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# *High Incidence of Myocardial Ischemia during Postpartum Hemorrhage*

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***Background:*** **Postpartum hemorrhage remains a major cause of global maternal morbidity and mortality, even in developed countries, despite the use of intensive care units. This study sought to (1) assess whether myocardial ischemia could be associated with and even aggravate hemorrhagic shock in young parturients admitted for postpartum hemorrhage, and (2) identify the independent risk factors for myocardial ischemia.**

***Methods:*** **On their referral to the intensive care unit, a multidisciplinary team managed parturients with severe postpartum hemorrhage. Ventilation, transfusion, catecholamines, surgery, or angiography with uterine embolization were provided as clinically indicated. Plasma cardiac troponin I levels were used as a surrogate marker of acute myocardial injury and electrocardiograms of myocardial ischemia.**

***Results:*** **A total of 55 parturients were referred with severe postpartum hemorrhage, all in hemorrhagic shock. Twenty-eight parturients (51%) had elevated serum levels of cardiac troponin I (9.4 μg/l [3.7–26.6 μg/l]), which were associated with electrocardiographic signs of ischemia and deteriorated myocardial contractility and correlated with the severity of hemorrhagic shock. Indeed, multivariate analysis identified low systolic and diastolic arterial blood pressure (< 88 and < 50 mmHg, respectively) and increased heart rate (> 115 beats/min) as independent predictors of myocardial injury. In addition, all patients who were given catecholamines also had elevated cardiac troponin I levels.**

***Conclusions:*** **These results suggest that treatment of postpartum hemorrhage–induced hemorrhagic shock should be coupled with concomitant prevention of myocardial ischemia, even in young parturients.**

SEVERE postpartum hemorrhage (PPHem) is a leading cause of maternal morbidity and death in the world, even in developed countries such as the United Kingdom,[1] France,[2] and United States,[3] in which severe PPHem remains among the two first causes of maternal deaths despite the use of intensive care units (ICUs).[4] Occurring in as many as 2–3% of deliveries, PPHem accounts for 25% of the half-million women who die annually of pregnancy-related complications worldwide.[1,5,6] Of all PPHem, severe PPHem accounts for 2–5%.[7–9] Although uncontrolled bleeding is an obvious cause of mortality related to severe PPHem in the ICU, precipitating factors such as acute myocardial dysfunction have been described, even after restoration of normovolemia, shortly after hemorrhagic shock.[10–12] However, both the incidence and mechanisms of this hemorrhagic shock–induced cardiac dysfunction in these young parturients with a very low risk for coronary artery disease remain unknown.

The rate of uterine bleeding is traditionally reduced by the administration of uterotonics, such as oxytocin, ergometrine, or, more recently, the uteroselective prostaglandin $E_1$ analog misoprostol[13] or $E_2$ analog sulprostone.[2,8] Although the safety profile of those uterotonics is generally good, debates about its associated cardiovascular risk–benefit issues remain unresolved. Numerous reports in recent years have implicated them, including sulprostone, as causative factors for the development of myocardial ischemia *via* coronary vasoconstriction and cardiac arrest during severe PPHem.[14–17] It is notable, however, that many precipitating factors of myocardial ischemia, including hypotension, severe anemia, and tachycardia, are coincident with severe PPHem.

Accordingly, the specific aims of this study were to (1) prospectively evaluate the incidence of myocardial ischemia, primarily by analyzing plasma cardiac troponin I (cTnI) levels and electrocardiographic changes,[18] in a cohort of women referred to our hospital for severe PPHem; and (2) identify independent risk factors for myocardial ischemia, including the use of uterotonics, by use of multivariate analysis.

This article is featured in "This Month in Anesthesiology." Please see this issue of ANESTHESIOLOGY, page 5A.

