Acute Myocardial Infarction in Pregnancy
A United States Population-Based Study
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Background—The purpose of this study was to determine the incidence, mortality, and risk factors for pregnancy-related acute myocardial infarction in the United States.

Methods and Results—The Nationwide Inpatient Sample for the years 2000 to 2002 was queried for all pregnancy-related discharges. A total of 859 discharges included a diagnosis of acute myocardial infarction, for a rate of 6.2 (95% confidence interval [CI] 3.0 to 9.4) per 100 000 deliveries. Among these, there were 44 deaths, for a case fatality rate of 5.1%. The odds of acute myocardial infarction were 30-fold higher for women aged 40 years and older than for women <20 years of age. Single independent variables that were statistically and clinically significant, including age, race, and certain medical conditions and obstetric complications, were entered into a multivariable logistic regression model. Hypertension (odds ratio [OR] 21.7, 95% CI 6.8 to 69.1), thrombophilia (OR 25.6, 95% CI 9.2 to 71.2), diabetes mellitus (OR 3.6, 95% CI 1.5 to 8.3), smoking (OR 8.4, 95% CI 5.4 to 12.9), transfusion (OR 5.1, 95% CI 2.0 to 12.7), postpartum infection (OR 3.2, 95% CI 1.2 to 10.1), and age 30 years and older remained as significant risk factors for pregnancy-related acute myocardial infarction. Black race was eliminated as a risk factor in the multivariable analysis, which suggests that the increased incidence among black women is explained by an increased prevalence of other cardiovascular risk factors.

Conclusions—Although acute myocardial infarction is a rare event in women of reproductive age, pregnancy increases the risk 3- to 4-fold. Certain medical conditions and complications of pregnancy increase the risk further and are potentially modifiable risk factors. (Circulation. 2006;113:1564-1571.)

Key Words: epidemiology ■ mortality ■ myocardial infarction ■ pregnancy ■ risk factors

Acute myocardial infarction has been reported to occur with a frequency of 3 to 10 cases per 100 000 deliveries.1,2 Although rare, acute pregnancy-related myocardial infarction is a devastating event that may claim the life of a mother and her unborn baby. The case fatality rate has been reported to be as high as 37%.3 Given that fewer than 12 women per 100 000 die in pregnancy,4 a single death due to acute myocardial infarction makes a substantial contribution to maternal mortality.

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Pregnancy itself has not usually been thought of as a risk factor for acute myocardial infarction, but pregnancy is accompanied by not only an increase in blood volume and altered hemodynamics5 but an increase in estrogen and progesterone. Oral estrogen and progestins, at least, have been implicated as a risk factor for cardiovascular disease. In the form of hormone replacement therapy, the risk of coronary heart disease (largely nonfatal myocardial infarction) is increased by 24%,6 and in the form of oral contraceptives, the risk of myocardial infarction is doubled.7 Any risk imposed by pregnancy may be compounded by other factors. Because the prevalence of certain cardiovascular risk factors, particularly advanced maternal age8 and obesity,9 is increasing, the incidence of pregnancy-related acute myocardial infarction may also be increasing, but there have been insufficient data to evaluate risk factors or trends.

Because of the rarity of pregnancy-related acute myocardial infarction, it is difficult to estimate its incidence, identify its risk factors, and report outcomes, such as mortality. Large population-based studies are required. One population-based study of pregnancy-related acute myocardial infarction in California has been published recently,10 but data for the United States as a whole have not. The majority of medical conditions and obstetric complications, however, are coded in hospital discharge data captured by the Nationwide Inpatient Sample (NIS), which allows for the investigation of risk factors for pregnancy-related acute myocardial infarction. The objective of the present study was to determine, with as complete an ascertainment as possible, the incidence, risk factors, and mortality from pregnancy-related acute myocardial infarction in the United States.
Methods

The research protocol used in this study was reviewed and approved by the Duke University Medical Center Institutional Review Board. The NIS, from the Healthcare Cost and Utilization Project (HCUP) of the Agency for Healthcare Research and Quality (AHRQ) was queried for all pregnancy-related discharge codes for the years 2000 to 2002 (the latest data available at the inception of the study). The NIS contains data from ~1000 hospitals and is the largest all-payer inpatient care database in the United States. It is a 20% stratified sample from a sampling frame that comprises 90% of all US hospital discharges. Included in the sample are general hospitals and academic medical centers.11,12 Rehabilitation hospitals, long-term hospitals, psychiatric hospitals, and alcoholism or chemical dependency treatment facilities are excluded. The hospitals are divided into strata based on ownership, bed size, teaching status, urban versus rural location, and region. Sampling probabilities are proportional to the number of hospitals in each stratum.

