Regular Article

Use of the Delphi method to facilitate antithrombotics prescription during pregnancy

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A B S T R A C T

Introduction: Management of pregnant women at risk for venous thromboembolism (VTE) remains complex. Guidelines do not definitively fix optimal strategies due to limited trial data. Our objective was to build an easy-to-use tool allowing individualised, risk-adapted prophylaxis.
Materials and Methods: A Delphi exercise was conducted to collect 19 French experts' opinions on pregnancy-related VTE.
Results: Experts with an active interest in clinical research and care of VTE and placental vascular complications were selected. The risk score was classified by an anonymous computer vote. A scoring system for VTE risk in pregnant women was developed, each score being associated with a specific treatment: graduated elastic compression stockings, aspirin, prophylactic Low Molecular Weight Heparin (LMWH: variable durations), or adjusted-dose of LMWH through pregnancy and postpartum.
Conclusions: Our simple consensual scoring system offers an individual estimation of thrombosis risk during pregnancy together with its related therapeutic strategy, in accordance with most of the new international recommendations. The accuracy of our individual risk score-based therapeutic guidance is currently being prospectively evaluated in a multicenter trial (Clinicaltrials.gov registry no: NCT00745212).

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Introduction

Pregnancy is well-known to be associated with hypercoagulability. In consequence, the risk of venous thromboembolism (VTE) has been evaluated to be six to ten times higher in pregnant women. Various recommendations for VTE, thrombophilia, antithrombotic therapy and pregnancy are available to practitioners via the French national recommendations in 2003 [1] to the consensus conference of the American College of Chest Physicians (ACCP) in 2004 [2], which was updated in 2008 [3]. Two main difficulties are currently encountered when applying these recommendations. First, the treatment must be adapted to patients with several simultaneous risk factors which have not been definitively associated with VTE. Currently, the few existing randomized studies on the treatment of pregnant women at risk for VTE do not give solid support for universal recommendations and the optimal care strategy for complex clinical cases remains unclear. Second, their complexity may dissuade practitioners and gynaecologists not currently involved in the VTE field from simply using them at all. Faced with complex situations, the ground health care agent often has to manage the gap between reality and recommendations. Recommendations may be easy to understand by those who currently treat VTE, but are difficult to apply by inexperienced practitioners and in daily practice. Nevertheless, as women at risk are not always clearly identified and monitored by specialists, gynaecologists are sometimes the first to take care of these women. This probably explains the tremendous disparity in the care of women at risk for VTE or placental vascular pathologies between medical teams, and even sometimes within the same team. Even in a simple situation, only 6.5% of practitioners follow current recommendations [4]. Thus, there is a real need for an easy-to-use risk score supporting which anti-thrombotic prophylaxis treatment to recommend at the beginning of pregnancy.

In the absence of hard evidence supporting clear treatment decisions, multiple expert opinions can be used to make therapeutic recommendations. Expert consensus concerning treatment options is thus a key element in creating those recommendations. Furthermore, this consensus must be drawn from multidisciplinary expertises, thus

avoiding inappropriate conclusions due to a preponderance of a single medical speciality in treatment decisions. Consensus from a wide range of experts is also more likely to find acceptance from the general medical community and ground practitioners. With these constraints in mind, it is logical to propose the Delphi method, recognized as the reference technique for building consensus among several experts [5–9], as a tool for building a risk assessment score supporting anti-thrombotic prophylaxis treatment options for pregnant women. Delphi is a well-recognized group process in the Social Sciences, and was considered best suited, among a number of potentially useful techniques, to establish consensus for diagnostic criteria [5]. The Delphi method is designed to synthesize information. It allows the inclusion of a large number of individuals from diverse locations and expertises and avoids the situation where a specific expert might dominate the process [10,11]. It has been frequently used in health care and permits a wider range of study types to be considered than is usually seen in statistical reviews[12]. Moreover, it gives a major role to the qualitative assessment of evidence.

The primary objective of this study is therefore to describe and use a Delphi procedure to construct a thrombotic risk score for pregnant women. Secondarily, this score and further expert consensus will be used to support referral to the various treatment options available. Score construction and treatment referrals will be prospectively validated in a later study.

Materials and Methods

To design the score and the corresponding therapeutic strategy, we conducted a Delphi exercise in 2006 and 2007 to collect expert opinions in the field of VTE during pregnancy [5–7,13,14]. The Delphi method was first applied to simple therapeutic cases (pregnant women with only one risk factor) using seven steps.

A Perifoetology Club meeting (a group of French national experts in foetal medicine) was used as an opportunity to contact, inform and select numerous experts (step 1). The group contained a multidisciplinary panel of anaesthesiologists, obstetricians, pharmacologists, haematologists, consultant physicians, angiologists and vascular medicine experts. We selected 20 lead practitioners on the basis of their active interest in clinical research and care of VTE and placental vascular complications, 19 of whom agreed to participate in this risk assessment (Table 1).