## Materials and Methods

### *Initial Management and Transfer of Parturients with Severe PPHem*

PPHem is defined as the loss of more than 500 ml of blood from the genital tract or a greater than 10% reduction in hemoglobin concentration during the first 24 h after delivery,[19] whereas a blood loss of more than 1,000 ml associated with hemorrhagic shock is termed *severe PPHem*.[1,7,8] Parturients had delivered in primary care centers located within or around Paris (Ile-de-France region). With the onset of PPHem, each primary institution tried to control hemorrhage by pharmacologic reinforcement of uterine contraction using intrave-

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nous oxytocin (Syntocinon®; Novartis Pharma, Rueil-Malmaison, France), followed by sulprostone infusion (Nalador®; Schering SA, Lys-lez-Lannoy, France) and surgical repair, when indicated, while homologous erythrocytes were transfused. If our advice was sought, we recommended the administration of sulprostone according to the following protocol: 500 μg infused over 1 h, continued, if necessary, with an additional 500 μg over 3 h; if bleeding persisted and uterine tone was unsatisfactory, then a third 500 μg was given over a period of 12 h. When locally available treatment options proved inefficient in controlling the bleeding, transfer to our tertiary care center, specializing in both the treatment of hemorrhagic shock and uterine embolization, was organized. During transfer by the French Emergency Medical Services (Service d'Aide Médicale Urgente), full ICU treatment options were available to the accompanying emergency physician and nurse–anesthetist.

*Management at the Tertiary Care Center*

The team of three specialists managing these parturients included an obstetrician, radiologist, and anesthesiologist–intensivist. On arrival, femoral arterial and venous (multilumen) catheters were inserted immediately, allowing continuous arterial blood pressure monitoring, blood sampling for laboratory tests, and intravenous drug and fluid therapy. After correction of immediate life-threatening hemodynamic disorders, the obstetrician evaluated the persistence and intensity of bleeding from the vagina and/or in the peritoneum by both physical examination and ultrasonography. Depending on the clinical findings, three therapeutic options were available: (1) (repeat) surgery for surgical hemostasis; (2) angiography with uterine embolization; or (3) if neither (1) nor (2) was immediately indicated because the bleeding had stopped or was minimal, the parturients remained in the ICU, under close observation, with both former options immediately available as necessary. After any invasive therapeutic intervention, parturients were always monitored within the ICU for at least 24 h.

*Data Collection*

The local ethical committee (Comité Consultatif pour la Protection des Personnes dans la Recherche Biomédicale, Paris Saint-Louis) approved the study and waived the necessity for patient consent.

Patient and obstetric characteristics of the parturients and details of their fluid and drug therapy were collected. The following hemodynamic variables were recorded: (1) systolic and diastolic arterial blood pressures and heart rate (HR) on admission and discharge from the ICU, and (2) the lowest systolic and diastolic blood pressures and the highest HR recorded during the first 24 h after ICU admission. We also recorded the administration of catecholamines, notably norepinephrine (Noradrénaline Aguettant®; Laboratoire Aguettant, Fougères, France), epinephrine (Adrénaline Renaudin®; Laboratoire Renaudin, Itxassou, France), dopamine (Dopamine Nativelle®; Procter & Gamble, Neuilly-sur-Seine, France), and dobutamine (Dobutrex®; Lilly, Saint-Cloud, France). Arterial blood sampling allowed determination of arterial blood gases (ABL 300; Radiometer, Copenhagen, Denmark), hemoglobin, prothrombin time (%), fibrinogen (normal range, 2.0–4.0 g/l), lactate (normal range $<$ 2.0 mM), aspartate aminotransferase (normal range $<$ 35 U/l), alanine aminotransferase (normal range $<$ 35 U/l), and γ-glutamyl transpeptidase (normal range $<$ 35 U/l) (Ektachem 700; Kodak, Rochester, NY). These were recorded both on admission and on discharge from the ICU.

*Quantification of Myocardial Ischemia and Injury*

Plasma cTnI was recently accepted by the Joint Committee of the European Society of Cardiology/American College of Cardiology as the standard marker for the diagnosis of acute myocardial injury.[20] It more efficiently pinpoints myocardial injury than does electrocardiogram analysis. In our study, cTnI values were measured at least twice a day in every parturient by the Axsym® system (Abbott, Chicago, IL). Results were expressed in micrograms per liter, with an analytic sensitivity of 0.3 μg/l and an upper limit of normal reference for adults of 0.4 μg/l. The Axsym cTnI specificity with concurrent skeletal muscle injury or renal disease remains 96% or greater.[21] Transthoracic echocardiographic examinations, including measurement of left ventricular ejection fraction (Simpson method), were performed within 24 h of ICU admission in parturients with high levels of plasma cTnI and were repeated in case of alteration of cardiac function.

