Peripartum cardiomyopathy and preeclampsia – two sides of the same coin?

RA Dyer
Professor and Second Chair
Department of Anaesthesia
University of Cape Town
OAA Westminster 2014
Peripartum cardiomyopathy: a diagnosis of exclusion.

- 1/300 – 1/3000
- Cardiac failure in the last month of pregnancy or within 5 months postpartum
- No identifiable cause of heart disease or cardiac failure
- Echocardiographic evidence of severe left ventricular systolic dysfunction

Sliwa, Lancet 2006
Preeclampsia is a major killer: South African Maternal Mortality by Cause (NCCEMD 2008-2010)
Learning objectives

• Recent research on maternal physiology
• The pathophysiology of preeclampsia and peripartum cardiomyopathy
• Transthoracic echocardiographic findings
  – Point of Care
  – Research
• Anaesthesia implications
• Long term cardiac outcomes
Physiology

• **Angiogenesis of pregnancy leads to physiological eccentric cardiac hypertrophy**
  – Neovascularization from pre-existing blood vessels in response to hypoxia or substrate demands of tissues
  – The endometrium, decidua and placenta are rich sources of angiogenic growth factors (VEGF, PI GF)
How can this go wrong?

IDIOPATHIC MYOCARDIAL DEGENERATION ASSOCIATED WITH PREGNANCY AND ESPECIALLY THE Puerperium.

By Benjamin A. Gouley, M.D.,
Thomas M. McMillan, M.D.,
and
Samuel Bellet, M.D.,

Am J Med Sci 1937
A Cathepsin D-Cleaved 16 kDa Form of Prolactin Mediates Postpartum Cardiomyopathy

Denise Hilfiker-Kleiner,¹,* Karol Kaminski,¹ Edith Podewski,¹ Tomasz Bonda,¹ Arnd Schaefer,¹ Karen Sliwa,³

Cell 128, 589–600, February 9, 2007
Fig. 1. Hypothesis: prolactin fragments generated by MMPs modulate PE and PPCM.
Cardiac angiogenic imbalance leads to peripartum cardiomyopathy

Ian S. Patten¹,²*, Sarosh Rana³*, Sajid Shahul⁴, Glenn C. Rowe¹, Cholsoon Jang¹, Laura Liu¹, Michele R. Hacker³, Julie S. Rhee³, John Mitchell⁴, Feroze Mahmood⁴, Philip Hess⁴, Caitlin Farrell¹, Nicole Kouliis¹, Eliyahu V. Khankin⁵, Suzanne D. Burke⁵, Leo, Igor Tudorache⁶, Johann Bauersachs⁷, Federica del Monte¹, Denise Hilfiker-Kleiner⁷, S. Ananth Karumanchi⁵,⁸ & Zoltan Arany¹

Nature, May 2012
Pathogenesis of peripartum cardiomyopathy

- PGC1-α: pro-angiogenic transcriptional coactivator
  - Knockout mice get cardiomyopathy
- Pro-angiogenic therapy in the form of vascular endothelial growth factor rescues the mice!
Pathogenesis of preeclampsia

- Marked elevations of the anti-angiogenic soluble form of endothelial growth factor (sFLT-1)
- May correlate with indices of diastolic dysfunction
- “Second hit” theory near end of pregnancy
Possible joint pathways of early pre-eclampsia and congenital heart defects via angiogenic imbalance and potential evidence for cardio-placental syndrome

Karen Sliwa¹* and Alexandre Mebazaa²

¹Hatter Institute for Cardiovascular Research in Africa & IIDMM, Cape Heart Centre, Department of Medicine, Faculty of Health Sciences, University of Cape Town, South Africa; and
²Inserm 942; University Paris Diderot, PRES Sorbonne Paris Cité; and AP-HP, Hôpitaux Universitaires Saint Louis-Lariboisière, Paris, France
Peripartum cardiomyopathy
Headache, cerebral edema, seizure
HELLP syndrome
Glomerular endotheliosis, proteinuria, edema, renal insufficiency
Hypertension, preeclampsia, endothelial dysfunction

Genetic factors
Nulliparity
Diabetes
Obesity
Metabolic syndrome
+
cytokines/ROS/coagulation factors

Spiral artery with reduced calibre, reduced blood flow & hypoxia
Angiogenic/antiangiogenic unbalance in maternal blood

