Obstetric hemorrhage: improving care by collaborating across borders

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Chapter 7

Maternal mortality due to obstetric hemorrhage by surgical injury during cesarean section: A nationwide study

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Abstract

Objectifs: Obstetric hemorrhage remains a largely preventable cause of maternal mortality globally. The contribution of uterine atony to hemorrhage-related maternal mortality has decreased in France while the contribution of other causes of obstetric hemorrhage such as surgical injury during cesarean has been reported to increase. However, little evidence exists regarding the risk factors and care processes of women who died from this cause of hemorrhage. Therefore, we aimed to describe the clinical profile, underlying mechanisms and preventability factors among women who died from obstetric hemorrhage by surgical injury during caesarean section.

Methods: Nationwide analysis of all hemorrhage-related maternal deaths by surgical injury during cesarean in France identified by the nationwide permanent enhanced maternal mortality surveillance system (ENCMM) between 2007-2018. We described characteristics of the women, delivery hospitals, circumstances of hemorrhage, features of obstetric and rescuscitation/transfusion care and main preventability factors.

Results: Between 2007-2018, hemorrhage-related maternal mortality in France decreased from 1.6/100,000 livebirths (95%CI 1.1-2.2) (39/2,472,650) in 2007-2009 to 0.8/100,000 livebirths (95%CI 0.5-1.3) (19/2,311,783) in 2016-2018. Hemorrhage-related maternal mortality ratio due to surgical injury during cesarean increased from 0.08 (95%CI 0.01-0.3) (2/2,472,650) to 0.2 (95%CI 0.07-0.5) (5/2,311,783) per 100,000 livebirths. Among the 18 women who died from surgical injury during cesarean over the 12-year study period, we report a high prevalence of obesity (67%,12/18), previous cesarean (72%,13/18), second-stage cesareans (56%,10/18). In 22%(4/18), cesarean section was performed in a hospital providing <1000 births annually, with no blood bank (39%,7/18) or no adult intensive-care (44%,8/18) on site. Overall preventability of deaths was 94%(17/18). Main preventability factors were related to delay in hemorrhage diagnosis (77%,14/18) due to late recognition of abnormal parameters (33%,6/18) and late bedside ultrasound (56%,10/18), and delay in management due to insufficient surgical skills (56%,10/18).

Conclusions: In France, surgical injury during cesarean section is an increasing, largely preventable, contributor to hemorrhage-related maternal mortality, as other causes of fatal hemorrhage have become less frequent. The profile of these women showed a high prevalence of obesity, previous cesarean section, second-stage cesarean section and delivery in hospitals with limited medical and surgical resources, which suggests explanatory mechanisms for the fatal outcome and opportunities for prevention.

Introduction

Obstetric hemorrhage remains a leading cause of severe maternal outcome globally.(1) Despite an increased awareness and sensibilization towards obstetric hemorrhage, resulting in the introduction of national professional guidelines and hemorrhage-care bundles, the majority of hemorrhage related maternal deaths remains preventable, suggesting persistent suboptimal management.(2–4) This stresses the need for global action to improve hemorrhage related maternity care.(5) In this context, the study of subpopulations or subcauses of obstetric hemorrhage may provide new insights.(6,7)

A study analyzing trends in hemorrhage related maternal mortality in France between 2001-2015 brought to light that while the contribution of uterine atony to fatal hemorrhage has declined, that of other causes of hemorrhage such as surgical injury during cesarean section has increased.(3) This finding is particularly relevant in the light of the burden of increasing cesarean section rates in many high-income countries.(8,9) However, to date, little high-level evidence exists as to the risk-factors and improvable care factors of women suffering severe maternal outcome following obstetric hemorrhage caused by surgical injury during cesarean section. Moreover, studies are hampered by inconsistency in definition and coding of this etiology, which is often classified as ‘obstetric trauma’, ‘genital tract trauma’ or ‘cesarean section related’, including lesions of the lower genital tract and uterine rupture.(10–12) This may bias the reported magnitude and understanding of this cause of hemorrhage.

Detailed analysis of maternal deaths, sentinel events at the end of the morbidity continuum, can provide key information on the factors leading to severe or even fatal outcomes in this context. Therefore, in this nationwide analysis of maternal deaths due to obstetric hemorrhage caused by surgical injuries during cesarean section, we aimed to describe the clinical profile, management, potential preventability and improvable care factors among women who died from this cause.

Methods

We conducted a nationwide retrospective study of all hemorrhage-related maternal deaths due to surgical injury during cesarean identified by the French nationwide permanent enhanced surveillance system for maternal mortality between 2007-2018. The ENCMM (Enquête Nationale Confidentielle sur les Morts Maternelles)

was established in 1996 under the authority of the National Public Health Agency (Santé Publique France) and the National Institute for Health Research (Institut National de la Santé et de la Recherche Médicale) to identify and document all maternal deaths in France, while overcoming the limitations of vital statistics in this field.

In the ENCMM system, deaths of women while pregnant or within 1 year after the end of pregnancy, regardless of the cause of death, are defined as pregnancy-associated deaths; they are identified through multiple sources described in details previously.(13, 14) In brief, deaths are identified from four sources: 1) self-report by clinicians 2)death certificates of women of reproductive age, 3) computer-based national linkage of the death register with the birth register, and 4) the national hospital discharge database. For each identified pregnancy- associated death, a team of assessors (either obstetrician or midwife and anesthesiologist) conducts a confidential inquiry using a standardized questionnaire to collect relevant information about the woman and her death through onsite interviews and manual review of medical records and autopsy reports. When a confidential inquiry is not possible, information from the death certificate and hospital discharge summary is analyzed.

Each death is then anonymously reviewed in a plenary session of the National Expert Committee on Maternal Mortality, which aims to agree unanimously on 1) the underlying cause of death; 2) whether it was a maternal death, defined as the death of a woman during pregnancy or within 1 year of the end of pregnancy, regardless of the duration or location of the pregnancy, from any cause related to or aggravated by the pregnancy or its management (but not accidental or incidental) and 3) the quality of care (optimal or nonoptimal) and maternal death preventability (categorized as probably or possibly preventable, not preventable, undetermined).

