Serious primary post-partum hemorrhage, arterial embolization and future fertility: a retrospective study of 46 cases

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BACKGROUND: The guidelines advise arterial embolization in case of post-partum hemorrhage. We evaluated its feasibility and the subsequent fertility. METHODS: A retrospective study has been conducted in our center for the past 10 years (1996–2005). Fifty-two patients experiencing a primary post-partum hemorrhage who were resistant to medical treatment underwent uterine artery embolization and/or hysterectomy. In case of arterial embolization, a follow-up of all the patients was realized, focusing on the preservation of fertility. RESULTS: Six (11.5%) patients underwent hysterectomy straightaway and 46 (88.5%) arterial embolization in the first instance including 35 arterial embolizations after Cesarean section. Embolization was successful among 41 patients (89.1%) and hysterectomy was performed on the 5 (10.9%) others. Overall, 11/24 398 women suffered from a definitive loss of fertility after post-partum hemorrhage. Fertility was studied at least 1 year after the delivery. All patients had a return of normal menses. Sixteen of 41 women (39%) wanted another child and 100% succeeded. Nineteen pregnancies, including two twin pregnancy and one early spontaneous abortion were observed. CONCLUSIONS: Embolization is a safe and effective non-surgical method to resolve post-partum hemorrhage and should be regarded as gold standard in a hemodynamically stable patient. Furthermore, subsequent fertility is not impaired by the procedure.

Keywords: embolization; primary post-partum hemorrhage; Cesarean section; fertility

Introduction
Post-partum hemorrhage remains one of the primary causes of maternal death with a mortality rate of 10 per 100 000 deliveries (Lewis and CEMACH, 2002). Diagnostic delays lead to late management of this condition and have serious repercussions in terms of maternal morbidity and mortality (Sergent et al., 2004). For this reason, numerous protocols have been developed allowing avoidance of serious hemorrhage in many cases. Immediately after diagnosis of primary post-partum hemorrhage, it is imperative to implement appropriate measures in accordance with the recommendations of RCOG (Royal College of Obstetricians and Gynaecologists) published in 2007 and ANAES (National Agency for Accreditation and Evaluation of Health) published in 2004 (Goffinet et al., 2005).

Since 1979, embolization was proposed as an alternative to surgical procedures (Brown et al., 1979; Duvaufrier et al., 1984; Greenwood et al., 1987). If all medical measures are unsuccessful, uterine artery embolization could be directly initiated if the patient is hemodynamically stable enough to be moved. Nevertheless, this point is still much debated. Even though hysterectomy remains the gold standard treatment to restore hemostasis in many cases, we wished to demonstrate through this study the place of arterial embolization, its efficiency, its safety and value in preserving fertility whatever the route of delivery.

Materials and Methods
This retrospective study was carried out in 2007 from studies of patients treated between 1996 and 2005 in the Department of Obstetrics and Gynecology of the University Hospital of Saint-Etienne. The first 12 cases treated between 1996 and 2001 were already described by Tourné et al. (2003) and other cases until 2005 were added for the present study.

Fifty-two patients experiencing a primary post-partum hemorrhage (>500 ml following French recommendations (Goffinet et al., 2005)) resistant to medical treatment underwent uterine artery embolization or hysterectomy. Fifty-one arrived directly at the University Hospital of Saint-Etienne for delivery and one was transferred from another hospital by helicopter. All embolizations were carried out in the intervention-suite of the radiology department.

For each patient undergoing arterial embolization, the following clinical and biological parameters were recorded: age, term, parity,
gestational age, obstetric history, mode of parturition, anesthesia, cause of hemorrhage (uterine atony, abruptio placentae, placenta praevia, cervix injury, placental accreta, percreta, myoma: diagnoses accepted by obstetricians and sometimes confirmed by an anatomicopathologic exam), hemoglobin level, number of packed red blood cell or platelet transfusions, failures of embolization, complications, menses and deliveries or pregnancies after embolization, fertility after embolization, pregnancy complications after embolization and birth weight.

