Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplementary Appendix

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Supplementary Methods

Definition of Pre-Existing Thrombotic Disease

We excluded patients with any recorded thrombotic disease prior to their first recorded labor and delivery by using the following *International Classification of Diseases, 9th Revision, Clinical Modification* (*ICD-9-CM*) codes in any emergency department or hospital discharge diagnosis code position: 253.2 (pituitary apoplexy), 410 (acute myocardial infarction), 415 (acute pulmonary heart disease), 430-438 (cerebrovascular disease), 443.21 (carotid artery dissection), 443.24 (vertebral artery dissection), 451 (phlebitis and thrombophlebitis), 453 (other venous embolism and thrombosis), 671 (venous complications in pregnancy and the puerperium), 673 (obstetrical pulmonary embolism), and 674.0 (cerebrovascular disorders in the puerperium). Intracranial hemorrhages were included in this definition because they may be the only documented manifestation of cerebral arterial or venous thrombosis with hemorrhagic transformation.[1]

Definitions of Outcomes

Ischemic stroke

Ischemic stroke was defined as *ICD-9-CM* codes 433.x1, 434.x1, or 436 in any hospital discharge diagnosis code position without a primary hospital discharge diagnosis code for rehabilitation (V57) or any accompanying codes for trauma (800-804 or 850-854), intracerebral hemorrhage (431), or subarachnoid hemorrhage (430). This algorithm has been validated by detailed medical record review to have a sensitivity of 86%, a specificity of 95%, and a positive predictive value of 90% for ischemic stroke, and to capture samples that comprise 88% incident cases.[2]

Acute myocardial infarction

Acute myocardial infarction was defined as *ICD-9-CM* code 410.x1 in the first or second hospital discharge diagnosis code position. All hospitalizations lasting >180 days were excluded, and any hospitalization lasting <3 days was excluded unless the patient died during that hospitalization. This algorithm has been validated to have a positive predictive value of 94% when compared with detailed medical record review.[3]

Venous thromboembolism

Venous thromboembolism consisted of a composite of deep venous thrombosis or pulmonary embolism, defined as *ICD-9-CM* codes 415.1, 451.11, 451.19, 451.2, 451.81, 451.9, 453.1, 453.2, 453.8, or 453.9 in any emergency department or hospital discharge diagnosis code position. This definition has been validated to have a positive predictive value of 96% when compared with detailed medical record review.[4]

Secondary composite outcome

As a secondary outcome, we assessed a composite of our primary outcome plus a broadly inclusive list of other thrombosis diagnoses. This secondary outcome was defined by the following *ICD-9-CM* codes in any emergency department or hospital discharge diagnosis code position: 253.2 (pituitary apoplexy); 410.x1 (acute myocardial infarction); 415 (acute pulmonary heart disease); 430 (subarachnoid hemorrhage); 431 (intracerebral hemorrhage); 432 (other and unspecified intracranial hemorrhage); 433.x1, 434.x1, or 436 (ischemic stroke); 437.2 (hypertensive encephalopathy); 437.6 or 671.5 (cerebral venous thrombosis); 443.21 (carotid artery dissection); 443.24 (vertebral artery dissection); 451 (phlebitis and thrombophlebitis); 453 (other venous embolism and thrombosis); 671.4 (postpartum deep venous thrombosis); 673 (obstetrical pulmonary embolism); and 674.0 (cerebrovascular disorders in the puerperium). Intracranial hemorrhages were included in this definition because they may be the only documented manifestation of cerebral arterial or venous thrombosis with hemorrhagic transformation.[1]

Definitions of Comorbidities

We identified risk factors for thrombosis using the following *ICD-9-CM* codes: 289.81 (primary hypercoagulable state); 642 (eclampsia or pre-eclampsia); 305.1, 649, 989.84, or V15.82 (smoking); and 74 (cesarean delivery).

Table S1. Numbers and Absolute Risks of Postpartum Thrombotic Events During Sequential 3-Week Intervals After Labor and Delivery.