The preventability decision by the expert committee aims to determine whether the death could, probably or possibly, have been avoided if one or more aspects of the chain of events leading to the fatal outcome had gone differently according to guidelines and standards of care at the time of the death. Among probably or possibly preventable maternal deaths, improvable care factors are classified as related to the inadequacy of care provided (notably failed or delayed diagnosis or inadequate treatment), to an inappropriate organization of care, or to an inadequate interaction between the patient and the care system, which are nonexclusive categories. The committee's assessment is collected with a standardized form for each death.(15) The main characteristics of the woman, her

pregnancy and care pathway, and the conclusions of the expert committee are entered into an electronic permanent database.

For this study, we included all maternal deaths from which the cause of death was considered as obstetric hemorrhage by surgical injury during cesarean section by the national expert committee. Maternal deaths were included from 2007-2018, which were the most recent available data.

Surgical injury during cesarean section was defined as 'any intra-abdominal surgical lesion related to cesarean section'. We classified the surgical lesions according to their anatomical origin of bleeding in five categories; Uterine incision site: bleeding from a large extension of the hysterotomy in the parametria or a tear of the lower uterine segment with notable bleeding; Arterial vessel injury: Bleeding from arterial injury of epigastric, uterine, vesical, or cervico-vaginal branches; Broad ligament hematoma: hematoma in the broad ligament which can either have a venous or arterial source, with the possibility to enter the retroperitoneal space; Injury of the bladder flap: Lesion at the level of the vesico-uterine pouch with or without omission of the bladder flap; Unknown: origin of bleeding not identified.

We extracted information for each included woman from the ENCMM database and a manual review of all available documents anonymously collected for each death. First, we described the following maternal, pregnancy and delivery characteristics: advanced maternal age (>35 years), obesity ((BMI$\geq$30 kg/m^2)), parity, history of obstetric hemorrhage, previous cesarean section, multiple gestation, macrosomia, hypertensive disorder, gestational age at birth <37 weeks, elective/emergency cesarean section (following the guidelines from the Collège National des Gynécologues et Obstétriciens Français (CNGOF), an elective cesarean was defined as a planned cesarean section whereas an emergency cesarean section was a cesarean section performed outside of a typical operative schedule because it needed to be performed earlier than planned due to, for example, earlier onset of labor, premature rupture of membranes or an unplanned cesarean section that became necessary during labor with varying degrees of urgency depending on the circumstance), 'red code' cesarean section (defined by the CNGOF as an extreme emergency with immediate vital danger for mother or fetus, necessitating fetal extraction within 15 minutes), indication of cesarean section, cesarean section performed during night hours (defined as a shift with working hours between 20h00-7h30), technical difficulties during cesarean, surgical technique for cesarean section (according to the national CNGOF recommendations, digital and vertical extension of the hysterectomy should be performed since these have been associated with a reduced incidence of surgical injury*).(*16, 17)

Then, we described the clinical features of the surgical injury and of the fatal hemorrhage: type of surgical injury, place and timing of hemorrhage diagnosis, ultrasound performed for diagnosis, time from initial symptoms to relaparotomy, call for surgical assistance, hemostatic hysterectomy performed, critical care (central venous catheter, tracheal intubation, invasive arterial pressure, cardiac arrest at induction of general anesthesia) and transfusion management (number of blood tests performed, red blood cell transfusion, time between diagnosis of hemorrhage and transfusion, platelet transfusion, fibrinogen, factor VII, tranexamic acid).

We also assessed organizational features of the maternity hospitals such as the annual number of births, availability of obstetrician/anesthesiologist 24h/24h, adult intensive care unit on site, blood supply availability, laboratory testing 24h/24h, interventional radiology unit, place of postpartum surveillance after cesarean section (labor ward, post anesthesia care unit), level of neonatal care (Level 1= care for neonates ≥ 36 weeks, level II: care for neonates ≥ 32 weeks, level III: care for neonates at all terms, neonatal intensive care unit). Of note, in France, hospitals either have a blood bank within the facility or an emergency blood stock available on site with a limited quantity of red blood cells, platelets and plasma and a pre-defined organization with the closest blood bank for situations when greater supply or mass transfusion is needed.

The main individual and delivery hospital characteristics of women who died from hemorrhage by surgical injury during cesarean were compared with representative samples of women who gave birth by cesarean in France from the 2010 and 2016 French National Perinatal Surveys (NPS), which were the editions compatible with our study period. Details pertaining to the design of these surveys have been described in detail elsewhere.(18-19)

Finally, we analyzed the conclusions of the national expert committee regarding preventability of deaths and improvable care factors classified as related to inadequate care provided (failed or delayed diagnosis or inadequate treatment), related to inadequate organization of care, or to inadequate interaction between the patient and the care system.

Maternal mortality ratios (MMR) were calculated as the number of maternal deaths up to 42 days after pregnancy end per 100,000 livebirths and were given with exact Poisson 95% confidence intervals. Data on the number of livebirths were obtained through the National Institute of Statistics and Economic Studies. MMR was

calculated for all hemorrhage-related maternal deaths, and for those due to cesarean related injury, per triennium between 2007-2018. Continuous variables were described by their median and the interquartile range (25th percentile to 75th percentile). Categorical variables were summarized by their frequency and percentage.

Statistical analysis was performed using Excel and Stata® v16 software.

Results

Between 2007-2009 and 2016-2018 in France, MMR up to 42 days after pregnancy end from obstetric hemorrhage decreased from 1.6/100,000 livebirths (95% CI 1.1-2.2) (39/2,472,650) to 0.8/100,000 livebirths (95%CI 0.5 - 1.3) (19/2,311,783). During the same period, the contribution of uterine atony to hemorrhage-related maternal mortality decreased from 54% (21/39) to 16% (3/19) and the corresponding uterine atony cause-specific MMR decreased from 0.9 (95% CI 0.52-1.3) (21/2,472,650) to 0.1 (95% CI 0.03-0.4) (3/2,311,783) per 100,000 livebirths; whereas surgical injury during cesarean section became the principal contributor to hemorrhage-related mortality (5% (2/39) in 2007-2009 to 26% (5/19) in 2016-2018). The corresponding surgical injury cause-specific MMR increased from 0.08 (95% CI 0.01-0.3) (2/2,472,650) to 0.2 (95% CI 0.07-0.5) (5/2,311,783) per 100,000 livebirths. Overall, during the 12 years study period, 18 out of 106 hemorrhage related maternal deaths could be attributed to surgical injury during cesarean section. (Figure 1 and Supporting Table 1)

