ESC guidelines for the management of cardiovascular diseases during pregnancy

The Committee for Practice Guidelines

How to manage anticoagulation in pregnant women

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Hemostatic changes during normal pregnancy:

- Concentration of coagulation factors $\uparrow$
- Concentration of fibrinogen $\uparrow$
- Platelet adhesiveness $\uparrow$
- Obstruction venous return $\downarrow$
- Increased risk of thrombo-embolic events
Anticoagulation therapy during pregnancy

- Not routinely necessary in pregnant women

- When indication arises:
  - risk of fetal complications with vit K ant. (OAC)
  - changing dose requirements for anticoagulants

(Plasma volume↑ and GFR↑)

Influences choice and monitoring of anticoagulation
Indications for anticoagulation during pregnancy

Atrial fibrillation
Indications for anticoagulation during pregnancy

Atrial fibrillation

Impaired ventricular function
Indications for anticoagulation during pregnancy

Atrial fibrillation

Impaired ventricular function

Pulmonary hypertension
Indications for anticoagulation during pregnancy

- Atrial fibrillation
- Impaired ventricular function
- Pulmonary hypertension
- Cyanotic heart disease, Fontan circulation
Indications for anticoagulation during pregnancy

Atrial fibrillation

Impaired ventricular function

Pulmonary hypertension

Cyanotic heart disease, Fontan circulation

Venous thrombosis, pulmonary emboli
Indications for anticoagulation during pregnancy

Atrial fibrillation

Impaired ventricular function

Pulmonary hypertension

Cyanotic heart disease, Fontan circulation

Venous thrombosis, pulmonary emboli

Valvular heart disease
Where in the guidelines?

Atrial fibrillation *chapter arrhythmias*

Impaired ventricular function *chapter cardiomyopathies*

Pulmonary hypertension

Cyanotic heart disease, Fontan circulation

Venous thrombosis, pulmonary emboli

Valvular heart disease *chapter valvular disease*

Chapter CHD and PH

Separate chapter
Indications for anticoagulation:
atrial fibrillation, 
impaired ventricular function, 
pulmonary hypertension:
comparable to non-pregnant patients

Choice of anticoagulant:
according to stage of pregnancy

LMWH 1st trim and > 36 weeks
OAC in 2nd / 3rd trim
- monitoring

* dabigatran
Anticoagulation in congenital heart disease:

- cyanotic heart disease without pulm hypert: thromboprophylaxis with LMWH if hemostasis normal (IIa)

- cyanotic heart disease with pulmonary arterial hypertension (Eisenmenger syndrome) consider on individual basis (risk bleeding)

- Fontan circulation: risk of thrombo- embolism is high; therapeutic anticoagulation should be considered
Venous thrombo-embolism - ch10

- occurs in 0.05 - 0.2% of pregnancies
- important cause of maternal mortality
Venous thrombo-embolism: risk assessment

- assessment of risk factors for venous thrombo-embolism is recommended in all pregnant women / women with pregnancy wish

- assign women to high, intermediate or low risk group according to presence of risk factors

management
Check list for risk factors for venous thromboembolism
(modified acc. to Royal College of Obstetricians and Gynecologists)

