AOGS
ACTA Obstetricia et Gynecologica Scandinavica

AOGS MAIN RESEARCH ARTICLE

Venous thromboembolism in pregnancy and the puerperal period: a study of 1210 events

RIE ADSER VIRKUS[1], ELLEN C.L. LØKKEGAARD[1], ØJVIND LIDEGAARD[2], JENS LANGHOFF-ROOS[3], LARS BJERREGAARD[4], CHARLOTTE W. SKOVLUND[2] & THOMAS BERGHOLT[1]

[1]Department of Obstetrics and Gynecology, Hillerød Hospital, University of Copenhagen, Hillerød, [2]Gynecological Clinic, Rigshospitalet, University of Copenhagen, Copenhagen, [3]Department of Obstetrics, Rigshospitalet, University of Copenhagen, Copenhagen, and [4]Department of Anesthesiology, Hillerød Hospital, University of Copenhagen, Hillerød, Denmark

Key words
Incidence rate, location, pregnancy, puerperal period, validation, venous thromboembolism

Correspondence
Rie Adser Virkus, Department of Obstetrics and Gynecology, Hillerød Hospital, Dyrehavevej 29, 3400 Hillerød, Denmark.
E-mail: rav@noh.regionh.dk

Conflict of interest
R.A.V., E.C.L., J.L.R., L.B., C.W.S. and T.B. declare that they have received no support from any organization for the submitted work. Ø.L. has within the last three years received honoraria for lectures on pharmacoepidemiological issues, and was an expert witness for a plaintiff in a legal US case in 2011. The study has not been funded by industry support.

Please cite this article as: Virkus RA, Løkkegaard ECL, Lidegaard Ø, Langhoff-Roos J, Bjerregaard L, Skovlund CW, Bergholt T. Venous thromboembolism in pregnancy and the puerperal period: a study of 1210 events. Acta Obstet Gynecol Scand 2013; 92:1135–1142.

Received: 1 November 2012
Accepted: 15 July 2013

DOI: 10.1111/aogs.12223

Abstract

Objective. The aim of this study was to describe venous thromboembolism (VTE) in pregnancy and the puerperal period, and to validate diagnoses of VTE. *Design.* Historical cohort study. *Population.* All pregnancies in Denmark from 1995 to 2009. *Methods.* VTE diagnoses were retrieved from national registries. *Main outcome measures.* Positive predictive value of a VTE diagnoses diagnosed during pregnancy or the puerperal period. Location of VTE. Incidence rate of confirmed, validated diagnoses of VTE and on all retrieved diagnoses of VTE. *Results.* In 1 297 037 pregnancies, 1436 women had a first-ever VTE diagnosis. Hospital records were retrieved for 1210 women (84.3%). Almost all women had relevant clinical symptoms and in 796 (65.8%), the diagnosis were confirmed by a positive diagnostic test or by instituted anticoagulation treatment. In all, 72.6, 53.7, 58.5 and 79.1% of the diagnoses were confirmed in the first, second, third trimester and the puerperal period, respectively. The 796 cases of VTE included 624 women with deep venous thrombosis only and 133 with pulmonary embolisms. Deep venous thrombosis was located in the left lower limb in 83.8% in pregnancy, compared with 67.9% in the puerperal period. *Conclusions.* The vast majority of women with a registered diagnosis of VTE had relevant symptoms. Diagnoses of VTE were confirmed in the medical records in two of three women. VTE diagnoses were most often confirmed when made in the first trimester and in the puerperal period. Left-sided deep venous thrombosis was the predominant type of VTE in pregnancy and the puerperal period.

Abbreviations: CI, confidence intervals; ICD, International Classification of Diseases; VTE, venous thromboembolism.

Introduction

Venous thromboembolism (VTE) is a serious complication in pregnancy and in the puerperal period. The risk increases throughout pregnancy with an average incidence rate of 1 per 1000 pregnancies (1,2). Discharge diagnoses

Key Message

Non-validated discharge diagnoses of venous thromboembolism in pregnant or puerperal women should be considered with care, especially in analytical epidemiology, but may provide realistic incidence estimates.

from national registries are a valuable source for epidemiological research concerning rare diseases such as VTE. Register-based cohort studies can be designed and performed at relatively low cost and, as data are prospectively collected, they are for most scientific purposes not influenced by recall or selection bias. However, the few studies that did investigate the validity of VTE diagnoses in pregnancy and the puerperal period have concluded that it is important to validate diagnoses when conducting such epidemiological analyses (3,4). The aim of this study was to describe and validate VTE diagnoses in pregnancy and the puerperal period.