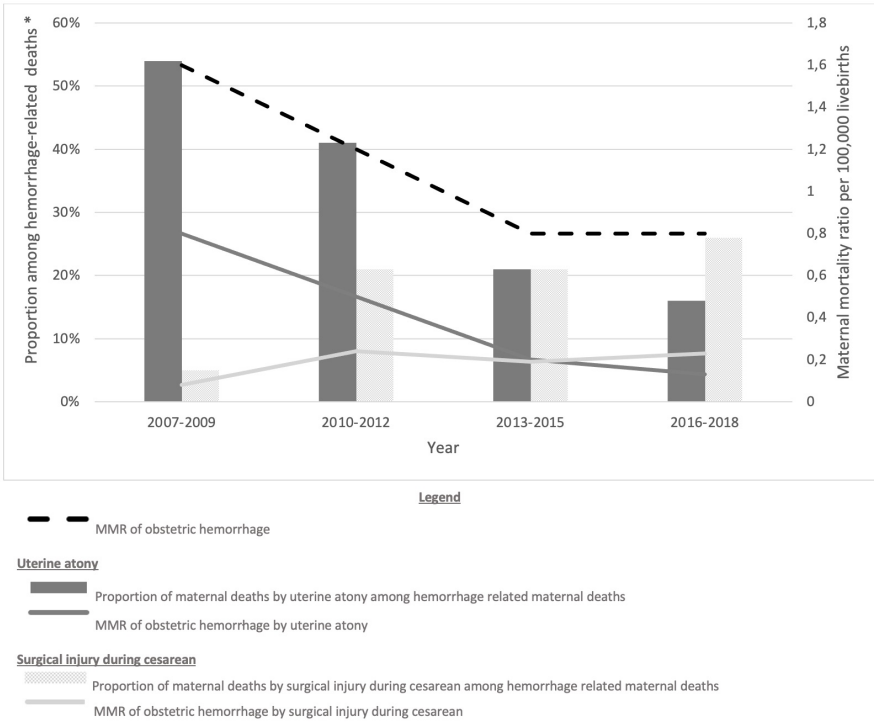

Figure 1. Trends in hemorrhage related maternal mortality in France between 2007 and 2018
** The proportion of cause-specific maternal deaths was calculated as the number of maternal deaths by cause divided by the total number of obstetric hemorrhage-related maternal deaths, for each triennium.*
Abbreviations: MMR = maternal mortality ratio

Table 1. Maternal, birth and maternity hospital characteristics in women who died from obstetric hemorrhage due to surgical injury during cesarean section, and in reference samples of parturients, France 2007-2018

	Women who died		**Reference populations**	
			2010	**2016**
	N=18		**n=2 965**	**n=2 457**
MATERNAL AND PREGNANCY CHARACTERISTICS	n	%	%	%
Age > 35 years	10	56	30	27
Obesity (BMI≥30 kg/m²)	12	67	15	19
Parity				
P0	1	6	48	48
P1	7	39	31	29
≥P2	10	56	21	22
History of obstetric hemorrhage	1	6	/	/
Previous cesarean section	13	72	35	34
>1 previous cesarean section	*6*	33		
Multiple gestation	2	11	4	5
Macrosomia	2	11	9	9
Hypertensive disorder	4	22	9	9
BIRTH CHARACTERISTICS	N	%	%	%
Gestational age at birth < 37 weeks	1	6	12	13
Cesarean section before labor	6	33	53	48
Elective	*1*	*6*	/	/
Emergency	*5*	*28*	/	/
Cesarean section during labor	12	67	47	52
First stage of labor	*1*	*6*	/	/
Second stage of labor	*11*	*56*	/	/
“Red code” cesarean section	5	28	/	/

Table 1. (continued)

	Women who died		Reference populations	
			2010	2016
	N=18		n=2 965	n=2 457
Indication of cesarean section				
Fetal indication[1]	*6*	*33*	*62*	*69*
Maternal indication[2]	*12*	*67*	*38*	*31*
Cesarean section performed during nighthours	15	83	/	/
Technical difficulties during cesarean section[3]	8	44	/	/
Cesarean section performed according to guidelines CNGOF[4]				
Digital extension of hysterotomy	*14*	*88*	/	/
Vertical extension of hysterotomy	*11*	*68*	/	/
MATERNITY HOSPITAL CHARACTERISTICS				
Number of annual births				
< 1000	4	22	16	16
1000-2000	3	17	35	35
2000-3000	5	28	28	29
>3000	6	33	21	20
No anaesthesiologist present in hospital 24h/24h	5	28	40	34
No obstetrician present in hospital 24h/24h	8	39	29	22
Facilities not available on site in the hospital				
No adult intensive care unit	8	44	55	61
No bloodbank	7	39	/	/
No laboratory testing available 24h/24h	4	22	/	/
No interventional radiology unit	11	61	/	/
Location of postpartum surveillance after cesarean section				
Labor ward	3	17	/	/
Post anesthesia care unit	15	83	/	/

Table 1. (continued)

	Women who died		Reference populations	
			2010	2016
	N=18		n=2 965	n=2 457
Level of neonatal care				
Level I	4	22	30	21
Level II	7	39	46	51
Level III	7	39	24	28

[1] Fetal indication: pathological heart rhythm (n=5), umbilical cord prolapsus (n=1)
[2] Maternal indication: non progression at full cervical dilation (n=8), preeclampsia or HELLP (n=3), stagnation of labor (n=1)
[3] Technical difficulties described as: difficult extraction of the impacted fetal head (n=4), adhesions (n=2), myoma previa (n=2)
[4] The surgical technique was described in the surgical report in 16/18 women

Among the women who died from surgical injury during cesarean section, 67% (12/18) were obese (BMI $\geq$30 kg/m^2), 56% (10/18) had advanced maternal age (> 35 years), 72% (13/18) had at least one prior cesarean section, and 33% (6/18) had >1 prior cesarean section. In total, 33% (6/18) of women gave birth by cesarean before labor, among which 5/6 were emergency cesareans (Table 1).

