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Population-based study of risk factors for severe maternal morbidity

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Summary

Background—Severe maternal morbidity (SMM) is a serious health condition potentially resulting in death without immediate medical attention, including organ failure, obstetric shock, and elcampsia. SMM affects 20,000 US women every year; however, few population-based studies have examined SMM risk factors.

Methods—We conducted a population-based case-control study linking birth certificate and hospital discharge data from Washington State (1987–2008), identifying 9,485 women with an antepartum, intrapartum, or postpartum SMM with ≥3-day hospitalization or transfer from another facility and 41,112 random controls. Maternal age, race, smoking during pregnancy, parity, preexisting medical condition, multiple birth, prior cesarean delivery, and BMI were assessed as risk factors with logistic regression to estimate odds ratios (OR) and 95% confidence intervals (CI), adjusted for education and delivery payer source.

Results—Older women [35–39: OR 1.65 CI 1.52, 1.79; 40+: OR 2.48 CI 2.16, 2.81], non-white women [Black: OR 1.82 CI 1.64, 2.01; American Indian: OR 1.52 CI 1.32, 1.73; Asian/Pacific Islander: OR 1.30 CI 1.19, 1.41; Hispanic: OR 1.17 CI 1.07, 1.27], and women at parity extremes [OR 1.83 CI 1.72, 1.95, nulliparous; OR 1.34 CI 1.23, 1.45, parity 3+] were at greater risk of SMM. Women with a preexisting medical condition [OR 2.10 CI 1.88, 2.33], a multiple birth [OR 2.54 CI 2.26, 2.82], and a prior cesarean delivery [OR 2.08 CI 1.93, 2.23] were also at increased risk.

Conclusion—The risk factors identified are not modifiable at the individual level; therefore, provider and system-level factors may be the most appropriate target for preventing SMM.

Introduction

The overall quality of maternal health care has traditionally been measured by maternal mortality.[1] However, in the United States and other industrialized countries where maternal death is rare, severe maternal morbidity (SMM), or “near miss”, has been utilized as a new indicator of the quality of maternal health.[2–5] SMM encompasses a broad category of serious health complications (organ failure, obstetric shock, pulmonary embolism, seizure) that would likely result in death without immediate medical attention and can occur

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antepartum, intrapartum, or postpartum.[3,4] These life-threatening conditions often involve separation of the mother from her newborn, lengthy hospital stays, significant health care costs, emotional distress to family members, and interference in bonding between a mother and her newborn.

SMM during delivery hospitalization was estimated to occur in 5.1 of every 1,000 U.S. deliveries from 1991–1993, affecting approximately 20,000 women annually.[3] Rates of SMM are increasing, with 4.5 per 1,000 deliveries in 1991–1994 and 5.9 per 1,000 deliveries in 1999–2003.[3] Only one population-based study has been conducted to examine risk factors for SMM in the US, and a higher incidence of SMM was observed in deliveries in the South or Northeast, in Black women, and in women <20 or >40 years of age.[3] This analysis did not include SMM that occurred antepartum and postpartum, which could have impacted the observed associations between SMM and various exposures. Although other population-based studies have been conducted in developed countries outside of the US, such as Canada[5,6] and the Netherlands[7], characteristics of pregnancy and delivery differ by region; therefore, these results may not be applicable to US populations. Factors associated with increasing risk of SMM reported in these studies included age ≥35 years, BMI≥25, nulliparity, prior cesarean delivery, induction of labor, use of ventouse/forceps, cesarean delivery, and multiple gestations.

The lack of population-based studies examining risk factors for SMM in the US indicates a gap in knowledge in the field of maternal and child health. A better understanding of these risk factors during pregnancy (antepartum), delivery (intrapartum), and postpartum may help identify areas for modification or improvement in the delivery of obstetric healthcare for high risk mothers and their infants. The purpose of this study was to identify risk factors for SMM occurring antepartum, intrapartum, and postpartum.

Methods

We conducted a population-based case-control study linking birth certificate records to hospital discharge data from the Comprehensive Hospital Abstract Reporting System (CHARS) for all Washington State singleton and multiple births from 1987–2008. The methods for linkage have been previously reported[8], and 95% of birth certificates are successfully linked with CHARS records via this approach.[9] The protocol was approved by the Institutional Review Board at the University of Washington.