Even though the analysis of electrocardiograms is less efficient than that of cTnI, two cardiologists separately evaluated the electrographic tracings (at least two per parturient, performed during their stay in the ICU), which were blinded and arranged in a random order, as previously described by Siscovick *et al.*[22] For each electrocardiogram, mean HR, electrocardiographic wave axis, PR interval, and electrocardiographic wave and cardiac output duration (milliseconds) were calculated, and the presence of incomplete or complete right or left bundle-branch block and/or arrhythmias such as atrial fibrillation or flutter were noted. Premature atrial or ventricular beats were counted on a 20-s recording. Abnormal ST segment shifts or abnormal T waves were assessed in all derivations. All of these factors were considered, because an ischemic score was attributed according to four predefined categories: no ischemia (0), ischemia unlikely (1), ischemia probable (2), or ischemia certain (3). Interindividual and intraindividual variations of the cardiologists' results were 2%.

**Table 1. Patient Characteristics (n = 55)**

| | |
|---|---|
| Gravidity | 2 [1–3] |
| Parity | 0 [0–1] |
| Mode of delivery | |
| Vaginal | 24 (44%) |
| Cesarean section | 19 (34%) |
| Forceps | 12 (22%) |
| Technique of anesthesia/analgesia | |
| Regional | 32 (58%) |
| General | 6 (11%) |
| None | 17 (31%) |
| Mode of treatment* | |
| Medical management | 27 (49%) |
| Embolization | 26 (47%) |
| Hysterectomy | 3 (6%) |
| Sulprostone | 46 (84%) |

Data are presented as median [interquartile range] or number (% of total).

* One parturient had both embolization and a hysterectomy.

*Data Analysis*

Results are expressed as median and interquartile range. Data were compared by use of the Mann–Whitney test. The chi-square test was used to compare the distribution of qualitative data among groups. Stepwise multiple logistic regression analysis, including all variables and all 55 parturients, was performed to identify independent factors predictive of myocardial injury in parturients with severe PPHem and to calculate the adjusted odds ratio and 95% confidence interval (Biomedical Data Package; University of California at Los Angeles, Los Angeles, CA). We used the median values of the predictive factors as cutoff values. A value of $P < 0.05$ was considered significant.

## Results

*Patient Characteristics and Hemodynamic Data*

Fifty-five consecutive parturients, median age 31 yr (range, 28–35 yr), were admitted with severe PPHem to our ICU. The median time elapsed between delivery of the infant and admission to our ICU was 5 h 30 min (range, 3 h 17 min–7 h 31 min). Patient and obstetric characteristics are shown in table 1. Forty-five parturients (82%) had no previous medical history. Comorbidities of the remaining 10 parturients (18%) included acute viral hepatitis (n = 3; 5%), asthma (n = 4; 7%), hypothyroidism (n = 1; 2%), and Raynaud syndrome (n = 1; 2%); one parturient had had a pulmonary embolus 2 months previously.

On admission, all parturients were in severe hemorrhagic shock (table 2), with systolic and diastolic hypotension, tachycardia, and lactic acidosis. Despite extensive homologous erythrocyte transfusion, the median hemoglobin level was 6.7 g/dl (range, 5.8–7.7 g/dl). Forty-four parturients (80%) received erythrocyte transfusion (5 units; range, 3–9 units) before ICU admission. In addition, 25 of these 44 parturients (57%) received 4 units (range, 2–7 units) of fresh-frozen plasma, and five were transfused with 5 units (range, 2–10 units) of platelets. Nineteen parturients (36%) were already intubated and ventilated (median duration, 23 h; range, 13–25 h), and nine received one or more catecholamines before and/or after admission to our ICU (norepinephrine, n = 4; epinephrine, n = 3; dopamine, n = 3; or dobutamine, n = 3). The length of stay in the ICU was 2 days (range, 1–3 days).

