Diagnosing Venous Thromboembolism in Pregnancy: Delivering Concepts

Wee-Shian Chan MD FRCPC MSc
McMaster University

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Objectives

- Provide an approach for the diagnosis of DVT and PE in pregnant patients
- Highlight difficulties in current approaches

Case

- 35yo G1P0 year old at 28w complains of left groin pain, bilateral leg swelling (L>R)
  - Of course you suspect DVT, how would you proceed with investigations?

Case

- Initial CUS is "negative"
- What would you do next?
  a) Just follow clinically
  b) Repeat CUS
  c) do D-dimer
  d) MRI
  e) one or none of the above

Diagnosis of DVT in Non-Pregnant Patients

- Start with Clinical Assessment of Pretest Probability of DVT

  → Low pretest probability of first lower extremity DVT,
  - Testing with D-dimer or CUS of the proximal veins

  → → Moderate pretest probability
  - Testing with a highly sensitive D-dimer, proximal CUS, or whole-leg US

  → → → High pretest probability
  - proximal compression or whole-leg US

Bates et al ACCP guidelines 2012

Clinical "Gestalt" PTP for Suspected DVT in Pregnancy

Author	Low	Intermediate	High
Chan et al 2009	1.5%	24.2%	
Le Gal et al 2012	1.9%	8.2%	72.2%

Assessing **PTP** in pregnant patients: "LeFt" Rule

"LEFt" Variables	Sensitivity (95% CI)	Specificity 95% CI	NPV 95% CI
No variables 1 or more variable(s)	100(77.1-100)	50.3 (42.7-57.9)	100(94.8-100.0)

L: Left

E: ≥ 2cm

Ft: First trimester

Chan WS, et al. Predicting deep venous thrombosis in pregnancy: out in "LEFt" field? Ann Intern Med. 2009 Jul 21;151(2):85-92.

D-Dimer:Utility in pregnancy?

- **Fibrin degradation product**

- **Assays getting more and more "sensitive"**

- **Increases with pregnancy, Preterm labour, Ruptured membrane, Labour, Pre-eclampsia, Abruptio, etc, etc, etc**
  - **►►precludes use????**

Test Characteristics of the 5 D-dimer Assays for Pregnancy

Assay	D-dimer level Cutpoints, μg /ml FEU	Sensitivity, % (95% Confidence Interval)	Specificity, % (95% Confidence Interval)	Negative Predictive value, % (95% Confidence Interval)	Negative Likelihood Ratio (95% Confidence Interval)
Vidas	Non-pregnant 0.50 / Pregnant 1.89	100 (74.7 -100) / 93.3 (68.1 to 99.8)	10.3 (6.63-15.5) / 78.8 (72.7-84.1)	100 (80.8- 100) / 99.4 (96.2- 100)	0.09 (0.01-0.56)
Asserachrome	Non-pregnant 0.50 / Pregnant 1.51	100 (74.7- 100) / 100 (78.2- 100)	12.3 (8.28 -17.8) / 73.9 (67.5-79.7)	100 (83.4- 100) / 100 (97.0- 100)	0 (-)†
IL Test*	Non-pregnant 0.23* / Pregnant 0.57*	100 (74.7- 100) / 80.0 (51.9- 95.7)	17.8 (13.0 -24.0) / 74.8 (68.3 -80.5)	100 (88.0 -100) / 98.1 (94.2 - 99.5)	0.27 (0.10-0.74)
STA-Lia Test	Non-pregnant 0.50 / Pregnant 1.38	100 (74.7 - 100) / 93.3 (68.1 - 99.8)	22.9 (17.5 -29.4) / 75.6 (69.3-81.2)	100 (90.6 -100) / 99.4 (96.1 -100)	0.09 (0.01-0.59)
Innovance	Non-pregnant 0.50 / Pregnant 1.50	100 (74.7-100) / 100 (74.7-100)	6.22 (3.49-10.6) / 61.2 (54.3-67.8)	100 (71.7-100) / 100 (96.4-100)	0 (-)†

Chan WS, et al. D-dimer testing in pregnant patients: towards determining the next 'level' in the diagnosis of deep vein thrombosis. J Thromb Haemost. 2010 May;8(5):1004-11

OK…Now CUS for pregnancy DVT

- How sensitive is it? ????