The case definition for SMM was modified from Callaghan et al.[3] Cases were defined as all women who had a hospitalization antepartum, intrapartum, or up to 90 days postpartum that included one or more of the ICD-9-CM codes listed in Appendix 1 and had a stay of at least three days or were transferred from another facility, as identified by the CHARS record. The SMM diagnosis-based codes included those for acute renal, liver, and respiratory failure; obstetric shock; cerebrovascular accident; pulmonary and amniotic fluid embolism; eclampsia; septicemia; and complications of anesthesia. Procedure-based codes included those for cardiac events and procedures (heart failure, cardiomyopathy, cardiac arrest, acute myocardial infarction, and conversion of cardiac rhythm); mechanical ventilation; transfusion; hysterectomy; and invasive hemodynamic monitoring. Since a shorter length of stay without transfer would be inconsistent with a severe morbidity diagnosis, women with an eligible ICD-9 code but with a shorter stay without a transfer were not eligible as cases. Controls were women who did not have an antepartum, intrapartum, or postpartum hospitalization with a three-day stay or transfer that included one of the selected ICD-9 codes from the case definition. If a woman had a hospitalization that included a selected ICD-9 code from the case definition, she was eligible for inclusion if the hospital stay was less than three days and she was not transferred from another facility; women transferred

from another facility or who had a stay of three days or more were also eligible as controls as long as they did not have one of the selected ICD-9 codes. Four controls were randomly selected per case and frequency matched by year of delivery. Controls and cases included women with singleton and multiple births.

We examined the number and percentage of all cases that qualified for each diagnosis or procedure. Because some women had more than one SMM within a single hospitalization or had multiple qualifying hospitalizations, some appeared in more than one category of diagnosis/procedure. In our analyses of the selected risk factors for SMM, women with more than one pregnancy were included, accounting for repeated measures; however, only one SMM *per pregnancy* was included.

The distribution of maternal demographic and obstetric characteristics among cases and controls was examined. Maternal characteristics included age, race, level of education, marital status, maternal smoking during pregnancy, payer source, parity, and preexisting conditions. Adequacy of prenatal care as measured by the Kotelchuck index[10], delivery method, having a multiple birth, delivering a low birthweight infant (<2500 but ≥500 grams), and preterm delivery (≥20 weeks but <37 weeks gestation) comprised the obstetric characteristics examined. All characteristics except for preexisting conditions and payer source were identified exclusively from birth certificate data. Payer source was identified from CHARS, and any woman for whom Medicaid/Medicare was listed as either one of the payment source variables was classified as having Medicaid/Medicare. A preexisting condition was identified from CHARS and defined as a hospitalization within the five years prior to conception that included an ICD-9 code for any one of the selected conditions in Table 1.

Body mass index (BMI) and income were potentially relevant to our analyses; however, because these values were missing in 40% of subjects, we used multiple imputation by chained equations to generate15 complete datasets to replace missing with plausible values.[11] Logistic regression analyses including income and BMI (Underweight: <18.5 kg/m^2, Normal: 18.5–24.99, Overweight: 25–25.99, Obese: ≥30) were performed using the pooled estimates from these imputed datasets; results are presented for imputed analyses.

The association between SMM and potential risk factors was evaluated using multiple logistic regression to estimate odds ratios (OR) and 95% confidence intervals (CI) using robust standard error estimates clustered on subject to account for multiple pregnancies per woman. Risk factors, determined *a priori,* were age, race, maternal smoking during pregnancy, parity, preexisting conditions, multiple birth, prior cesarean delivery, and BMI. Confounding by payer source, marital status, income, and education was assessed for the model because they were associated with one or more of the risk factors and also SMM, but were not of primary interest as risk factors. Ultimately, education and payer source were included in the model (in addition to all risk factors) because adjustment for these confounders altered the crude odds ratios substantially. Both multiple birth and the presence of a preexisting condition were assessed for an interaction with age for SMM; however, we found no evidence of effect modification (Wald p-value: 0.15 and 0.39, respectively). All analyses were performed using Stata 10.0 (Stata Corporation, College Station, TX).