Information included in the NIS is what can be derived from a typical discharge abstract, with safeguards to protect the privacy of individual patients, physicians, and hospitals. These data include primary and secondary diagnoses; primary and secondary procedures; admission and discharge status; demographic information such as gender, age, race, and median income for ZIP code; expected payment source; total charges; length of stay; and hospital characteristics. Although the data are limited, the NIS is the most reliable source of data on hospital admissions and discharges. Reliability is supported by agreement between the NIS, a telephone survey, and the National Health Interview Survey (a national, door-to-door survey). Invalid or inconsistent diagnostic codes are flagged.11,12

The pregnancy-related discharge records included in the sample from 2000 to 2002 were identified with the International Classification of Diseases, 9th Revision (ICD-9) and were classified as to whether they were an admission during pregnancy or postpartum. A pregnancy admission was defined as any discharge record with a pregnancy-related code (ICD-9 codes 630 to 648) or delivery code (ICD-9 codes 74 for cesarean delivery and 72, 73, 75, v27, or 650 to 659 for vaginal delivery). A postpartum admission was defined as any discharge record that included a postpartum diagnosis (ICD-9 codes 660 to 677) and did not also include a delivery code.

The ICD-9 code used for acute myocardial infarction was 410.4. For comorbidities, both the ICD-9 code for a particular condition in pregnancy and the general ICD-9 code for that condition were utilized. If the pregnancy-related code was not specific, it was not used.

Data were analyzed on the basis of the NIS sampling design, a multistaged sampling frame that consists of 3 stages. The 3 stages are strata (geographic region, urban versus rural location, teaching status, type of ownership, and bed size), hospitals within the strata, and individual discharges weighted by population counts and controlled for missing data. STATA 9.0 (Stata Corp LP, College Station, Tex) software, with its SVY (survey data) commands utilizing these 3 stages, were used for all analyses, both descriptive and inferential. Two-way χ² analyses were performed, to account for the complex survey design of the NIS. The 2-way χ² analyses yielded cell frequencies and their confidence intervals. Cell frequencies were divided by the number of deliveries to compute rates (ratios).

Logistic regression analyses were used to compute odds ratios (ORs) with 95% confidence intervals (CIs) for age, race, medical conditions, and obstetric complications. The statistically and clinically significant risk factors, from the analyses of single independent variables, were entered into a multivariable logistic regression model.

The authors had full access to the data and take full responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results

During the period from 2000 to 2002, there were 12 595 624 deliveries among 13 801 499 pregnancy-related discharges. Among the pregnancy-related discharges, there were 859 cases of acute myocardial infarction. Of these, 626 (73%) occurred during pregnancy, and 233 (27%) occurred postpartum, requiring readmission to the hospital (Table 1). The mean age was 33 years for those with acute myocardial infarction and 27 years for those without. The overall risk of pregnancy-related acute myocardial infarction was 6.2 (95% CI 3.0 to 9.4) per 100 000 deliveries. There were 44 deaths due to acute myocardial infarction, for a case fatality rate of 5.1% and a mortality rate of 0.35 per 100 000 deliveries.

The mean length of stay differed by location of acute myocardial infarction and ranged from 4.4 to 12.7 days (Table 2). Anterior-wall acute myocardial infarction, reported in 20% of cases, was more common than lateral or inferior-wall infarcts. Cardiac procedures are listed in Table 3. Among the women with acute myocardial infarction, 45% were reported to have undergone cardiac catheterization and 37% to have undergone angioplasty, stent placement, or bypass surgery. Fifty-five percent of white women and 53% of black women underwent catheterization, whereas only 11% of Hispanic women had the procedure.