Material and methods

All Danish women 15–49 years of age in the period 1 January 1995 to 31 December 2009 were identified from the Central Person Registry. A woman was included at the age of 15 years, and she was excluded after her 50th birthday. Emigrants were excluded from the date of emigration.

The Danish Central Person Registry includes a 10-digit personal identification number for all citizens, given at birth or immigration, and has daily updated information on present address and vital status. The personal identification number is a unique personal identifier used in all public registries, allowing reliable linkage between different registries.

The National Registry of Patients was established in 1977 and collects discharge diagnoses classified according to World Health Organization's International Classification of Diseases (ICD) version 8 until the end of 1993 and version 10 from 1994. From this database all pregnancy periods occurring during the study period were identified, as were the outcomes of pregnancy (miscarriages, abortions, ectopic pregnancies, hydatidiform mole or delivery).

The ICD-10 codes used to identify VTE events included VTE codes for non-pregnant women as well as codes specifically for use in pregnancy or the puerperal period (Table 1). A pregnancy period was defined as starting on the day of conception (14 days after the first day of last period) until 12 weeks after delivery. If the pregnancy was not completed (miscarriages, abortions, ectopic pregnancies or hydatidiform mole), the period ended four weeks after termination of the pregnancy. The date of a VTE event was defined as the admission date.

To ensure that only first-ever VTEs were included, women with a previous VTE were identified and excluded, using ICD-8 codes 450, 451.00, 451.08, 451.99, 452, 453.02, 631, 634.99, 671.01, 671.01, 671.08, 671.09 and 673, and from 1994 till inclusion in the study by the ICD-10 codes listed in Table 1. Diagnoses of amniotic or air embolism were included to see whether they masked venous thromboemblic events. If not, these women were excluded from the cohort.

Two of the authors (R.A.V. and L.B.) retrieved all medical records, which were reviewed by R.A.V. The following information was recorded from the medical records: initial clinical symptoms of deep venous thrombosis, location, respiratory symptoms, examinations done to verify the VTE, whether anticoagulation in therapeutic dosages was initiated, and whether a woman had received prophylactic anticoagulation treatment prior to the diagnosis.

A VTE diagnosis was confirmed if at least one of the following diagnostic tests was positive; ultrasonography, venography, ventilation-perfusion lung scan, computertomography or magnetic resonance scan. We decided that diagnosis of VTE was also confirmed if a woman was treated with anticoagulation therapy for the rest of the pregnancy and the puerperal period, or for at least three months in therapeutic doses. The exact date of the confirmatory diagnostic test or the beginning of treatment was noted as a date of diagnosis. To evaluate the interobserver variability of VTE diagnosis, 313 medical records were additionally reviewed by author L.B., who was blinded to the conclusions of R.A.V. In the case of differing conclusions of R.A.V. and L.B., two specialists in obstetrics and gynecology (E.L. and T.B.) additionally reviewed the medical records and their conclusions were based on consensus. Finally, E.L. and T.B. reviewed the medical records with doubtful confirmation after primary chart evaluation and the final conclusions were based on their consensus.

The diagnostic validity was calculated as the number of patients with confirmed VTE diagnoses after reviewing the medical records divided by the total number of patients with a discharge diagnosis of VTE. The validity was calculated for all pregnancy diagnoses of VTE and for all VTE codes for non-pregnant women and, in addition, according to the time of occurrence, i.e. first, second and third trimester or during the puerperal period. Incidence rates per 10 000 exposure-years according to gestational age and time after delivery were calculated for both all retrieved diagnoses (using the admission date) and for the confirmed diagnoses (using the date for diagnosis). All proportions were calculated with 95% confidence intervals. We analyzed data using PREDICTIVE ANALYTIC SOFTWARE STATISTICS 18 (PASW).