Results

Between 1987 and 2008, 9,485 women had one or more SMM in Washington State. Women with SMM were more likely to be older, non-white race/ethnicity, unmarried, have a lower level of education, at the extremes of parity, to have a preexisting medical condition, and to receive Medicaid/Medicare (Table 2) compared to controls. Women with SMM were more

likely to have a multiple birth, to deliver by cesarean, to deliver a low birthweight or preterm infant, and to have received intensive prenatal care as compared to controls.

The majority of cases had an SMM at the time of delivery (73.7%, n=6990 vs. 17.9%, n=1694 postpartum and 11.0%, n=1039 antepartum), although a small number of cases (233) had SMM during more than one time period, and five women had SMM at all three time periods (data not shown). Receipt of a blood transfusion was the most common qualifying SMM and occurred in nearly half of all cases, followed by hysterectomy (11.2%), and respiratory failure (10.9%) (Table 3). The mean length of hospital stay for the delivery hospitalization was 5.6 days for cases and 2.2 days for controls. For the delivery hospitalization, 3.4% of cases and 0.5% of controls were transferred from another facility.

Older women were at greater risk of SMM as compared to women ages 25–29 (ages 30–35: OR 1.17 [CI 1.09, 1.25]; ages 35–39: OR 1.65 [CI 1.52, 1.79]; ages 40+: OR 2.48 [CI 2.16, 2.81]) (Table 4). Non-white women were also at increased risk of SMM as compared to white women, with Black and American Indian women at highest risk (OR 1.82 [CI 1.64, 2.01]; OR 1.52 [CI 1.32–1.73], respectively), followed by Asian/Pacific Islander women (OR 1.30 [CI 1.19, 1.41]) and Hispanic women (OR 1.17 [CI 1.07, 1.27]). Women at the extremes of parity were at increased risk of SMM, with nulliparous women at 1.8 times the risk [CI 1.72, 1.95], women with two prior deliveries at 1.1 times the risk [CI 1.02, 1.19], and women with three or more prior deliveries at 1.3 times the risk [CI 1.23, 1.45], as compared to women with one prior delivery. The distribution of qualifying preexisting conditions varied among cases and controls, with almost every condition being more common among cases (Table 1). Women with a preexisting condition were at more than two times the risk of SMM as women without a preexisting condition [CI 1.88, 2.33]; and women with a multiple birth were at 2.5 times the risk [CI 2.26, 2.82] of SMM as women with a singleton birth. Women with a prior cesarean delivery were also at more than two times the risk [CI 1.93, 2.23] of SMM as compared to those without a prior cesarean delivery. Women who were underweight or obese were also at slightly increased risk of SMM as compared to women of normal BMI.

Discussion

In our population-based case-control study, we found the majority of cases had an SMM intrapartum, and the most common SMM were transfusion, hysterectomy, and respiratory failure. Maternal age of 40 years and older, the presence of a preexisting medical condition, a multiple birth, and a prior cesarean delivery were the strongest risk factors for SMM. In addition, nulliparity and being a minority, particularly Black, were also strong risk factors for SMM.

Our results are consistent with a large US population-based study in which transfusion was also the most common SMM (48.4%), followed by eclampsia (14.0%) and hysterectomy (11.9%)[3]; notably eclampsia was observed in only 7.8% of our cases. Another population-based study from the Netherlands combined antepartum, intrapartum, and postpartum SMM and found the largest SMM rates for eclampsia, major obstetric hemorrhage, and uterine rupture, respectively;[7] a population-based Canadian study reported rates of intrapartum SMM were largest for transfusion, puerperal sepsis, hysterectomy, and cardiac events.[5] Our study did not assess severe hemorrhage and uterine rupture as unique SMM categories, although transfusion is a surrogate for severe hemorrhage and uterine rupture commonly is associated with hysterectomy.

