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**Literature search results**

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**Search details**

Risk stratification for diagnosis of pulmonary embolism

**Resources searched**

NHS Evidence; TRIP Database; Cochrane Library; CINAHL; EMBASE; MEDLINE; Google Scholar

**Database search terms:** pulmonary adj2 emboli*; pulmonary adj2 embol*; PULMONARY EMBOLISM; lung* adj2 embol*; LUNG EMBOLISM; pregnan*; PREGNANCY; pre-natal; prenatal; ante-natal; antenatal, gravid, gestation; diagnos*; exp DIAGNOSIS; ident*; detect*; spot*; "risk stratification*; risk* adj2 stratif*; RISK ASSESSMENT; STRATIFICATION; d-dimer; d-dimer adj2 threshold*; D-DIMER; FIBRIN FIBRINOGEN DEGRADATION PRODUCTS

**Evidence / Google Scholar search string(s):** (pregnant OR pregnancy OR antenatal OR prenatal OR gestation OR gravid)("lung embolism" OR "lung emboli" OR "pulmonary emboli" OR "pulmonary embolism") (diagnosis OR diagnose OR identify OR identification OR identified OR detected OR detect OR detection OR d-dimer) "risk stratification"

**Summary**

There is some research on risk stratification for pulmonary embolism for pregnant women, which I hope you will find useful.

**Guidelines and Policy**

American College of Emergency Physicians
Critical issues in the evaluation and management of adult patients presenting to the emergency department with suspected pulmonary embolism 2011

American College of Chest Physicians

Diagnosis of DVT: antithrombotic therapy and prevention of thrombosis 2012

In hospitalized and other acutely ill patients commonly affected by DVT and pulmonary embolism, D-dimer testing has less usefulness because of the high frequency of false-positive results.

NICE

CG144 Venous thromboembolic diseases: two-level Wells score - templates for deep vein thrombosis and pulmonary embolism 2013

Two-level DVT and PE Wells scores are recommended in the guideline to help you estimate the clinical probability of DVT and PE respectively. This document provides templates for local adaptation to allow the two-level Wells score for DVT or PE to be calculated and recorded in a format suitable for filing in the patient record.

University of Michigan Health System

Venous thromboembolism (VTE) 2014

Evidence-based reviews

BestBETs

Diagnostic utility of chest xray for investigation of pulmonary embolism 2009

A chest X-ray alone is of little value in the diagnosis of pulmonary embolus. Its main value is in ruling out other causes of the presenting symptoms, or as part of a risk stratification strategy to inform a further investigative protocol.

Biomed central

The prognostic value of pulmonary embolism severity index in acute pulmonary embolism: a meta-analysis 2012

PESI has discriminative power to predict the short-term death and adverse outcome events in patients with acute pulmonary embolism, the PESI and the sPESI have similar accuracy, while sPESI is easier to use. However, the calibration for predicting prognosis can’t be calculated from this meta-analysis, some prospective studies for accessing PESI predicting calibration can be recommended.

British Medical Journal

Diagnosis and management of pulmonary embolism 2013

Database of Abstracts of Reviews of Effects

D-dimer for risk stratification in patients with acute pulmonary embolism 2013

Published research – Databases

1. Cardiovascular disorders in pregnancy: Diagnosis and management

Author(s) Westhoff-Bleck M., Podewski E., Hilfiker A., Hilfiker-Kleiner D.

Citation: Best Practice and Research: Clinical Obstetrics and Gynaecology, December
Abstract: Cardiovascular diseases (CVDs) are a major cause of complications in pregnancy worldwide and the number of patients who develop cardiac problems during pregnancy is increasing. This review summarises recent literature on the aetiology and the underlying pathophysiology, diagnostic tools, risk stratification and prognosis in women who develop heart failure during pregnancy and in the peri-partum phase as well as in patients with pre-existing cardiomyopathies undergoing pregnancy. We specifically highlight peri-partum cardiomyopathy, valvular disease and Marfan's syndrome. Furthermore, we provide overviews on established treatment concepts and novel therapeutic strategies for these different disease types, stressing the point that pregnancy-associated cardiac disease requires interdisciplinary concepts for diagnosis, management and treatment. 2013 Elsevier Ltd. All rights reserved.

Source: EMBASE

2. 16th Tri-country Congress of the Austrian, German and Swiss Society of Angiology

Author(s)

Citation: Vasa - Journal of Vascular Diseases, September 2013, vol./is. 42/(13) (12 Sep 2013)