- How specific is it? ????

- Can I do a single CUS in pregnancy?

Anatomical Distribution of DVT

- Non-pregnant patients
  - Isolated calf vein thrombosis: 12 to 28%
  - proximal vein thrombi with calf vein involvement: 58-87%
  - Proximal vein thrombi without calf vein involvement: 0-13%
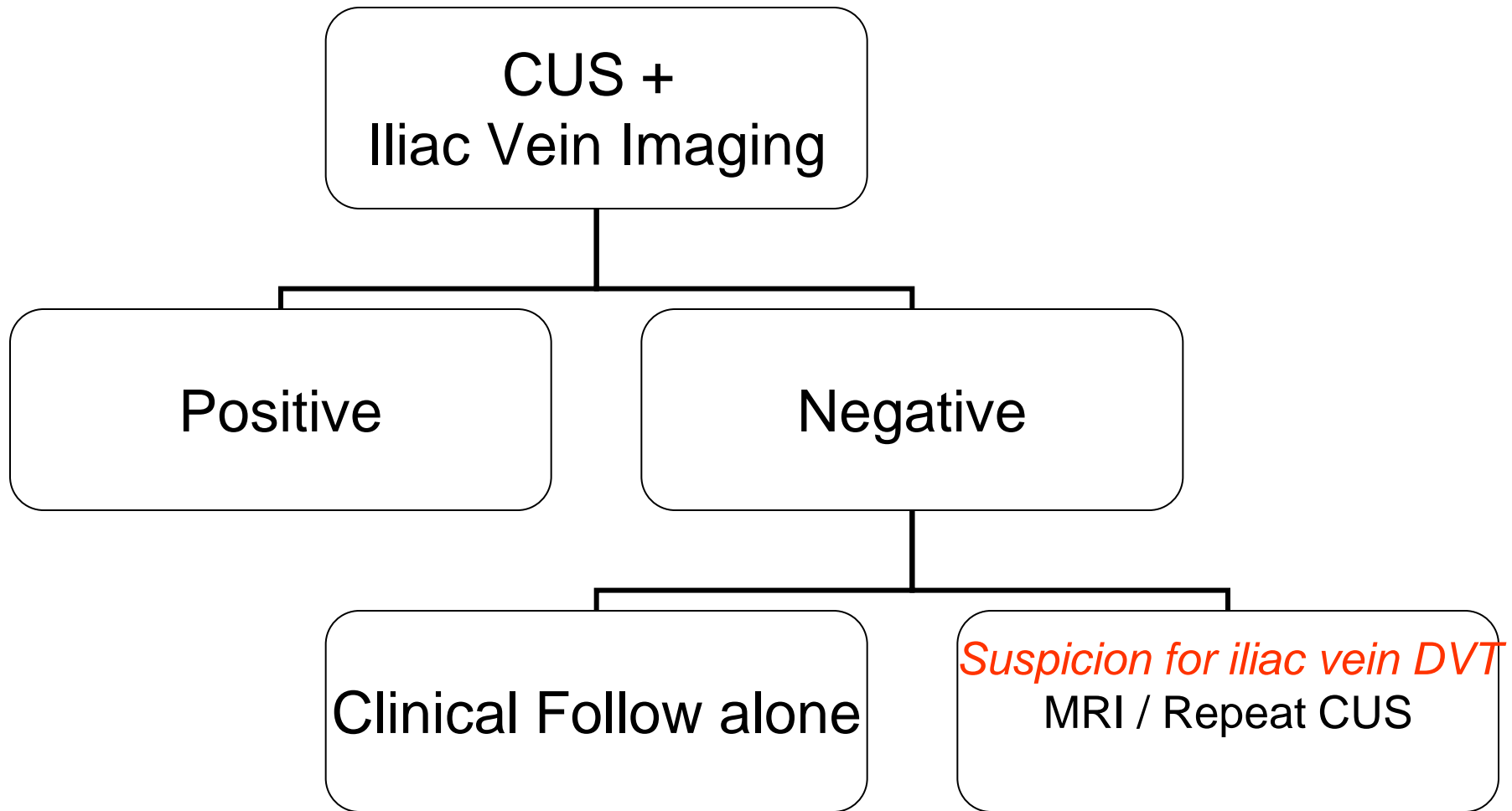 - Ileofemoral/femoral/iliac vein thrombi vein thrombi: 1-5%