**Table 2. Comparison of Hemodynamic and Biochemical Variables on Admission and Discharge from the ICU**

| | Values | | |
|---|---|---|---|
| Variable | ICU Admission | ICU Discharge | *P* |
| Systemic Blood Pressure, mmHg | | | |
| Systolic | 88 (70–124) | 117 (106–128) | < 0.005 |
| Diastolic | 50 (35–60) | 68 (60–76) | < 0.001 |
| HR, beats/min | 115 (97–130) | 94 (83–100) | < 0.001 |
| pH | 7.39 (7.34–7.44) | 7.45 (7.41–7.46) | < 0.005 |
| Lactate, mmol/l | 2.7 (2.0–4.1) | 1.1 (0.9–1.6) | < 0.001 |
| Hemoglobin, g/dl | 6.7 (5.8–7.7) | 7.9 (6.7–8.9) | < 0.005 |
| Prothrombin time, % | 52 (34–67) | 78 (68–91) | <0.001 |
| Fibrinogen, g/l | 1.6 (0.9–2.5) | 4.0 (3.1–5.0) | < 0.001 |

n = 54 (the parturient who died of amniotic fluid embolism was excluded from this analysis).

HR = heart rate; ICU = intensive care unit.

Conservative medical management alone achieved control of the hemorrhage, including hemodynamic stabilization in 27 parturients (47%). Two parturients (4%) had a hysterectomy immediately after initial assessment because of extensive uterus injury and uncontrollable uterine atony, respectively. In the remaining 26 cases, bleeding through the vagina remained active despite sulprostone. These parturients underwent angiography and subsequent embolization of the bleeding (predominantly the uterine) arteries. In 25 parturients (45%), embolization was successful. One more hysterectomy was performed on another parturient in whom two embolization procedures could not control the bleeding. Despite intensive resuscitation efforts, she died 2 days later from multiple organ failure. Postmortem examination confirmed amniotic fluid embolism.

*Myocardial Ischemia–induced Injury Associated with Severe PPHem*

Twenty-eight of the 55 parturients (51%) had an elevated serum level of cTnI (cTnI+ group). Of these, 24 already had elevated cTnI levels on arrival at our hospital. During the first 6 h after admission, the median cTnI of all 28 parturients was 6.6 μg/l (range, 2.8–18.9 μg/l). In 19 of 28 parturients, cTnI levels remained elevated for more than 48 h. The median levels of cTnI peaked 24 h after admission (9.4 μg/l; range, 3.7–26.6 μg/l) and decreased after 48 h (fig. 1). In contrast, cTnI values never

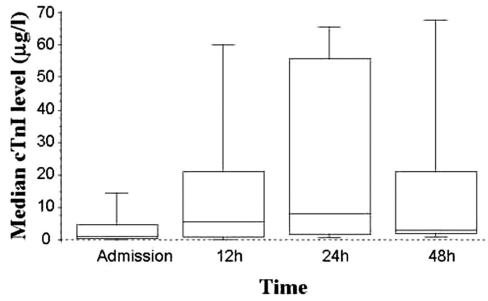


**Fig. 1. Evolution of plasma cTnI levels (median and interquartile range) in the cTnI+ group during the first 48 h after admission.**

reached abnormal levels in the other 27 parturients (cTnI− group).

Electrocardiogram tracings suggestive of myocardial ischemia (electrocardiogram severity score ≥ 2) were observed in 17 parturients (31%): 13 in the cTnI+ group *versus* 4 in the cTnI− group ($P < 0.05$). In almost all of these cases, T-wave inversions and/or electrocardiographic wave segment elevations were present. Echocardiography in the six parturients with the highest levels of cTnI (> 20 µg/l) showed a global hypokinetic left ventricle, with a decreased left ventricular ejection fraction as low as 25%, within 24 h after ICU admission. Left ventricular wall motion began to recover and ejection fraction increased by more than 10% within 3 days.