The risk of acute myocardial infarction increased dramatically with age (Table 4) and was highest among women aged

<table>
<thead>
<tr>
<th>Location</th>
<th>ICD-9 Code</th>
<th>Percent of Cases</th>
<th>Mean Length of Stay, d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterolateral</td>
<td>410.0</td>
<td>5</td>
<td>12.7</td>
</tr>
<tr>
<td>Anterior</td>
<td>410.1</td>
<td>20</td>
<td>6.2</td>
</tr>
<tr>
<td>Inferolateral</td>
<td>410.2</td>
<td>3</td>
<td>5.7</td>
</tr>
<tr>
<td>Inferoposterior</td>
<td>410.3</td>
<td>2</td>
<td>4.4</td>
</tr>
<tr>
<td>Other inferior wall</td>
<td>410.4</td>
<td>15</td>
<td>8.2</td>
</tr>
<tr>
<td>Other lateral wall</td>
<td>410.5</td>
<td>2</td>
<td>4.7</td>
</tr>
<tr>
<td>True posterior wall</td>
<td>410.6</td>
<td>1</td>
<td>7.0</td>
</tr>
<tr>
<td>Subendocardial infarction</td>
<td>410.7</td>
<td>37</td>
<td>5.9</td>
</tr>
<tr>
<td>Other specified sites</td>
<td>410.8</td>
<td>1</td>
<td>4.9</td>
</tr>
<tr>
<td>Unspecified site</td>
<td>410.9</td>
<td>15</td>
<td>6.5</td>
</tr>
</tbody>
</table>
40 years and older (30.2 per 100,000 deliveries). The risk of acute myocardial infarction also differed by race or ethnicity (Table 4). Black women had the highest risk of myocardial infarction (11.4 per 100,000 deliveries) compared with Hispanic women (4.2 per 100,000 deliveries) or white women (7.6 per 100,000 deliveries). Within all 3 racial or ethnic groups, women aged 35 years and older had a higher risk of acute myocardial infarction (22.5 per 100,000 deliveries for white, 40.9 for black, and 14.6 for Hispanic women). For white women aged 35 years and older, the odds of having an acute myocardial infarction were 5 times higher (OR 5.1, 95% CI 3.1 to 8.4) than for their younger counterparts, but the highest risk of acute myocardial infarction was among black women aged 35 years and older, whose odds were 8 times higher (OR 8.4, 95% CI 4.2 to 16.9) than for white women younger than 35 years old.

Table 5 presents the single-variable analyses of various medical conditions and acute myocardial infarction. Medical conditions that were strongly associated with acute myocardial infarction included thrombophilia (OR 22.3, 95% CI 8.2 to 61.1), hypertension (OR 11.7, 95% CI 6.9 to 21.2), and smoking (OR 6.2, 95% CI 4.1 to 9.5). Other medical conditions that were significantly associated with acute myocardial infarction included anemia (OR 2.0, 95% CI 1.3 to 3.2), diabetes mellitus (OR 3.2, 95% CI 1.5 to 6.9), and migraine headaches (OR 4.2, 95% CI 1.0 to 17.1). There were no cases of myocardial infarction among pregnant women who also had a diagnosis of lupus or sickle cell disease.

Table 6 presents the single-variable analyses of obstetric complications and acute myocardial infarction. Complications of pregnancy that were significantly associated with acute myocardial infarction were preeclampsia (OR 1.6, 95% CI 1.0 to 2.5), postpartum hemorrhage (OR 2.1, 95% CI 1.1 to 3.9), transfusion (OR 7.4, 95% CI 3.3 to 16.2), postpartum infection (OR 2.5, 95% CI 1.0 to 5.9), and fluid and electrolyte imbalance (OR 10.9, 95% CI 6.3 to 18.9).