Abstract: The proceedings contain 142 papers. The special focus in this conference is on Angiology. The topics include: Serum angiogenin which influences vascular repair is related to macrovascular complications of diabetes, but not to diabetes per SE; longterm evaluation on the impact of thrombus formation on the course of abdominal aortic diameter expansion; preserved thrombin inducible platelet activation in thienopyridine-treated patients; prasugrel reduces agonists' inducible platelet activation and leukocyteplateletlet interaction more efficiently than clopidogrel; recent trends in morbidity and in-hospital outcomes of inpatients with peripheral arterial disease - a nationwide population-based analysis; infrapopliteal arterial lesion morphology in patients with critical limb ischemia; proton pump inhibitor intake and outcome after percutaneous intervention for symptomatic iliac artery occlusive disease; percutaneous transluminal angioplasty (PTA) versus primary stenting in patients with severe claudication and critical limb ischemia with infrapopliteal vascular lesions-EXPAND study; treatment of in-stent-restenosis with silverhawk atherctomy; care of patients with aortic abdominal aneurysms within an interdisciplinary vascular center improves patients' outcome and is economically effective; pulse wave velocity predicts lifetime survival - a 50-year longitudinal study; outcome of patients with reduced ankle brachial index (ABI) undergoing open heart surgery with cardiopulmonary bypass; prognostic value of neutrophils in patients with asymptomatic carotid artery disease; influence of the inflammatorical burden and plaque stability on the 11-year mortality after carotid endarterectomy; differentiation of superficial femoral artery restenosis by optical coherence tomography (OCT); assessment of disease activity in extracranial giant cell arteries with positron emission tomography; endovenous laser ablation of the great saphenous vein using the new radial fiber slim - 1 month follow-up; endovenous laser ablation of varicose veins with the 1470 diode laser using a radial fibre - 1 year follow-up; hemodynamic prerequisites triggering venous reflux as well as reflux recurrence; pharmacomechanical thrombectomy of pulmonary embolism - a case series; longterm mortality after percutaneous transluminal angioplasty in PAD patients with chronic kidney disease; cardiovascular risk in peripheral arterial disease; an unusual cause for the usual case of intermittent claudication; derived neutrophil-to-lymphocyte ratio and its association with critical limb ischemia in PAOD patients; the interdisciplinary challenge; successful infrarenal aortic replacement with superficial femoral vein; transapical endovascular aortic repair to treat complex aortic pathologies; lightweight personal protection devices for superior radiation protection in fluoroscopy-guided interventions; sensitivity and specificity of fluorescence microlymphography for detecting lymphedema of the lower extremity; imaging characterization of central conducting lymphatic anomalies; the interaction between circadian rhythms of endothelial function; gender related disparity in hospitalization and in-hospital outcome of patients with peripheral arterial disease; vascular malformations in particular syndromes with regional overgrowth; D-dimer levels over time and the risk of recurrent venous thromboembolism; cardiovascular risk profile of individuals.
with pulmonary embolism with and without history of deep vein thrombosis; D-dimer; prevalence of established risk factors for venous thromboembolism according to age; impact of the interventionist on success and outcome of carotid artery stenting in a real life scenario; retrograde recanalization technique after failed antegrade angioplasty in chronic femoral artery occlusions; clinical evaluation of a unique stent with 3D helical geometry - 12-month data from the mimics study; optic coherence tomography of tack optimized balloon angioplasty; ultrasound-accelerated vs standard catheter-directed thrombolysis for treatment of iliofemoral deep vein thrombosis; 6 month outcomes for a below the knee use of a novel balloon catheter first in man clinical study; twelve-month results of the BIOULX P-i first-in-man study comparing a paclitaxel-releasing balloon catheter versus an uncoated catheter in femoropopliteal lesions; vaspin in patients with peripheral arterial disease; injection of vascular resident progenitor cells enhances collateral growth; vascular progenitor cells following massive weight loss induced by bariatric surgery; catestatin for the treatment of myocardial ischemia; transmembraneous activation of the proteasome in vascular resident endothelial progenitor cells reduces collateral growth; secretoneurin gene therapy improves hindlimb and cardiac ischemia in apo E-/- mice without influencing systemic atherosclerosis; management of NOAC bleeding complications - findings from the dresden NOAC registry; peri-interventional management of NOAC patients - results from the Dresden NOAC registry; incidence and causes of heparin-induced skin lesions in postmenopausal women; recurrent cerebral ischaemia in a pregnant woman with PFO and thrombophilia under therapy with LMWH; evaluation of assay performance monitoring new oral anticoagulants; response to antiplatelet therapy and platelet reactivity to thrombin receptor activating peptide-6 in cardiovascular interventions; clinically driven need for secondary interventions after endovascular revascularization of tibial arteries in patients with critical limb ischemia; early recoil after plain balloon angioplasty of tibial arterial obstructions in patients with critical limb ischemia; lymphocyte-to-monocyte ratio; correlation between intima-media thickness (IMT) and flow-mediated dilation (FMD); gene therapy in peripheral arterial disease; fibromuscular dysplasia of the superior mesenteric artery - a rare cause of angina abdominalis; the impact of red cell distribution width on outcome in patients with atherosclerosis; phosphorus-rich diet specifically induces media calcification in the abdominal aorta; wall shear stress in the stented superficial femoral artery in patients with peripheral arterial disease; short term effectiveness of paclitaxel-eluting stents in femoropopliteal lesions; two years follow-up after endovascular repair of a symptomatic aneurysm of the posterior circumflex humeral artery; short- and long-term success of thrombin occluded aneurysm spuria in 632 patients; complications and mortality; standard radial approach for coronary catheterization and access site complications - an observational registry; monocyte vaccination for therapeutic collateralization; a case of successful critical limb ischaemia treatment by pharmacomechanical thrombectomy; soluble P-selectin, D-dimer and high-sensitivity C-reactive protein after acute deep vein thrombosis of the lower limb; D-dimer for risk stratification in hemodynamic stable patients with acute pulmonary embolism; ethiodol in sclerotherapy of venous malformations; nucleoside triphosphates inhibit ADP, collagen, and epinephrine-induced platelet aggregation; essential thrombocythemia and abdominal angina; post-interventional evaluation of stent-perfusion with vascular ultrasonography; late structural damage of the thoracic aorta in patients with giant cell arteritis; pictorial review of fibro-adipose vascular anomaly (FAVA); risk factors for puncture site complications after endovascular procedures in peripheral arterial disease patients; foreign body pulmonary embolism; endovascular therapy for a huge subclavian aneurysm in the elderly; PTA registry for diabetic foot syndrome; stenting of the popliteal artery - a single center experience with 5 year follow up; monolateral intermittent claudication revealing renal graft ischemia; acute wiitis representing as thrombosis of the inferior vena cava and left pelvic veins; statin medication and incidence of recurrent deep venous thrombosis; the complex DVT-case; intraprocedural complications for sclerotherapy in venous malformations; insights to prostanooid therapy in CLI by indocyanine fluorescent angiography; acute effects of dark chocolate on vascular function in patients with peripheral artery disease; contribution of non invasive diagnostic in dialysis associated steal syndrome; microvascular reactivity as function of sex and age; impact of cytochrome 2c9 allelic variants on clopidogrel-mediated platelet inhibition; the efficacy of antiplatelet therapy with aspirin in patients after ischemic stroke; indirect local fibrinolysis as therapy for subacute digital ischemia; blue toe syndrome - a description of positive evolutions through patient adapted therapy; tinnitus and hypercoagulable state; use of radial approach for stenting of left carotid artery stenosis in patients with bovine aortic arch; ambulatory negative pressure wound therapy with a
miniaturized system shortens in-hospital stay; from ollier to maffucci; aortic aneurysm im
giant cell arteritis; functional stenosis of the right iliac artery in a young healthy road cyclist;
accidental injection of epinephrine in the thumb and AGXT2 plays important role in
regulation of urine ADMA levels after acute ADMA loading in mice.

