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Original Article

Outcomes of hypogastric artery ligation and transcatheter uterine artery embolization in women with postpartum hemorrhage

Chen-Yu Wang [a], Hsueh-Hsing Pan [b], Cheng-Chang Chang [a], Chi-Kang Lin [a, *]

[a] Department of Obstetrics and Gynecology, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan
[b] School of Nursing, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

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ABSTRACT

Objective: This study aimed to report our experience of emergent bilateral hypogastric (internal iliac) artery ligation (HAL) in the management of intractable postpartum hemorrhage (PPH) in a tertiary care center.

Materials and methods: Patients with severe postpartum hemorrhage that could not be controlled with conservative management were retrospectively reviewed from January 2013 to December 2017. Data were retrieved from patients' hospital records. Two cases involving both transcatheter uterine artery embolization (TAE) and HAL were excluded. A total of 40 patients were included in the analysis during this period. The inclusion criteria were gestational age ≥24 weeks and primary severe PPH (blood loss ≥1500 mL within 24 h after birth).

Results: A total of 40 patients with intractable PPH were included after a thorough review of their medical records. Nine of them required HAL during the study period. Causes of PPH included uterine atony, placental abruption, vaginal/cervical laceration, uterine rupture, and placenta accreta. Hemorrhage was effectively controlled in 8 of 9 patients (88.9%) in the group undergoing bilateral HAL even though their initial conditions were poor. All patients with HAL did not have to undergo hysterectomy. No immediate complications developed. There were two maternal deaths in the group undergoing TAE.

Conclusion: Bilateral HAL is an effective life-saving procedure for severe intractable PPH and should be performed as soon as possible when obstetric emergency conditions are indicated.

Introduction

Postpartum hemorrhage (PPH) is the major cause of maternal mortality and morbidity worldwide. In the United States, the incidence of PPH rose from 1.6% in 1994 to 2.4% in 2008, and severe PPH (estimated blood loss [EBL] >1500 mL) doubled during the period with estimated maternal mortality about 30% and severe adverse maternal sequelae about 26.7% worldwide resulted from severe PPH [1,2]. Every year, about 140,000 pregnant women die of PPH, which is one-quarter of the maternal deaths globally [3]. Intractable PPH can lead to complications with severe hypovolemic shock, coagulopathy (disseminated intravascular coagulation [DIC]), emergent hysterectomy, pituitary gland necrosis (Sheehan's syndrome), and prolonged hospitalization. All of them may increase the direct and indirect costs and delay the patient's return to work or normal daily life.

The major cause of PPH is uterine atony. The risk factors include uterine overdistention, anesthesia with halogenated agents, rapid or prolonged labor, oxytocin stimulation, chorioamnionitis, and obesity [4]. However, PPH is unpredictable and could occur even without prior predisposing risk factors. Management of PPH includes administration of uterotonic agents, bimanual uterine massage, intrauterine balloon tamponade, transcatheter uterine artery embolization (TAE), bilateral hypogastric artery ligation (HAL), uterine compression sutures, and, finally, emergent abdominal hysterectomy.

If conservative treatment such as bimanual uterine massage and uterotonic agent administration fails to stop the bleeding, surgical intervention should be considered without hesitation. Emergent abdominal hysterectomy for intractable PPH is uncommon and is always performed as the definite life-saving procedure during or immediately after delivery, including cesarean section and vaginal delivery [5,6]. The incidence rate of emergency abdominal

* Corresponding author. 5F, 325, Section 2, Cheng-Gong Rd., Nei-Hu District, 114, Taipei, Taiwan. Fax: +2 87927207.
E-mail address: kung568@gmail.com (C.-K. Lin).

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hysterectomy in intractable obstetric bleeding was found to be approximately 0.8–2.28 per 1000 deliveries in the United States [7–9]. Even with this low incidence rate of emergency postpartum hysterectomy, it is associated with a relatively high morbidity and mortality rate. The greatest benefit of this procedure is the preservation of fertility in young women of reproductive age and decreased subsequent physical or mental sequelae [10–12]. Other adverse effects include additional surgical intervention, iatrogenic trauma of the bladder or ureter, extensive blood loss and need for massive blood transfusion, perioperative infection, and mortality [9].

