Venous thromboembolism (VTE) is a critical complication after surgery. Although pregnancy is a known risk factor of VTE, available data on the risk of postoperative VTE are scarce. Using the American College of Surgeons National Surgical Quality Improvement Program database between 2006 and 2012, we matched 2,582 pregnant women to 103,640 nonpregnant women based on age, race, body mass index, and modified Rogers score. Pregnant women, compared with matched nonpregnant women, experienced higher incidence of VTE (0.5% vs 0.3%; odds ratio 1.93, 95% confidence interval 1.1 to 3.37, \( p = 0.02 \)). Pregnant women also showed higher risk of pneumonia, ventilator dependence \( \geq 48 \) hours, bleeding, and sepsis than did the counterparts. In conclusion, pregnancy was associated with higher risk of VTE after surgery as well as other postoperative complications. The absolute risk difference was small, and careful evaluation against the potential risk and benefit should be given when surgical treatment is considered among pregnant women.© 2017 Elsevier Inc. All rights reserved. (Am J Cardiol 2017;120:479–483)
large, medium, and small differences.\textsuperscript{6,7} Statistical significance was defined as a p value of $<0.05$. All analysis was performed using Stata 13.1 (StataCorp LP, College Station, Texas).

Results

Among 2,596 pregnant and 189,958 nonpregnant women in the complete case cohort, 2,582 (99.5%) pregnant women were matched to 103,640 nonpregnant women. There were large differences in age, body mass index, and modified Rogers score between pregnant versus nonpregnant women in the complete case cohort, and these differences were diminished in the weighted matched cohort (Table 1). Among the components of modified Rogers score, pregnant women had lower preoperative serum sodium levels and higher prevalence of emergent surgery in both the entire and weighted matched cohort. The incidence of VTE among pregnant and nonpregnant patients was 0.5% versus 0.4% in the complete case cohort and 0.5% versus 0.3% in the matched cohort, respectively (Table 2). After matching, the incidence of other postoperative complications also decreased among nonpregnant women.

Pregnant women, compared with nonpregnant women, showed higher risk of VTE and other complications except for surgical site infection after adjustment for age, race, and body mass index in the matched cohort (Figure 2). Consistent associations were observed in the matched cohort (OR 1.93, 95% confidence interval [CI] 1.11 to 3.37, \( p = 0.02 \) for VTE; OR 1.79, 95% CI 1.06 to 3.00, \( p = 0.03 \) for pneumonia; OR 2.24, 95% CI 1.49 to 3.35, \( p < 0.001 \) for ventilator dependency $>48$ hours; OR 2.36, 95% CI 1.79 to 3.10, \( p < 0.001 \) for bleeding; and OR 1.52, 95% CI 1.11 to 2.07, \( p = 0.009 \) for sepsis). Sensitivity analyses including emergent surgery as a matching factor showed an attenuation in the risk of pneumonia, ventilator dependency, and sepsis, but the risk of VTE and bleeding remained significant (OR 2.26, 95% CI 1.29 to 3.97, \( p = 0.004 \); and OR 2.25, 95% CI 1.70 to 2.98, \( p < 0.001 \), respectively).

Discussion

This study demonstrated the association of pregnancy with increased risk of postoperative VTE. The risk of other postoperative complications (i.e., pneumonia, ventilator dependency $>48$ hours, bleeding, and sepsis) was also significantly higher among pregnant patients than nonpregnant female patients.

The absolute rate of postoperative VTE in this study was consistent with previous studies.\textsuperscript{8–10} A recent US population-based study by Abbasi et al\textsuperscript{9} also showed that among pregnant women who developed acute appendicitis during the hospital stay for delivery, the risk of postoperative VTE was 60% higher than nonpregnant women after adjustment for age, race, obesity, income, insurance, and hospital type. Our study included all types of surgical procedures that were ever performed for pregnant women during the antepartum period, and confirmed the association between pregnancy and postoperative VTE even after matching on factors related to VTE.

Previous studies also showed that pregnant women had higher risk of postoperative adverse events including
infection, sepsis, pneumonia, and mortality.\textsuperscript{8,9} Patients with severe complications, especially those who are ventilator dependent, usually require complete bed rest, and immobility is a major cause of postoperative VTE.\textsuperscript{11} Additionally, infection and systemic inflammation may increase the risk of VTE through Virchow triad (i.e., stasis of

