Print ISSN: 0009-7322. Online  
ISSN: 1524-4539

- Blinded clinical, prospective single-centre, randomized, open-label proof-of-concept trial of women with newly diagnosed PPCM, receiving standard care (PPCM-Std, n=10,) versus standard care plus bromocriptine for 8 weeks (PPCM-Br, n=10).
- Bromocriptine: 2.5 mg twice daily for 2 weeks, followed by 2.5 mg daily for 6 weeks.
- Blinded clinical, hemodynamic and echocardiographic assessment were performed at baseline and 6 months post diagnosis, cardiac MRI was performed 4-6 weeks post diagnosis in PPCM-Br.
- 6-month outcome of their children (n=21) was studied, as mothers receiving bromocriptine could not breast feed.

# Bromocriptine promotes recovery of cardiac function and survival in patients with PPCM - first randomized proof-of-concept pilot study

*Sliwa K, Blauwet K, Tibazarwa K, Libhaber E, et al (Circulation 2010)*

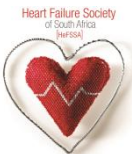


Change in left ventricular ejection fraction from baseline to either death, or survival, at 6 months.

PPCM Br: 28 to 56% *versus* PPCM Std: 28-36%,  $p=0.006$

PPCM Bromo: 10 % Mortality

PPCM Standard Care: 40% Mortality

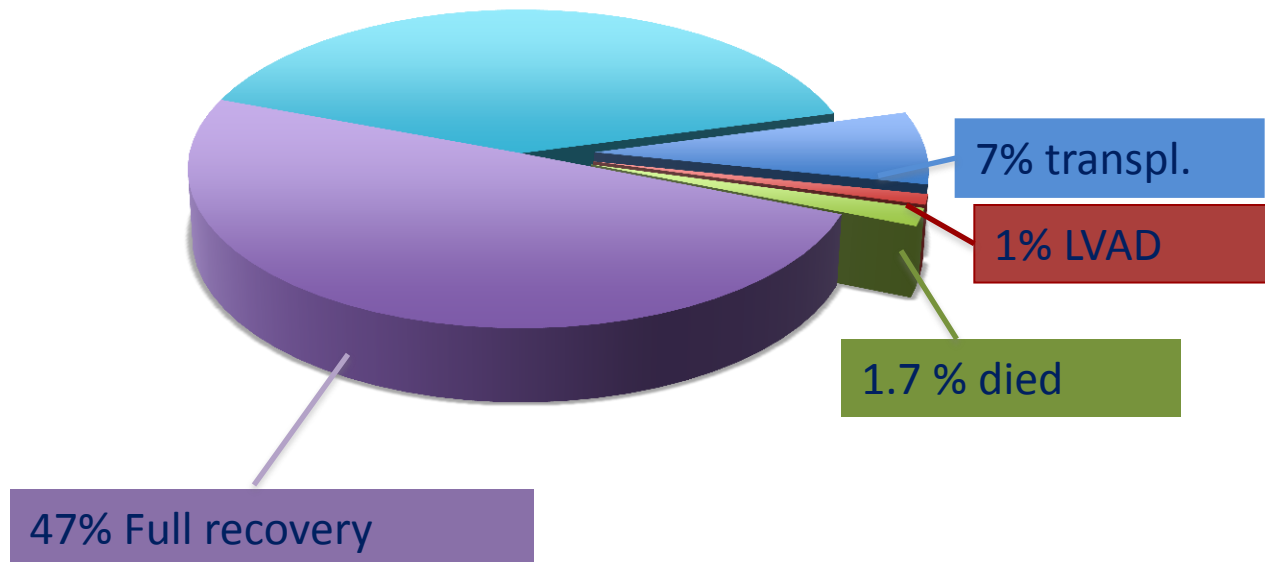


## Phenotyping and outcome on contemporary management in a German cohort of patients with peripartum cardiomyopathy

A. Haghikia · E. Podewski · E. Libhaber · S. Labidi · D. Fischer ·  
P. Roentgen · D. Tsikas · J. Jordan · R. Lichtinghagen · C. S. von Kaisenberg ·  
I. Struman · N. Bovy · K. Sliwa · J. Bauersachs · Denise Hilfiker-Kleiner