In total, 67% (12/18) of the women who died gave birth by a cesarean during labor, from which the large majority (92%, 11/12) was performed during the second stage of labor. Most cesareans were performed during night hours (83%, 15/18). Technical difficulties during cesarean were reported in 44% (8/18). In 4/11 women who died after cesarean during the second stage of labor, a difficult extraction of the fetal impacted head was reported. In 83% (15/18) women, the surgeon extended the hysterotomy digitally and in 61% (11/18) hysterotomy was vertically extended. (Table 2 and Table S2)

Table 2. Characteristics of the hemorrhage and the clinical care provided in women who died from obstetric hemorrhage due to surgical injury during cesarean section, France 2007-2018

	Women who died N=18	
	n	**%**
HEMORRHAGE CHARACTERISTICS		
Type of surgical injury		
Uterine incision site	6	33
Arterial vessel injury	8	44
Broad ligament hematoma	1	6
Injury of the bladder flap	2	11
Unidentified	1	6
Location where obstetric hemorrhage was diagnosed		
Operating room	2	11
Recovery ward	9	50
Maternity ward	5	28
Intensive care unit	1	6
Emergency room	1	6
OBSTETRIC CARE		
Time caesarean section - diagnosis obstetric hemorrhage (median (min-max)) (min)[1]	122	30-14400
Hemorrhage diagnosed < 120 minutes after caesarean section	8	44
Ultrasound performed	8	44
Relaparotomy	15	83
Time diagnosis obstetric hemorrhage – relaparotomy (median (min-max)) (min) (minutes)	105	20-420
Call for surgical assistance	10	56
Hemostatic hysterectomy performed	11	61

Table 2. (continued)

	Women who died N=18	
	n	**%**
CRITICAL CARE AND TRANSFUSION MANAGEMENT		
Central venous catheter	13	72
Tracheal intubation	16	89
Invasive arterial pressure	8	44
Number of blood tests performed (median (min-max))	2	0-6
Cardiac arrest at induction of general anaesthesia	2	12
RBC transfusion[2]	16	89
Number of RBC units per woman (median (min-max))	15	3-42
Time diagnosis obstetric hemorrhage - transfusion (median (min-max)) (min) (*((minutes)	75	9-370
FFP transfusion	16	89
Number of FFP units per woman (median (min-max))	11	2-46
Platelets transfusion	11	65
Number of platelets units per woman (median (min-max))	2	1-13
Fibrinogen	12	67
Factor VII	8	44
Tranexamic acid	9	50

[1]Including one maternal death which was diagnosed 10 days postpartum. This woman was brought to the emergency room while being in hypovolemic shock. A CT-angio scan confirmed active hemorrhage from the uterine artery when she arrived at the hospital. She died from cardiac arrest during transport from the scan to the operating room. She received intravascular resuscitation but no blood transfusion. When excluding this woman from this analysis, the median time between cesarean and hemorrhage diagnosis was 120 (30-840) minutes.

[2] Two women did not receive any blood loss transfusion. The first woman gave birth in a hospital with < 1000 births annually without presence of an anesthesiologist during night. When she was found at the maternity ward she was in hypovolemic shock (220 minutes after cesarean). She was brought to the operating room for relaparotomy and had cardiac arrest upon her arrival. She never recovered. The other woman concerned the same woman as described in footnote.

Abbreviations: RBC= Red blood cells, FFP= fresh frozen plasma, min= minimum; max= maximum, (min) = minutes

The characteristics of the hospitals where the women who died gave birth are presented in Table 1 and Table 2. In total, 22% (4/18) of women who died gave birth in a maternity hospital with < 1000 births annually as compared to 16% in the reference population, and 39% (7/18) in a hospital where no obstetrician was present 24h/24h versus 29-22% in the reference population. In total, 44% (8/18) of the women who died gave birth in a hospital without an adult intensive care, 39% (7/18) in a hospital without a blood bank on-site and 17% (3/18) in a hospital where post-cesarean surveillance was organized at the labor ward instead of the post anesthesia care unit.

Arterial vessel injuries, particularly those of the uterine artery, were the most frequent etiology of surgical injury related hemorrhage (44%, 8/18) followed by bleeding from the uterine incision site (33%, 6/18). In less than half of fatal cases (44%, 8/18), hemorrhage was detected within two hours after cesarean (median of 122 minutes (min-max 30-14400)). In 44% (8/18) of women, the obstetrician performed an ultrasound to screen for intrabdominal bleeding. A relaparotomy was performed in 83% (15/18) of women with a median time of 105 minutes after cesarean (min-max 20-420). In more than half of the women (56%, 10/18) there was a call for surgical assistance from either a senior obstetrician or a vascular or general surgeon to perform hemostatic surgery. (Table 2 and Table S2)

Critical care interventions such as invasive arterial pressure were performed in 44% (8/18) of women who died. In total, 16/18 (89%) of women received a red blood cell transfusion and the median time before transfusion therapy start was 70 minutes after diagnosis of hemorrhage. Fresh frozen plasma was administered in 89% (16/18) of women, fibrinogen in 67% (12/18), tranexamic acid in 50% (9/18) and factor VII in 44% (8/18) (Table 2).

In Table 3 we present the preventability and improvable care factors of the eighteen women who died, as assessed by the national expert committee. In total, 83% (15/18) of maternal deaths were considered probably preventable and 11% (2/18) as possibly preventable. Initial improvable care factors included unjustified emergency indication of cesarean birth in 17% (3/18) of women. In 77% (14/18), delay in hemorrhage diagnosis was considered to have contributed to maternal death. Contributive factors to the delay in hemorrhage diagnosis were inadequate post-cesarean surveillance with no surveillance documented in 22% (4/18) women, and no or late recognition of abnormal vital signs in 33% of women (6/18). In 10/18 (56%) of women, ultrasound to diagnose intra-abdominal bleeding was not or too late performed. In 28% (5/18) of women, diagnosis of hemorrhage was missed as surgical injury was not raised as a cause of bleeding due to the absence of vaginal

bleeding; this falsely targeted treatment in the direction of other causes of shock such as amniotic fluid embolism. In 56% (10/18), adequate management of the hemorrhage was delayed because of insufficient skills to perform hemostatic surgery as the team had to wait for the arrival of a senior obstetrician or vascular/abdominal surgeon. Limited resources such as the lack of an on-site adult intensive care unit and limited quantity of blood products immediately available were considered contributive to maternal death in 17% (3/18) and 33% (6/18) of maternal deaths respectively. The lack of resources was considered to have contributed to preventability of death in all women who gave birth in a hospital <1000 births/year.