CHD
Pulmonary artery catheter: Filling pressures and cardiac work – untreated preeclampsia

Young, Johanson, Best Pract Res Clin Obstet Gynecol 2001
An “inovasoconstrictor” state

Healthy pregnant woman

Woman with untreated preeclampsia

- Increased LV mass
- Altered ventricular movement
- Increased left atrial size
- Altered filling of heart
- Pericardial effusion
**Results**: Fourteen women (93%) had severe PE. Women were similar in body mass index, parity and age.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Healthy</th>
<th>Untreated PE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestation (weeks)</td>
<td>40 ± 1.8</td>
<td>36 ± 5.6*</td>
</tr>
<tr>
<td>Haemoglobin (g/l)</td>
<td>10.7 ± 1.42</td>
<td>10.3 ± 1.9</td>
</tr>
<tr>
<td>Mean arterial pressure (mmHg)</td>
<td>84 ± 15.2</td>
<td>120 ± 11.9*</td>
</tr>
<tr>
<td>Cardiac index (l/min/m²)</td>
<td>3.1 ± 0.70</td>
<td>3.6 ± 0.94</td>
</tr>
<tr>
<td>SVR (dyne.s/cm²)</td>
<td>1237 ± 321</td>
<td>1592 ± 531*</td>
</tr>
<tr>
<td>Cardiac output (l/min)</td>
<td>5.7 ± 1.3</td>
<td>6.6 ± 2.1</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>66 ± 14</td>
<td>79 ± 15.8*</td>
</tr>
<tr>
<td>CWI (mmHg.l/m²)</td>
<td>266 ± 77.7</td>
<td>425 ± 109.7*</td>
</tr>
<tr>
<td>LV ED diameter (cm)</td>
<td>4.6 ± 0.44</td>
<td>4.5 ± 0.49</td>
</tr>
<tr>
<td>LV mass (g)</td>
<td>170 ± 40.4</td>
<td>216 ± 32.2*</td>
</tr>
<tr>
<td>Fractional shortening (%)</td>
<td>40 ± 8.8</td>
<td>40 ± 7.1</td>
</tr>
<tr>
<td>Heart rate (BPM)</td>
<td>88 ± 13.1</td>
<td>83 ± 14.2</td>
</tr>
<tr>
<td>Septal s’ velocity (cm/s)</td>
<td>9.3 ± 1.7</td>
<td>8.4 ± 1.6</td>
</tr>
<tr>
<td>Biphasic septal s’ wave</td>
<td>6 (15)</td>
<td>7 (47)*</td>
</tr>
<tr>
<td>Mitral valve E/Septal e’</td>
<td>7.7 ± 2.13</td>
<td>10.5 ± 3.3*</td>
</tr>
<tr>
<td>TAPSE</td>
<td>2.6 ± 0.39</td>
<td>2.6 ± 0.36</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>21 (53)</td>
<td>10 (67)</td>
</tr>
<tr>
<td>Size of effusion (cm)</td>
<td>0.3 ± 0.28</td>
<td>0.5 ± 0.24*</td>
</tr>
<tr>
<td>Longitudinal Strain (%)</td>
<td>-</td>
<td>-18.1 ± 3.7</td>
</tr>
</tbody>
</table>
Prevalence of severe LVH, diastolic and systolic dysfunction in early- and late onset preeclampsia

Melchiorre, Hypertension 2011
At 24 weeks:
- Early onset disease: High SVR, low cardiac output
- Late onset disease: Low SVR, high cardiac output

Early onset:
- Greater percentage > 35 yoa
- Lower percentage raised BMI
Echocardiographic differences between preeclampsia and peripartum cardiomyopathy

A.T. Dennis, a J.M. Castro b

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bDepartment of Cardiology, St Vincent’s Hospital, Fitzroy, Australia

Differing emphasis on systolic and diastolic dysfunction, chamber enlargement, and cardiac output
Cardiac abnormalities in pulmonary oedema associated with hypertensive crises in pregnancy

D. K. Desai Consultant, J. Moodley Professor, D. P. Naidoo Consultant, I. Bhorat Senior Registrar
MRC/UN Pregnancy Hypertension Research Unit, Faculty of Medicine, University of Natal, Durban, South Africa