- Pregnant Patients
  - Isolated calf vein thrombosis: 6%
  - proximal vein thrombi with calf vein involvement: 21%
  - Proximal vein thrombi without calf vein involvement: 74%
  - Ileofemoral/femoral/iliac vein thrombi: 61%

Chan WS, et al. Anatomic distribution of deep vein thrombosis in pregnancy. CMAJ. 2010 Apr 20;182(7):657-60.

Diagnostic value of a single complete compression ultrasonography in pregnant and postpartum women with suspected deep vein thrombosis: Prospective study

- Le gal et al BMJ 2012;344:e2635 Apr 24, 2012
- 226 pregnant and postpartum (20.5%)
- Single proximal and distal compression ultrasonography, iliac imaging with doppler
- **Results**
  - **Prevalence of DVT 10.5%**
  - **Risk of VTE in follow-up after negative test: 1.1% (95%CI 0.3-4.0%)**

Diagnosis of DVT in Pregnancy

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           ┌─────────────────────┐
           │       CUS +         │
           │  Iliac Vein Imaging │
           └─────────────────────┘
                      │
           ┌──────────┴──────────┐
  ┌────────────────┐      ┌────────────────┐
  │                │      │                │
  │    Positive    │      │    Negative    │
  │                │      │                │
  └────────────────┘      └────────────────┘
                              │
                   ┌──────────┴──────────┐
          ┌────────────────────┐  ┌────────────────────────────┐
          │                    │  │ Suspicion for iliac vein DVT│
          │ Clinical Follow    │  │   MRI / Repeat CUS          │
          │      alone         │  │                            │
          └────────────────────┘  └────────────────────────────┘
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Case

- 35 yo, 9w GA, c/o rt sided upper back to mid back pain.
  - Of course you suspect PE, how would you investigate?

Investigation of PE

- a) VQ
- b) CTPA
- c) D-dimer?
- d) CXR, EKG, ABGs, bilateral leg CUS, Echo…then call thrombo/hematologist….

Diagnosis of PE in Non-pregnant Patients

- Clinical Assessment (Well's, PERC, Geneva)
  - Followed by D-dimer testing
    - Diagnostic Imaging: VQ or CT

Clinical Assessment of PE in Pregnancy

- "Gestalt"

Can we use D-dimer to rule out PE in pregnancy?

- To MS, Hunt BJ, Nelson-Piercy C. **A negative D-dimer does not exclude venous thromboembolism (VTE) in pregnancy.** J Obstet Gynaecol. 2008 Feb;28(2):222-3.

- Levy MS, Spencer F, Ginsberg JS, Anderson JA. **Reading between the (Guidelines). Management of submassive pulmonary embolism in the first trimester of pregnancy.** Thromb Res. 2008;121(5):705-7. Epub 2007 Aug 17.

- Damodaram M, Kaladindi M, Luckit J, Yoong W. **D-dimers as a screening test for venous thromboembolism in pregnancy: is it of any use?** J Obstet Gynaecol. 2009 Feb;29(2):101-3.