For fertility reserve, other fertility-sparing surgical interventions should be considered in nulliparous women. TAE could be first considered in stable patients, but low quality of evidence and weak strength of recommendation were introduced by the World Health Organization (WHO) guidelines in case of severe PPH [12]. HAL was first performed by Sir Kelly in 1893 to control severe hemorrhage during hysterectomy in women with advanced uterine carcinoma [13]. This procedure was mainly used in women with gynecologic malignancy for many decades after development. In 1960, HAL was first introduced to control intractable PPH and then obtained popularity in controlling severe pelvic bleeding in women undergoing gynecologic and obstetric surgeries [14–16]. Recently, many studies indicated that HAL could be effective in controlling intractable PPH and help prevent subsequent DIC [17–19]. HAL should be considered as the first line of management in emergent severe PPH cases and has a variable success rate ranging from 40 to 100% [19,20]. However, only few studies discussed the outcomes of HAL and TAE in severe PPH. The aim of this study was to clarify the outcomes in patients with severe PPH who were managed using either HAL or TAE.

Materials and methods

Study design and participants

A retrospective analysis was performed in a tertiary medical center in northern Taiwan. We screened all charts of patients with PPH from January 2013 to December 2017. Two cases involving both TAE and HAL were excluded. One of these two cases underwent hysterectomy because of DIC developed with intractable uterine bleeding. A total of 40 patients were included in the analysis during this period. The inclusion criteria were gestational age ≥24 weeks and primary severe PPH (blood loss ≥1500 mL within 24 h after birth). Ethical approval was obtained from the Institutional Review Board of Tri-Service General Hospital (TSGHIRB1-106-05-077).

Outcomes and variables

Details of outcomes including the procedure time of HAL and TAE, re-procedure or not, pre-, intra-, or post-procedure total blood loss, laboratory data of blood examination pre- and post-procedure (Hb, Hct, PLT), transfusion, using recombinant coagulation factor VIIa (rFVIIa, NovoSeven®), hospital stay, intensive care unit (ICU) stay, DIC, maternal mortality, and fetal mortality were recorded.

Data including characteristics of the study population such as age, body mass index (BMI), gestational age, history of uterine surgery, gravida, para, route of delivery, singleton or twin, Apgar score at 1 and 5 min after birth, cause of PPH, and transfer to our hospital or not, were collected by a resident physician with more than 5 years of experience in gynecologic and obstetric care.

Statistical analysis

The data were analyzed using IBM SPSS software (SPSS 20.0 for Windows). The means and standard deviations were used for the continuous variables, and frequencies and proportions for the categorical variables. Normality was analyzed by Shapiro–Wilk test. Nonparametric statistics, including Mann–Whitney U test and chi-square with Fisher's correction one-tailed test were also used in this study. A p value < 0.05 was considered statistically significant.

Results

Characteristics of the study population undergoing HAL and TAE are presented in Table 1. The two groups of women with PPH exhibited no significant differences in baseline characteristics ($p > 0.05$).

Differences in the mean values of the procedure time (120.3 ± 72.8 vs. 158.2 ± 31.4, $p = 0.012$); total blood loss (5747.8 ± 2553.1 vs. 3586.1 ± 3494.0, $p = 0.005$), especially pre- (4147.3 ± 2053.0 vs. 1131.2 ± 475.0, $p < 0.001$) and intra-procedure (1009.1 ± 727.0 vs. 1064.0 ± 572.6, $p = 0.044$); pre-procedure hemoglobin level (6.7 ± 2.1 vs. 9.2 ± 2.6, $p = 0.025$); transfusion of packed RBC (PRBC) (19.9 ± 11.1 vs. 12.8 ± 23.6, $p = 0.005$) and fresh frozen plasma (FFP) (16.3 ± 10.4 vs. 11.2 ± 23.8, $p = 0.016$); and length of ICU stay (4.0 ± 2.6 vs. 2.2 ± 3.4, $p = 0.030$) between the HAL and TAE groups were all statistically significant. The HAL group had shorter procedure time but worse initial clinical conditions, which led to greater blood loss, more blood transfusions, and longer hospital stay. The most common cause of PPH in our retrospective study was uterine atony, followed by placental abruption. All uteruses were preserved in our retrospective analysis. Two

Table 1
Characteristics of the study population undergoing HAL and TAE.