Results  Echocardiography diagnosed impaired left ventricular systolic function in 4 of 16 (25%) patients with HCP and pulmonary oedema. In the remaining 12 patients with preserved systolic function, left ventricular diastolic filling abnormalities were demonstrated in a significant proportion compared to control hypertensive and normotensive groups. Fifteen of 16 (94%) study patients presented with pulmonary oedema antepartum; in seven of these patients, the use of dexamethasone to enhance fetal lung maturity appeared to be a contributing factor in precipitating pulmonary oedema.
Pulmonary oedema

A00 Transthoracic echocardiography in patients with preeclampsia and pulmonary oedema

AT Dennis, RA Dyer*, M Gibbs*, L Nel*, JM Castro†, JL Swanevelder*

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*Anaesthesia, Groote Schuur Hospital & University of Cape Town, Cape Town, South Africa, †Cardiology, St Vincent's Hospital, Melbourne, Australia

Introduction: Pulmonary oedema (PO) is a life-threatening complication of preeclampsia (PE). In hypertensive PO assumptions are often made regarding cardiac function (CF) without appropriate investigations such as transthoracic echocardiography (TTE). TTE is recommended in PO but rarely used in the obstetric setting. We present 3 cases in which TTE performed at the time of PO confirmed diagnosis, assessed CF & assisted with management.

<table>
<thead>
<tr>
<th></th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>23</td>
<td>30</td>
<td>41</td>
</tr>
<tr>
<td>Booking weight (Kg)</td>
<td>60</td>
<td>54</td>
<td>52</td>
</tr>
<tr>
<td>Booking Systolic BP (mmHg)</td>
<td>120</td>
<td>90</td>
<td>138</td>
</tr>
<tr>
<td>Booking Diastolic BP (mmHg)</td>
<td>90</td>
<td>60</td>
<td>88</td>
</tr>
<tr>
<td>Haemoglobin (g/l)</td>
<td>7.1</td>
<td>8.9</td>
<td>9.3</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>190</td>
<td>150</td>
<td>150</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>145</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Fractional shortening (%)</td>
<td>19</td>
<td>25</td>
<td>28</td>
</tr>
<tr>
<td>Ejection fraction (EF) (%)</td>
<td>15</td>
<td>45</td>
<td>45</td>
</tr>
<tr>
<td>LV End diastolic diameter (cm)</td>
<td>4.7</td>
<td>5.3</td>
<td>5.5</td>
</tr>
<tr>
<td>HR (BPM)</td>
<td>126</td>
<td>70</td>
<td>80</td>
</tr>
<tr>
<td>Mitral valve E/ septal e’</td>
<td>9.7</td>
<td>8.7</td>
<td>12.2</td>
</tr>
<tr>
<td>Treatment after TTE</td>
<td>Hydralazine</td>
<td>Frusemide</td>
<td>Frusemide</td>
</tr>
</tbody>
</table>

LV=left ventricle, CS=caesarean section, HR=heart rate
Cardiovascular Management in Pregnancy

Cardiovascular Implications in Preeclampsia
An Overview

Karen Melchiorre, MD, PhD; Rajan Sharma, MD, MRCP; Basky Thilaganathan, MD, PhD, FRCOG

*Circulation.* 2014;130:703-714
Implications for Anaesthesia?
Anaesthesia in PPCM

British Journal of Anaesthesia 1995; 75: 97–101

CASE REPORTS

Peripartum cardiomyopathy presenting as a cardiac arrest at induction of anaesthesia for emergency Caesarean section

A. K. McInDOE, E. J. HAMMOND AND P. C. B. BABINGTON

Need high index of suspicion
CASE REPORT

Low dose combined spinal-epidural anaesthesia for caesarean section in a patient with peripartum cardiomyopathy

M. Pirlet, M. Baird, S. Pryn, M. Jones-Ritson, S. M. Kinsella
Sir Humphry Davy Department of Anaesthesia, St Michael's Hospital, Bristol, UK

SUMMARY. A patient with peripartum cardiomyopathy was scheduled for elective caesarean section after stabilization on medical therapy. We performed a combined spinal epidural using one ml 0.5% hyperbaric bupivacaine (5 mg) with 0.3 mg diamorphine for the spinal. The epidural was topped up with 10 mL bupivacaine 0.5%. Significant haemodynamic changes consisted of reduction in heart rate and hypotension after the spinal, and tachycardia after delivery. The benefits and risks of this approach are discussed. © 2000 Harcourt Publishers Ltd

Use of remifentanil in a patient with peripartum cardiomyopathy requiring Caesarean section

Department of Clinical Anaesthesia, Royal Victoria Hospital, Grosvenor Road, Belfast BT12 6BA, UK

*Corresponding author

We describe a case of a 26 yr old primigravida at 39 weeks' gestation, with a diagnosis of peripartum cardiomyopathy, requiring urgent Caesarean section. The patient presented in severe heart failure and active labour. A general anaesthetic, using a target-controlled infusion of propofol and an intravenous infusion of remifentanil, was used to provide stable anaesthesia and analgesia for a successful delivery. The unusual diagnosis of peripartum cardiomyopathy and the potential benefits of the use of remifentanil in high-risk obstetric surgery are discussed.