<table>
<thead>
<tr>
<th>Pre-existing risk factors</th>
<th>Obstetric risk factors</th>
<th>Transient risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous recurrent VTE*</td>
<td>Pre-eclampsia</td>
<td>Current systemic infection</td>
</tr>
<tr>
<td>Previous VTE—unprovoked or oestrogen related*b</td>
<td>Dyhydration/hyperemesis/ovarian hyperstimulation syndrome</td>
<td>Immobility</td>
</tr>
<tr>
<td>Previous VTE—provoked</td>
<td>Multiple pregnancy or assisted reproductive therapy</td>
<td>Surgical procedure in pregnancy or &lt;6 weeks post-partum</td>
</tr>
<tr>
<td>Family history of VTE</td>
<td>Emergency caesarean section</td>
<td></td>
</tr>
<tr>
<td>Known thrombophilia*c</td>
<td>Elective caesarean section</td>
<td></td>
</tr>
<tr>
<td>Medical co-morbidities, e.g. heart or lung diseases, SLE, cancer, inflammatory conditions, nephritic syndrome, sickle cell disease, i.v. drug use</td>
<td>Mid-cavity or rotational forceps</td>
<td></td>
</tr>
<tr>
<td>Age &gt;35 years</td>
<td>Prolonged labour (&gt;24 hours)</td>
<td></td>
</tr>
<tr>
<td>Obesity, BMI &gt;30 kg/m²d</td>
<td>Peripartum haemorrhage (&gt;1 L or transfusion)</td>
<td></td>
</tr>
<tr>
<td>Risk groups</td>
<td>Definition according to risk factors listed in Table 17</td>
<td></td>
</tr>
<tr>
<td>-------------</td>
<td>----------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>High risk</td>
<td>Patients with:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(i) Previous recurrent VTE (&gt;1) or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(ii) VTE unprovoked / oestrogen–related</td>
<td></td>
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<tr>
<td></td>
<td>or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(iii) Single previous VTE + thrombophilia or family history</td>
<td></td>
</tr>
<tr>
<td>Intermediate risk</td>
<td>Patients with:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(i) 3 or more risk factors other than listed above as high risk</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(ii) 2 or more risk factors other than listed as high risk if patient is admitted to hospital</td>
<td></td>
</tr>
<tr>
<td>Low risk</td>
<td>Patients with:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;3 risk factors.</td>
<td></td>
</tr>
<tr>
<td>Risk groups</td>
<td>Definition according to risk factors listed in Table 17</td>
<td>Preventive measures according to risk group</td>
</tr>
<tr>
<td>------------</td>
<td>--------------------------------------------------------</td>
<td>-------------------------------------------</td>
</tr>
<tr>
<td><strong>High risk</strong></td>
<td>Patients with: (i) Previous recurrent VTE (&gt;1) or (ii) VTE unprovoked / oestrogen-related or (iii) Single previous VTE + thrombophilia or family history</td>
<td>High risk patients should receive antenatal prophylaxis with LMWH as well as post-partum for the duration of 6 weeks. Graduated compression stockings are also recommended during pregnancy and post-partum.</td>
</tr>
<tr>
<td><strong>Intermediate risk</strong></td>
<td>Patients with: (i) 3 or more risk factors other than listed above as high risk (ii) 2 or more risk factors other than listed as high risk if patient is admitted to hospital</td>
<td>In intermediate risk patients antenatal prophylaxis with LMWH should be considered. Prophylaxis is recommended postpartum for at least 7 days or longer, if &gt;3 risk factors persist. Graduated compression stockings should be considered during pregnancy and postpartum.</td>
</tr>
<tr>
<td><strong>Low risk</strong></td>
<td>Patients with: &lt;3 risk factors.</td>
<td>In low risk patients early mobilization and avoidance of dehydration is recommended.</td>
</tr>
</tbody>
</table>
Diagnosis and management of pulmonary embolism
(avoid CT if possible)
Diagnosis and management of pulmonary embolism

D-dimer
- negative
  - CUS -
    - no anticoag.
  - CUS +
    - no anticoag.
  - CUS -
  - CUS +
- positive
  - MRI iliac vein
    - negative
    - undecided
    - positive
      - CT pulm. angiogr.
      - anticoag
      - anticoag
Venous thrombo-embolism: treatment

- LMWH (according to weight, with anti X-a monitoring) = standard therapy

- renal failure, massive emboli: iv UFH

- thrombolysis: only for massive emboli with hypotension or shock

- newer drugs (fondaparinux, rivaroxaban): not recommended
Valvular heart disease

Mechanical valve prostheses

controversy: LMWH / UFH or vit K antagonists?

- How toxic are vitamin K antagonists for the foetus?

- How effective are LMWH / UFH to prevent mechanical valve thrombosis?
How toxic are vitamin K antagonists for the foetus?