Time Interval After Labor and Delivery	Case Period[a]	Crossover Period[b]	Absolute Risk Difference[c]	Odds Ratio[d]
0 through 3 weeks				
Stroke, MI, or VTE[e]	329 (19.5)	18 (1.1)	18.4 (16.2-20.7)	18.3 (11.4-29.4)
Stroke	103 (6.1)	9 (0.5)	5.6 (4.3-6.9)	11.4 (5.8-22.6)
MI	13 (0.8)	1 (0.1)	0.7 (0.2-1.2)	13.0 (1.7-99.4)
VTE	213 (12.6)	8 (0.5)	12.2 (10.4-13.9)	26.6 (13.1-53.9)
Stroke, MI, VTE, or other[f]	2006 (118.8)	43 (2.6)	116.3 (111.0-121.6)	46.7 (34.5-63.1)
4 through 6 weeks				
Stroke, MI, or VTE	82 (4.9)	20 (1.2)	3.7 (2.4-4.9)	4.1 (2.5-6.7)
Stroke	16 (0.9)	5 (0.3)	0.7 (0.1-1.2)	3.2 (1.2-8.7)
MI	0 (0)	0 (0)	0 (-0.1-0.1)	N/A[g]
VTE	66 (3.9)	15 (0.9)	3.0 (1.9-4.1)	4.4 (2.5-7.7)
Stroke, MI, VTE, or other	247 (14.6)	56 (3.3)	11.3 (9.2-13.4)	4.4 (3.3-5.9)
7 through 9 weeks				
Stroke, MI, or VTE	59 (3.5)	25 (1.5)	2.0 (0.9-3.1)	2.4 (1.5-3.8)
Stroke	9 (0.5)	6 (0.4)	0.2 (-0.3-0.7)	1.5 (0.5-4.2)
MI	4 (0.2)	2 (0.1)	0.1 (-0.2-0.5)	2.0 (0.4-10.9)
VTE	46 (2.7)	17 (1.0)	1.7 (0.7-2.7)	2.7 (1.6-4.7)
Stroke, MI, VTE, or other	125 (7.4)	49 (2.9)	4.5 (2.9-6.1)	2.6 (1.8-3.5)
10 through 12 weeks				
Stroke, MI, or VTE	36 (2.1)	19 (1.1)	1.0 (0.1-1.9)	1.9 (1.1-3.3)
Stroke	6 (0.4)	3 (0.2)	0.2 (-0.2-0.6)	2.0 (0.5-8.0)
MI	4 (0.2)	0 (0)	0.2 (-0.1-0.5)	N/A[g]
VTE	26 (1.5)	16 (0.9)	0.6 (-0.2-1.4)	1.6 (0.9-3.0)
Stroke, MI, VTE, or other	72 (4.3)	45 (2.7)	1.6 (0.3-2.9)	1.6 (1.1-2.3)
13 through 15 weeks				
Stroke, MI, or VTE	32 (1.9)	16 (0.9)	0.9 (0.1-1.8)	2.0 (1.1-3.6)
Stroke	7 (0.4)	3 (0.2)	0.2 (-0.2-0.7)	2.3 (0.6-9.0)
MI	1 (0.1)	1 (0.1)	0 (-0.2-0.2)	1.0 (0.1-16.0)
VTE	24 (1.4)	12 (0.7)	0.7 (-0.1-1.5)	2.0 (1.0-4.0)[h]
Stroke, MI, VTE, or other	56 (3.3)	40 (2.4)	0.9 (-0.2-2.1)	1.4 (0.9-2.1)
16 through 18 weeks				
Stroke, MI, or VTE	23 (1.4)	23 (1.4)	0 (-0.8-0.8)	1.0 (0.6-1.8)
Stroke	2 (0.1)	6 (0.4)	-0.2 (-0.6-0.2)	0.3 (0.1-1.7)
MI	1 (0.1)	1 (0.1)	0 (-0.2-0.2)	1.0 (0.1-16.0)
VTE	20 (1.2)	16 (0.9)	0.2 (-0.5-1.0)	1.3 (0.6-2.4)
Stroke, MI, VTE, or other	43 (2.6)	55 (3.3)	-0.7 (-1.9-0.5)	0.8 (0.5-1.2)
19 through 21 weeks				
Stroke, MI, or VTE	31 (1.8)	22 (1.3)	0.5 (-0.4-1.4)	1.4 (0.8-2.4)
Stroke	8 (0.5)	6 (0.4)	0.1 (-0.4-0.6)	1.3 (0.5-3.8)
MI	3 (0.2)	1 (0.1)	0.1 (-0.2-0.4)	3.0 (0.3-28.8)
VTE	20 (1.2)	15 (0.9)	0.3 (-0.5-1.0)	1.3 (0.7-2.6)
Stroke, MI, VTE, or other	49 (2.9)	45 (2.7)	0.2 (-0.9-1.4)	1.1 (0.7-1.6)

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22 through 24 weeks				
Stroke, MI, or VTE	21 (1.2)	31 (1.8)	-0.6 (-1.5-0.3)	0.7 (0.4-1.2)
Stroke	8 (0.5)	9 (0.5)	-0.1 (-0.6-0.5)	0.9 (0.3-2.3)
MI	2 (0.1)	1 (0.1)	0.1 (-0.2-0.3)	2.0 (0.2-22.1)
VTE	11 (0.7)	21 (1.2)	-0.6 (-1.3-0.1)	0.5 (0.3-1.1)
Stroke, MI, VTE, or other	49 (2.9)	68 (4.0)	-1.1 (-2.4-0.2)	0.7 (0.5-1.0)[i]

Abbreviations: MI, myocardial infarction; VTE, venous thromboembolism.