According to Danish legislation, ethical approval was not required. The Danish Data Protection Agency approved the study (J.no. 2009-41-3483).

Results

In 1 320 353 pregnancies from 1995 to 2009, leaving 1 297 037 after exclusions, we identified 1452 first-ever

Table 1. Validity of venous thromboembolism (VTE) discharge diagnoses according to time in pregnancy and specific International Classification of Diseases (ICD)-10 codes.

		Confirmed		
	n	*n*	%	95% CI
Overall validity	1210	796	65.8	63.1–68.4
Validity of VTE diagnosed in the first trimester	124	90	72.6	64.2–79.9
Validity of VTE diagnosed in the second trimester	134	72	53.7	45.3–62.0
Validity of VTE diagnosed in the third trimester	482	283	58.7	54.3–63.1
Validity of VTE diagnosed in the puerperal period	402	318	79.1	74.9–82.9
Excluded[a]	68	33	48.5	36.8–60.3
Non-pregnancy VTE codes	702	469	66.8	63.3–70.2
DI26 Pulmonary embolism	191	115	60.2	53.1–67.0
I26.0 Pulmonary embolism with cor pulmonal	0			
I26.9 Pulmonary embolism without cor pulmonal	191	106	55.5	53.1–67.0
DI676 Cerebral venous thrombosis	3	3	100	
DI80 Deep venous thrombosis	465	326	70.1	65.8–74.1
I80.1 Thrombophlebitis of femoral vein	35	31	88.6	74.7–96.3
I80.2 Thrombophlebitis of other deep vessels of lower extremities	70	56	80.0	69.4–88.1
I80.3 Thrombophlebitis of lower extremities, unspecified	360	239	66.4	61.4–71.1
DI81 Portal vein thrombosis	4	2	50.0	9.4–90.6
DI82 Embolism and thrombosis of other veins	39	23	59.0	43.1–73.5
I82.2 Embolism and thrombosis of vena cava	3	3	100	
I82.3 Embolism and thrombosis of renal vein	0			
I82.8 Embolism and thrombosis of other specified veins	3	1	33.3	1.7–87.0
I82.9 Embolism and thrombosis of unspecified vein	33	19	57.6	40.4–73.4
Pregnancy or puerperal VTE codes	508	327	64.4	60.1–68.4
DO08.2 Embolism following abortion, and ectopic and mole	0			
DO08.7 Venous complications following abortion, ectopic or mole	1	1	100	
DO22.3 Deep phlebothrombosis in pregnancy	299	222	74.2	69.0–79.0
DO22.5 Cerebral venous thrombosis in pregnancy	4	1	25	1.2–75.8
DO22.8 Other venous complications in pregnancy	18	2	12.5	2.2–35.5
DO22.9 Venous complication in pregnancy, unspecified	24	2	8.3	1.4–24.9
DO87 Venous complications in the puerperal period	127	80	63.0	0.54–71.3
O87.1 Deep phlebothrombosis in the puerperal period	106	72	67.9	58.6–76.3
O87.3 Cerebral venous thrombosis in the puerperal period	8	5	62.5	27.8–89.4
O87.8 Other venous complications in the puerperal period	5	2	40.0	7.3–81.8
O87.9 Venous complication in the puerperal period, unspecified	8	1	12.5	0.6–48.0
DO88.2 Obstetric blood-clot embolism	35	19	54.3	43.9–79.4

[a]Pregnancy started before 1995 or ended in 2010 or age not between 15 or 50 years.

VTE events in pregnancy or the puerperal period. Among these 1452 events, 16 were diagnosed with amnion or air embolism, and were excluded, as chart review confirmed these diagnoses. From the remaining 1436 women with VTE, 1210 (84.3%) medical records were retrievable. Of the 226 non-retrievable medical records, 127 admissions were more than 10 years old and therefore had been allowed to be shredded, and in 57 cases the departments were closed. For different reasons the remaining 42 medical records could not be retrieved in the departments.

Of the 313 doubly reviewed medical records there was disagreement in three cases, which were assessed by the two specialists. Of the 1210 retrieved medical records, 796 (65.8%) were confirmed in the records (Table 1).