Source: EMBASE


Author(s) Barco S, Nijkeuter M, Middeldorp S

Citation: Seminars in Thrombosis & Hemostasis, July 2013, vol./is. 39/5(549-58), 0094-
6176;1098-9064 (2013 Jul)

Publication Date: July 2013

Abstract: Pregnancy and the postpartum period are associated with an increased risk of
venous thromboembolism (VTE), which complicates 1 to 2 of 1,000 pregnancies and
represents a leading cause of mortality during pregnancy in developed countries. Strong
evidence for the management of pregnancy-related VTE is missing, mostly because
pregnant women have been excluded from all major trials investigating different diagnostic
tools and treatment regimens. Nevertheless, proper evaluation of the involved risk factors is
mandatory to reduce the incidence of pregnancy-related VTE and improve outcomes. Low-
molecular-weight heparins are considered as a first-line option in the management of
pregnancy-related VTE. With regard to future research, there is a need for methodologically
strong studies in pregnant women, especially with respect to risk stratification, optimal
heparin doses, usefulness of anti-FXa levels and their correlation with clinical outcomes,
and correct management of anticoagulation during delivery. Thieme Medical Publishers
333 Seventh Avenue, New York, NY 10001, USA.

Source: Medline

4. Evaluation of redundant studies for the diagnosis of pulmonary embolism

Author(s) Cohen E.

Citation: Clinical Nuclear Medicine, June 2013, vol./is. 38/6(486-487), 0363-9762 (June
2013)

Publication Date: June 2013

Abstract: Objectives: The aim of this study was to determine the frequency and
rationalization for ordering both a ventilation/perfusion lung scan and a CT pulmonary
angiogram for suspected acute pulmonary embolism. Methods: Data was collected from
(227) consecutive patients at Loyola University Medical Center between June 2007 and
November 2012 who underwent both a ventilation/perfusion lung scan (V/Q) and a CT
pulmonary angiogram (CTPA) within a 48 hour time period. Information obtained from the
hospital's HER included patient age, sex, time of study, setting (emergency room or
inpatient), imaging findings, D-dimer, and Wells score. Retrospective analysis was
performed using raw numbers (n) and percentages. Results: Despite a definitive diagnosis
with either V/Q scan or CTPA, 23% of patients (53/227) also underwent the other exam,
which did not change the diagnosis or management. Common justifications for a second
exam included disbelief of the radiologic diagnosis or a misunderstanding of the limitations
of the exam. Technical difficulties in performing CTPA were another frequent indication for
subsequent V/Q scans: 37% (85/227) of CTPAs were non-diagnostic due to an inadequate
bolus, usually performed after normal business hours. An indeterminate or intermediate
probability V/Q resulted in a follow-up CTPA in 11% of patients (24/227). An equivocal
interpretation by the radiologist or nuclear medicine physician led to an alternate exam in
11% of patients (24/227). Only 1% of patients (3/227) had discordant results. Of the total
patients, 35% (79/227) were women ages 45 and younger, four of whom were also
pregnant. An elevated D-dimer was used for risk stratification in 48% of patients (109/227),
but only eight were ultimately diagnosed with a pulmonary embolism. Seventeen patients
with D-dimer levels in the normal range underwent both V/Q and CTPA exams which were
negative for pulmonary embolism. Only five patients had a documented Wells score in the
chart; two of these patients had a calculated risk of 1-3% and underwent both diagnostic
studies which were negative for pulmonary embolism. Conclusion: There is a high
incidence of redundant studies for the diagnosis of pulmonary embolism, resulting in added medical costs and excess radiation exposure. This study has identified several factors contributing to the problem and necessitates better education of referring physicians.

Source: EMBASE

5. Update of D-dimer testing [German] Einsatz der D-Dimerbestimmung - ein Update

Author(s): Rosler A.E., Orth M.