Variable	HAL n = 9	TAE n = 31	*p*-value
	M±SD/n (%)	M±SD/n (%)	
Age, year	33.6 ± 3.0	34.5 ± 4.5	0.516[a]
BMI, kg/m^2	24.7 ± 2.1	26.8 ± 3.9	0.099[a]
Gestational age, week	38.9 ± 0.7	37.9 ± 3.2	0.770[a]
History of uterine surgery			0.590[b]
Yes	1 (11.1)	5 (16.1)	
No	8 (88.9)	26 (83.9)	
Gravida			0.177[b]
1 time	3 (33.3)	18 (58.1)	
≥2 times	6 (66.7)	13 (41.9)	
Para			0.064[b]
0 time	2 (22.2)	18 (58.1)	
≥1 times	7 (77.8)	13 (41.9)	
Route of delivery			0.406[b]
NSD	6 (66.7)	17 (54.8)	
CS	3 (33.3)	14 (45.2)	
Baby			0.344[b]
Singleton	9 (100)	27 (87.1)	
Twin	0 (0)	4 (12.9)	
Weight, gm	3250.2 ± 180.5	3110.0 ± 872.4	0.400[a]
Apgar			
1 min after birth	6.8 ± 2.6	6.7 ± 1.9[#]	0.385[a]
5 min after birth	7.9 ± 3.0	8.3 ± 1.6[#]	0.736[a]
Cause of PPH			0.091[b]
Atony	5 (55.6)	24 (77.4)	
Abruption	1 (11.1)	3 (9.7)	
Vaginal/cervical laceration	1 (11.1)	2 (6.5)	
Rupture	2 (22.2)	0 (0)	
Accreta	0 (0)	2 (6.5)	
Transfer to our hospital			0.225[b]
No	3 (33.3)	17 (54.8)	
Yes	6 (66.7)	14 (45.2)	

HAL = hypogastric (internal iliac) artery ligation, TAE = transcatheter uterine artery embolization, BMI = body mass index, NSD = normal spontaneous delivery, CS = caesarean section, PPH = postpartum hemorrhage.
[a] Mann–Whitney U test.
[b] Chi-square with Fisher's one-tailed correction test.
[#] missing data.

maternal deaths in the TAE group due to intractable DIC were noted. All details are shown in Table 2.

Discussion

In this study, we demonstrated that HAL had a shorter procedure time than TAE in women with severe PPH, and the difference was statistically significant. However, higher total blood loss, especially pre- and intra-procedure, lower Hb count (before intervention), more PRBC transfusions, and longer hospital and ICU stay were noted in the HAL group in comparison to the TAE group. After a thorough review of the charts, all patients in the HAL group were hemodynamically unstable and had greater blood loss in initial inspections. Because of preoperative hemodynamic instability and uncontrolled obstetric bleeding, invasive surgical intervention should be first considered without hesitation [18].

Emergent abdominal hysterectomy could be one of the alternative management methods but should never be considered first because of its irreversible impact on fertility in young women who desire to bear children in the future. In contrast to hysterectomy, bilateral HAL has been reported as a safe and effective method for the management of intractable PPH, with the preservation of fertility and reduced maternal death rate [19,21–23]. According to some prior hemodynamic studies of patients who underwent bilateral HAL, the effectiveness of this procedure could be attributed to 49% reduction in pelvic blood flow and 85% reduction in pulse pressure, thus rapidly promoting hemostasis. Every obstetrician should be familiar with this procedure and use it as the first line of treatment for intractable PPH with life-threatening conditions [19,24].

The timing of emergent interventions for severe PPH is still controversial and mainly depends on the experience and technique of the operator. Few studies suggested that the procedures for control of severe PPH should be initiated at an EBL lower than that meeting the standard criteria for PPH [25]. Some studies indicate that current definition of PPH is not strong enough for early identification of severe PPH. They introduced shock index (SI) instead of estimating the amount of blood loss for early diagnosis of severe PPH. The SI, quotient of heart rate divided by systolic blood pressure, which was first introduced in 1967 for recognition of gastrointestinal bleeding [1]. Patients with SI > 0.9 or heart beating greater than systolic blood pressure may indicate the necessity of emergent interventions [1]. In our study, all of the cases in the HAL group had elevated heart rates and decreased systolic blood pressures, the SI were all more than 0.9. According to our review and experience, HAL should be performed immediately in cases with persistent and severe uterine bleeding and unstable vital signs (SI > 0.9) after delivery, both abdominally and vaginally. In our survey of medical records, most of the patients (n = 6, 66.7%) in the HAL group were referred from other obstetric clinics with critical condition and unstable vital signs (hypovolemic shock, tachycardia, and disturbance of consciousness). Massive blood transfusion was administered with adequate PRBCs, FFP, and platelets as part of initial urgent resuscitation in the emergency department. All 6 patients, on average, were sent to our operating room within 15 min after initial resuscitation. All patients underwent bilateral HAL as soon as possible and had no immediate complications. All uteruses were preserved [26].