The VTE diagnoses were divided into non-pregnancy ICD-10 codes (58.1%) and pregnancy-related ICD-10 codes (41.9%). The diagnoses were confirmed in 66.8 and 64.4%, respectively. The validity of the specific ICD-10 codes is described in Table 1. During pregnancy, 51.4% were diagnosed with pregnancy ICD-O codes, whereas 26.8% were diagnosed with ICD-O codes in the puerperal period. The remaining were diagnosed by non-pregnancy ICD-I codes. The validity of the ICD-I codes was 53.3% in pregnancy and 65.9% in the puerperal period, and the validity of the ICD-O codes was 47.4 and 73.6%, respectively. The anatomical distribution of confirmed cases and additional information of the non-confirmed cases of VTE is presented in Figure 1.

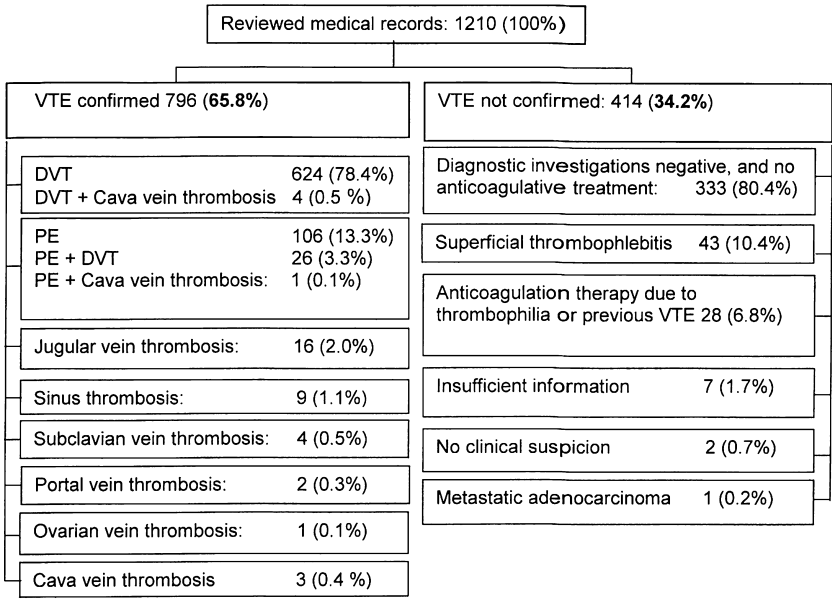

Figure 1. Distribution of confirmed and unconfirmed venous thromboembolism.

Among the 1210 retrieved medical records, 64.8% of the diagnoses occurred during pregnancy and 35.2% in the puerperal period, according to the admission date. In the 796 women with confirmed diagnoses, information on the date of diagnosis was retrievable in 739 (92.8%). We calculated that 78.8% (582/739) of the women had dates of admission according to the National Registry of Patients in an interval of seven days from the date of validated diagnosis of VTE. If this date for diagnosis of VTE was used instead of admission date, 58.3% were diagnosed during pregnancy and 41.7% in the puerperal period. A majority of confirmed deep venous thrombosis events were diagnosed during pregnancy (60.9%), whereas confirmation of pulmonary embolism was equally distributed during pregnancy and the puerperal period (Table 2).

Of the 654 confirmed events of deep vein thrombosis, 586 (89.6%) were diagnosed by ultrasonography, magnetic resonance imaging or venography. Of 133 pulmonary embolisms, 109 (82.0%) were confirmed by ventilation-perfusion lung scan or computer-tomography (Table 2). Of the confirmed deep venous thromboses, the proportion with a positive diagnostic test rose from 87.7% in pregnancy to 97.2% in the puerperal period (Table 3). In total, 8.4% (55/654) women were diagnosed with deep venous thromboses based on clinical judgment and relevant anticoagulative therapy without a positive diagnostic test result. During pregnancy, 79.4% of the confirmed deep venous thromboses were located in the left lower limb compared with 67.7% in the puerperal period (Table 3).

Table 2. Time of deep venous thrombosis (DVT) or pulmonary embolism (PE) in the confirmed events.