### Table 3. Cardiac Procedures

<table>
<thead>
<tr>
<th>Location</th>
<th>CPT Code</th>
<th>Frequency (% of All Cases)</th>
<th>Percent With Heart Catheterization Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart catheterization</td>
<td>37.21, 37.22, 37.23</td>
<td>386 (45)</td>
<td>...</td>
</tr>
<tr>
<td>Arterial catheterization</td>
<td>38.91</td>
<td>17 (2)</td>
<td>76</td>
</tr>
<tr>
<td>Angioplasty</td>
<td>36.01, 36.02, 36.05</td>
<td>135 (16)</td>
<td>87</td>
</tr>
<tr>
<td>Stent</td>
<td>36.06</td>
<td>127 (15)</td>
<td>89</td>
</tr>
<tr>
<td>Pulsation balloon</td>
<td>37.61</td>
<td>62 (7)</td>
<td>82</td>
</tr>
<tr>
<td>Bypass</td>
<td>36.11, 36.12, 36.13, 36.14, 36.15, 36.19</td>
<td>51 (6)</td>
<td>61</td>
</tr>
<tr>
<td>Defibrillator</td>
<td>35.2</td>
<td>20 (2)</td>
<td>20</td>
</tr>
</tbody>
</table>


### Table 4. Pregnancy-Related Acute Myocardial Infarction by Age and Race

<table>
<thead>
<tr>
<th>Demographic Variable</th>
<th>No. of Cases</th>
<th>Rate per 100 000 Deliveries (95% CI)</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (all races), y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20 (Referent)</td>
<td>14</td>
<td>1.0 (0.5–1.6)</td>
<td>1</td>
<td>...</td>
</tr>
<tr>
<td>20–24</td>
<td>70</td>
<td>2.3 (0.7–3.9)</td>
<td>2.4 (4.6–9.1)</td>
<td>0.20</td>
</tr>
<tr>
<td>25–29</td>
<td>133</td>
<td>4.0 (2.0–6.0)</td>
<td>4.3 (1.3–14.3)</td>
<td>0.02</td>
</tr>
<tr>
<td>30–34</td>
<td>265</td>
<td>8.8 (6.2–11.4)</td>
<td>9.5 (3.0–30.4)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>35–39</td>
<td>280</td>
<td>19.0 (13.4–24.6)</td>
<td>20.5 (6.4–65.4)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>≥40</td>
<td>97</td>
<td>30.2 (17.2–43.2)</td>
<td>31.6 (9.4–105.7)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White (referent)</td>
<td>377</td>
<td>7.6 (5.4–89.8)</td>
<td>1</td>
<td>...</td>
</tr>
<tr>
<td>Black</td>
<td>143</td>
<td>11.4 (6.9–15.9)</td>
<td>1.4 (0.9–2.2)</td>
<td>0.12</td>
</tr>
<tr>
<td>Hispanic</td>
<td>87</td>
<td>4.2 (2.3–6.1)</td>
<td>0.5 (0.3–0.9)</td>
<td>0.02</td>
</tr>
<tr>
<td>Age and race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White &lt;35 y (referent)</td>
<td>185</td>
<td>4.5 (2.6–6.4)</td>
<td>1</td>
<td>...</td>
</tr>
<tr>
<td>White ≥35 y</td>
<td>192</td>
<td>22.5 (14.9–30.1)</td>
<td>5.1 (3.1–8.4)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Black &lt;35 y</td>
<td>87</td>
<td>7.8 (3.5–12.1)</td>
<td>1.6 (0.9–3.0)</td>
<td>0.12</td>
</tr>
<tr>
<td>Black ≥35 y</td>
<td>56</td>
<td>40.9 (17.6–64.2)</td>
<td>8.4 (4.2–16.9)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hispanic &lt;35 y</td>
<td>56</td>
<td>3.0 (1.3–4.7)</td>
<td>0.7 (0.3–1.3)</td>
<td>0.25</td>
</tr>
<tr>
<td>Hispanic ≥35 y</td>
<td>30</td>
<td>14.6 (2.8–26.4)</td>
<td>3.2 (1.4–7.8)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>
Statistically and clinically significant risk factors, from the analyses of single independent variables, were entered into a multivariable logistic regression model. The results, presented in Table 7, revealed that when controlled for other risk factors, age, hypertension, thrombophilia, diabetes mellitus, smoking, transfusion, and postpartum infection remained significant, whereas race, anemia, preeclampsia, and postpartum hemorrhage did not.