The therapeutic strategy was based on a consensus reached by obstetricians, anesthesiologists and interventional radiologists (Fig. 1). Once the decision had been taken to perform embolization, the patient was transported to the Radiology Department, accompanied by a gynecologist and an anesthesiologist. If she was transferred from one of the surrounding hospitals, an intracavity balloon was placed for the transport by the emergency ambulance. The patient was monitored by cardiovascular monitoring and kept under oxygen and prostaglandins infusion throughout the procedure.

Embolization was performed under local anesthesia via the right femoral artery to allow the selective study of and access to both internal iliac arteries and branches, and to ideally perform a selective embolization of both uterines arteries. If catheterization is difficult, embolization of the anterior division of both internal iliac arteries should be considered. In case of bleeding from the cervico-vaginal region, selective evaluation and embolization of cervico-vaginal branches should be performed (Pelage et al., 1998; Deux et al., 2001).

An initial assessment was performed by arteriography (angiography catheters 4 or 5 French), sometimes permitting visualization of a hemorrhagic extravasation. After catheterization of the left uterine artery, resorbable gelatine sponge pledgets were injected by the radiologist to perform embolization. The same procedure was then done to the right uterine artery.

The main criterion for success was a cessation of external bleeding, estimated using a collecting bag. A further arteriographic assessment was performed at the end of the procedure in order to stop it when the blood flow stopped. The patient was then transferred to the intensive care department and monitored for at least 24 h.

All patients whose references could be found were subsequently contacted by phone in 2007 and asked the following questions: ‘When did you have a return of normal menses?’, ‘Did you become pregnant again?’, ‘If so, when and how did you give birth?’, ‘If not, why? Do you intend to have more children?’ and ‘Have you resorted to medically assisted methods of conception?’.

Figure 1: Delivery hemorrhage protocol.
Results

Overall results
From 1996 to 2005, 24,398 deliveries took place in the University Hospital of Saint-Etienne. During this period, 980 patients (4.0%) experienced post-partum hemorrhage (>500 ml), including 52 who were primary hemorrhages resistant to medical treatment, considered as serious and treated as follows: (i) six patients underwent hysterectomy straightaway [three in 1996, the year in which arterial embolization procedure was introduced, and three additional between 1998 and 2005, due to technical problems (absence of free operating theater or radiologists)] and (ii) 46 patients (0.19% of deliveries and 4.6% of primary post-partum hemorrhages) underwent arterial embolization.

Arterial uterine embolization

Patient characteristics
The median age of these patients was 27.3 years (range 19–41); 9 patients were primiparous and 37 were multiparous (Table I). Nine patients had unassisted vaginal deliveries (two involving twins), 2 had instrumented vaginal deliveries (one involving twins) and 35 underwent Cesarean section (1 patient giving birth to triplets, 6 to twins and 28 to a single child) including 19 elective and 16 during the course of labor. All the patients having given birth by vaginal delivery, emergency or elective Cesarean section were given an epidural anesthetic or neuraxial anesthesia. Four patients having undergone a Cesarean section were operated under general anesthesia. The median hemoglobin concentration measured immediately before embolization was 8.04 g/dl, after they had been transfused or not. Twenty-seven patients experienced disseminated intravascular coagulation, 39 were transfused with packed red blood cells, 25 with fresh frozen plasma and 1 with four platelet transfusions.

Cause of hemorrhage
Uterine atony was the most frequent cause of hemorrhage (32 patients; 69.5%), followed by placenta accreta or percreta [8 patients; 17.3% (1 patient with percreta placenta was treated by conservative management)], placenta praevia (3 patients; 6.5%), abruptio placentae (1 patient; 2%), myoma and atony (1 patient; 2%) and a parametrical dissecting hematoma (1 patient; 2%). Embolization was successful in 41 out of 46 patients (89.1%).