Complications of HAL include external or internal iliac vein injury, bladder atony, ischemia of the gluteal muscles, and, rarely, external iliac artery thrombosis [19,27]. Pulsation of the dorsalis pedis artery at both feet should be checked after bilateral HAL to promptly identify errors in external iliac artery ligation. The success rate of bilateral HAL during our study period was 88.9%, and only one patient in this group needed further coagulant agent (NovoSeven®). However, some previous studies indicated that abnormal placentation (placenta previa, accreta, increta, and percreta) can lead to failure of hemostasis through this procedure and lower success rate [28]. There was no abnormal placentation in our review of medical records.

In the TAE group, most patients were relatively hemodynamically stable after adequate fluid resuscitation or blood transfusion. However, two patients in the HAL group died due to severe hypovolemic shock during TAE. Compared to HAL, TAE needed longer surgical time from needle insertion to localization of the bleeding source. It took more time to perform Gelfoam embolization to achieve hemostasis. However, the TAE group is not available whenever the patients need in some settings. In our institution, it may cost 30 min or even longer to wait for gathering the members to operate TAE in the midnight. This limits the clinical practice of TAE in patients with intractable PPH plus hemodynamic instability who need immediate interventions. A clinical study indicated that TAE may be effective in severe PPH even with unstable hemodynamic conditions. The success rate was 79% [29]. In our knowledge

Table 2
Different outcomes of HAL and TAE in the study population.

Variable	HAL n = 9	TAE n = 31	*p*-value
	M±SD/n (%)	M±SD/n (%)	
Procedure time, min	120.3 ± 72.8	158.2 ± 31.4	0.012[a]
Re-open			0.596[b]
Yes	0 (0)	2 (6.5)	
No	9 (100)	29 (93.5)	
Total blood loss, mL	5747.8 ± 2553.1	3586.1 ± 3494.0	0.005[a]
Pre-procedure	4147.3 ± 2053.0	1131.2 ± 475.0	<0.001[a]
Intra-procedure	1009.1 ± 727.0	1064.0 ± 572.6	0.044[a]
Post-procedure	2037.3 ± 843.8	4582.7 ± 1018.0	0.662[a]
Blood examination			
Hb, mg/dL			
Pre-procedure	6.7 ± 2.1	9.2 ± 2.6	0.025[a]
Post-procedure	9.9 ± 1.1	9.6 ± 1.6	0.475[a]
Hct, mg/dL			
Pre-procedure	22.6 ± 5.6	36.0 ± 45.4	0.060[a]
Post-procedure	28.6 ± 3.6	27.3 ± 5.5	0.466[a]
PLT, $*10^3$ u/L			
Pre-procedure	134.1 ± 73.4	145.5 ± 76.1	0.697[a]
Post-procedure	101.9 ± 40.4	123.6 ± 65.8	0.486[a]
Transfusion, unit			
PRBC	19.9 ± 11.1	12.8 ± 23.6	0.005[a]
FFP	16.3 ± 10.4	11.2 ± 23.8	0.016[a]
SD	2.2 ± 1.9	2.2 ± 3.8	0.354[a]
WB	0.2 ± 1.1	0.7 ± 2.0	0.159[a]
Cry	6.9 ± 11.3	8.1 ± 29.0	0.430[a]
Coagulant agent (NovoSeven®)			0.496[b]
Yes	1 (11.1)	6 (19.4)	
No	8 (88.9)	25 (80.6)	
Hospital stay, day	8.1 ± 4.4	5.8 ± 3.1	0.144[a]
ICU			0.011[b]
Yes	9 (100)	17 (54.8)	
No	0 (0)	14 (45.2)	
Stay, day	4.0 ± 2.6	2.2 ± 3.4	0.030[a]
DIC			0.594[b]
Yes	4 (44.4)	13 (41.9)	
No	5 (55.6)	18 (58.1)	
Maternal mortality			0.596[b]
Yes	0 (0)	2 (6.5)	
No	9 (100)	29 (93.5)	
Fetal mortality			0.775[b]
Yes	0 (0)	1 (3.2)	
No	9 (100)	30 (96.8)	