Citation: LaboratoriumsMedizin, March 2012, vol./is. 36/2(65-75), 0342-3026;1439-0477 (01 Mar 2012)

Publication Date: March 2012

Abstract: D-dimer concentrations are elevated in a variety of clinical situations with hypercoagulability, such as venous thromboembolism (VTE), disseminated intravascular coagulation (DIC), ischemic cardiopathy, stroke, acute aortic dissection, malignomas, pregnancy, after surgery, traumas, and burns. D-dimer testing has become an essential tool for the diagnosis of VTE and pulmonary embolism because of its high negative predictive value, especially when used in conjunction with a clinical pretest score. D-dimer testing can be used for the diagnosis of DIC and other thrombotic diseases. It is also helpful for risk stratification in coronary artery disease, in first and recurrent thrombotic events, and for the timing of the duration of oral anticoagulation after a first episode of VTE. The use of D-dimer testing is limited in certain clinical conditions in which elevated D-dimer concentrations render the test unsuitable for the detection of acute thrombotic events. 2012 by Walter de Gruyter Berlin Boston.

Source: EMBASE

6. The application of a clinical risk stratification score may reduce unnecessary investigations for pulmonary embolism in pregnancy

Author(s): O’Connor C., Moriarty J., Walsh J., Murray J., Coulter-Smith S., Boyd W.

Citation: Journal of Maternal-Fetal and Neonatal Medicine, December 2011, vol./is. 24/12(1461-1464), 1476-7058;1476-4954 (December 2011)

Publication Date: December 2011

Abstract: Objective: To examine the use of the modified Wells score in pregnancy as a risk stratification tool in the diagnosis of pulmonary embolism (PE). Methods: All pregnant or post-partum patients who were referred for CT Pulmonary Angiography (CTPA) to evaluate suspected PE over a 5-year period were included in the study. Patient records were used to apply the modified Wells score (MWS) and analyze their risk of PE. Results: A total of 125 women were referred for CTPA over 5 years. A MWS of 6 or greater (“High Risk”) was 100% sensitive and 90% specific with a positive predictive value of 36% for PE on CTPA. No patients with a low MWS (less than 6) had a PE, giving a negative predictive value of 100%. p<0.001. D-dimers, chest X-ray, blood gases and EKG were significantly less effective than the MWS in aiding the diagnosis of PE. Conclusion: Current methods employed for the diagnosis of PE are inadequate. Risk stratification using the MWS may allow safe exclusion of PE before resorting to CTPA. To the best of our knowledge this is the first study to have used the MWS in a pregnant patient group. 2011 Informa UK, Ltd.

Source: EMBASE

Available in fulltext from Journal of Maternal-Fetal & Neonatal Medicine at EBSCOhost

7. Thromboprophylaxis in antenatal women admitted to hospital: A snapshot view

Author(s): Lancastle A., Milling Smith O.

Citation: Journal of Obstetrics and Gynaecology, 2011, vol./is. 31/(31), 0144-3615 (2011)

Publication Date: 2011
Abstract: Background: Pulmonary embolism is the leading direct cause of maternal deaths in the UK. The UK Obstetric Surveillance System Cohort showed in a study of 143 cases that approximately 70% of fatal and nonfatal pulmonary embolisms in antenatal women had identifiable risk factors. The Royal College of Obstetricians and Gynaecologists produced the Greentop guideline "Reducing the risk of thrombosis and embolism during pregnancy and the puerperium" in November 2009. This guideline advises that all women should undergo a documented assessment of risk factors for VTE prophylaxis in early pregnancy or before pregnancy. This assessment should be repeated if the woman is admitted to hospital for any reason or develops other intercurrent problems. Aim: To clarify whether the unit met the recommendations from the RCOG for a new documented antenatal VTE risk assessment for each new admission and whether risk stratification occurred based on known risk factors. To see whether the hospital's population of antenatal patients followed the nationwide trend of increasing age and BMI. Methods: Over a five day period, all antenatal patients that were admitted had their notes reviewed to answer the above aims. The patients were asked to clarify any information not apparent from the notes. Results: 19 antenatal patients were admitted over the 5 day period. Six patients were excluded due to contraindications to LMWH. No new patient had a documented VTE risk assessment completed. 69% met RCOG criteria for consideration of LMWH however no patient was prescribed it 76.9% of patients were either > 35years or obese at the time of booking. Conclusion: The unit are not meeting guidelines set by RCOG with regards to antenatal thromboprophylaxis. A new checklist will be introduced in the department soon and the cycle will be completed to see if this improves outcomes. This study shows increasing incidence of obese and older mothers demonstrated in previous studies.

Source: EMBASE
Available in fulltext from Journal of Obstetrics & Gynaecology at EBSCOhost
Available in fulltext from Journal of Obstetrics & Gynaecology at EBSCOhost

8. Pulmonary embolism in pregnancy: Do the diagnostic algorithms from non-pregnant populations apply?

Author(s) Bastek J.A., Dainty E., Srinivas S.K., Adamczak J.E., Elovitz M.A.