### *Factors Predictive of Myocardial Injury in Severe PPHem*

Comparison between the cTnI+ and cTnI− groups showed no difference in age, obstetric characteristics, technique of anesthesia/analgesia, or method of delivery. However, hemorrhagic shock was more severe in the cTnI+ group than in the cTnI− group (table 3). This is demonstrated by the cTnI+ group's lower systolic and diastolic arterial blood pressure values, higher HR, higher number of erythrocyte units transfused, more severely altered biochemical values, and greater number of mechanically ventilated parturients compared with the cTnI− group ($P = 0.01$) (table 3). Catecholamines were required only among cTnI+ parturients, with no parturient in the cTnI− receiving catecholamines. Those cTnI+ parturients receiving one or more catecholamines had higher peak cTnI values (n = 9, 12.4 µg/l [range, 4.3–32.0 µg/l]) than those not requiring inotropic support (n = 19, 4.3 µg/l [range, 1.0–15.2 µg/l], $P < 0.05$).

Factors associated with elevated cTnI according to univariate analysis were hemoglobin of 6.0 g/dl or lower on admission, systolic blood pressure of 88 mmHg or lower and diastolic blood pressure of 50 mmHg or lower, HR greater than 115 beats/min, or 9 units or more of erythrocyte transfused during the first 24 h. Subsequent multivariate analysis revealed that low systolic and diastolic blood pressure and increased HR were indepen-

**Table 3. Comparison of Hemodynamic and Biologic Variables between cTnI− and cTnI+ Groups**

| Time, Variable | cTnI+ (n = 28) | cTnI− (n = 27) | *P* Value |
|---|---|---|---|
| First 24 h on ICU | | | |
| Minimum systolic BP, mmHg | 80 (70–110) | 102 (97–110) | < 0.05 |
| Minimum diastolic BP, mmHg | 40 (30–60) | 53 (40–70) | < 0.05 |
| Maximum HR, $min^{-1}$ | 124 (112–144) | 104 (93–114) | < 0.001 |
| RBC transfused, U | 9 (5–14) | 3 (0–5) | < 0.001 |
| Embolization, n | 14 | 12 | NS |
| Stay in ICU | | | |
| Electrocardiographic ischemic score ≥ 2 | 13 (46%) | 4 (15%) | < 0.05 |
| Discharge from ICU | | | |
| Systolic BP, mmHg | 116 (105–127)† | 116 (106–128) | NS |
| Diastolic BP, mmHg | 69 (62–77)† | 68 (57–72)* | NS |
| HR, beats/min | 92 (84–97)† | 95 (77–100)* | NS |
| Catecholamines | 9/28 | 0/27 | < 0.01 |
| Mechanical ventilation, n | 14/28 | 5/27 | < 0.05 |
| Sulprostone, n | 23/28 | 23/27 | NS |
| Hemoglobin, g/dl | 6.0 (5.4–6.9) | 7.3 (6.7–8.4) | < 0.01 |
| PT, % | 39 (30–57) | 63 (46–75) | < 0.005 |
| Fibrinogen, g/l | 1.3 (0.7–1.8) | 2.0 (1.4–2.8) | < 0.01 |
| AST, U/l | 23 (19–29) | 18 (16–21) | NS |
| ALT, U/l | 16 (12–20) | 11 (9–15) | < 0.05 |
| γ-GT, U/l | 12 (11–13) | 13 (12–15) | NS |
| pH | 7.38 (7.32–7.41) | 7.42 (7.38–7.47) | < 0.05 |
| $HCO_3^-$, mmol/l | 17 (16–21) | 20 (19–22) | < 0.05 |
| Lactate, mmol/l | 3.2 (2.3–6.3) | 2.2 (1.8–3.3) | < 0.05 |

NS = not significant.

Red blood cell count (RBC) corresponds to the total number of homologous red blood cell units transfused before and during intensive care unit (ICU) stay. Hemoglobin, prothrombin time (PT), fibrinogen, aspartate aminotransferase (AST), γ-glutamyl transferase (γ-GT), pH, bicarbonate ($HCO_3^-$), and lactate returned to within normal range in the plasma cardiac troponin I (cTnI)+) group on ICU discharge.

* $P < 0.03$, † $P < 0.001$ both *versus* first 24 h on ICU.

BP = blood pressure.