**Discussion**

Our estimate of the incidence of pregnancy-related acute myocardial infarction, 6.2 (95% CI 3.0 to 9.4) per 100 000 deliveries, is in the broad range of 3 to 10 per 100 000 deliveries that has been reported previously. We found a higher incidence (6.2 versus 2.8 per 100 000 deliveries) and a lower case fatality rate (5.1% versus 7.3%), however, than a recent analysis that used data from a California database. Because the California estimate of incidence was based on data from 1991 to 2000, our estimate may reflect improved identification of cases or may reflect a true increase in the number of births to older women, who may have more cardiac risk factors. Between 2002 and 2003, the birth rate rose 6% for women aged 35 to 39 years and 5% for women aged 40 to 44 years. Another possible explanation for the higher incidence is better ascertainment of cases in the NIS database.

Our estimate of the case fatality rate, 5.1%, is not only lower than the California study estimate of 7.3% but is remarkably lower than the other previously reported rates of 21% and 37%. Because the California estimate was based on data from the previous decade, diagnosis and treatment may have improved over time. The other rates, derived from cases published before 1996 in the review by Roth and Elkayam and before 1985 in the review by Hankins et al, may reflect not only higher mortality from an earlier time period but also a bias toward reporting severe or fatal cases.

**TABLE 5. Medical Conditions* and the Risk of Pregnancy-Related Acute Myocardial Infarction**

<table>
<thead>
<tr>
<th>Medical Condition</th>
<th>ICD-9 Codes</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>401–405</td>
<td>11.7 (6.9–21.2)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Thrombophilia</td>
<td>273.8, 286.9, V12.51, 286.5, 289.8, 289.9, 795.79</td>
<td>22.3 (8.2–61.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Anemia</td>
<td>648.2, 285.0</td>
<td>2.0 (1.3–3.2)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>648.8, 250</td>
<td>3.2 (1.5–6.9)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Obesity</td>
<td>278.0</td>
<td>2.0 (0.8–4.9)</td>
<td>0.11</td>
</tr>
<tr>
<td>Migraine headaches</td>
<td>346.0, 346.1</td>
<td>4.2 (1.0–17.1)</td>
<td>0.05</td>
</tr>
<tr>
<td>Alcohol and substance abuse</td>
<td>648.3, 305.0, 305.2, 305.3, 305.5, 305.6, 305.7</td>
<td>1.9 (0.8–4.3)</td>
<td>0.15</td>
</tr>
<tr>
<td>Smoking</td>
<td>305.1, V15.82</td>
<td>6.2 (4.1–9.5)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

*There were no cases of acute myocardial infarction among women who also had a diagnosis of thrombocytopenia, sickle cell disease, or lupus, conditions that were also queried.

**TABLE 6. Obstetric Complications* and the Risk of Pregnancy-Related Acute Myocardial Infarction**

<table>
<thead>
<tr>
<th>Pregnancy or Delivery Complication</th>
<th>ICD-9 Codes</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm labor</td>
<td>644</td>
<td>0.6 (0.3–1.2)</td>
<td>0.13</td>
</tr>
<tr>
<td>Antepartum hemorrhage</td>
<td>640.9, 641.1, 641.2, 641.3, 641.8, 641.9,</td>
<td>0.9 (0.3–2.4)</td>
<td>0.84</td>
</tr>
<tr>
<td>Preeclampsia, eclampsia, and gestational hypertension</td>
<td>642</td>
<td>1.6 (1.0–2.5)</td>
<td>0.03</td>
</tr>
<tr>
<td>Postpartum hemorrhage</td>
<td>666, 667, 669.1</td>
<td>2.1 (1.1–3.9)</td>
<td>0.02</td>
</tr>
<tr>
<td>Transfusion</td>
<td>CPT codes 9900, 9902, 9904, 9907</td>
<td>7.4 (3.3–16.2)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Postpartum infection</td>
<td>670, 672</td>
<td>2.5 (1.0–5.9)</td>
<td>0.04</td>
</tr>
<tr>
<td>Fluid and electrolyte imbalance</td>
<td>276</td>
<td>10.9 (6.3–18.9)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>