Citation: American Journal of Obstetrics and Gynecology, January 2011, vol./is. 204/1 SUPPL.(S317), 0002-9378 (January 2011)

Publication Date: January 2011

Abstract: OBJECTIVE: Pulmonary Embolism (PE) is the leading cause of pregnancy-related death in the US. In non-pregnant patients, the Wells criteria provide risk stratification for pretest assumption of PE. However, neither this score, nor any other pretest probability algorithm, exist to risk stratify pregnant patients for PE. Therefore, our objective was to determine whether the Wells criteria can accurately predict which pregnant / post-partum patients are most likely to be diagnosed with PE. STUDY DESIGN: We performed a retrospective cohort study of all pregnant / post-partum patients with a CT PE protocol study at a single urban institution (2001-2009). Significant associations between PE and demographic variables of interest, Wells Score, and individual Wells criteria were determined using chi-square and Fisher's exact tests. The relative risk of PE was calculated for each symptomatic complaint. RESULTS: The prevalence of PE was 14% (N=143). There was no association between demographic variables or medical history and PE. All patients with PE had a total Wells score between 2-4. No patient had a total Wells score of 6-7. There was a significant association between total Wells score and PE (p=0.024). When each criterion was assessed individually for association with PE, only Wells Criteria #2 (other diagnoses less likely) was significant (p< 0.001). Patients with chest pain were 3 times more likely (95%CI 1.26-7.33) and patients with shortness of breath were twice as likely (95%CI 0.92-6.20) to be diagnosed with PE than those without these symptoms (Table). CONCLUSIONS: The prevalence of PE in an OB population with clinical suspicion for PE is similar to the prevalence in an at-risk non-pregnant population (9-17%). Since pregnant patients with and without documented PE had similar Wells scores, this algorithm does not appear to be an effective tool to risk stratify pregnant patients. Likewise, clinical suspicion for PE is a poor predictor in pregnancy. Scoring systems pertinent to the pregnant population must be developed to more accurately assess risk of this potentially fatal event.(Table presented).
9. Thromboprophylaxis in pregnancy the practical implications of guidelines

Author(s) Hayes-Ryan D., Byrne B.

Citation: American Journal of Obstetrics and Gynecology, January 2011, vol./is. 204/1 SUPPL.(S315-S316), 0002-9378 (January 2011)

Publication Date: January 2011

Abstract: OBJECTIVE: Pregnancy increases the risk of thromboembolic disease (TED) such that it is reported to complicate one in 500 to 2000 maternities. The case fatality rate for pulmonary embolism (PE) is high, however, making TED the leading direct cause of maternal mortality in the UK and Northern Ireland (1.94 per 100,000 maternities). Recent guidelines have been produced by the RCOG in the UK that have been rapidly adopted by hospital trusts. Pregnant women are assessed for risk of thrombosis (low, intermediate or high) using a combination of multiple risk factors at booking, during hospital admission antenatally and around the time of delivery. Low Molecular Weight Heparin (LMWH) administration is recommended for those deemed to be at intermediate or high risk. The aim of this study was to determine how this risk stratification would apply to our obstetric population and what number of patients would potentially receive LMWH. STUDY DESIGN: The charts of the first 100 women who delivered at the CWIUH in 2010 were reviewed and risk stratification applied at the relevant time points. RESULTS: Out of this population, a total of 51 women i.e. 51% were deemed to be at high or intermediate risk of TED at the some point during pregnancy; 5 at booking, 7 during an antenatal admission, and 39 peri-partum. Of these peri-partum cases, 14 had undergone either elective or emergency caesarean section while the remainder of 25 were deemed at intermediate risk due to having a combination of two or more of the following; parity greater than or equal to 3, smoking, BMI > 30 or age greater than 35 years. CONCLUSIONS: Identification of women at high risk of TED in pregnancy remains paramount and the RCOG guidelines are excellent in this regard. However, the use of multiple risk factors cumulatively (that individually have low impact on thrombotic risk in pregnancy) places many women into an intermediate risk category. The efficacy, safety and cost effectiveness of treating one out of every two women in order to prevent a complication that occurs at most in only one out of every 500 maternities needs greater evaluation.

Source: EMBASE

10. Strategies for diagnosis and prevention of venous thromboembolism during pregnancy

Author(s) Bagaria S.J., Bagaria V.B.

Citation: Journal of pregnancy, 2011, vol./is. 2011/(206858), 2090-2735 (2011)

Publication Date: 2011

Abstract: Pregnancy and the postpartum period have an increased incidence of venous thromboembolism (VTE). The condition is unique during this period for several reasons. Primarily, because there is complexity in diagnosing this condition in view of altered physiology and preexisting edema in pregnancy and also because there are restrictions on the use of certain drugs and a need for vigilant monitoring of anticoagulant activities of drugs during the period. The problem is compounded and assumes the highest order of significance since two lives are involved and all the investigations and management done should also take into account the potential adverse effects on the foetus. In order to prevent the development of VTE during pregnancy, sound clinical evaluation for risk factors, risk stratification, and optimal use of resource both mechanical and pharmacological is necessary. This paper details strategies in preventing development of deep vein thrombosis and treatment of VTEs.

Source: EMBASE

Available in fulltext from Journal of Pregnancy at National Library of Medicine

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Available in fulltext from Journal of Pregnancy at National Library of Medicine
Venous thromboembolism (VTE) affects pregnant women from five to fifty times more frequently than non-pregnant women of similar age. In developed countries, while mortality from other causes has been reduced and hemorrhage is successfully treated or prevented, VTE has emerged as a leading cause of maternal death (1) with an incidence of fatal pulmonary embolism in the UK (where data are the most accurate) of 1.56/100000 maternities (2). Many antenatal VTE events occur in the first trimester and therefore prophylaxis, if given, should begin early in pregnancy; however the highest risk period for VTE and pulmonary embolism in particular is during the post-partum period. Caesarean section (CS) is a significant risk factor but women having vaginal deliveries are also at risk since 55% of the postpartum deaths from VTE in the UK between 1997 and 2005 occurred in women who had a vaginal delivery (3). A cohort study from Rochester, showed that the annualized incidence of VTE was five times higher in postpartum compared to pregnancy period (4). A large population-based case-control study from Netherlands found a 60-fold increase in the risk of VTE in the first three months after delivery compared to non-pregnant controls (5). Although the relative risk of VTE in pregnancy is increased, the absolute risk remains low with an overall incidence of 1-2/10000(2), therefore some form of risk stratification is required to identify the women that will need a pharmacological thromboprophylaxis. Virchow's triad, described almost 150 years ago, consists of venous stasis, changes in the vessel wall and changes in the composition of the blood. Pregnancy affects all three factors. Firstly, progesterone-mediated blood vessels changes cause venous stasis, which starts from the end of the first trimester and is greatest at 36 weeks.