Women with a preexisting condition, as compared to those without, were at two times the risk of SMM. This observation is similar to two case-control studies in which women with a

history of a chronic medical condition[12] were at two times the risk of SMM, and women with a previous or preexisting illness[13] were 2.5 times more likely to have an ICU admission during pregnancy. Although the case definitions and ascertainment methods differed in these studies, preexisting conditions were consistently identified as strong risk factors for SMM. It has been well established that conditions such as those listed in Table 1 lead to a number of adverse health and pregnancy outcomes.[14,15]

We also observed that women with a multiple birth were at 2.5 times the risk of SMM as compared to women with a singleton birth. Prior studies note that the risk of SMM in women with a multiple birth is 2–5 times greater than in women with singleton births,[5,7,13,16] most likely related to increased risks of hypertensive disease, diabetes, hemorrhage and operative vaginal and cesarean deliveries.[17–21] Additionally, we found that prior cesarean delivery was strongly associated with SMM. Prior cesarean delivery is known to be associated with preeclampsia, placenta previa, placenta accrete, placental abruption,[22] uterine rupture, postpartum infection, transfusion, and admission to the intensive care unit.[23]

Black race was identified as another strong risk factor for SMM, which is consistent with previous studies noting 2 to 7.5 times the risk of SMM among Black women as compared to white women.[3,24,25] This increased risk may result from a greater prevalence of disease due to genetic factors or underlying poor health, more severe disease, less access to prenatal care, or a combination of these factors.[26] Hypertension and gestational diabetes (GDM), differ by race and ethnicity and the severity of these morbidities may be increased in minority women.[27] Maternal obesity in pregnancy also differs by race/ethnicity, with minorities at increased risk of overweight and obesity, which is associated with a number of pregnancy complications.[27] However, we simultaneously controlled for factors that could confound the association between race and SMM [preexisting conditions, BMI, other measures of SES (education and payer source)] and the increased risk associated with maternal race/ethnicity persisted, indicating that this finding is likely not an artifact of improper adjustment. These results may reflect genetic differences or disparities in access to and utilization of medical care.

Lastly, we observed an increased risk of SMM at parity extremes. Nulliparous women had nearly two times the risk of SMM as women with one prior delivery. This finding has been observed in other studies[12,28] but not consistently.[29] Nulliparous women have been observed to be at increased risk of GDM, pregnancy-induced hypertension, premature rupture of membranes (>24 hours), postpartum hemorrhage, and third-degree tears.[30] We also observed an increased risk for multiparous women with three or more prior births; pregnancy complications and adverse pregnancy outcomes are associated with increasing parity.[31,32]

Some of the important demographic risk factors for SMM (also classified as “near miss”) identified by our study are also risk factors for maternal mortality. In a study of maternal deaths in New York City, women ≥35 years were at increased risk of maternal mortality as compared to women 15–19.[33] Another US study noted increasing parity was associated with risk of maternal mortality.[34] The risk for pregnancy-related death was observed to increase with increasing live birth order.

Our study had several limitations. As discussed by Callaghan et al, conventional obstetric ICD-9 codes often are not specific and do not provide information about the severity of the condition, both of which are limitations to identifying “near-miss” morbidities.[3] However, our case definition focused on codes that could identify severe complications by using codes for conditions/procedures occurring as a result of only *severe* complications (e.g. cerebrovascular accident, blood transfusion, or artificial ventilation in the case of severe

preeclampsia).[3] Although the selected SMM codes could still result in misclassification of cases as controls, the rarity of these morbidities and the very large number of controls in this study would likely result in this misclassification having little or no impact on our results. We further strengthened our definition by restricting cases to women who had a hospital stay of at least three days or who were transferred from another facility, as a shorter stay without transfer would be inconsistent with the severity of a true SMM. In addition, although our definition of preexisting conditions using hospitalizations within the five years prior to the index delivery may have not captured all women with these conditions, using this method ensured the condition was present before the pregnancy and was significant enough to result in hospitalization. Compared to using birth certificate data, hospital discharge data are more accurate for obtaining preexisting medical conditions.[35] An additional limitation of our preexisting condition definition is that women who delivered before 1992 had less than five years of data because CHARS became available in 1987. Nevertheless, because this information would be missing equally for cases and controls, misclassification is likely non-differential and would attenuate observed associations. We performed a sensitivity analysis with an alternate definition of preexisting conditions derived from birth certificates and results were almost identical.