*There were no cases of acute myocardial infarction among women who also had a diagnosis of multiple gestation or hyperemesis, conditions that were also queried.
There are several limitations to the present analysis. Similar to the recent analysis using cases from the California database, the present study data are limited to information derived from discharge record abstractions. Detailed and precise information on diagnosis and treatment are not available to validate acute myocardial infarction and other comorbidities. Additionally, the discharge abstracts do not allow for attribution of the timing of events. Therefore, it is possible that some of the conditions, such as fluid and electrolyte imbalance, occurred after acute myocardial infarction and not before. Because the discharge abstracts are de-identified and patients are not tracked, the 24 patients (3% of the total) who were transferred to another NIS facility may have been counted twice, which would result in a slight overestimation of the number of cases. Another factor that could have resulted in a slight overestimate in the rate of acute myocardial infarction is the exclusion from the denominator of the 1% of deliveries that would have occurred outside of the hospital. Alternatively, patients who died of acute myocardial infarction outside of the hospital would not have been counted at all, which would result in an underestimate in both the incidence and mortality.

We do not have the incidence of acute myocardial infarction for women who were not pregnant. Petitti et al. published the incidence of myocardial infarction among reproductive-aged women in a large health maintenance organization. Using the age-specific rates of myocardial infarction per 100 000 women-years derived from that study and applying them to the age distribution of the women in the present study, we would have expected to find 250 myocardial infarctions as opposed to the 859 found. Therefore, the risk of acute myocardial infarction appears to be approximately 3 to 4 times higher in pregnancy.

We found that anterior-wall acute myocardial infarction was more common than lateral or inferior-wall infarcts. In a review of 150 published cases of acute myocardial infarction in pregnancy, a preponderance of anterior-wall infarcts was noted. Interestingly, in a series of 16 women younger than 45 years of age who experienced acute myocardial infarction and were also oral contraceptive users, either normal coronary angiography or single-vessel disease, mainly affecting the left anterior descending artery, was observed. These findings may suggest a common mechanism in acute myocardial infarction associated with pregnancy or oral contraceptive use.

The number of cardiac catheterizations may have been underreported, because only 60% to 90% of women who were reported to have undergone an intervention were also reported to have had a catheterization. Nonetheless, fewer than half of the women were reported to have undergone cardiac catheterization. This figure is low and may imply that the diagnosis of acute myocardial infarction is not suspected as often as it should be in this population, or that there is a reluctance to intervene, even if the diagnosis is suspected. Of those who were reported to have undergone catheterization, however, 313 of 386, or 81%, a high percentage, had significant disease that required a corrective procedure. Unlike other studies that have reported a discrepancy between the rate of catheterization for white versus black patients, the rate of catheterization for black women (53%) was essentially the same as the rate for white women (55%) but was remarkably lower for Hispanic women (11%). This discrepancy for Hispanic patients warrants further investigation.

We found that age >35 years and black race were significant risk factors for pregnancy-related myocardial infarction. Because the risk of myocardial infarction increases with age and is higher among black women, the increased risk of pregnancy-related myocardial infarction among black women and women aged 35 years and older is not surprising. The magnitude of the increased risk, with odds >5-fold higher for black women aged 35 years and older, has not been appreciated previously. The multivariable analysis, however, eliminated race as a risk factor, which suggests that the increased incidence among black women is explained by an increased prevalence of other risk factors. Cardiovascular risk factors that are reported to be more prevalent among black women include hypertension, physical inactivity, obesity, diabetes mellitus, and an increased risk of thrombosis.

In accord with previous publications, we found the known cardiac risk factors of hypertension, diabetes mellitus, and smoking to be associated with pregnancy-related acute myocardial infarction. The magnitude of the risk associated with smoking, with odds 8-fold higher in the multivariable analysis, has not been appreciated previously. Although