Table 1
Clinical characteristics in complete case analysis and weighted matched cohort

| Variables                          | Complete case cohort (n=192,554) | Weighted matched cohort (n=106,222) |
|------------------------------------|----------------------------------|----------------------------------|
| Age, mean ± SD, (years)            | Pregnant (n=2,596) | 29 ± 6 | 29 ± 6 | 0 |
| Body mass index, median (IQR), (kg/m\textsuperscript{2}) | Non-pregnant (n=189,958) | 37 ± 9 | 37 (24.0, 32.9) | 30.4 (24.4, 39.4) | -0.33 |
| Race                               | Pregnant (n=2,582) | 27.9 (24.0, 32.9) | 29 ± 6 | 29 ± 6 | 0 |
| Black                              | Non-pregnant (n=103,640) | 37 (24.0, 32.9) | 29 ± 6 | 29 ± 6 | 0 |
| Asian                              | 1,651 (64%) | 130,354 (69%) | 1.12 | 1,644 (64%) | 70,494 (68%) | 0.09 |
| Other + Unknown                    | 422 (16%) | 29,526 (16%) | -0.02 | 419 (16%) | 14,505 (14%) | -0.06 |
| Modified Rogers score              | 81 (3%) | 4,673 (2%) | -0.04 | 81 (3%) | 2,668 (3%) | -0.03 |
| Work relative value unit           | 442 (17%) | 25,408 (13%) | -0.10 | 438 (17%) | 15,973 (15%) | -0.04 |
| Disseminated cancer                | 8 (6, 9) | 8 (6, 10) | -0.14 | 8 (6, 9) | 8 (6, 9) | 0 |
| ASA classification                 | 2 (2, 3) | 2 (2, 3) | -0.08 | 2 (2, 3) | 2 (2, 3) | -0.05 |
| Chemotherapy for malignancy       | 12 (10, 18) | 12 (10, 18) | -0.51 | 12 (10, 18) | 12 (10, 18) | -0.18 |
| Serum sodium ≥145 mEq/L            | 913 (0.5%) | 913 (0.5%) | 0.06 | 913 (0.5%) | 913 (0.5%) | 0.07 |
| Transfusions RBCs before operation | 15 (0.6%) | 15 (0.6%) | -0.03 | 15 (0.6%) | 15 (0.6%) | -0.02 |
| Ventilator dependent              | 20 (0.8%) | 20 (0.8%) | -0.06 | 20 (0.8%) | 20 (0.8%) | -0.05 |
| Wound class (clean /contaminated)  | 1,284 (49%) | 1,284 (49%) | -0.14 | 1,284 (49%) | 1,284 (49%) | -0.01 |
| Dyspnea                            | 54 (2%) | 54 (2%) | -0.07 | 54 (2%) | 54 (2%) | 0.07 |
| Emergent surgery                   | 1,425 (55%) | 1,425 (55%) | -0.60 | 1,425 (55%) | 1,425 (55%) | 0.07 |
| Type of surgery                    | 1,809 (70%) | 1,809 (70%) | -0.12 | 1,809 (70%) | 1,809 (70%) | 0.07 |
| Integument                         | 169 (7%) | 169 (7%) | -0.25 | 169 (7%) | 169 (7%) | 0.11 |
| Hernia                             | 103 (4%) | 103 (4%) | -0.10 | 103 (4%) | 103 (4%) | 0.05 |
| Mouth, palate                      | 13 (0.5%) | 13 (0.5%) | -0.08 | 13 (0.5%) | 13 (0.5%) | 0.07 |
| Thoracoabdominal aneurysm,         | 24 (0.9%) | 24 (0.9%) | -0.01 | 24 (0.9%) | 24 (0.9%) | 0.03 |
| embolectomy/thrombectomy,          | 1,805 (70%) | 1,805 (70%) | -0.12 | 1,805 (70%) | 1,805 (70%) | 0.07 |
| venous reconstruction, and         | 1,805 (70%) | 1,805 (70%) | -0.12 | 1,805 (70%) | 1,805 (70%) | 0.07 |
| endovascular repair                | 1,805 (70%) | 1,805 (70%) | -0.12 | 1,805 (70%) | 1,805 (70%) | 0.07 |
| Stomach, intestines                | 950 (0.5%) | 950 (0.5%) | 0.02 | 950 (0.5%) | 950 (0.5%) | 0.06 |
| Aneurysm                           | 158 (0.1%) | 158 (0.1%) | -0.04 | 158 (0.1%) | 158 (0.1%) | -0.05 |
| Hematocrit, mean ± SD, (%)         | 34.1 ± 4.2 | 38.0 ± 4.2 | 0.93 | 34.1 ± 4.2 | 37.8 ± 4.2 | 0.87 |
| Serum bilirubin, median (IQR), (mg/dl) | 0.5 (0.3, 0.7) | 0.5 (0.7, 0.8) | -0.06 | 0.5 (0.3, 0.7) | 0.5 (0.3, 0.7) | -0.14 |
| Serum albumin, mean ± SD, (g/dl)   | 3.4 ± 0.7 | 4.0 ± 0.6 | 0.89 | 3.4 ± 0.7 | 4.0 ± 0.6 | 0.88 |

\textsuperscript{a} ASA = American Society of Anesthesiology; RBCs = red blood cells.