Although this study investigated risk factors at the level of the patient, both provider and health care system factors may also play a critical role in the development of SMM.[26] In a study investigating the preventability of maternal mortality and severe morbidity, 45% of near-miss morbidities were deemed preventable; provider factors were identified as the source of preventability in approximately 93% of these instances, including failure to identify high-risk status, lack of referral to a tertiary care center, and in the greatest proportion incomplete or inappropriate management.[24] Patient factors only accounted for 13% and system factors 47% of the cases of preventable near-miss morbidities. The majority of risk factors we identified cannot be modified at the level of the individual, including age, race, parity, multiple birth, and prior cesarean delivery, which suggests that improvements at the provider or system-level may be the key to reducing SMM. For example, if preeclampsia is identified early and proper treatment is initiated, progression to eclampsia is rare; however 738 women in our population were diagnosed with eclampsia, likely indicating some error in identification or management. Further studies investigating the specific provider and system factors that contribute to preventable SMM are necessary develop interventions that reduce the risk of SMM.

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Table 1

Distribution of Preexisting Medical Conditions Among Women With and Without Severe Maternal Morbidity

		Cases		Controls	
		N=9485		N=41112	
	ICD-9 code	n[a]	%[a]	n[a]	%[a]
Established diabetes	250.0–250.93	68	0.72	71	0.17
Chronic hypertension	401.0–405.99	53	0.56	65	0.16
Cardiac Conditions	412, 413, 414.00–.05, 414.8–.9, 416, 424–426, 428.22, 428.32, 428.42	132	1.39	70	0.17
Renal Conditions	581, 582, 585–588, 590.00– .01, 595.1–.2	69	0.73	55	0.13
Pulmonary Conditions	491–496, 500, 502–505, 501, 515, 516, 517	135	1.42	238	0.58
Skin and Subcutaneous Tissues	695.4, 699	0		0	
Diseases of the Musculoskeletal System and Connective Tissue	710, 710.1, 710.2, 712.0–.9, 714.0–.9, 720, 732.0–.6	31	0.33	19	0.05
Diseases of the Digestive System	555.0–.2, .9	8	0.08	17	0.04
Diseases of the Blood and All Blood-Forming Organs	281–289	128	1.35	157	0.38
Mental Disorders	290–305.0, 305.2–319	328	3.46	680	1.65
Other Disorders of the Central Nervous System	340–346	55	0.58	67	0.16
Chronic Rheumatic Heart Disease	393–398	10	0.11	3	0.01
Diseases of the Arteries, Arterioles, and Capillaries	444, 445	3	0.03	0	
Diseases of Veins and Lymphatics, and Other Diseases of the Circulatory System	453.0–.4, .8, .9	10	0.11	12	0.03

[a]Numbers exceed totals and percents exceed 100% due to multiple qualifying conditions

Table 2

Characteristics of Women With and Without Severe Maternal Morbidity, Washington State, 1987–2008

	Cases (N=9485)		Controls (N=41112)	
	n[a]	%[b]	n[a]	%[b]
Maternal age				
<20	1166	12.3	3990	9.7
20–24	2132	22.5	9753	23.7
25–29	2299	24.2	11779	28.7
30–34	2069	21.8	9887	24.1
35–39	1379	14.5	4725	11.5
40+	438	4.6	970	2.4
Race				
White	6103	66.2	29999	74.9
Black	670	7.3	1535	3.8
American Indian	355	3.9	944	2.4
Asian/Pacific Islander	840	9.1	3191	8.0
Hispanic	1248	13.5	4382	10.9
Education				
Less than high school	1843	24.8	6242	18.9
High school	2167	29.1	9128	27.7
Some college/technical school	1983	26.7	9121	27.7
Graduated college	924	12.4	5385	16.3
Grad school or beyond	522	7.0	3066	9.3
Married[c]	5872	62.3	29154	71.1
Smoked during pregnancy[d]	1443	16.0	5532	13.9
Medicare/Medicaid[e]	4650	49.0	15591	37.9
Parity (at conception)				
0	4217	45.7	16506	41.1
1	2240	24.3	13092	32.6
2	1369	14.8	6317	15.7
3	754	8.2	2525	6.3
4+	643	7.0	1760	4.4
Preexisting condition	656	6.9	1220	3.0
Adequacy of prenatal care				
Inadequate	1021	17.8	3634	13.5
Intermediate	960	16.7	5928	22.1
Adequate	2030	35.3	12203	45.4
Intensive	1737	30.2	5092	19.0
Delivery method				
Vaginal	3378	36.5	28172	68.9
Vaginal with Forceps or Vacuum	664	7.2	3375	8.2