	DVT		PE	
	n	%	*n*	%
Time of diagnoses				
Pregnancy	398	60.9	62	46.6
Puerperal period	217	33.2	60	45.1
Not applicable	39	6.0	11	8.3
Total	654	100.0	133	100.0
Result of diagnostic tests				
Positive[a]	586	89.6[b]	109	82.0
Negative[c]	15	2.3	3	2.3
Inconclusive[c]	12	1.8	10	7.5
Missing description of diagnostic test[c]	41	6.3	11	8.3
Total	654	100.0	133	100.0

[a]Positive diagnostic test (phlebography, ultrasonography, venography, ventilation-perfusion lung-scan, computer tomography or magnetic resonance scan).
[b]Phlebography was used for 32 patients.
[c]Confirmation of these cases was a combination of a clinically relevant case and anticoagulative treatment in therapeutic doses.

From the medical records, the time of first clinical symptoms of VTE was described in 525 of 654 women with deep venous thrombosis and 98 of 133 of the women with pulmonary embolism. The mean number of

Table 3. Diagnostic test results and left/right distribution of the confirmed deep venous thrombosis.

	Pregnancy, n = 398[a]		1st Trimester, n = 76[a]		2nd Trimester, n = 65[a]		3rd Trimester, n = 257[a]		Puerperal period, n = 217[a]	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Diagnostics										
Positive test[b]	349	87.7	74	97.4	62	95.4	213	82.9	211	97.2
Negative test[b,c]	18	4.5	1	1.3	1	1.5	11	4.3	5	2.3
Inconclusive test[b,c]	14	3.5	0		1	1.5	13	5.1	1	0.5
No diagnostic test[b,c]	17	4.3	1	1.3	1	1.5	20	7.8	0	
Location										
Left lower limb	316	79.4	63	82.9	49	75.4	204	79.4	147	67.7
Right lower limb	69	17.3	13	17.1	10	15.4	46	17.9	60	27.6
Not applicable	13	3.3	0		6	9.2	7	2.7	10	4.6

[a]In 39 cases the time of diagnosis was missing.

[b]Tests included Doppler ultrasound, magnetic resonance imaging or phlebography.

[c]A 'negative' test result was a diagnostic test that did not diagnose a deep venous thrombosis. An 'inconclusive' test was a test describing an inconclusive result regarding the presence of deep venous thrombosis. 'No' diagnostic test was the situation in which a diagnostic test was performed without a description of the test result in the medical record. Deep venous thrombosis with a negative or inconclusive test result, or no test result was confirmed if relevant anticoagulative therapy was initiated due to relevant clinical symptoms.

days with clinical symptoms before admission with deep venous thrombosis and pulmonary embolism was 5.8 days (SD = 9.1) and 8.0 days (SD = 12.4), respectively.

A majority (98.8%) of the 414 unconfirmed events showed relevant symptoms of VTE, but the diagnosis was not confirmed by positive diagnostic tests or treatment initiated (Fig. 1). Of the 414 unconfirmed events, 43 women (10.4%) had superficial thrombophlebitis, corresponding to 3.6% (43/1210) of women diagnosed with VTE.

The incidence rate of all VTE events (confirmed and unconfirmed) was 1436/1 377 286 pregnancies, or 1.0/1000 pregnancies. The incidence rate after validating the diagnoses should include the true VTEs among the 226 medical records we did not have access to. Extrapolating the findings from the retrieved records, these 226 events would be expected to contribute with an additional 149 events. Our validated incidence rate of VTE was consequently estimated to be 945/1 377 286 pregnancies, or 0.7/1000 pregnancies.

The validity was lowest in the second and third trimester, with 53.7 and 58.7% confirmed diagnoses, compared with 72.6% in first trimester and 79.1% in the puerperal period. The incidence rate for all and confirmed diagnoses according to gestational age is shown in Figure 2. When known, the diagnosis was used to confirm the exact date of VTE (n = 739); if unknown (n = 57) the admission date was used. The admission date was used for all VTE. The difference between the two curves was significantly different from week 39 until delivery.

The rate of confirmed cases of VTE with a positive diagnostic test did not change in the period from 2006 to 2009 compared with 1995–2005 (over 15 years) according to the specific diagnostic tests. The incidences and the anatomical location of VTE also did not change significantly in these two periods.