Table I. Patient characteristics

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Median hemoglobin concentration g/dl (before or after transfusion)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embolization (N = 41)</td>
<td>8.1</td>
</tr>
<tr>
<td>Hysterectomy (N = 6)</td>
<td>8.33</td>
</tr>
<tr>
<td>Embolization + hysterectomy (N = 5)</td>
<td>7.42</td>
</tr>
</tbody>
</table>

Post-partum hemorrhage and arterial embolization

Procedure
The mean time between delivery and embolization was 263 min (range 90–750). The transfer of the patient to the radiology department took approximately 15 min.

Then, the radiologists performed uterine artery embolizations. Five patients underwent additional procedures. One of them presented a parametrical dissecting hematoma as a result of vascular injury during Cesarean section and thus, embolization was completed by the insertion of a coil into the right uterine artery. Another underwent ovarian artery embolization. For a third patient, the hypogastric artery was catheterized and embolization was performed beyond the gluteal artery. A fourth patient underwent superselective embolization of the internal iliac artery branch and for the last one, embolization was performed after ligation of the hypogastric arteries (embolization of the residual stump of hypogastric artery and anastomotic pelvic tracts).

Complications
During the embolization procedure, the following complications were encountered: allergy to iodine (one case), acute pulmonary edema related to massive volume expansion (one case), cardiovascular instability leading to the embolization procedure being stopped because of an hematoma from the puncture site of the right Scarpas’s fascia, proximal to the common femoral artery, resolving after application of a compression bandage (one case), and one major hemoperitoneum related to dissection of the epigastric artery, overlooked at the time of embolization (one case). This last patient was re-operated four times, undergoing hysterectomy and ovariotomy; during the second operation, she experienced cardiac arrest but recovered rapidly; she received a total of 60 transfusions of packed red blood cells, 60 transfusions of fresh frozen plasma and four platelet transfusions.

One patient with a case of placenta percreta was treated with in situ methotrexate in conjunction with embolization and died four months after the embolization procedure because of the methotrexate-related nephrotoxicity.

Hysterectomies
Since 1996, 11 hysterectomies for vascular hemostasis have been performed in our department including six as first-line treatment (Table I). In these cases, the median hemoglobin concentration measured immediately before hysterectomy was 8.33 g/dl (before or after transfusion). The other five...
hysterectomies have been performed after failure of embolization. Among these five cases, (i) one patient with placenta accreta underwent subtotal hysterectomy after the embolization procedure had to be stopped due to cardiovascular instability; (ii) because of recurrence of hemorrhage, hysterectomy was performed 3 h after embolization in one patient with placenta accreta; (iii) hysterectomy was performed following injury to the epigastric artery during the embolization procedure, as embolization was not carried out at the cut side, resulting in the continuation of the hemorrhage and (iv) placenta percreta was diagnosed in one patient who had undergone five previous Cesarean sections. The placenta was left in place and embolization was performed in conjunction with in situ methotrexate treatment (50 mg/m²). Then, the patient experienced aplasia, complicated by a major pelvic infection and died as a result of methotrexate-related nephrotoxicity, (v) hysterectomy was performed following hemorrhagic shock triggered by vascular injury during the Cesarean section.

In one patient presenting placenta accreta, recurrence of hemorrhage on Day 11 necessitated curettage under general anesthesia.

**Evaluation of fertility after embolization**

Of the 41 surviving patients who had undergone embolization, all had a return of normal menses, with the timing depending on breastfeeding and use of contraception (Table II). When women did not breastfeed, their menses normally recurred between 6 and 8 weeks after delivery. Eight patients using levonorgestrel-releasing intrauterine device or levonorgestrel were fully treated by medical measures and thus another embolization was not necessary. There were 19 pregnancies (46.3%), two of which were twin pregnancy (one spontaneous and one after clomiphene citrate) and one was an early spontaneous abortion. Finally, one patient was pregnant at the time of this report. All but four studied patients, who could not be contacted, provided information concerning their fertility: 16 did not wish to have any further children, 5 had no present wish to have another child and 16 (39%) wanted another child. When they decided to become pregnant again, it happened 1–11 months later. The earliest delivery occurred 1 year after the embolization, by vaginal birth.