VQ versus CT

- Safety of Fetus/Mother
  - Contrast agent
  - Radiation
- Test characteristics
  - Sensitivity?
  - Does specificity matter?
  - Technical issues

Fetal Radiation Dose

- VQ scan
  - **Perfusion lung scan**
    0.06-0.12mGy
  - **Ventilation lung scan**
    0.01-0.35mGy

- Spiral CT
  - Radiation dose
    - 1st trimester:
      0.003-0.020mGy
    - 2nd trimester:
      0.008-0.077mGy
    - 3rd trimester:
      0.051-0.131mGy

Threshold for childhood malignancies >50mGy

Spiral CT & Maternal Radiation Exposure

- **Average calculated effective minimum dose to the breast of an average 60kg woman during CT *20 mGy* per breast**

- **2-view mammogram: 3 mGy**

- **VQ scan 0.28 mGy**

- **Cancer risk threshold in acute exposure ≈10-50 mGy**

Observational "Pregnant" PE Studies

Author (year)	VQ/Q	Both	CT	Results
Balan 1997	82	0	0	22%H, 17% I, 23% L, 38% N
Chan 2002	119	1	1	2% H, 25% ND, 74%N
Scarsbrook 2007	92	2	9	1% H, 7% ND, 92% N CT: 0% positive
Shamir 2010	97	2	106	VQ: 0% H, 2 % ND, 98% N CT: 3.7% positive
Bourjeilly 2011	0	0	343	2.9% positive

ND: non-diagnostic   N:Normal   H:High
I:Intermediate

"Technical Difficulties" CT vs VQ

Author, year	Case (CT)	Comparison group	Frequency of "Indeterminates"
U-King-Im et al, 2008	40 pregnant	40 non-pregnant	27.5% vs 7.5% (p=0.015)
Cahill et al, 2009	108 CT (preg+pp)	196 VQ (preg+pp)	17% vs 13%* (ns)
Ridge et al, 2009	28 CT	25 VQ	35% vs 4% (p=0.0058)
Shahir et al, 2010	106 CT	99 Q	5.6% vs 1% (p<0.05)
Revel et al 2011	43 CT	91 VQ	19% vs 19%* (ns)

Why is CT likely to be more often "Inadequate" in pregnancy?

- Most non-diagnostic CTA studies showing an artifact due to transient interruption of contrast material by unopacified blood from the IVC.

- Increased IVC pressure combined with the expected decrease in intrathoracic pressure during deep inspiration may increase venous return owing to the thoracoabdominal gradient.