Table 3. Preventability of death and identified improvable care factors among the women who died of hemorrhage due to surgical injury during cesarean section, France 2007-2018

Preventability of maternal death	**N=18**	**%**
Not preventable	0	0
Probably preventable	15	83
Perhaps preventable	2	11
Not enough information to conclude	1	6
Improvable care factors related to clinical care	N*	%
Inadequate antenal assessment of the woman's risk profile[1]	3	17
Unjustified emergency indication for cesarean birth[2]	3	17
Inadequate indication of cesarean birth[3]	4	22
Delay in diagnosis of hemorrhage	14	77
Inadequate postpartum surveillance due to no or late recognition of abnormal vital signs[4]	6	33
No or late performance of bedside ultrasound to detect internal bleeding	10	56
Missed diagnosis of obstetric hemorrhage[5]	5	28
Delay in adequate management of hemorrhage	10	56
Insufficient surgical skills to arrest bleeding	10	56
No hysterectomy performed while indicated	7	39

Table 3. (continued)

Preventability of maternal death	N=18	%
Improvable care factors related to the organization of the health care system		
Equipment and materials		
Lack of blood products	6	33
Absence of adult intensive care unit on site	3	17
Communication		
Lack of leadership	4	22
Communication difficulties between obstetrician and anesthesiologist	4	22
Transportation		
Inadequate indication to transfer the patient	4	22
Poorly organized transfer	2	11
Documentation		
No trace in the case-files of postpartum surveillance	4	22
Improvable care factors related to the inteaction of the patient with the healthcare system		
None		

*Multiple improvable care factors could be identified for each woman who died

[1] Inadequate assessment of the hemorrhage risk profile of the woman resulted in birth in a maternity unit not adapted to this risk profile in terms of equipment and resources.

[2] A "red code" cesarean was performed in two women for cardiac rhythm abnormalities and in one woman for preeclampsia while the experts esteemed these cesareans could have been performed as less urgent 'orange code' cesarean.

[3] In 2/4 women cesarean was performed at full cervical dilatation while instrumental delivery should have been attempted according to the national expert committee: 1/4 cesarean was performed during the second stage labor for inadequate analgesia which the experts hypothesized not all options to optimized analgesia were explored; and 1/4 cesarean was performed during labor because of a scarred uterus while vaginal delivery was not considered an option in a patient motivated for vaginal birth.

[4] The following vital signs were not interpreted correctly: Arterial pressure (n=6), heart rate (n=6), diuresis (n=4), abdominal pain (n=3), consciousness (n=1)

[5] In 5 women, the diagnosis of surgical injury was not raised as an explanation of the clinical condition of the woman. In 2/5 women, an amniotic fluid embolism was suspected, in 2/5 women the cause of bleeding was suspected to be uterine atony, in 1/5 women it was suspected that the intra-abdominal bleeding was caused by diffuse intravascular coagulation rather than by a surgical injury.

Individual details of each woman who died from obstetric hemorrhage due to surgical injury during cesarean section in our study period are provided in the supporting information (Table S2).

Discussion

Surgical injury during cesarean section is an increasing and largely preventable contributor to hemorrhage-related maternal mortality in France, as other causes of fatal hemorrhage have become less frequent. The dominant profile of these women was characterized by a high prevalence of obesity, previous cesarean section, second-stage cesareans and a delivery hospital with limited medical and surgical resources. Main improvable care factors were related to delay in adequate diagnosis and surgical management of hemorrhage.

The number of women with a previous cesarean section among the women who died from surgical injury emphasizes the need to be particularly vigilant in these women as the risk of surgical injury multiplies with the number of previous cesareans.(20, 21) The proportion of women with obesity, which was three times as high as compared to overall maternal deaths in France and 4 times that of the general population of parturients, may reflect the more difficult surgical repair and more challenging clinical surveillance and reanimation among these women. (22, 23) Maternity-care workers should be aware of the risks and complications of second stage cesareans.(24, 25) Simulation trainings to improve skills on delivery of the impacted fetal head, which has been associated to surgical injury, could be implemented to reduce the incidence of surgical injury.(26)

An association between some organizational characteristics of the delivery hospitals and maternal mortality by hemorrhage has been reported in a previous study in France (27). The contribution of human and equipment resources to preventable mortality we found here further stresses the need to define at national levels minimum standards for acute maternal care provision in all maternity units, as has been proposed by the American College of Obstetrics and Gynecology.(28)

The relative increase of the contribution of surgical injury during cesarean section to fatal hemorrhage cannot be explained by increasing cesarean section rates in France which remained stable over the study period: 20.4% in 2019 and 20.3% in 2016 versus 21.4% in 2021.(18,19) More likely, this can be explained by a relative decrease in the contribution of uterine atony to fatal hemorrhage due to increased awareness and sensibilization towards uterine atony after introduction of the French guidelines on the prevention and management of postpartum hemorrhage. Cross-country comparisons on the incidence and burden of surgical injury during cesarean section are very difficult as heterogeneity exists in the classification of this cause of hemorrhage. Although several studies have addressed the rate and risk factors for obstetric hemorrhage during cesarean section, these analyses did

not distinguish between the different causes of obstetric hemorrhage such as placenta accreta spectrum disorders, uterine atony or surgical trauma.(29–31) To improve our understanding of the incidence of surgical injury during cesarean, international consensus is needed on the definition of this cause of hemorrhage as well as on the subclassification.

Main improvable care factors were related to delay in hemorrhage diagnosis which can be challenging in the absence of vaginal bleeding since vital parameters such as tachycardia, tachypnea and hypotension appear late due to the hemodynamic physiology in pregnant women.(32,33) There may be an interest for early warning systems as threshold values indicating when to call the anesthesiologist/ obstetrician may reduce delays in diagnosis. The shock-index has been poorly investigated as an early warning tool in post-cesarean surveillance but may be a promising early warning tool.(34,35) Bedside ultrasound may also contribute to earlier detection of intra-abdominal bleeding but its use remains limited in case of retroperitoneal bleeding.(36,37)

Delay in adequate management of hemorrhage was mainly due to the absence of skills to perform hemostatic surgery among the team in charge. Indeed, the arrival of less invasive interventions to treat obstetric hemorrhage, such as intrauterine balloon tamponade, may have decreased the experience with hemostatic surgery. This emphasizes the need to involve an experienced obstetrician when hemostatic surgery is considered as is currently already recommended in some guidelines from professional societies on the prevention and management of obstetric hemorrhage. (38) Universal obstetric training in hysterectomy seems mandatory and could be achieved and maintained by simulation-based learning. Also, obstetricians could take turns scrubbing in with the gynecology (oncology) surgeons for planned hysterectomies or for planned cesarean-hysterectomies.