HAL = hypogastric (internal iliac) artery ligation, TAE = transcatheter uterine artery embolization, SD = standard deviation, Hb = hemoglobin, Hct = hematocrit, PLT = platelet, PRBC = packed RBC, FFP = fresh frozen plasma, SD = single donor platelet, WB = whole blood, Cry = cryoprecipitate, ICU = intensive care unit, DIC = disseminated intravascular coagulation.

[a] Mann–Whitney U test.

[b] chi-square with Fisher's one-tailed correction test.

and experience, the risk in hemodynamically unstable patients with PPH who underwent TAE is higher than those who underwent HAL according to our retrospective study. Early performance of TAE in one study found that patients who underwent interventions for PPH with lower EBL of 500–700 mL had better outcomes than those with EBL >700 mL [30]. There is no clear cutoff point for EBL indicating initiation of TAE. There was one hysterectomy in the excluded group because of DIC with intractable uterine bleeding after both TAE and HAL. In our review of records, this patient was referred from other obstetric institution because of intractable uterine bleeding after vaginal delivery with relative stable vital signs. It took about 3 h from arrangement to completion of the TAE procedure. However, persistent uterine bleeding with elevated heart pulsation was observed even after the procedure. We kept blood transfusion during this period. Then we performed HAL about 12 h after TAE because DIC developed. In the end of the surgery, persistent vaginal bleeding was still noted. After discussion with her family, we shifted the surgery to subtotal hysterectomy instead. Ultimately, the DIC was corrected and the patient discharged without immediate complications.

The higher DIC rate in the HAL group in our study may have resulted from massive bleeding that had developed before the patients were transferred to our hospital. After successful bilateral HAL and adequate blood transfusion, DIC was corrected, and there was no mortality in the HAL group. Other coagulating agents, a rFVIIa (NovoSeven®), has been administered to patients with coagulation factor deficiency for a long time. It provides excellent ability to control bleeding effectively. However, it has still not been certified in the field of surgical hemostasis. The WHO guideline in PPH management suggests administration of rFVIIa for control of intractable PPH, which reduces the risk of maternal death [12]. According to the studies in the guideline, rFVIIa could be effective as the “last resort” if inadequate hemostasis is noted even after or before surgical interventions. However, due to its cost and off-label use, it should not be administered routinely [12].

One study suggested uterine artery ligation (UAL) as a better method than bilateral HAL in uncontrolled PPH with a success rate of >90% and a remarkably low complication rate [31]. However, dissection and identification of the bilateral uterine arteries can take more time than that for the exposure of hypogastric arteries, and the surgical field may be disturbed by the engorged uterus in UAL. Ligation of the main trunk of the pelvic vessel is relatively easy to approach. In fact, pelvic circulation after bilateral HAL had been studied in few elegant reports, and collateral circulation developed after ligation, which adequately maintained blood supply to the pelvic organs [32]. There was no obvious adverse effect after bilateral HAL in subsequent fertility and pregnancy outcome in a critical review, but intrauterine growth restriction should be assessed closely according to these studies [17]. However, we need a further cohort study to assess fertility outcomes and adverse effects after bilateral HAL. The main limitation of our study was that this is a retrospective study without a control group and further long-term follow-up of complications and fertility outcome is needed.

Conclusion

Severe PPH with hemodynamic instability is fatal, and further management should not be delayed. In such conditions, early recognition of severe PPH and emergent surgical interventions should be immediately considered by the obstetrician. Bilateral HAL could be a life-saving and fertility-sparing procedure when performed by a reliable skilled operator. This skill should be introduced in all gynecologic and obstetric training programs and always kept in mind when encountering intractable PPH. We suggest that TAE should be the first choice and always be considered in hemodynamically stable patients with persistent bleeding after conservative management of severe PPH. In contrast, in patients with severe PPH with unstable vital signs, especially when SI is more than 0.9, emergent bilateral HAL must be the first priority. The procedure should be performed as soon as possible.

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Conflict of interest

The authors declare that there is no financial and conflicts of interest that could be perceived as prejudicing the impartiality of the research reported.

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