### TABLE 7. Multivariable Analysis of Significant Risk Factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20 (Referent)</td>
<td>1</td>
<td>...</td>
</tr>
<tr>
<td>20–24</td>
<td>1.9 (0.5–7.7)</td>
<td>0.37</td>
</tr>
<tr>
<td>25–29</td>
<td>3.3 (0.9–11.3)</td>
<td>0.06</td>
</tr>
<tr>
<td>30–34</td>
<td>6.7 (2.0–22.2)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>35–39</td>
<td>16.0 (4.9–51.7)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>≥40</td>
<td>15.2 (4.2–54.8)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White (referent)</td>
<td>1</td>
<td>...</td>
</tr>
<tr>
<td>Black</td>
<td>1.4 (0.9–2.3)</td>
<td>0.17</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0.8 (0.5–1.3)</td>
<td>0.42</td>
</tr>
<tr>
<td>Medical condition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>21.7 (6.8–69.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Thrombophilia</td>
<td>25.8 (9.2–71.2)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Anemia</td>
<td>1.6 (0.9–2.9)</td>
<td>0.14</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>3.6 (1.5–9.3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Smoking</td>
<td>8.4 (5.4–12.9)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Pregnancy or delivery complication</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>0.1 (0.0–0.6)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Postpartum hemorrhage</td>
<td>1.8 (0.8–3.8)</td>
<td>0.14</td>
</tr>
<tr>
<td>Transfusion</td>
<td>5.1 (2.0–12.7)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Postpartum infection</td>
<td>3.2 (1.2–10.1)</td>
<td>0.02</td>
</tr>
</tbody>
</table>
female smokers are reported to have a 2-fold increased risk of myocardial infarction. Female smokers taking oral contraceptives are reported to have a 7- to 100-fold increased risk of myocardial infarction. The increased levels of estrogen and progesterone in pregnancy, like the increased levels of estrogen and progestins associated with oral contraceptives, may compound the risk of acute myocardial infarction among women who smoke. Vascular reactivity, which is believed to be increased during pregnancy, may also compound the risk. Although the effects of smoking on both maternal health and pregnancy outcome are recognized, the fact that pregnancy further increases the cardiac risks associated with smoking has not been emphasized. This should not be ignored, because the risks associated with smoking are real and preventable.

Although recognized as a risk factor for myocardial infarction in young women, thrombophilia has not been reported as a risk factor for acute myocardial infarction in pregnancy. That thrombophilia would be a risk factor is not surprising, because the hypercoagulability of pregnancy, which is further increased in the presence of thrombophilia, is considered a risk factor for acute myocardial infarction in pregnancy. It is possible, however, that the diagnosis of thrombophilia was more common among the women who experienced acute myocardial infarction only because they were more likely to have been tested.

Migraine headaches, not usually thought of as a risk factor for myocardial infarction, were a risk factor in the present study, with an OR of 4.2 (95% CI 1.0 to 17.1). One possible explanation is that migraine headaches may be a manifestation of a “generalized vasospastic disorder” that includes susceptibility to coronary artery spasm. Another possible explanation is that migraine headaches were more likely to be diagnosed by treating physicians who were suspicious of vasospasm.

In the analysis of single independent variables, we found that thrombophilia was a significant risk factor for acute myocardial infarction, including preeclampsia, postpartum hemorrhage, transfusion, and postpartum infection. Ladner et al also found preeclampsia to be a risk factor. Preeclampsia, particularly in association with preterm delivery, has been identified as a risk factor for myocardial infarction later in life. Endothelial dysfunction, which accompanies preeclampsia and contributes to the pathogenesis of cardiovascular disease later in life, has been found to persist in women with a history of preeclampsia for up to 1 year postpartum. In the multivariable analysis, before race and hypertension were added to the logistic regression model, preeclampsia remained a significant risk factor, with an OR of 1.6. When race was added to the model, however, the OR dropped to 0.7, and when hypertension was added, it dropped further. Therefore, in the multivariable analysis, preeclampsia was eliminated as a risk factor. Hypertension, a risk factor for preeclampsia and a condition more prevalent among black women, appears to be the explanation for the association between pregnancy-related acute myocardial infarction and either preeclampsia or black race.

Hemorrhage results in a hypercoagulable response, which may increase the risk of coronary artery thrombosis. Although postpartum hemorrhage did not remain a significant risk factor in the multivariable analysis, transfusion, a marker of severe hemorrhage, did, with odds >5-fold. A possible etiologic factor in acute myocardial infarction associated with severe hemorrhage is the use of methylergonovine maleate to treat uterine atony. Methylergonovine has been used diagnostically to provoke coronary vasospasm, and acute myocardial infarction has resulted as a complication. Not surprisingly, there are multiple case reports of women who experienced acute myocardial infarction after receiving methylergonovine. The use of methylergonovine to treat uterine atony, or a hypercoagulable response to hemorrhage, or even hypotension from blood loss could partially explain the increased risk of acute myocardial infarction associated with transfusion. Transfusion itself, however, may be a risk factor. Storage and preservation of red blood cells increases their tendency to aggregate, possibly increasing the risk of coronary artery thrombosis.