The role of night-hours in suboptimal delivery care may need to be further explored. During nightshifts, alerts are often delayed to avoid disturbing the doctor, hence the interest for early warning systems. Although reduced fitness to perform among obstetricians during night-hours may increase the risk for surgical injuries and suboptimal postpartum surveillance, the literature is conflicting as to whether this is related rather to day versus night shifts or to the duration of shifts.(39,40)

Strengths of our study are the detailed data obtained through the ENCMM system, allowing us to explore chronology of diagnosis and interventions in the course of obstetric hemorrhage as important determinants of quality of hemorrhage related maternity care. The comparison of our data with a reference population of women

in France who gave birth by cesarean provided better understanding of the specific characteristics of women who died from surgical injury. Thanks to the national population-based design and enhanced identification method, selection bias was absent.(41) Obstetric hemorrhage guidelines did not change significantly during the study period, guaranteeing findings are representative for current clinical practices. The small study-size is inherent to the rarity of maternal mortality, but maternal deaths are sentinel events that provide unique information. Study power could have been increased by including women with severe morbidity yet these data are more difficult and costly to collect and maternal mortality may serve as a proxy for severe maternal morbidity. In 4/18 cases, postpartum surveillance was not documented. We cannot make assumptions on the quality of postpartum surveillance care in those cases and how they would have modified our findings, yet the absence of documentation of care in such cases is in itself a marker of improvable quality of care.

Conclusion

This study provides insight in the specific profile and care process of the women who died from surgical injury during cesarean section, raising awareness among maternity-care workers of the risks and complications of second stage cesareans particularly among women with obesity and previous cesarean section. We suggest avenues to improve care in this context and provide opportunities to prevent surgical injury during cesarean section such as by implementing simulation-based learning on difficult cesareans and increasing awareness of cesareans at high-risk of surgical injury. Care improvement may include the implementation of simulation training for hemostatic surgery and specific and evidence-based regulations on availability of medical and human resources to provide optimal maternal critical care. Specific guidance to improve post-cesarean surveillance by implementing early warning systems may result in earlier detection of hemorrhage. Our findings suggest future research may focus on the role of nightshifts in substandard maternity care. In addition, the role of other parameters to detect postoperative bleeding such as the shock index may need to be investigated in this context.

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Supplemental information

Supplemental Table S1. Maternal mortality due to obstetric hemorrhage by 3-year periods in France, overall and by subcause (atony or surgical injury during cesarean section)

	2007-2009	2010-2012	2013-2015	2016-2018
Live births	**2 472 650**	**2 477 240**	**2 412 720**	**2 311 783**
MM by obstetric hemorrhage				
n	39	29	19	19
MMR (/100 000 live births)	1.6	1.2	0.8	0.8
MM by uterine atony				
n	21	12	4	3
MMR (/100 000 live births)	0.8	0.5	0.2	0.1
% of maternal deaths by obstetric hemorrhage by uterine atony	54%	41%	21%	16%
MM by surgical injury during cesarean				
n	2	6	4	5
MMR (/100 000 live births)	0.08	0.2	0.2	0.2
% of maternal deaths by obstetric hemorrhage by surgical injury	5%	21%	21%	26%

Abbreviations: MM = Maternal mortality, MMR = maternal mortality ratio

Supplemental Table S2. Individual details of women who died from obstetric hemorrhage due to surgical injury during cesarean section in France between 2007-2018

Case	Type surgical injury	Age	Obstetric history	BMI	Complications during pregnancy	Mode of birth	Code red cesarean	Night time	Size delivery hospital (# annually)	Time delivery-hemorrhage (min) [1]	Time delivery-death (min)[2]	Clinical circumstances of death
1	Arterial vessel injury	≥35	>1 previous cesarean section	≥30	-	Emergency cesarean, second stage	Yes	Yes	>3000	120	300	Uncomplicated cesarean for fetal bradycardia at full cervical dilatation. Patient hypotensive during postpartum surveillance. Bedside ultrasound shows a hematoma next to the uterus. Decision for expectant management. Finally, relaparotomy for hemodynamic instability, bringing to light an actively bleeding lesion of the uterine artery, difficult to repair. Cardiorespiratory arrest during relaparotomy.

Supplemental Table S2. (continued)

Case	Type surgical injury	Age	Obstetric history	BMI	Complications during pregnancy	Mode of birth	Code red cesarean	Night time	Size delivery hospital (# annually)	Time delivery-hemorrhage (min) [1]	Time delivery-death (min)[2]	Clinical circumstances of death
2	Arterial vessel injury	≥40	>1 previous cesarean section	Less than 25	Gestational hypertension	Emergency cesarean, first stage	No	Yes	<1000	310	3 days	Uncomplicated cesarean for multi-scarred uterus and spontaneous contractions. No documentation of vital parameters during postpartum surveillance but patient reports abdominal pain. Los of consciousness is initially interpreted as an eclampsia. Bedside ultrasound showing hemoperitoneum. Emergent relaparotomy with active bleeding from uterine artery. Transfer to ICU. Hysterectomy performed 1 day later because of hemodynamic instability. Cardiorespiratory arrest during hysterectomy with successful reanimation. Dies from multiorgan failure at ICU.

Supplemental Table S2. (continued)

Case	Type surgical injury	Age	Obstetric history	BMI	Complications during pregnancy	Mode of birth	Code red cesarean	Night time	Size delivery hospital (# annually)	Time delivery-hemorrhage (min) [1]	Time delivery-death (min)[2]	Clinical circumstances of death
3	Arterial vessel injury	Less than 35	previous cesarean section	Less than 25	Multiple gestation	Emergency cesarean, second stage	No	Yes	>3000	90	4 days	Uncomplicated cesarean for non-engagement of first twin in breech. Hypotension during postpartum surveillance at recovery ward with an abdominal ultrasound being made 1h after first hypotension showing a hemoperitoneum. Initial repair during relaparotomy of uterine artery lesion and embolization. Persistence of hemodynamic instability and diffuse intravascular coagulation. Hysterectomy on D1 for hemodynamic instability. Dies at ICU, multiorgan failure.