To deal with potential selection bias from admissions more than 10 years ago and diagnoses not being validated due to closure of departments, we performed separate validity analyses for diagnoses only made in the last 10 years. These analyses demonstrated no differences in the validity of diagnoses compared with the findings using the whole study period.

Discussion

We reviewed 1210 medical records from women diagnosed with VTE during pregnancy or in the puerperal period in Denmark from 1995 to 2009. Based on our criteria for confirmed VTE, which was a positive diagnostic test or relevant anticoagulation treatment, we were able to confirm 65.8% of the VTE diagnoses. The validity was highest in the puerperal period, perhaps due to more specific symptoms in this period, compared with late pregnancy, where pain, tenderness and leg edema are common. Furthermore, as the uterus enlarges, it becomes increasingly difficult to visualize the central veins by ultrasonography and confirm a diagnosis of deep venous thrombosis.

Previous validation of ICD codes for VTE in pregnant or puerperal women is not quite consistent. However, all studies have used confirmatory criteria matching those used in this study. Larsen et al. (5) reviewed 304 medical records from 1980 to 2001 in North Jutland County in Denmark. They were able to confirm 74.5% (95% CI

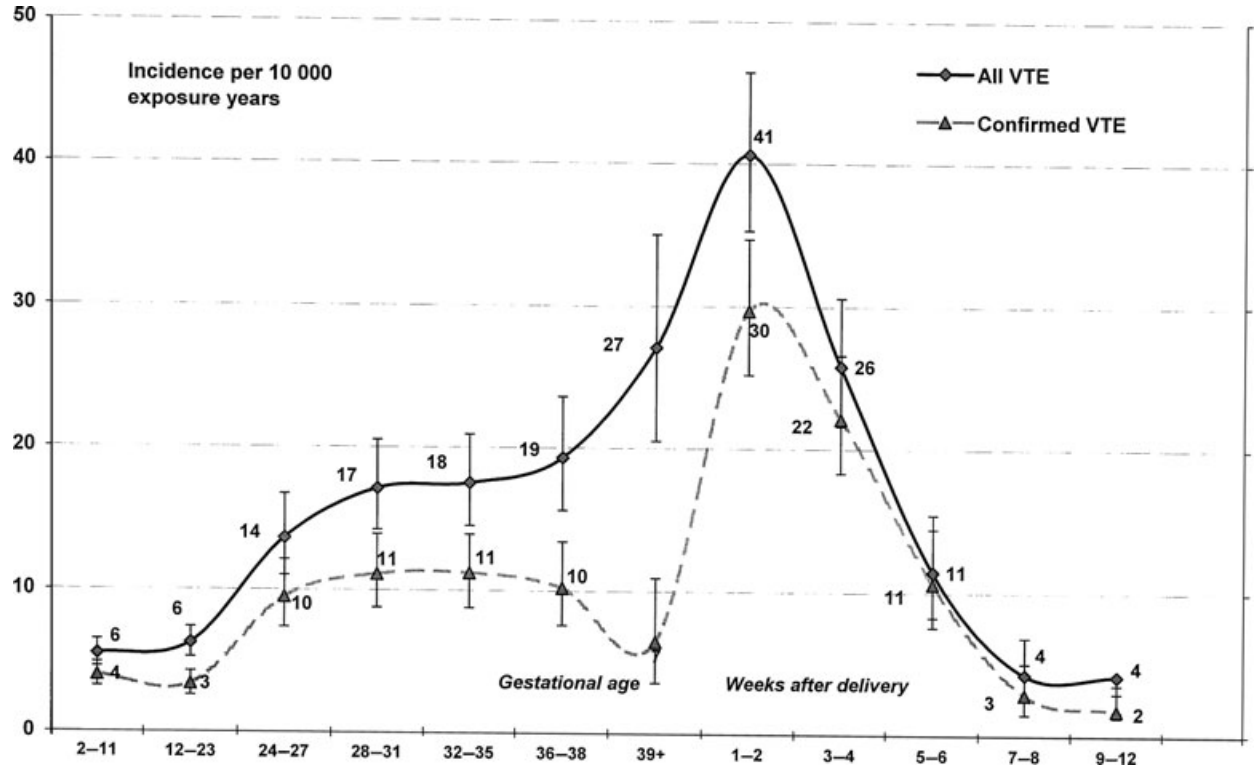

Figure 2. Incidence rate (IR) by 10 000 exposure-years and 95% confidence intervals for confirmed and for all venous thromboembolism (VTE) events according to time of occurrence in pregnancy or the puerperal period.