- *embryopathy*: mainly nasal hypoplasia
  sometimes severe abnormalities

 0% if avoided from week 6-12

- *vitamin K ant throughout pregnancy*:

  Chan (review, 549 pregn): 6.4%
  v Driel (review, 394 pregn): 6.0%

*older studies, high dose*

Chan 2000, van Driel 2002
How toxic are vitamin K antagonists for the foetus?

4 more recent studies 1999-2007:

287 pregnancies, no embryopathy, 1 x hydrocephalus

lower INR - lower dose? reliability?

How toxic are vitamin K antagonists for the foetus?

- embryopathy: *dose effect* (<5 mg warfarin)
  2 small studies, probably overlap:
  1x 0%, 1x 2.6%

- miscarriage: literature N=1477:
  no difference between heparin and warfarin

Vitale 1999, Cotrufo 2002
How toxic are vitamin K antagonists for the foetus?

-CNS abnormalities:

- Vit K ant. 1st trimester: review van Driel N=689:1% half had bleeding during vaginal delivery (guidelines: CS when delivery starts while mother on vit K ant, IC)

- vit K ant only in 2nd and 3rd trimester: Wesseling N=307 (vitK ant) vs N=267 (control) normal IQ and development vit K ant : minor neurologic dysfunction (OR 1.9)

Van Driel 2002
Wesseling 2001
How effective are LMWH / UFH to prevent valve thrombosis during pregnancy?

<table>
<thead>
<tr>
<th></th>
<th>vit K ant</th>
<th>UFH wk 6-12</th>
<th>UFH</th>
</tr>
</thead>
<tbody>
<tr>
<td>valve thrombosis</td>
<td>4%</td>
<td>9%</td>
<td>33%</td>
</tr>
<tr>
<td>maternal death</td>
<td>2%</td>
<td>4%</td>
<td>15%</td>
</tr>
</tbody>
</table>

*older valves, adequate dosing of UFH?*

Chan 2000

Newer series N=287: valve thrombosis vit K ant 2,4%

How effective are LMWH / UFH to prevent valve thrombosis during pregnancy?

LMWH: valve thrombosis rate higher when no anti Xa monitoring

LMWH throughout pregnancy, with antiXa monitoring and dose adjustment: N=111 valve thrombosis 9%

Noncompliance? Too low target anti Xa levels?

High risk thrombosis /risk vit K ant low 2nd/3rd trim (guidelines: vit K ant in 2nd/3rd trim until wk 36, IC)

Abildgaard 2009; Quinn 2009; Yinon 2009; McLintock 2009
How effective are LMWH / UFH to prevent valve thrombosis during pregnancy?

LMWH 1st trimester only with antiXa monitoring and dose adjustment:

N=56  valve thrombosis 3.6 %

Peak anti-Xa levels: 0.7-1.2 U/l (ACC guidelines)
However: pre-dose levels then often too low

Monitoring pre-dose levels not yet reported in women with mech. valves (no recommendation)

Barbour 2004, Friedrich 2010
Recommendations in new guidelines

Anticoagulation during first trimester in women with mechanical valves:

*Risk of embryopathy is low with low dose vit K ant*
*Risk of valve thrombosis is higher with UFH / LMWH*

Continuation of vit K ant in the first trimester (wk 6-12) when vit K ant dose is low (<5 mg warfarin or eq)  
**IIa**

*substitute by UFH / LMWH*  
**IIb**
Recommendations in new guidelines

Anticoagulation during first trimester in women with mechanical valves:

*Higher dose requirement; probably more embryopathy*

When vit K ant dose is higher: dose adjusted UFH or LMWH monitoring APTT / anti Xa levels)(weekly) in the first trimester (wk 6-12) IIa

*Continue vit K antagonist instead IIb*
mother Vit K antagonist baby

Safe pregnancy but risk of embryopathy
False dilemma

risk of valve thrombosis  but baby is safe

mother  LMWH / UHF  baby
Valve thrombosis

mother

baby
Valve thrombosis

mother

t

†
surgery

baby

t
t
neurological damage

No risk-free options, no easy choices
guidelines for management of cardiovascular diseases during pregnancy

The best care for the mother with a mechanical valve and for her child