Supplemental Table S2. (continued)

Case	Type surgical injury	Age	Obstetric history	BMI	Complications during pregnancy	Mode of birth	Code red cesarean	Night time	Size delivery hospital (# annually)	Time delivery-hemorrhage (min) [1]	Time delivery-death (min)[2]	Clinical circumstances of death
4	Arterial vessel injury	Less than 35	previous cesarean section	≥30		Emergency cesarean, second stage	No	Yes	2000-3000	372	2 days	Uncomplicated cesarean during which patient presents a hyperthermia. After cesarean, tachycardia and hypotension interpreted as a septic shock by the anesthesiologist. Hemorrhage is diagnosed by bedside ultrasound by obstetrician who is called because of clinical deterioration of the patient despite effective treatment for septic shock. Transfer to another hospital for surgical management. Patient dies from cardiorespiratory arrest during transport.
5	Arterial vessel injury	≥35	>1 previous cesarean section	≥35		Emergency cesarean, second stage	Yes	Yes	>3000	120	2 days	Cesarean for failure of forceps because of fetal bradycardia. Difficult fetal extraction but no other complications described. No documentation of postpartum surveillance. Patient was found in hypovolemic shock 2h after cesarean. Despite adequate surgical and resuscitation management afterwards she dies from multiorgan failure at ICU.

Supplemental Table S2. (continued)

Case	Type surgical injury	Age	Obstetric history	BMI	Complications during pregnancy	Mode of birth	Code red cesarean	Night time	Size delivery hospital (# annually)	Time delivery-hemorrhage (min) [1]	Time delivery-death (min)[2]	Clinical circumstances of death
6	Arterial vessel injury	≥35	>1 previous cesarean section	≥30		Emergency cesarean, second stage	No	Yes	2000-3000	425	3 days	Uncomplicated cesarean for non-engagement at full cervical dilation. No documentation of postpartum surveillance. Patient found unconscious in bed at postpartum wards. Emergent relaparotomy performed. Call for vascular surgeon because of uterine artery injury. Hysterectomy performed. Transfer to ICU. Instable. CT-angioscanner: acitvely bleeding lesion at the level of the iliac artery. Embolization. Patient dies from multiorgan failure at ICU.

Supplemental Table S2. (continued)

Case	Type surgical injury	Age	Obstetric history	BMI	Complications during pregnancy	Mode of birth	Code red cesarean	Night time	Size delivery hospital (# annually)	Time delivery-hemorrhage (min) [1]	Time delivery-death (min)[2]	Clinical circumstances of death
7	Arterial vessel injury	Less than 35	previous cesarean section	Less than 25		Elective cesarean	No	No	2000-3000	90	180	Elective cesarean at 31weeks of pregnancy for suspicion of placenta percreta. Patient not referred to a reference center for placenta accreta disorders. Cesarean hysterectomy without complication. Patient hemodynamically unstable during postpartum surveillance at recovery ward. Relaparotomy: Injury of uterine artery, hemoperitoneum of 3L. Patient dies from cardiorespiratory arrest during relaparotomy.

Supplemental Table S2. (continued)

Case	Type surgical injury	Age	Obstetric history	BMI	Complications during pregnancy	Mode of birth	Code red cesarean	Night time	Size delivery hospital (# annually)	Time delivery-hemorrhage (min) [1]	Time delivery-death (min)[2]	Clinical circumstances of death
8	Arterial vessel injury	≥35	previous cesarean section	Less than 25	Gestational hypertension	Emergency cesarean, before labor	No	No	<1000	80	1740	Cesarean for eclampsia Patient transferred to ICU at another hospital after cesarean while not being hemodynamically stable. At arrival in other hospital, immediate relaparotomy for hemodynamic instability, important hemoperitoneum, no lesion identified. After relaparotomy, persistence of hemodynamic instability. Angioscanner shows a lesion of the uterine artery lesion. Failure of embolization. Hysterectomy. Multiorgan failure.

Supplemental Table S2. (continued)

Case	Type surgical injury	Age	Obstetric history	BMI	Complications during pregnancy	Mode of birth	Code red cesarean	Night time	Size delivery hospital (# annually)	Time delivery-hemorrhage (min) [1]	Time delivery-death (min)[2]	Clinical circumstances of death
9	Uterine incision site	Less than 35		Less than 25		Emergency cesarean, before labor	Yes	Yes	<1000	30	205	Emergency cesarean because of rupture of membranes while contra-indication of vaginal birth (macrosomia). Cesarean complicated by myoma previa needing a corporeal incision and difficult fetal extraction. Important perioperative bleeding with difficulties to detect bleeding source. Second obstetrician is called but bleeding persists. 2,5L of bleeding during CS because of large tears fusing into the round ligaments coming from the hysterotomy. After cesarean, postoperative surveillance at the postpartum maternity ward where she is found death 3h after giving birth. Autopsy shows an important hemoperitoneum.

Supplemental Table S2. (continued)

Case	Type surgical injury	Age	Obstetric history	BMI	Complications during pregnancy	Mode of birth	Code red cesarean	Night time	Size delivery hospital (# annually)	Time delivery-hemorrhage (min) [1]	Time delivery-death (min)[2]	Clinical circumstances of death
10	Uterine incision site	Less than 35	>1 previous cesarean section	≥35	-	Emergency cesarean, second stage	No	Yes	1000-2000	90	6 days	Uncomplicated cesarean after failure of forceps. Difficult fetal extraction. Supraphysiological exteriorized bleeding, pain and tachycardia during postpartum surveillance. Suspicion of uterine atony for which sulprostone is started. Deterioration of the clinical condition of the patient several hours after cesarean. Emergent relaparotomy showing active bleeding from the right angle of the uterotomy, repaired with senior obstetrician. Patient dies from multiorgan failure at ICU.

Supplemental Table S2. (continued)

Case	Type surgical injury	Age	Obstetric history	BMI	Complications during pregnancy	Mode of birth	Code red cesarean	Night time	Size delivery hospital (# annually)	Time delivery-hemorrhage (min) [1]	Time delivery-death (min)[2]	Clinical circumstances of death
11	Uterine incision site	Less than 35	previous cesarean section	≥30	Osteochon-droplasia	Emergency cesarean, before labor	No	Yes	>3000	90	240	Uncomplicated cesarean because of spontaneous rupture of membranes and maternal contra-indication for vaginal birth (scarred uterus and limited pelvis due to ostechondroplasia). Patient found unconsciousness 90 minutes after cesarean. Emergency relaparotomy, showing active bleeding lesion from the left angle of the uterotomy. Cardiac arrest during relaparotomy.
12	Uterine incision site	Less than 35	previous cesarean section	Less than 25		Emergency cesarean, second stage	Yes	Yes	2000-3000	30	360	Code red cesarean for fetal bradycardia, without complications. 30 minutes after cesarean, tachycardia and hypotension and absence of diuresis. Transfer to postpartum maternity unit 3h after cesarean where she experiences cardiorespiratory arrest. Autopsy shows hemoperitoneum with important hematoma fusing from the uterotomy.