66.8–81.2) diagnoses of deep venous thrombosis and 63.6% (95%CI 40.7–82.8) diagnoses of pulmonary embolism, figures comparable to ours. White et al. (6) evaluated 214 events from California, USA, with specific ICD-9 codes for VTE in pregnant or puerperal women, and they were able to confirm 39% (95% CI 33–46). This positive predictive value was based on all admissions, including emergency room visits, which might explain the low value. Furthermore, the data were collected in another time period, using ICD-9 codes, which complicates any comparison.

Severinsen et al. (4) reviewed 1100 non-pregnant women over 50 years of age with a VTE diagnosis in the National Patient Registry from two regions in Denmark. They confirmed 75.0% (95%CI 71.9–77.9) of the events. Diagnoses from emergency room visits were less valid than diagnoses from wards and consequently we did not include diagnoses from emergency rooms in the present study.

We found differences between the incidence rates of confirmed VTE and all retrieved diagnoses of VTE, according to when a VTE was diagnosed in pregnancy or the puerperal period. Using the dates for diagnosis instead of admission dates, 6.5% of VTE changed from pregnancy to the puerperal period, probably including those that developed the VTE just before delivery and had it diagnosed shortly after delivery. In our previously published study based only on non-validated diagnoses from 1995–2005, 69.3% of women were diagnosed by their admission date during pregnancy (1). In the present study we found 64.8% of diagnoses using admission dates among the non-validated data and 58.3% for confirmed events using the date of diagnosis.

The present study covered a time of early discharge policies after delivery. Consequently, symptoms of VTE in the puerperal period would result in a new admission and the timing in relation to birth would be correctly classified using the registry-based admission date. This could explain the slightly differing results compared with the incidence rates in our previous study (1). However, the precise time of the VTE initiation of deep venous thrombosis and pulmonary embolism was 5.8 and 8.0 days before admission, respectively, according to chart review, which would move some VTEs categorized as puerperal to late pregnancy. Additionally, we did not have knowledge on the length of the period from the initiation of the formation of a VTE until symptoms arose – the induction time. Therefore, the admission date would in most cases be close to the true initiation of relevant symptoms. However, few of the women had been admit-

ted for a long period before the thrombus developed and in these cases the date for diagnosis would be closer to the date of the thrombus generation.

The "true" rate is difficult to determine even in a validation study like this. A lack of diagnostic confirmation of a VTE does not exclude the presence of a true VTE. Reviewing the medical records revealed that nearly all women had relevant clinical symptoms of VTE. In cases with negative diagnostic tests, this could be due to a small thrombus that was not detectable with the equipment available at the time, or a spontaneous resolution. Such women could be discharged with a VTE diagnosis in view of the lack of a more appropriate diagnosis. Therefore, we have considered women with symptoms, who were treated with low molecular weight heparin, "confirmed cases" even though diagnostic tests were negative or inconclusive. The rate of false positive diagnoses, on the other hand, was probably low.

Excluding emergency rooms visits would miss some true VTEs, but only a few women with suspected VTEs would not be admitted to wards, leaving only a small underestimation of the true rate. The very small numbers on rare locations of VTE in our study could be caused by a lack of coding knowledge or inexperience with registering thromboses-related diagnoses in ICD-10.

ICD-10 codes for superficial thrombophlebitis were not included in the present study. Consequently, we would not capture women with VTE if coded with a superficial thrombophlebitis diagnosis. However, we expect that there would only have been a small number of these, due to the relatively high positive predictive value of the diagnosis (88.0%) found in a similar population by Larsen et al. (5). The exclusion of superficial thrombophlebitis diagnoses would not have influenced the positive predictive value of a VTE diagnosis, but would have contributed to a slight underestimation of the true VTE incidence rate. Previous cohort studies have shown incidence rates of VTE in pregnancy and the puerperium of between 1 and 2/1000 pregnancies (2,7–9), which is higher than our confirmed incidence rate of 0.7/1000.