	Cases (N=9485)		Controls (N=41112)	
	n[a]	%[b]	n[a]	%[b]
Cesarean Section	5224	56.4	9363	22.9
Multiple birth	587	6.2	1116	2.7
Low birthweight[f]	2203	23.6	2382	5.8
Preterm delivery[g]	2732	29.2	3262	8.0
Transfer from another facility[h]	323	3.4	201	0.5

[a] May not add to totals due to missing information;

[b] Percent of non-missing observations;

[c] 60 cases, 113 controls missing data;

[d] 461 cases, 1327 controls missing data;

[e] 3 controls missing data;

[f] 133 cases, 180 controls missing data;

[g] 1158 cases and 4760 controls missing data;

[h] 1 case missing data

Table 3

Distribution of Severe Maternal Morbidity-Qualifying Diagnosis and Procedures, Washington State 1987–2008

	N=9485	
	n[a]	%[a]
Diagnosis		
Acute Renal Failure	322	3.4
Liver Failure	23	0.2
Respiratory Failure	1035	10.9
Obstetric Shock	106	1.1
Cerebrovascular Accident	407	4.3
Pulmonary Embolism	444	4.7
Amniotic Fluid Embolism	63	0.7
Eclampsia	738	7.8
Septicemia	780	8.2
Complications of Anesthesia	451	4.8
Procedure		
Cardiac Events/Procedures	576	6.1
Mechanical Ventilation	425	4.5
Transfusion	4630	48.8
Hysterectomy	1059	11.2
Invasive Hemodynamic Monitoring	302	3.2

[a]Numbers exceed totals and percents exceed 100% due to multiple SMM-qualifying diagnoses

Table 4

Risk Factors Associated with Severe Maternal Morbidity in Washington State, 1987–2008

	aOR[a]	95% CI	
Age			
<20	0.99	0.89	1.08
20–24	0.94	0.87	1.01
25–29	1.00	reference	
30–34	1.17	1.09	1.25
35–39	1.65	1.52	1.79
40+	2.48	2.16	2.81
Race			
White	1.00	reference	
Black	1.82	1.64	2.01
American Indian	1.52	1.32	1.73
Asian/Pacific Islander	1.30	1.19	1.41
Hispanic	1.17	1.07	1.27
Smoked during pregnancy (yes vs. no)	1.08	1.01	1.16
Parity (at conception)			
0	1.83	1.72	1.95
1	1.00	reference	
2	1.11	1.02	1.19
3+	1.34	1.23	1.45
Preexisting condition (present vs. absent)	2.10	1.88	2.33
Multiple birth (vs. singleton)	2.54	2.26	2.82
Prior cesarean section (vs. no prior)	2.08	1.93	2.23
BMI			
Underweight	1.11	0.99	1.23
Normal	1.00	reference	
Overweight	1.07	1.00	1.15
Obese	1.17	1.08	1.26

[a]Adjusted for education, payer source, and all other factors in the table

Appendix 1

Diagnosis or procedure and ICD-9 codes for markers of severe maternal morbidity[a]

Morbidity Group	ICD-9 code
Diagnosis-based	
Acute renal failure	584; 586; 669.30, 2, 4
Liver failure	570
Respiratory failure	518.4; 518.5; 518.81,2,4; 799.1
Obstetric shock	669.10,1,2,3,4
Cerebrovascular accident	430; 431; 432; 433; 434; 436; 671.50,1,2,3,4; 674.00,1,2,3,4
Pulmonary embolism	673.00,1,2,3,4; 673.20,1,2,3,4; 673.30,1,2,3,4; 673.80,1,2,3,4; 415.11; 415.19
Amniotic fluid embolism	673.10,1,2,3,4
Eclampsia	642.60,1,2,3,4
Septicemia	038
Complications of anesthesia	668.00,1,2,3,4; 668.10,1,2,3,4; 668.21,1,2,3,4
Procedure-based	
Cardiac events/procedures	428; 425; 427.5; 410; 99.60; 99.62; 99.63; 99.64; 99.69
Mechanical ventilation	96.70; 96.71; 96.72
Transfusion	99.03; 99.04
Hysterectomy	68.3; 68.4; 68.9
Invasive hemodynamic monitoring	89.60–64

[a]Adapted from Callaghan et al, 2008[3]