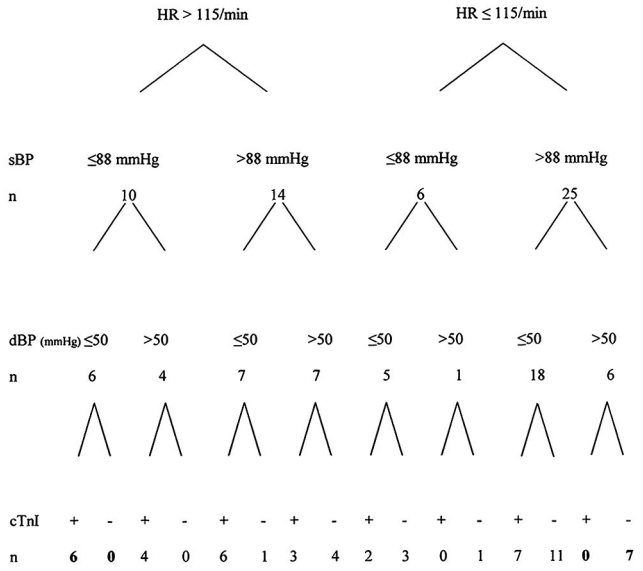


**Fig. 2. Multivariate analysis showed that HR and systolic (sBP) and diastolic (dBP) arterial blood pressure are predictive factors for elevation in cTnI levels. The risk of myocardial injury was 100% in the presence of all three factors, 75% in the presence of any two of the three, 38% in the presence of any one of the three, and 0% in the absence of all risk factors.**

dent predictors of myocardial injury (fig. 2). The adjusted odds ratios were 0.10 (CI, 0.01–0.84) for systolic blood pressure, 0.06 (0.01–0.69) for diastolic blood pressure, and 21.40 (2.16–213.00) for HR. In addition, as mentioned above, all patients who were administered catecholamines also had elevated cTnI levels. By contrast, all other hemodynamic and biologic parameters measured, including the number of erythrocyte transfusions, hemoglobin level, and use of uterotonics (sulprostone or oxytocin), did not influence the occurrence of myocardial injury.

## Discussion

In this study, 51% of parturients admitted to our ICU with severe PPHem were shown to have a myocardial ischemia–induced injury, the presence of which correlated strongly with the severity of hemorrhagic shock. Use of uterotonics neither predicted the occurrence of myocardial injury nor contributed to its incidence.

Increased cTnI levels were used as a surrogate marker of myocardial injury in this study. Elevated levels of this long-lived marker have been found previously to be highly sensitive and specific for myocardial injury and have correlated positively with the development of new areas of regional dysfunction.[18,23–26] The diagnostic value of cTnI in myocardial injury is particularly high in the pregnant population, because cTnI has been shown to be the only biochemical marker that remains undetectable throughout all three stages of labor in healthy women,[27] with increased levels being observed only during myocardial injury associated with pregnancy and labor.[28] Thus, the high plasma cTnI concentrations observed in the parturients in this study were indicative of the occurrence of myocardial cellular necrosis. Moreover, cTnI was an early marker of myocardial injury, because 24 of 28 parturients (86%) exhibited increased cTnI levels on admission (which was at 5 h 30 min after delivery and the ensuing onset of hemorrhagic shock).

Although myocardial injury occurring during acute noncardiac disease in the ICU is not a novel phenomenon, the underlying mechanisms remain poorly understood. Septic and hypovolemic shock have been shown to induce increased cTnI concentrations,[29,30] but many patients studied to date had previously diagnosed coronary artery disease and/or one of the major risk factors for coronary artery disease.[30–32] In the present study, despite pregnant parturients being young, healthy, and at very low risk for coronary artery disease, electrocardiogram analysis showed myocardial injury to be related to myocardial ischemia. Our study further showed that myocardial ischemia was probably related to a significant alteration in the myocardial oxygen supply–demand ratio in parturients with otherwise "normal" coronary arteries. Indeed, in the cTnI+ group, myocardial oxygen supply was impaired by lowered arterial blood pressure, whereas increased HR resulted in an increased myocardial oxygen demand. The myocardial oxygen supply–demand ratio was further compromised in our study by the low hemoglobin concentrations and by the use of vasopressor therapy (in 9 of 27 cTnI+ parturients) to maintain minimal organ perfusion pressures. One cannot exclude the possibility that because of the physiologic changes affecting the heart during the whole of the pregnancy, the heart becomes more susceptible to imbalances of myocardial oxygen supply and demand.

