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*Original Research*

# Intrauterine Vacuum-Induced Hemorrhage-Control Device for Rapid Treatment of Postpartum Hemorrhage

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**OBJECTIVE:** To evaluate the effectiveness and safety of an intrauterine vacuum-induced hemorrhage-control device for postpartum hemorrhage treatment.

**METHODS:** A multicenter, prospective, single-arm treatment study of a novel intrauterine device that uses low-level vacuum to induce uterine myometrial contraction to achieve control of abnormal postpartum uterine bleeding and postpartum hemorrhage was undertaken at 12 centers in the United States. The primary effectiveness endpoint was the proportion of participants in whom use of the intrauterine vacuum-induced hemorrhage-control device controlled abnormal bleeding without requiring escalating interventions. The primary safety endpoint was the incidence, severity, and seriousness of device-related adverse events. Secondary outcomes included time to bleeding control, rate of transfusion, and device usability scored by each investigator using the device.

**RESULTS:** Of 107 participants enrolled with primary postpartum hemorrhage or abnormal postpartum uterine bleeding, 106 received any study treatment with the device connected to vacuum, and successful treatment was observed in 94% (100/106, 95% CI 88–98%) of these participants. In those 100 participants, definitive control of abnormal bleeding was reported in a median of 3 minutes

See related editorial on page 874.

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(interquartile range 2.0–5.0) after connection to vacuum. Eight adverse events deemed possibly related to the device or procedure were reported, all of which were outlined as risks in the study and all of which resolved with treatment without serious clinical sequelae. Transfusion of 1–3 units of red blood cells was required in 35 participants, and five participants required 4 or more units of red blood cells. The majority of investigators reported the intrauterine vacuum-induced hemorrhage-control device as easy to use (98%) and would recommend it (97%).

**CONCLUSION:** Intrauterine vacuum-induced hemorrhage control may provide a new rapid and effective treatment option for abnormal postpartum uterine bleeding or postpartum hemorrhage, with the potential to prevent severe maternal morbidity and mortality.

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Postpartum hemorrhage is the leading cause of maternal mortality worldwide and is responsible for 25% of maternal deaths from obstetric causes.[1] Moreover, the problem is growing, particularly in the United States, where rates of severe maternal morbidity and transfusions have increased[2] despite commensurately increasing utilization rates of first- and second-line postpartum hemorrhage treatment modalities.[3] Many important efforts have been developed to address these trends, notably comprehensive safety bundles inclusive of recognition and prevention of abnormal postpartum bleeding, readiness with improved training and transfusion protocols, and robust quality reporting,[4–6] and yet there have been few innovative approaches to treat abnormal postpartum bleeding or postpartum hemorrhage before morbidity occurs.

Uterine atony causes up to 80% of all postpartum hemorrhages.[7] After most deliveries, constriction of the uterine vasculature occurs when contraction of the interlacing muscle fibers of the myometrium control bleeding after placental delivery.[8–11] In an atonic uterus, vessels are not constricted and hemorrhage ensues, prompting first-line therapy. When medical management alone is deemed unsuccessful, tamponade is currently the next treatment option added to control uterine atony. Tamponade directly compresses the vascular bed to impede bleeding as a temporizing measure. By using outward pressure on the uterine walls for 12–24 hours,[12,13] the uterus may then involute and regain normal tone.[14] Although tamponade has been demonstrated to be effective in controlling hemorrhage in 87% (95% CI 84–90%) of atony-related cases,[15] the mechanism of action of using outward pressure to control bleeding from uterine atony is counterintuitive if the ultimate goal is uterine contraction. Additional drawbacks of tamponade include the need for prolonged monitoring and observation, the risk of occult bleeding, potential expulsion or displacement through the cervix, cervical tears, vaginal laceration, acute colonic pseudoobstruction, uterine incision rupture, uterine perforation, and infection.[15–17] The frequency of complications attributed to uterine balloon tamponade use was up to 6.5% in the recent meta-analysis by Suarez et al.[15] Most protocols[18,19] recommend using tamponade or packing after at least 1,000 mL of blood have been lost and, with ongoing bleeding, up to 1,500 mL. Up until this point, there have been few other options appropriate for early use in the management of abnormal bleeding unresponsive to uterotonics alone or in a patient who has limited options for uterotonics owing to contraindications. Beyond these modalities, other treatment options consist of increasingly invasive procedures.