Compression of the pelvic veins adds in late pregnancy affecting the left side in particular (almost 90% of deep venous thrombosis (DVT) is on the left side and 72% of them is ileofemoral and therefore more likely to embolize). Secondly, the endothelium of the pelvic veins may be damaged during vaginal delivery or caesarean section (CS). Thirdly, clotting factors alter in pregnancy. There are increases in factors II, VII, VIII, IX, X, von Willebrand factor and fibrinogen. Plasminogen activator inhibitor type 1 (PAI-1) levels are fivefold increased and levels of PAI-2, produced by the placenta, dramatically increase during the third trimester (6). At the same time a normal pregnancy is accompanied by a decrease in anticoagulant proteins, as free protein S, and fibrinolysis. These changes, which may not completely return to baseline until more than 8 weeks postpartum, begin with conception and result in the hypercoagulable state of pregnancy (7, 8). The diagnosis of VTE is critical because many of the classic symptoms of VTE as tachycardia, tachypnea, dyspnea and leg swelling may also be associated with a normal pregnancy. The two most common initial symptoms, present in more than 80% of women with pregnancy-associated deep vein thrombosis are pain and swelling in an extremity (9). D-dimer testing with currently available assays is not helpful in excluding VTE, as pregnancy is accompanied by an increase in D-dimer levels and a high proportion of false positive results (6). Certainly VTE mainly occurs in pregnant women with other risk factors. The attention must be focused on identifying these women and targeting prophylactic measures. 

At the Sant'Orsola University Hospital in Bologna, Italy, the use of a protocol for thromboembolic prophylaxis is a practice routine approved by all the physicians daily involved in this field, according to the most recent international guidelines (2-10-11). Pregnant women are evaluated by an individual schedule to identify the best prophylaxis depending on the seriousness of the risk (table 1). Recommendation is related to the risk factors: Very high risk: Women with previous venous thromboembolism, LAC, antithrombin deficit, homozygous thrombophilia, asymptomatic double heterozygosis have to be treated with LWME at full dose during pregnancy and to continue the prophylaxis for almost 6 weeks after the delivery. High risk: Women with asymptomatic heterozygous thrombophilia or with single alterations have to be treated with LWME at full dose after the delivery for 6 weeks. Mild risk: Women with bed
rest, BMI>30kg/m2, dead fetus induction, emergency CS, surgical procedures in postpartum or in puerperium and with two or more of the following conditions: Age > 38, number of child-births > 2, lower limbs varicose veins. CS, have to be treated with LWME at low dose for 7 days (unless complications). Low risk: All the other conditions, women don't need any treatment. The use of thromboembolic deterrent stockings (TED) stockings is always recommended when varicose veins, post phlebitic syndrome or relevant chronic venous insufficiency are present. Very High Risk: Previous venous thromboembolism-LAC-antithrombin deficit-homozygous thrombophilia, asymptomatic double heterozygosis) Full dose LMWE, individual treatment started during pregnancy, in close consultation with angiologist. To be continued during the puerperium (6 weeks). High Risk: asymptomatic heterozygous thrombophilia or single alterations Full dose LMWH started after delivery (6-8h), to be continued during the puerperium (6 weeks) Mild Risk: bed rest-BMI>30kg/m2 dead fetus induction-CS in emergency-surgical procedures in postpartum or puerperium two or more of the following conditions: age>38, child-births>2, lower limbs varicose veins, Cesarean Section Low dose LWMH per 7 days (unless complications) started after delivery (6-8h) Low Risk: All other conditions No prophylaxis. The preferred agents for anticoagulation in pregnancy are heparin compounds. Neither heparin nor low-molecular-weight heparin crosses the placenta and both are considered safe in pregnancy. Unique aspects of anticoagulation with heparins in pregnancy include an increase from 40% to 50% in maternal blood volume, an increase in the volume of distribution (6), and, additionally, an increased protein binding of heparin (7); heparins have consequently shorter half-lives and lower peak plasma concentrations, usually necessitating higher doses and more frequent administrations in order to maintain peak concentrations (8). Unfractionated heparin (UFH) used as anticoagulant agent since the 1940’s is available both as intravenous sodium heparin or as subcutaneous calcium heparin. The anticoagulant effects of UFH are unpredictable and require monitoring due to:- Heterogeneity of molecular size, anticoagulant activity, and pharmacokinetic properties.- A high degree of binding to plasma proteins.(12-13-14) IV Sodium Heparin is currently used in women with very high risk for VTE (proximal DVT or PE within 4 weeks of delivery) They can be switched from low molecular weight heparin to therapeutic IV UFH which is then discontinued about 4 h prior to the expected time of delivery. With this approach, the duration of time without therapeutic anti-coagulation can be shortened considerably. Moreover it’s possible to monitor the anticoagulant effect with the aPTT and, if necessary, to reverse the anti-coagulation with protamine sulphate The subcutaneous UFH (calcium hepar-arin) was widely used in the past for the thromboprophylaxis but has to be considered out-dated due to the variable and not predictable anticoagulant effect (there is a risk of major bleeding episodes in 2-10%). Calcium heparin use may be still justified in women with severe renal failure where it does not accumulate. Significant side effects of unfractionated heparin in pregnancy include:- Risk of reduced bone density and osteoporosis (2-36%). Osteoporosis is dose dependent. Mean bone loss is 5% with approximately 1/3 of patients suffering >/= 10% decrease in bone density(15).- Risk of heparin induced thrombocytopenia (HIT) in 2 variants:- Non immune form within first few days of therapy, that resolves by 5 days.- Immune form (IGG) seen in 3% within 5-14 days. Platelets should be checked on day 5 and then periodically for the first two weeks of therapy(14). Low molecular weight heparin (LMWH) are the agents of choice for antenatal prophylaxis (10).