[a]Data represent the number (frequency per 100,000) of patients with an outcome during the indicated time interval after labor and delivery.

[b]Data represent the number (frequency per 100,000) of patients with an outcome during the indicated time interval plus 1 year after labor and delivery.

[c]Data represent the difference per 100,000 deliveries (95% confidence interval) in the number of events between the case and crossover periods. Discrepancies between the reported risks for individual and composite endpoints or for different periods are due to rounding.

[d]Conditional logistic regression was used to calculate each patient's odds (95% confidence interval) of a thrombotic event during the case period as compared with the crossover period.

[e]The primary outcome was a composite of ischemic stroke, acute MI, or VTE (see preceding section of supplementary appendix for diagnosis definitions).

[f]The secondary outcome comprised the primary outcome plus a broader set of thrombosis diagnoses, including cerebral venous thrombosis (see preceding section of supplementary appendix for diagnosis definitions).

[g]Odds ratio was not estimable due to insufficient numbers of events.

[h]$P = 0.05$.

[i]$P = 0.08$.

Table S2. Subgroup Analyses of Thrombotic Risk During the 0-6 Week Postpartum Period.

Characteristic	Case Period[a]	Crossover Period[b]	Odds Ratio[c]	P value for interaction
Age:				
>35 years	115 (42.3)	11 (4.0)	10.5 (5.6-19.4)	
≤35 years	296 (20.9)	27 (1.9)	11.0 (7.4-16.3)	0.90
Eclampsia or pre-eclampsia:				
Yes	109 (82.7)	6 (4.6)	18.2 (8.0-41.3)	
No	302 (19.4)	32 (2.1)	9.4 (6.6-13.6)	0.15
Primary hypercoagulable state:				
Yes	7 (465.7)	0 (0)	N/A[d]	
No	404 (24.0)	38 (2.3)	10.6 (7.6-14.8)	N/A[d]
Smoking:				
Yes	16 (53.5)	1 (3.3)	16.0 (2.1-120.6)	
No	395 (23.8)	37 (2.2)	10.7 (7.6-15.0)	0.70
Method of delivery:				
Cesarean	246 (44.8)	12 (2.2)	20.5 (11.5-36.6)	
Vaginal	165 (14.5)	26 (2.3)	6.3 (4.2-9.6)	0.001

[a]Data represent the number (frequency per 100,000) of patients with an outcome during the indicated time interval after labor and delivery.
[b]Data represent the number (frequency per 100,000) of patients with an outcome during the indicated time interval plus 1 year after labor and delivery.
[c]Conditional logistic regression was used to examine each patient's odds (95% confidence interval) of a thrombotic event during the 0-6 week postpartum period versus the same 6-week period 1 year later.
[d]Odds ratios and P values for interaction were not estimable in these subgroups due to insufficient numbers of events.

Table S3. Subgroup Analyses of Thrombotic Risk During the 7-12 Week Postpartum Period.

Characteristic	Case Period[a]	Crossover Period[b]	Odds Ratio[c]	P value for interaction
Age:				
>35 years	24 (8.8)	7 (2.6)	3.4 (1.5-8.0)	
≤35 years	71 (5.0)	37 (2.6)	1.9 (1.3-2.9)	0.22
Eclampsia or pre-eclampsia:				
Yes	25 (19.0)	9 (6.8)	2.8 (1.3-6.0)	
No	70 (4.5)	35 (2.2)	2.0 (1.3-3.0)	0.46
Primary hypercoagulable state:				
Yes	1 (66.5)	0 (0)	N/A[d]	
No	94 (5.6)	44 (2.6)	2.1 (1.5-3.1)	N/A[d]
Smoking:				
Yes	3 (10.0)	0 (0)	N/A[d]	
No	92 (5.5)	44 (2.7)	2.1 (1.5-3.0)	N/A[d]
Method of delivery:				
Cesarean	41 (7.5)	19 (3.5)	2.2 (1.3-3.7)	
Vaginal	54 (4.7)	25 (2.2)	2.2 (1.3-3.5)	0.99

[a]Data represent the number (frequency per 100,000) of patients with an outcome during the indicated time interval after labor and delivery.

[b]Data represent the number (frequency per 100,000) of patients with an outcome during the indicated time interval plus 1 year after labor and delivery.

[c]Conditional logistic regression was used to examine each patient's odds (95% confidence interval) of a thrombotic event during the 7-12 week postpartum period versus the same 6-week period 1 year later.

[d]Odds ratios and P values for interaction were not estimable in these subgroups due to insufficient numbers of events.

Supplementary References

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