Postpartum infection increased the risk of acute myocardial infarction, with odds of 2- to 3-fold. Although chronic infection and long-standing inflammation are recognized risk factors for acute myocardial infarction, acute infection is not generally considered a risk factor but has been suggested.

We found that several of the risk factors for pregnancy-related acute myocardial infarction are unique to pregnancy, which suggests that some of the mechanisms may be unique as well. Coronary artery dissection is a rare cause of acute myocardial infarction. In one series, however, 20% of cases involved women who had recently delivered. Postpartum degeneration of the ground substance of the connective tissue in the intima and media of the coronary arteries has been proposed as a mechanism. A susceptibility to coronary artery dissection in pregnancy may explain why, in the present study, hypertension was so strongly associated with acute myocardial infarction. Hypertension may further damage blood vessels already weakened by hemodynamic stress or altered by other factors associated with pregnancy. In a review of 125 reported cases of pregnancy-related acute myocardial infarction, information on coronary artery anatomy was available in 68. Coronary artery dissection was found in 16%, thrombus without atherosclerotic disease in 21%, normal coronary arteries in 29%, and atherosclerosis with or without intracoronary thrombus in 43% of those cases. In contrast, the vast majority of cases of acute myocardial infarction outside of pregnancy are due to coronary thrombosis overlying a disrupted atherosclerotic plaque.

In summary, although acute myocardial infarction in pregnancy and the puerperium is rare, pregnancy does confer an increased risk. The risk increases dramatically with age and is significantly higher among black women, women with certain medical conditions or obstetric complications, and smokers. Understanding the cause of pregnancy-related acute myocardial infarction and identification of women at risk are the first steps toward
prevention. Screening and preventive measures should focus on women with advanced maternal age, known coronary risk factors, thrombophilia, or postpartum complications and women who smoke.

Acknowledgments
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Disclosures
None.

References
40. Sutaria N, O’Toole L, Northridge D. Postpartum acute MI following routine ergometrine administration treated successfully by primary PTCA. Heart. 2000;83:97–98.
Acute myocardial infarction is a rare event among women of childbearing age. The incidence among women who are not pregnant is 5 per 100,000 women-years, but among women who are pregnant, the risk is increased 3- to 4-fold, with a risk of death of 0.3 per 100,000 deliveries. Combined with the risk of death due to stroke, which is 1.4 per 100,000 deliveries, the risk of death due to arterial thromboembolism in pregnancy exceeds the risk from venous thromboembolism by 50%. Considerable attention has been directed to reducing the risk of pregnancy-related venous thromboembolism, but similar efforts have not been directed to reducing the risk of arterial thromboembolism, possibly because events are rare and risk factors are not well understood. Our study has helped elucidate the risk factors for acute myocardial infarction in pregnancy. Compared with venous thromboembolism, age, hypertension, and smoking are much more important. The risk of venous thromboembolism is not quite doubled for women aged 40 years and older compared with women <20 years of age, but the risk of acute myocardial infarction is increased 30-fold. Hypertension doubles the risk of venous thromboembolism but increases the risk of acute myocardial infarction 20-fold. Smoking doubles the risk of venous thromboembolism but increases the risk of acute myocardial infarction 8-fold. Currently, the rate of maternal mortality is 7.5 deaths per 100,000 live births, whereas the target rate for the United States’ Healthy People 2010 initiative is 3.3 per 100,000 live births. Reducing the incidence of pregnancy-related acute myocardial infarction might help us achieve our goal.
Acute Myocardial Infarction in Pregnancy: A United States Population-Based Study
Andra H. James, Margaret G. Jamison, Mimi S. Biswas, Leo R. Brancazio, Geeta K. Swamy
and Evan R. Myers

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