Hundred percentage of patients who wished another child conceived one or two other children (one of the women needed a treatment by clomiphene citrate for polycystic ovary syndrome but that was also the case for her first pregnancy). Fifty percentage of these women gave birth by Cesarean section. Six patients had more than one pregnancy after the embolization: one had a preterm delivery (twin) with fetal growth restriction (2030 and 2250 g) and the others were at term, without any major incident (Table II). The babies weights were between 2030 and 4140 g (Table II). Only one repetition of obstetric hemorrhage was observed and successfully treated by medical measures and thus another embolization was not necessary. There were 19 pregnancies (46.3%), two of which were twin pregnancy (one spontaneous and one after clomiphene citrate) and one was an early spontaneous abortion.

**Table II. Pregnancy after embolization**

<table>
<thead>
<tr>
<th>No</th>
<th>Pregnancy</th>
<th>Assisted reproduction</th>
<th>Duration of attempt to conceive (months)</th>
<th>Complications</th>
<th>Delivery</th>
<th>Birth weight g</th>
<th>Centiles*</th>
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<tbody>
<tr>
<td>1</td>
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<td>41+3</td>
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<tr>
<td>3</td>
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<td></td>
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</tr>
<tr>
<td>8</td>
<td>2003</td>
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<td>10</td>
<td></td>
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</tr>
<tr>
<td>10</td>
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<td>No</td>
<td>5</td>
<td></td>
<td>38+2</td>
<td>Cesareans sections</td>
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</tr>
<tr>
<td>12</td>
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<td>3</td>
<td></td>
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<tr>
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<td>2003 twins</td>
<td>Clomifene citrate</td>
<td>11</td>
<td>Preterm delivery</td>
<td>35+5</td>
<td>Cesarean section</td>
<td>2960</td>
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<tr>
<td>18</td>
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<td>2</td>
<td></td>
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</tr>
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<tr>
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<td>4</td>
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<td>2007 twins</td>
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<td>6</td>
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<tr>
<td>32</td>
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<tr>
<td>34</td>
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<tr>
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<td>Gestational diabetes</td>
<td>38+5</td>
<td>Cesarean section</td>
<td>3630</td>
</tr>
</tbody>
</table>

*From Salomon et al. (2007).*
In our series, 68% of hemorrhages were due to uterine atony, within the range reported in the literature (from 45% to 78%) (Pelage et al., 1998; Vandelet et al., 2001; Deux et al., 2001; Boulleret et al., 2004).

Reported primary success rate (i.e. rate of success of the first embolization) for this same indication ranges from 73% to 100%; in our series it was 89.1% and we did not have to resort to secondary embolization. According to published data, secondary embolization is generally required in 8–15% patients (Vedantham et al., 1997; Pelage et al., 1998; Deux et al., 2001; Boulleret et al., 2004) and gives a very satisfactory final success rate of 96%.

Since 1996, only 11 hysterectomies for vascular hemostasis have been performed in our department, including five after failure of embolization. These cases included three patients with placenta accreta and two patients with arterial lesions. The rate of successful embolizations in our study was 89.1% and thus, is in the range of published data, comprised between 73% and 100% (Vedantham et al., 1997; Pelage et al., 1998; Vandelet et al., 2001; Deux et al., 2001; Boulleret et al., 2004; Tsang et al., 2004). As described in the literature, we also observed that abnormal placental insertion increased the risk of failure of conservative methods (Palacios Jaraquemada, 1999; Sergent et al., 2004). In our series, 60% of embolization failures were due to placenta accreta, when compared with 50% in the studies reported by Sergent et al. (2004) and Chou et al. (2004) and only 13% in that of Vandelet et al. (2001) and 29% in that of Descargues et al. (2001). It should be noted that the rate of successful embolization for our subgroup of eight patients with placenta accreta is 62.5%.