Supplemental Table S2. (continued)

Case	Type surgical injury	Age	Obstetric history	BMI	Complications during pregnancy	Mode of birth	Code red cesarean	Night time	Size delivery hospital (# annually)	Time delivery-hemorrhage (min) [1]	Time delivery-death (min)[2]	Clinical circumstances of death
13	Uterine incision site	Less than 35	previous cesarean section	≥30		Emergent second stage cesarean	No	Yes	>3000	10 days	10 days	Emergent cesarean for abnormal fetal heart rhythm at full cervical dilatation. Cesarean complicated by postpartum hemorrhage of 2.5L from the uterine incision site. Uncomplicated postpartum surveillance afterwards. Patient brought in at emergency room 10 days after cesarean because of cardiorespiratory arrest. Autopsy shows important hemoperitoneum and necrosis of the uterine incision site where a large hematoma is localized. No injury of vessels reported.

Supplemental Table S2. (continued)

Case	Type surgical injury	Age	Obstetric history	BMI	Complications during pregnancy	Mode of birth	Code red cesarean	Night time	Size delivery hospital (# annually)	Time delivery-hemorrhage (min) [1]	Time delivery-death (min)[2]	Clinical circumstances of death
14	Uterine incision site	≥40		≥30	Gestational diabetes	Emergency cesarean, second stage	No	Yes	>3000	480	4 days	Cesarean for non-engagement at full cervical dilatation. Surgeons do not report any complications during cesarean but patient receives RBC and FFP transfusion during cesarean because of tachycardia and hypotension. Relaparotomy for hemodynamic instability. Active bleeding from uterine incision site. Senior obstetrician called in for ligatures, followed by hysterectomy for ongoing bleeding. Transfer to ICU where she dies from multiorgan failure.

Supplemental Table S2. (continued)

Case	Type surgical injury	Age	Obstetric history	BMI	Complications during pregnancy	Mode of birth	Code red cesarean	Night time	Size delivery hospital (# annually)	Time delivery-hemorrhage (min) [1]	Time delivery-death (min)[2]	Clinical circumstances of death
15	Injury of the bladderflap	≥35	>1 previous cesarean section	≥30	Gestational hypertension, HELLP syndrome, multiple gestation	Emergency cesarean, before labor	No	No	1000-2000	240	23 days	Emergency cesarean because of HELLP syndrome, uncomplicated. Prolonged postoperative surveillance at recovery ward because of supraphysiological exteriorized bleeding. No postpartum surveillance documentation. Nurse calls obstetrician 1h after cesarean because of tachycardia and hypotension. Obstetrician advises to give intravenous iron but does not clinically evaluate the patient. Patient is found 3h after cesarean in hemorrhagic shock. Emergent relaparotomy showing active bleeding with hemoperitoneum at the level of the bladder flap. Ligatures iliac artery by senior obstetrician, transfer to ICU in another hospital where second laparotomy with hysterectomy because of hemodynamic instability. Patient dies at ICU from multiorgan failure.

Supplemental Table S2. (continued)

Case	Type surgical injury	Age	Obstetric history	BMI	Complications during pregnancy	Mode of birth	Code red cesarean	Night time	Size delivery hospital (# annually)	Time delivery-hemorrhage (min) [1]	Time delivery-death (min)[2]	Clinical circumstances of death
16	Injury of the bladder flap	≥35		≥40		Emergency cesarean, second stage	Yes	Yes	1000-2000	67	2 days	Complicated cesarean, code red, for fetal bradycardia at full cervical dilatation. Difficult fetal extraction and many adhesions probably due to previous endometriosis surgery. During postoperative surveillance, hypotension and absence of diuresis. Anesthesiologist and obstetrician are not alerted. Anesthesiologist is called 60 minutes after to reinject in the epidural because of abdominal pain. Patient unconsciousness by then. Rapid bedside ultrasound showing hemoperitoneum confirmed by relaparotomy showing injury of the bladder flap and of the bladder, actively bleeding. Call for general surgeon to assist during the laparotomy. Hysterectomy performed. Two cardiac arrests during procedure with successful resuscitation. Total blood loss: 5.5L. Transfer to ICU academic hospital where patient dies from multi organ failure.

Supplemental Table S2. (continued)

Case	Type surgical injury	Age	Obstetric history	BMI	Complications during pregnancy	Mode of birth	Code red cesarean	Night time	Size delivery hospital (# annually)	Time delivery-hemorrhage (min) [1]	Time delivery-death (min)[2]	Clinical circumstances of death
17	Broad ligament hematoma	≥40		≥30		Emergency cesarean, second stage	No	Yes	<1000	840	3 days	Uncomplicated cesarean for non-engagement at full cervical dilatation. Patient hypotensive and tachycardic during postpartum surveillance at post anesthesia care unit but this does not alert the medical team. Patient found unconscious at postpartum ward several hours after birth. Emergent relaparotomy. Important broad ligament hematoma extending to the retroperitoneum. Hysterectomy performed. Cardiorespiratory arrest during hysterectomy with aggressive reanimation. Patient dies from multiorgan failure at ICU.

Supplemental Table S2. (continued)

Case	Type surgical injury	Age	Obstetric history	BMI	Complications during pregnancy	Mode of birth	Code red cesarean	Night time	Size delivery hospital (# annually)	Time delivery-hemorrhage (min) [1]	Time delivery-death (min)[2]	Clinical circumstances of death
18	Unidentified	≥35		≥35	HIV, HELLP syndrome Gestational hypertension	Emergency cesarean, before labor	No	Yes	2000-3000	420	840	Emergency cesarean for HELLP syndrome complicated by difficult hemostasis and 2L of perioperative blood loss, Redon left intra-abdominally and compressive bandage with transfer to ICU. Massive transfusion. Ongoing hemodynamic instability with suspicion of DIC in the context of HELLP syndrome (while DIC is not confirmed by hemostatic testing which remain normal). Relaparotomy performed by obstetrician and vascular surgeon showing important hemoperitoneum. Decision to perform hysterectomy. Cardiorespiratory arrest during hysterectomy.

[1]Time between delivery and diagnosis of hemorrhage, reported in minutes. [2] The time of death is reported in minutes (M), hours (H) or days (D) postpartum, relative to delivery.

FFP = fresh frozen plasma, RBC= red blood cells, ICU = intensive care unit, DIC= diffuse intravascular coagulation, CS= cesarean section, L= liters, HELLP = hemolysis, elevated liver-enzymes and low platelets