**Source:** EMBASE

Available in fulltext from Regional Anesthesia and Pain Medicine at the ULHT Library and Knowledge Services’ eJournal collection


**Author(s)** Carman T.L., Gegaj F.

**Citation:** Current Treatment Options in Cardiovascular Medicine, April 2010, vol./is. 12/2(168-184), 1092-8464 (April 2010)

**Publication Date:** April 2010

**Abstract:** The morbidity and mortality of venous thromboembolism remain underrecognized and underappreciated. Suspected pulmonary embolism should be risk stratified using a validated clinical risk prediction tool; intermediate to high clinical suspicion requires objective diagnostic testing to confirm or refute the diagnosis. Therapy with unfractionated heparin, low molecular weight heparin, or fondaparinux should be initiated while diagnostic testing is pursued. Conversion to vitamin K antagonists requires a minimum of 5 days’ overlap between the parenteral agent and the vitamin K antagonist.
Anticoagulation should be continued for a minimum of 3 to 6 months. Longer or even indefinite therapy may be required with a persistent hypercoagulable state. In patients with cancer, low molecular weight heparin monotherapy for the initial 3 to 6 months is preferred. In stable patients with normal biomarkers and a normal echocardiogram, accelerated discharge and outpatient therapy may be considered. In patients with hemodynamic instability, systemic thrombolytic therapy, catheter-directed therapy, or surgical embolectomy may be considered. Cancer screening and/or thrombophilia testing should be pursued only if the findings will directly affect patient therapy or long-term care. Springer Science+Business Media, LLC 2010.

Source: EMBASE

13. Pulmonary embolism in pregnancy

Author(s) Bourjeily G., Paidas M., Khalil H., Rosene-Montella K., Rodger M.

Citation: The Lancet, 2010, vol./is. 375/9713(500-512), 0140-6736 (20100206/12)

Publication Date: 2010

Abstract: Pulmonary embolism (PE) is the leading cause of maternal mortality in the developed world. Mortality from PE in pregnancy might be related to challenges in targeting the right population for prevention, ensuring that diagnosis is suspected and adequately investigated, and initiating timely and best possible treatment of this disease. Pregnancy is an example of Virchow's triad: hypercoagulability, venous stasis, and vascular damage; together these factors lead to an increased incidence of venous thromboembolism. This disorder is often suspected in pregnant women because some of the physiological changes of pregnancy mimic its signs and symptoms. Despite concerns for fetal teratogenicity and oncogenicity associated with diagnostic testing, and potential adverse effects of pharmacological treatment, an accurate diagnosis of PE and a timely therapeutic intervention are crucial. Appropriate prophylaxis should be weighed against the risk of complications and offered according to risk stratification. 2010 Elsevier Ltd. All rights reserved.

Source: EMBASE

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Available in print at Louth County Hospital Medical Library

14. Biomarkers for the diagnosis of venous thromboembolism

Author(s) Perrier A.

Citation: Pathophysiology of Haemostasis and Thrombosis, 2010, vol./is. 37/(P20), 1424-8832 (2010)

Publication Date: 2010

Abstract: Among the various biomarkers that have been evaluated in the context of venous thromboembolism (VTE), only D-dimer has proved useful for diagnosis, mainly for ruling out VTE when negative. Natriuretic peptides (BNP or NTproBNP) and troponin are restricted to risk stratification in patients with diagnosed pulmonary embolism (PE). Nevertheless, there are numerous D-dimer assays, among which only a fraction have been properly validated by prospective outcome studies or by measurement in plasma samples from outcome studies. ELISA and ELISA-derived assays have the highest sensitivity (above 95%) and can be used to rule out VTE in patients with a low or intermediate clinical
probability of DVT or PE, or, when using twolevel prediction rules for clinical assessment, in patients with an "unlikely" ruling for DVT or PE. In contrast, latex-derived assays have a lower sensitivity (around 90 to 95%) and must be restricted to patients with a low clinical probability or a DVT or PE "unlikely" ruling. No D-dimer assay is sensitive enough to allow safely ruling out VTE in patients with a high clinical probability, a population in whom D-dimer results are very rarely negative. In outpatients, D-dimer measurement combined with clinical assessment should be the first step in a diagnostic algorithm for DVT or PE as it allows ruling out VTE in around 30% of patients with a clinical suspicion of VTE. In other populations such as inpatients, elderly patients, patients with cancer, or pregnant women, its use should be considered on a case-by-case basis due to a significantly lower diagnostic yield. Efforts are under way to simplify the decision rules for assessing clinical probability and establishing variable cut-offs for D-dimer to improve their exclusion rate in the elderly.