Ridge et al. Pulmonary Embolism in Pregnancy: Comparison of Pulmonary CT Angiography and Lung Scintigraphy. AJR November 2009 193:1223
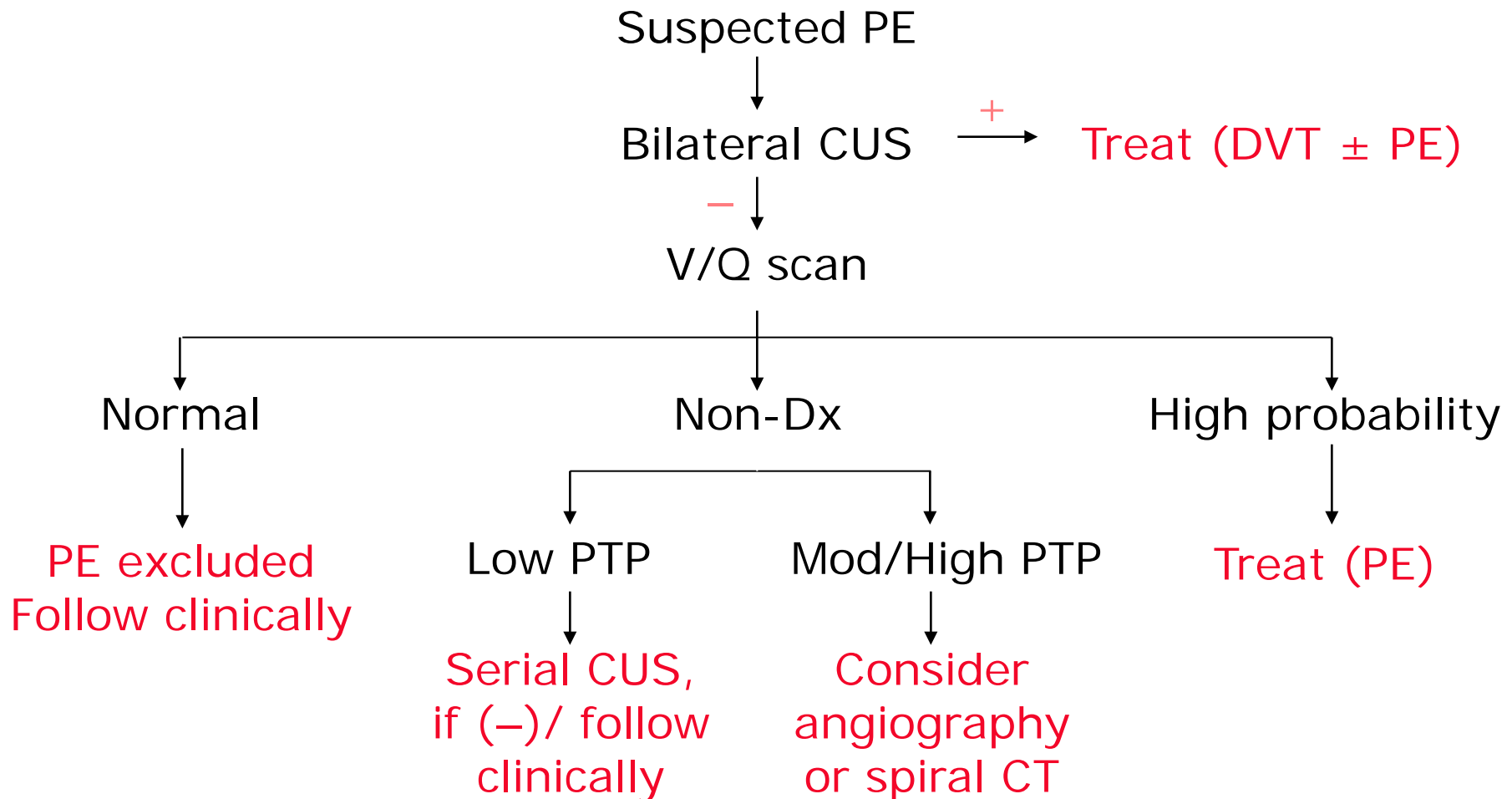
Methods to improve the image quality and to reduce the radiation dose of CTA for acute PE during pregnancy

- Short scan duration (choose the fastest scanner)
- High iodine influx (↑ increase of flow and / or iodine concentration, e.g., 6ml /s and 400 mg Iodine/ml)
- No maximal inspiration or even shallow breathing
- Take images during shallow-held inspiration
    - Hartmann et al, EJR 74 (2010) 40–49

Test Characteristics: VQ vs CT

- Prevalence of PE in pregnant patients lower than that of non-pregnant patients
- Both CT/VQ are likely sensitive.
- Specificity: Unknown.
- More Technical difficulties with spiral CT scan
  - 5-36% inadequate scan with CT vs 1-2% with VQ scan

Diagnosis of PE in Pregnancy (I still prefer VQ in 2012)

Suspected PE

↓

Bilateral CUS —— + ——→ Treat (DVT ± PE)

– ↓

V/Q scan

- **Normal**
  ↓
  PE excluded
  Follow clinically

- **Non-Dx**
  - **Low PTP**
    ↓
    Serial CUS,
    if (–)/ follow
    clinically
  - **Mod/High PTP**
    ↓
    Consider
    angiography
    or spiral CT

- **High probability**
  ↓
  Treat (PE)

Chan WS & Ginsberg JS (2002). *Thromb Res*, 107:85-91

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