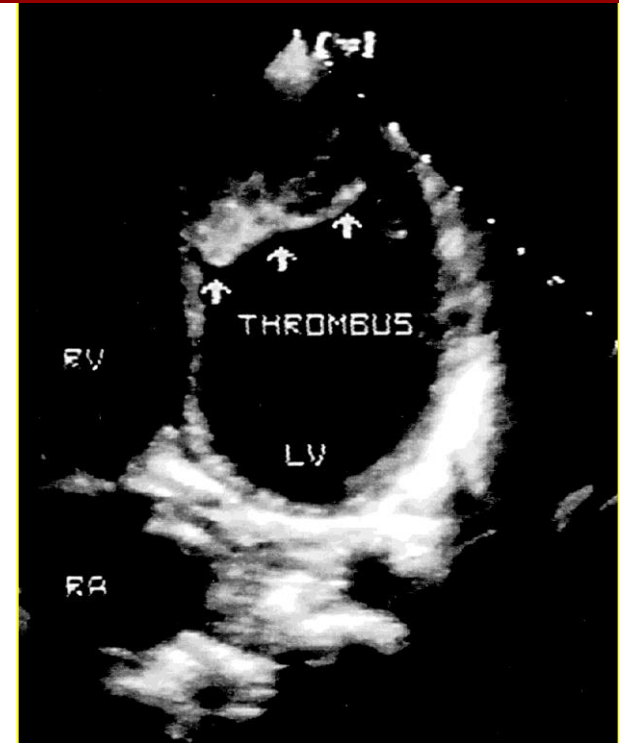
85% Improver (IMP)

15% Non-Improver (NIMP)



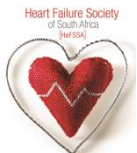
# Anticoagulation

- Thromboembolic phenomena have been reported frequently in PPCM.
- Hypercoagulable state of late pregnancy may persist up to 8 weeks post partum.
- Low ejection fraction (<35%) - LV thrombus common.
- **Warfarin is preferred postpartum and low-molecular weight heparin agent of choice in the last weeks of pregnancy in particular if EF < 35% or LV clot has been documented.**
- In more than 100 patients treated with Bromocriptine in Germany & South Africa thrombotic events were not observed – *unpublished observation.*



# Breast Feeding

- Based on the postulated negative effects of prolactin sub-fragments (*Hilfiker-Kleiner Cell 2007*), breast feeding is not advised in patients with suspected PPCM, even if this practice is not fully evidence-based.
- Several ACE-inhibitors (captopril, enalapril and quinapril) have been adequately tested in breast feeding women.



# Case Follow up 1

## Follow up

**Patient was seen 1 month, 3 month and 6 month post diagnosis. Her symptoms improved on medication and she was asymptomatic at the 6 months visit.**

## **Medication:**

**Beta-blockers ( carvedilol) was up-titrated to maximal dose**

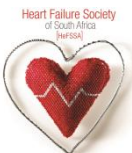
**Ace-inhibitor ( perindopril) was only tolerated at 4 mg daily as BP remained at 100 mmHg systolic**

**No digoxin was added as no evidence to use in this condition**

**Furosemide was stopped and replaced with low dose Hydrochlorothiazide.**

**Bromocriptine was given at 6.25 daily for 2 weeks followed by 6.25 daily for another 4 weeks**

**Warfarin was not given as patient had no access to regular INR testing**



# Case Follow up 2

## Follow up II

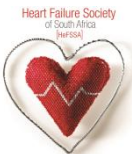
Echocardiography was repeated after 6 month:

The contractility had improved ( LVEF 45%) but not normalized

The patient was advised to continue on medical therapy for another 6 months and to repeat the investigation

Advise on a subsequent pregnancy:

The patient was advised to continue on her contraception and to not plan another pregnancy until the heart had fully recovered ( minimum to wait- 2 years)



# Conclusion and way forward

- PPCM remains a difficult condition to both diagnose and treat.
- PPCM symptoms mimic typical symptoms of pregnancy/ early post-partum period. High index of suspicion warranted.
- Treatment with standard medication and bromocriptine needs to be investigated in larger trials and registries.
- Need to identify biomarkers for facilitating early diagnosis and predicting outcome
- Long-term prognosis is not well established
- More awareness for the disease is important!

# HeFSSA Practitioners Program 2015

## Theme - Women and Heart Failure

08:00 - 08:20	Registration & Breakfast
08:20 - 08:25	Welcome and Thank You to Sponsors
08:25 - 08:30	HeFSSA smartphone patient app (video)
08:30 - 09:15	Implantable devices, women and heart failure
09:15 - 10:00	Peri-partum cardiomyopathy
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