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15. Application of a clinical risk stratification score in pregnancy and the puerperium - Can unnecessary investigations for pulmonary embolism be avoided?

Author(s) O'Sullivan C., Moriarty J., Walsh J., Coulter-Smith S., Boyd W.

Citation: American Journal of Obstetrics and Gynecology, December 2009, vol./is. 201/6 SUPPL. 1(S68), 0002-9378 (December 2009)

Publication Date: December 2009

Abstract: OBJECTIVE: Pulmonary Embolism remains the number one cause of direct maternal death in the developed world with an almost 10 fold increased incidence in pregnancy versus the non-pregnant population. The diagnostic imaging tool of choice, CT Pulmonary Angiography, is costly and hazardous due to radiation and iodinated contrast administration. Our aim was to retrospectively evaluate the efficacy of the Modified Wells score as a risk stratification tool in the antenatal and post natal setting. STUDY DESIGN: This study was carried out in a large tertiary referral centre in Ireland. All pregnant or post-partum patients who were referred for CT Pulmonary Angiography (CTPA) over a 5 year period were included in the study cohort. Developed by Wells et al in 2000, the Modified Wells Score (MWS) combines clinical history and signs to obtain a probability score (6 or more =high risk). Its use in adult medicine is well validated. Patients records were used to retrospectively apply a MWS and hypothesis analysis was performed using the Chi squared test. RESULTS: A total of 125 women were referred for CTPA over a 5 year time period (97 pregnant, 28 post-partum). 5 positive for PE on CTPA. MWS of 6 or greater ("High Risk") = 100% sensitive, 90% specific, positive predictive value of 36% negative predictive value of 100% for the diagnosis of PE. P = <0.001. D-dimers, chest X-ray, blood gases and ECG data was also analysed. The sensitivity and specificity of these commonly used tests were found to be significantly lower than the MWS for the diagnosis of PE. CONCLUSION: The diagnosis of PE in pregnancy and the puerperium represents a significant diagnostic challenge. Risk stratification using the Modified Wells Score may allow safe and timely exclusion of PE, as it has been shown in this study to have a negative predictive value of 100%. This may reduce the use of expensive and potentially toxic diagnostic tools, such as CT Pulmonary Angiography, in a large majority of cases. To the best of our knowledge this is the first study to have used the modified wells score in the maternity setting.

Source: EMBASE
New directions in the diagnosis and treatment of pulmonary embolism in pregnancy

BA Cutts, D Dasgupta, BJ Hunt - American journal of obstetrics and ..., 2013 - Elsevier
... of Nuclear Medicine is that V/Q SPECT become the gold standard for the diagnosis of PE in all patients (pregnant and nonpregnant ... FIGURE 2. V/Q spect for the detection of pulmonary embolism V/Q SPECT thermal imaging coronal posterior sections in a female ... PE in pregnancy. ...

Diagnostic imaging and risk stratification of patients with acute pulmonary embolism

SK Burns, LB Haramati - Cardiology in review, 2012 - journals.lww.com
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Recommendations for the diagnosis and treatment of deep venous thrombosis and pulmonary embolism in pregnancy and the postpartum period

C McLintock, T Brighton, S Chunilal... - Australian and New ..., 2012 - Wiley Online Library
... 34 A further study reported antenatal bleeding in 6% of women receiving LMWH, with no ... 4. 7 Chan WS , LeeA, SpencerFAet al.D-dimer testing in pregnant patients: towards ... 15 Revel MP, CohenS, SanchezOet al.Pulmonary embolism during pregnancy: diagnosis with lung ...

Strategies for diagnosis and prevention of venous thromboembolism during pregnancy

... system activation and thrombin potential in healthy pregnant women with ... at Publisher · View at Google Scholar; M. Knight, “Antenatal pulmonary embolism: risk factors ... J. Hirsh, “Venous thromboembolism, thrombophilia, antithrombotic therapy, and pregnancy: American college ... 

D-dimers as a screening test for venous thromboembolism in pregnancy: Is it of any use?

... It is also well established that clinical diagnosis in the antenatal period is notoriously difficult, as many of the signs and symptoms associated with pulmonary embolism (PE) are similar to the physiological changes of pregnancy (RCOG 2007). In non-pregnant women, D-dimers ...

D-dimers and efficacy of clinical risk estimation algorithms: sensitivity in evaluation of acute pulmonary embolism

RT Gupta, RK Kakarla… - American Journal of ..., 2009 - Am Roentgen Ray Soc
... Acute pulmonary embolism (PE) is a serious condition that affects approximately 69 persons per 100,000 ... were excluded from the study if they had renal insufficiency, were pregnant, or chose not ... Many of the decisions regarding pulmonary CTA in the diagnosis of acute PE are ...

A risk score for the management of pregnant women with increased risk of venous thromboembolism: a multicentre prospective study

Y Dargaud, L Rugeri, MC Vergnes… - British journal of ..., 2009 - Wiley Online Library
... Screening for PS deficiency was performed in women with no oral contraceptive use and before falling pregnant or delayed until 12 weeks postpartum. ... According to the VTE risk level evaluated with this score in early pregnancy, an antenatal thromboprophylaxis by LMWH ...

Pulmonary embolism, part I: Epidemiology, risk factors and risk stratification,
pathophysiology, clinical presentation, diagnosis and nonthrombotic pulmonary ... 

... history of thromboembolic disease; or in women who experienced thrombosis or PE during pregnancy and plan to become pregnant again. ... To explain, a subanalysis of the International Cooperative Pulmonary Embolism Registry (ICOPER) data showed the presence of ... 

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