The Jada System (novel intrauterine vacuum-induced hemorrhage-control device) was specifically designed to offer rapid treatment by applying low-level intrauterine vacuum to facilitate the physiologic forces of uterine contractions to constrict myometrial blood vessels and achieve hemostasis. The device was evaluated in a prior feasibility study outside the United States that showed promise as a rapid treatment for abnormal postpartum uterine bleeding or postpartum hemorrhage.[20] The study reported herein was conducted in the United States to evaluate the effectiveness and safety of the intrauterine vacuum-induced hemorrhage-control device to control abnormal postpartum uterine bleeding or postpartum hemorrhage in a larger patient population.

## ROLE OF THE FUNDING SOURCE

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## METHODS

This was a prospective, observational, multicenter treatment study (clinicaltrials.gov NCT02883673). The aim of the study was to evaluate the effectiveness and safety of the intrauterine vacuum-induced hemorrhage-control device for the control of postpartum hemorrhage. The intrauterine vacuum-induced hemorrhage-control device is made of medical-grade silicone, with an elliptical intrauterine loop on the distal end and, on the proximal end, a vacuum connector that allows connection using standard tubing to an in-line graduated canister and regulated vacuum source (Fig. 1). In this study, the regulated vacuum source included standard wall suction and, in some cases, a transportable vacuum source. The inner surface of the intrauterine loop has 20 vacuum pores that facilitate creation of vacuum within the uterine cavity. The outer surface is covered by a shield that overhangs the vacuum pores to protect maternal tissue from the vacuum and to prevent the vacuum pores from clogging with tissue or blood clot. The intrauterine loop and other components are soft and smooth to limit the chance of tissue damage during insertion, treatment, and removal of the device.

A manual sweep of the uterine cavity is customarily performed to evaluate for retained products and to assess the integrity of the uterine cavity; in the case of ongoing bleeding, it is performed again before device placement to clear any organized clot from the uterus before treatment. The device is then introduced through the cervix into the uterine cavity with direction either by the user's hands or with the assistance of standard instrumentation such as sponge forceps. The goal of placement is to place the intrauterine loop within the uterine cavity, with the donut-shaped cervical seal just outside the external cervical os at the top of the vagina, which limits vacuum application to the uterus only. The cervical seal is filled with sterile fluid (60–120 mL), and low-level vacuum (80±10 mm Hg) is applied using a regulated vacuum source with an in-line canister. Pooled blood is evacuated from the uterus as the uterus collapses, which can be observed directly when the abdomen remains open during cesarean delivery or by abdominal palpation or real-time ultrasound scan after vaginal delivery. The volume of blood initially evacuated from the uterus and any ongoing blood loss is quantified in the canister during treatment. Control of abnormal bleeding or postpartum hemorrhage was defined in the protocol as the first report that abnormal bleeding had been stopped. Control is considered definitive when there is an absence of recurrence without need for additional escalation of treatment.

The intrauterine vacuum-induced hemorrhage-control device remains in place (Fig. 2), with the vacuum applied for at least 1 hour after control of hemorrhage. With the uterine cavity collapsed and bleeding controlled, the continued application of vacuum allows time for physiologic or medication-induced myometrial contractions that collapse the uterine cavity and occlude vessels. Control is evaluated by direct observation of blood flow through the system while feeling for a firm uterus. This contracted state, which mirrors the natural process after delivery, is designed to provide sustained control of bleeding. After active therapy is completed, the vacuum is disconnected and the cervical seal emptied. The device is left in place for a minimum of 30 minutes to allow close observation for any return of atony or abnormal