\textsuperscript{b} 0.8, 0.5, and 0.2 in absolute values are considered large, medium, and small differences.

\textsuperscript{c} Not shown because of a limited number of patients as per the NSQIP policy.

\textsuperscript{d} Missing frequency was 2%, 27%, and 31% for hematocrit, bilirubin, and serum albumin.

Table 2
Incidence of postoperative complications among pregnant versus nonpregnant women

| Variable                          | Complete case cohort (n=192,554) | Weighted matched cohort (n=106,222) |
|-----------------------------------|----------------------------------|----------------------------------|
| Venous thromboembolism            | Pregnant (n=2,596) | 13 (0.5%) | 271 (0.3%) | 0.87 |
| Surgical site infection\textsuperscript{a} | Non-pregnant (n=189,958) | 742 (0.4%) | 6,597 (3%) | 38.0 ± 4.2 |
| Pneumonia                         | 83 (3%) | 6,597 (3%) | 0.93 | 34.1 ± 4.2 | 37.8 ± 4.2 | 0.87 |
| Ventilator >48 hours              | 16 (0.6%) | 924 (5%) | -0.06 | 0.5 (0.3, 0.7) | 0.5 (0.3, 0.7) | -0.14 |
| Bleeding                          | 28 (1%) | 1,955 (10%) | 0.89 | 3.4 ± 0.7 | 4.0 ± 0.6 | 0.88 |
| Sepsis                            | 42 (2%) | 2,567 (1%) | 0.07 | 42 (2%) | 1,117 (1%) | 0.05 |

\textsuperscript{a} Surgical site infection is defined as superficial surgical site infection, deep surgical site infection, organ/space surgical site infection, or wound disruption.
blood flow, endothelial injury, and hypercoagulability).\textsuperscript{12,13} Bleeding activates coagulation system, and transfusion may also increase the risk of VTE.\textsuperscript{14} Meanwhile, pulmonary embolism may cause other complications including respiratory dysfunction and sepsis in turn, and anticoagulant therapy increases bleeding risk, creating a vicious cycle among these complications.

Hypernatremia is an index of dehydration which may lead to postoperative VTE,\textsuperscript{17} as included in Rogers score.\textsuperscript{2} Despite the physiological increase in body fluid during the antepartum period as partly reflected by lower serum sodium levels, pregnancy was associated with postoperative VTE. These results suggested the involvement of other factors such as increased procoagulant factors (i.e., fibrinogen, factor VIII, and von Willebrand factor)\textsuperscript{18} and reduced anticoagulant factors (i.e., protein C and protein S),\textsuperscript{19} as well as venous compression by enlarged uterus.\textsuperscript{2}

The higher prevalence of emergent surgery among pregnant women may reflect an effort of physicians to avoid surgical complications. However, delayed treatment may result in adverse consequences. Abbasi et al\textsuperscript{7} reported that conservative treatment was more common than expected and associated with septic shock, peritonitis, and VTE among pregnant women. We also found that the risk of pneumonia, ventilator dependence, and sepsis was attenuated after adding emergent surgery into matching variables, suggesting the contribution of preoperative conditions to these complications. The postoperative VTE risk remained significant, but the absolute rate difference was 0.2%.

Therefore, surgical procedures for pregnant women should be considered with the risk-benefit balance between surgical versus conservative treatment on an individual basis. Further studies are necessary to identify high-risk patients who need careful monitoring and aggressive prophylaxis.

Several limitations should be noted. First, there may be residual confounding and/or effect modification by type of surgery.\textsuperscript{20} However, type of surgery was contained in Rogers score,\textsuperscript{2} and we selected those ever performed in pregnant women. Second, there may also be unmeasured confounding by hereditary thrombophilia (i.e., antithrombin, protein C, or protein S deficiency),\textsuperscript{21} smoking, a history of VTE, and the use of prophylactic and therapeutic drugs and devices. Third, the incidence of VTE may be underestimated in this study because the NSQIP database contains only clinically observed outcomes within 30 days after surgery. Indeed, a previous study showed that the risk of VTE among middle aged women was substantially increased in the first 12 postoperative weeks.\textsuperscript{10} Finally, gestational period was not recorded in the NSQIP database. The incidence rate of venous thromboses may be consistent across the trimesters,\textsuperscript{22} but the physiological changes in the course of pregnancy may alter the risk of VTE among pregnant women, which need further investigation.

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Disclosures

The authors have no conflicts of interest to disclose.

Supplementary Data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.amjcard.2017.04.053.

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