The frequent left-side localization of deep VTE is in accordance with other studies (10–12) and has been explained by the increasing pressure from the growing uterus during pregnancy on the left iliac vein crossing the lumbar column. The influence of the uterine pressure on the risk of deep venous thrombosis in pregnancy is supported by the finding of a higher proportion of left-sided deep venous thrombosis in pregnancy than in the puerperal period. The distribution of VTE in our study is in accordance with previously published studies (2,13).

This national cohort study reviewing 1210 medical records is the first national validation study of incident VTE discharge diagnoses in pregnancy and the puerperal period. Of the 1436 women diagnosed with VTE, 184 medical records were not retrievable and they included more than 10-year-old admissions and admissions to departments no longer operational. The remaining 42 medical records are unlikely to have led to appreciable selection bias in our results.

Conclusions

The validity of VTE diagnoses changes during pregnancy and the puerperal period, and is highest in the first trimester and the puerperal period. Left-sided deep venous thrombosis is the predominant type of VTE during pregnancy and the puerperal period. Registry-based discharge diagnoses in pregnant or puerperal women may slightly overestimate the incidence of VTE. Inclusion of only validated events may underestimate the real occurrence of VTE in pregnancy and the puerperal period, but will ensure more valid estimates of VTE risk factors and of the clinical consequences of venous thrombosis.

Acknowledgments

We thank Anne Kirstine Nielsen for assistance in the management of data and in performing the statistical analysis.

Funding

The study was funded by the Research Foundation at Hillerød Hospital, University of Copenhagen.

References

1. Virkus RA, Lokkegaard EC, Bergholt T, Mogensen U, Langhoff-Roos J, Lidegaard O. Venous thromboembolism in pregnant and puerperal women in Denmark 1995–2005. A national cohort study. Thromb Haemost. 2011;106:304–9.
2. Jacobsen AF, Skjeldestad FE, Sandset PM. Incidence and risk patterns of venous thromboembolism in pregnancy and puerperium – a register-based case-control study. Am J Obstet Gynecol. 2008;233:e1–7.
3. Sorensen HT, Schulze S. Danish health registries. A valuable tool in medical research. Dan Med Bull. 1996;43:463.
4. Severinsen MT, Kristensen SR, Overvad K, Dethlefsen C, Tjonneland A, Johnsen SP. Venous thromboembolism discharge diagnoses in the Danish National Patient Registry should be used with caution. J Clin Epidemiol. 2010;63:223–8.
5. Larsen TB, Johnsen SP, Moller CI, Larsen H, Sorensen HT. A review of medical records and discharge summary data found moderate to high predictive values of discharge

diagnoses of venous thromboembolism during pregnancy and postpartum. J Clin Epidemiol. 2005;58:316–9.
6. White RH, Brickner LA, Scannell KA. ICD-9-CM codes poorly indentified venous thromboembolism during pregnancy. J Clin Epidemiol. 2004;57:985–8.
7. Heit JA, Kobbervig CE, James AH, Petterson TM, Bailey KR, Melton LJ 3rd. Trends in the incidence of venous thromboembolism during pregnancy or postpartum: a 30-year population-based study. Ann Intern Med. 2005;143:697–706.
8. Martineau M, Nelson-Piercy C. Venous thromboembolic disease and pregnancy. Postgrad Med J. 2009;85:489–94.
9. James AH. Pregnancy and thrombotic risk. Crit Care Med. 2010;38(2 Suppl):S57–63.
10. James AH, Tapson VF, Goldhaber SZ. Thrombosis during pregnancy and the postpartum period. Am J Obstet Gynecol. 2005;193:216–9.
11. Ray JG, Chan WS. Deep vein thrombosis during pregnancy and the puerperium: a meta-analysis of the period of risk and the leg of presentation. Obstet Gynecol Surv. 1999;54:265–71.
12. Greer IA. Thrombosis in pregnancy: maternal and fetal issues. Lancet. 1999;353:1258–65.
13. Blanco-Molina A. Venous thromboembolism during pregnancy, postpartum or during contraceptive use. Thromb Haemost. 2007;103:306–11.