Br J Anaesth 2001; 86: 135–8

Keywords: anaesthesia, obstetric; complications, cardiomyopathy; analgesics opioid, remifentanil
Acute and critically ill peripartum cardiomyopathy and ‘bridge to’ therapeutic options: a single center experience with intra-aortic balloon pump, extra corporeal membrane oxygenation and continuous-flow left ventricular assist devices

Sofie Gevaert1⁎, Yves Van Belleghem2, Stefaan Bouchez3, Ingrid Herck4, Filip De Somer2, Yasmina De Block1,2, Fiona Tromp1, Els Vandecasteele1, Floor Martens4, Michel De Pauw1

6 Patients had IABP
1 ECMO, 4 LVAD
3 Heart transplants
Case report

- 30 year old G2P1
- 38 weeks’ gestation
- Pulmonary oedema
- Caesarean section
- Heart rate 160
- BP 60/30
- CVP 22 cm H₂O
Hemodynamic Changes Associated with Spinal Anesthesia for Cesarean Delivery in Severe Preeclampsia


* CO change from baseline (L/min)

Sitting Spinal Supine L Tilt Skin Uterine Post-delivery End surg Recovery

Time intervals

CO change from baseline (L/min)
Recommendations in preeclampsia

- Regional anaesthesia preferable and safe in uncomplicated severe disease
  - Caution in pulmonary oedema – consider CSE

- Should general anaesthesia be required
  - Hypertension, diastolic dysfunction:
    - Rapid pre-determined dose of thiopentone/propofol, magnesium sulphate, suxamethonium
  - Pulmonary oedema, systolic hypofunction:
    - Careful titration, balance risk of aspiration and hypoxaemia against acute hypotension
Long term recovery?
Preeclampsia

- Increased 10 year cardiovascular risk
- 2 fold risk for hospitalisation for heart failure or atrial/ventricular dysrhythmias 7-8 years later
- Higher risk of death if in first pregnancy
- Increased risk of end stage renal disease

Prevalence of moderate to severe LV functional abnormality 1 year postpartum

Melchiorre, Hypertension 2011
Starting EF>35%, mortality close to zero, high percentage recover
Data from 22 studies (n=979 patients) on peripartum cardiomyopathy were included. The pooled prevalence of 22% (95% CI, 16-28%) was more than quadruple the 5% average worldwide background rate of preeclampsia in pregnancy (p<0.001).
Hypertension and haemodynamics in pregnant women – is a unified theory for pre-eclampsia possible?

- Supply demand mismatch
- Pre-, placental, post-placental conditions
- Relative hypoxaemia
- Vasoconstrictors/vasodilators produced
- Increased perfusion of vascular beds
- Endothelial damage, hypertension
Conclusions: Preeclampsia and Peripartum Cardiomyopathy

- Abnormal angiogenesis in both, possible shared pathways
- Clear distinction in the *typical* presentation of the disease
  - Severe hypertension
  - Diastolic versus systolic dysfunction
  - Biomarkers in preeclampsia
  - Long term cardiovascular sequelae are different
- Severe systolic dysfunction may occur in both
- *In genetically susceptible individuals with subclinical systolic dysfunction (rare), severe hypertension in pregnancy (common) may predispose to the development of cardiomyopathy and severe heart failure*
- *Individual diagnosis and management: echocardiography*
“Ridiculous extrapolations are being made from studies on a few rats. I take care of humans”
Thank you!
References

- Sliwa K et al. Possible joint pathways of early preeclampsia and congenital heart defects via angiogenic imbalance and potential evidence for cardio-placental syndrome. European Heart Journal 2014;
- Melchiorre K et al. Cardiovascular implications in preeclampsia: an overview. Circulation 2014; 130: 703-714