The present study also provides evidence of an apparent dissociation between the use of uterotonics and myocardial injury during severe PPHem. Indeed, on adherence to the sulprostone treatment protocol described previously, the incidence of myocardial injury was found to be independent of the total amount of sulprostone administered. A similar result was found with oxytocin in the present study. These findings challenge several published case reports that describe the occurrence of myocardial ischemia after the administration of uterotonic and potentially vasoactive drugs, including sulprostone, oxytocin, and ergometrine.[14–16] The apparent discrepancy between these results may be attributable to differences in the method and/or site of drug administration. In contrast to the slow infusion recommended in our treatment protocol, sulprostone was given as an intravenous bolus or directly into the uterine wall in these published reports, thus causing a rapid and dramatic increase in plasma drug concentration. More important, however, these cases showed severe PPHem to be associated with a hemoglobin level of less than 5 g/dl,

a HR of more than 110 beats/min, and/or hypotension, with no indication of the cTnI levels before sulprostone administration. According to the results of the present study, any one of these hemodynamic alterations could be responsible for inducing myocardial ischemia. Thus, although potential effects of sulprostone on PPHem-associated myocardial injury cannot be excluded, we observed no significant association between the use of uterotonic drugs and myocardial injury. With regard to the role of arterial embolization in myocardial ischemia, our results show that the cTnI+ parturients already had increased cTnI levels before embolization. In conjunction with the observation that the cTnI levels of the cTnI− parturients remained normal throughout the postembolization period, despite the comparable incidence of embolization in both groups (table 3), we do not think this therapeutic intervention is a potential causative factor for myocardial ischemia.

*Study Limitations*

Our study population experienced very specific physiologic changes both before and during pregnancy, which limits the applicability of the study to other subpopulations of hemorrhagic shock. This study did not assess whether the observed myocardial injury had any short- or long-term consequences or whether the myocardial injury in all parturients receiving catecholamines was a result of the vasoconstrictive drug action itself or merely a reflection of the presence of all three predictive factors of myocardial injury, which were later masked by this "iatrogenic" interference. Arlati *et al.*[30] and Edouard *et al.*[25] focused on cTnI elevation in hypovolemic shock caused by several mechanisms, including hemorrhage. For the first time, we have shown the susceptibility to myocardial injury in a group of 55 patients exclusively in severe hemorrhagic shock. Still, further studies will be necessary to show whether timely correction, or preferably prevention, of these risk factors actually averts myocardial injury.

*Recommendations*

Because previous studies have shown that correction of hypovolemia and low hemoglobin levels alone do not guarantee successful outcome, the therapeutic goal of severe PPHem is to avoid myocardial ischemia together with any potential short- or long-term complication and to prevent any intervention that would influence the quality of life of either the mother or the newborn (*e.g.*, hysterectomy). Because our study showed no association between myocardial ischemia and the use of sulprostone, we recommend the early initiation of specific treatment directed at controlling hemorrhage (*i.e.*, administration of a sulprostone, strictly according to our protocol as a continuous intravenous infusion and, if available, uterine artery embolization). In parallel, clinical objectives for the management of hemorrhagic shock in this patient subpopulation should focus on the early simultaneous restoration of blood pressure and hemoglobin levels and the reduction of tachycardia if prevention fails. It is anticipated that such a two-pronged clinical attack will enable the postulated vicious circle of ischemia and hemorrhagic shock to be broken.

In summary, we have demonstrated the novel finding that myocardial ischemia–induced injury associated with hemorrhagic shock is likely to increase the incidence of PPHem-associated cardiac complications. We therefore suggest that treatment of hemorrhagic shock in isolation is insufficient in severe PPHem, because with other causes of hemorrhagic shock, the concomitant prevention of myocardial ischemia is essential. Although PPHem usually occurs in a young and otherwise healthy population, rapid and rigorous restoration of hemodynamic variables is warranted.

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