Table 1
Experts agreed to participate in this risk assessment.

Name	Location	Speciality
Pr D. BENHAMOU	Paris le Kremlin-Bicêtre	Anesthesiology
Dr C. BIRON-ANDREANI	Montpellier	Haematology
Pr JY.BORG	Rouen	Haematology
Dr C.CHAULEUR	Saint-Etienne	Obstetrics and Gynaecology
Pr J. CONARD	Paris	Haematology
Pr L. DROUET	Lariboisière, Paris	Haematology
Dr E. DEMAISTRE	Dijon	Haematology
Dr P. EDELMAN	Paris	Obstetrics and Gynaecology
Pr J EMMERICH	Paris	Vascular medecine
Pr P. GAUCHERAND	Lyon	Obstetrics and Gynaecology
Pr J.C. GRIS	Nîmes	Haematology
Pr Y GRUEL	Tours	Haematology
Pr B JUDE	Lille	Haematology
Pr J.L. LORENZINI	Dijon	Haematology
Pr P MISMETTI	Saint-Etienne	Pharmacology and Vascular Medicine
Dr E. PASQUIER	Brest	Vascular Medicine
Dr G. PERNOD	Grenoble	Vascular Medicine
Dr B TARDY	Saint-Etienne	Haematology
Dr N. TRILLOT	Lille	Haematology

In order to construct a highly representative list of VTE risk factors and the effects of their associated prophylaxis regimes, we performed a literature review (step 2). The selected studies were performed between 1980 and 2006, and found in the MEDLINE® and EMBASE® electronic databases and the Cochrane Library, using the following search strategies: (1) deep-vein thrombosis or thromboembolism or pulmonary embolism or thrombophilia and pregnancy, (2) deep-vein thrombosis and pregnancy and prophylaxis, (3) deep-vein thrombosis and epidemiology, (4) deep-vein thrombosis or thromboembolism or pulmonary embolism and guidelines, and (5) thrombophilia and pre-eclampsia or foetal loss or placental abruption or intra-uterine growth restriction. The identified risk factors were thereafter sent via email to the aforementioned experts [5–7,13].

After presenting a detailed description of the aims and procedure of the exercise, we asked the experts to evaluate the intensity of the VTE risk associated with each of the identified factors (step 3). To accomplish this, we provided a Visual Analogue Scale ranging from zero to ten (from low to high risk).

After having completed this first round, the 19 experts were invited to the second round of risk assessment (step 4). The risk intensity appreciation of each risk factor was asked to be reclassified according to the same method, but after gathering all previous first answers from the experts [5–7,13]. From these data, the median risk value (MRV) associated with each risk factor was calculated from the 19 experts' opinions. The scale was then divided into 5 classes as follows: $0 \leq MRV \leq 2$; $2 < MRV \leq 4$; $4 < MRV \leq 6$; $6 < MRV \leq 8$; $8 < MRV \leq 10$.

For a given pregnant woman bearing only the risk factor under focus, each expert then had to choose an antithrombotic treatment (step 5). For this, they evaluated all putative therapeutic strategies which duration could be modulated: (1) no treatment, (2) prophylactic LMWH six weeks postpartum, (3) prophylactic LMWH third trimester and postpartum, (4) prophylactic LMWH second and third trimester and postpartum, (5) prophylactic LMWH through pregnancy and postpartum, (6) LMWH adjusted-dose through pregnancy and postpartum, (7) Low-dose aspirinthat could also be associated with one of the other treatment.

Risk factors sharing the same MRV class and for which at least 60% of the 19 experts proposed the same treatment option were regrouped into *risk categories* (step 6) [5–7,13]. When such a therapeutic consensus could not be achieved, the given risk factor was discussed a third time (step 7) during a scheduled final meeting to propose the final risk factors taken into account for the risk factor score. Individual votes were requested and followed by a discussion and a new vote in the case of insufficient concordance (<60%) until the collection of at least 60% identical choices.

When a consensus was reached for individual risk factors and their corresponding treatment proposals, we moved to a methodology describing the VTE risk in women cumulating various risk factors, and proposed a given treatment. To accomplish this, we first had the experts study complex clinical cases. They were required to vote on a therapeutic strategy (using an anonymous computerized system during the final meeting) for 60 cases where two, three or four risk factors had been associated. If at least 60% of experts gave the same treatment (type, dose, beginning and end of treatment...), it was retained for this case. Otherwise, the clinical case was discussed and resubmitted to a vote until a consensus was obtained [5–7,13].

Treatments were thus defined for 32 isolated risk factors (steps 1 to 7) and 60 risk factor combinations, giving a data base of 92 elements. These were further classified according to identical proposed treatments and used to validate cases for the accuracy of the final risk score.

For practical reasons, the main clinical and biological risk components were classified into 4 different categories: (1) VTE antecedents, (2) placental vascular complication antecedents, (3) known thrombophilia, and (4) other risk components. Each risk component category was then assigned a preliminary weight and tested on the validating