The results of numerous studies nevertheless encourage the use of embolization in patients with previously diagnosed placenta accreta, while leaving the placenta in location and in some cases injecting methotrexate (Descargues et al., 2000, 2001; Bennet and Sen, 2003; Courbiere et al., 2003; Clement et al., 2004). In our study, the only patient benefiting from such conservative treatment for placenta percreta after five Cesarean sections unfortunately died as a result of intolerance to methotrexate.

The other reported causes of failure of embolization are uterine artery spasm (Deux et al., 2001), scarred uterus, previous arterial ligation hampering catheterization (Vedantham et al., 1997; Vandelet et al., 2001), embolization of a single artery, or embolization too proximal for development of collateral networks (Deux et al., 2001).

According to published reports, four rare types of complication may be encountered: arterial dissection, allergy to the contrast medium, hematoma at the site of catheter insertion and pain (Vedantham et al., 1997; Boulleret et al., 2004; Goffinet et al., 2005). In our study, one patient experienced injury to the epigastric artery secondary to catheterization initially overlooked. This patient had to undergo four additional operations before the arterial lesion was detected. In another patient, catheterization was complicated by the formation of a hematoma of Scarpa’s fascia, proximal to the common femoral artery. Finally, one patient presented an allergic reaction to iodine.

The other types of complications are directly related to embolization and may take the form of infection, amenorrhea or premature menopause (Vedantham et al., 1997; Wang and Carmel, 2003; Chou et al., 2004; Goffinet et al., 2005) and also, in exceptional cases, uterine ischemia when polyvinyl alcohol particles are used for embolization (Cottier et al., 2002). No complications of this type occurred in our series.

There are guidelines that recommend arterial embolization for patients with uterine atony or who are hemodynamically stable, whereas artery ligation is preferred if patients are hemodynamically unstable or during a Cesarean section (Ledeet et al., 2001; Vandelet et al., 2001; Sergent et al., 2004).

In our series, as in many others, we consider that embolization is the initial treatment for post-partum and post-Cesarean pelvic bleeding. Indeed, failed arterial ligation can render later embolization difficult whereas surgical ligation and B-Lynch stitch are always available after embolization (Vedantham et al., 1997; Sergent et al., 2004; Hong et al., 2006). Sometimes we used intracavitary balloons for patients transferred from another hospital or when the operating theatre was not available. Balloon tamponade could be an effective adjunct in the treatment of severe post-partum hemorrhage when medical therapy fails (Dabelea et al., 2007).

A further objective of our study was to demonstrate the preservation of fertility after embolization. Unfortunately, four patients could not be contacted at the time of our data collection due to the length of the study and six patients were not relevant, as the time elapsing since embolization was too short (14.2%). Among the patients who answered our phone call, 16 wished to become pregnant again and succeeded with a delivery at term without major incident (100%), including one patient who already had recourse to assisted reproduction treatment and needed it again. One patient is currently pregnant without having had recourse to medically assisted procreation.

Many studies have reported that fertility is not diminished after embolization (Stancato-Pasik et al., 1997; Ornan et al., 2003, Salomon et al., 2003; Wang and Carmel, 2003; Boulleret et al., 2004; Descargues et al., 2004; Goffinet et al., 2005). We confirm here that fertility is not hampered by embolization. In the literature, the proportion of women resuming normal menstrual cycles after embolization varies from 91% to 100%. This high proportion is explained by the mechanism of embolization, permitting a temporary and rapidly reversible decrease in arterial flow (Stancato-Pasik et al., 1997; Tsang et al., 2004; Goffinet et al., 2005). We used resorbable gelatine sponge pledgets which allowed the revascularization of the uterine artery. Descargues et al. (2004) showed that reabsorption occurs without deterioration of the vascular endothelium in the embolized site.

Nevertheless, an analysis of 50 published cases (Goldberg et al., 2002) identified a number of complications during pregnancies following embolization; these included abnormal modes of presentation (17%), low gestational age (28%), low birth weight (7%), recourse to Cesarean section (58%) and hemorrhage (13%). In our case, 50% of patients gave birth by Cesarean section, but all of them had already had one or more Cesarean sections. One patient had premature delivery and fetal growth restriction but it was a twin pregnancy. As


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