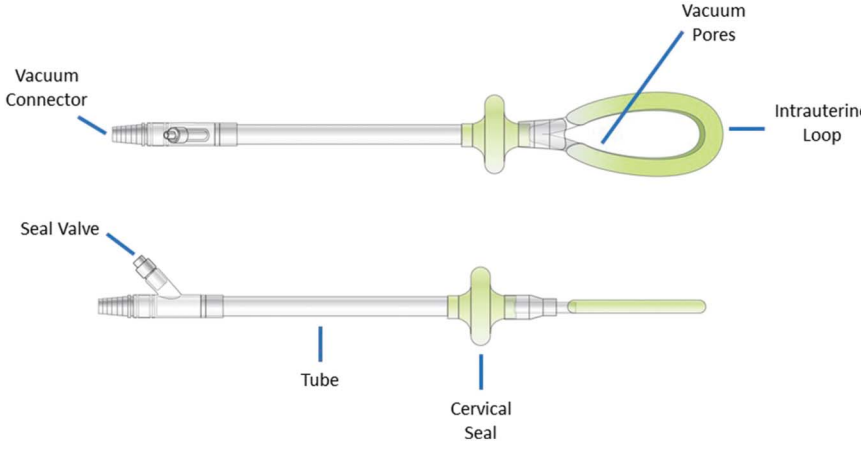


**Fig. 1.** The intrauterine vacuum-induced hemorrhage-control device (The Jada System). Image courtesy of Alydia Health. Used with permission.
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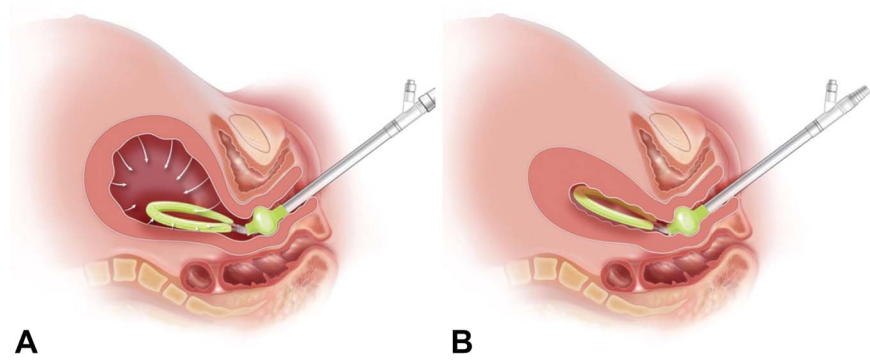


**Fig. 2.** Placement of intrauterine vacuum-induced hemorrhage-control device with low-level vacuum connected (**A**) and uterine contraction (**B**). Images courtesy of Alydia Health. Used with permission.

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bleeding necessitating further treatment before removal. Finally, to remove the device, one hand is placed on the abdomen to support the uterine fundus while the other hand slowly withdraws the device through the vagina. The device is not intended to be left within the uterus for more than 24 hours. Prophylactic antibiotic administration was not specifically required as part of the study protocol but could be prescribed based on the clinical judgment of the investigator and their local postpartum hemorrhage–management guidelines.

Women were eligible for participation in the study if they were 18 years of age or older, able to consent, delivered at 34 weeks of gestation or later, had normal uterine anatomy (women with uterine leiomyomas not excluded) and normal placentation, and had atony-related pre–device placement estimated blood loss of 500–1,500 mL after vaginal delivery or 1,000–1,500 mL after cesarean delivery (device placed transvaginally after hysterotomy closure) unresponsive to treatment with uterotonics and uterine massage. Initial quantitative blood loss was not required, because many sites were not universally calculating real-time quantitative blood loss. However, if quantitative blood loss was available before placement of the vacuum-induced hemorrhage-control device, it was captured and used instead of estimated blood loss. Blood loss criteria for inclusion were developed acknowledging that the reVITALize[21] definition for postpartum hemorrhage was published in 2014, with the American College of Obstetricians and Gynecologists Practice Bulletin[22] subsequently updated for consistency to a cumulative blood loss of 1,000 mL or greater.[21,22] However, both reVITALize and the American College of Obstetricians and Gynecologists highlight that a blood loss of 500–999 mL should trigger increased supervision and potential interventions as clinically indicated. Large state-wide perinatal-quality collaboratives continue to cite blood loss greater than 500–999 mL as abnormal,[18,19] and care teams often initiate treatment in this abnormal range to minimize ongoing blood loss.[3] Exclusion criteria included retained placenta without easy manual removal, uterine rupture, purulent infection, coagulopathy, or blood loss greater than 1,500 mL at time of device placement. Additional medications could be continued during or after treatment according to standard care at each clinical site, provided maximum dosing was not exceeded.

Enrollment occurred from February 2018 to January 2020 at 12 hospitals across the United States. Race and ethnicity were categorized on the study case report forms according to National Institutes of Health standards and were abstracted from medical record review, reliant on patient self-report. Women were approached by trained research staff in the prenatal setting or the labor and delivery unit for consent. Informed consent was obtained before the diagnosis of postpartum hemorrhage to ensure the participants were not consented while in a state of duress. Women who gave consent were enrolled if they reached the estimated blood loss inclusion requirement and had suspected uterine atony that was determined to be refractory to initial treatment with uterine massage, prescribed uterotonics, and possibly tranexamic acid. If the participant underwent cesarean delivery, a minimal cervical dilation of 3 cm was required to attempt placement of the intrauterine vacuum-induced hemorrhage-control device. Only investigators who were trained on device placement and study procedures were permitted to place the device. Training for investigator participation included both a didactic session on the study protocol and use of the device and hands-on simulation using a task trainer uterine model to ensure proficiency using the device. The training included content on the protocol requirement to visualize or palpate uterine collapse after connection of the vacuum during the

steps of using the device as an outcome of interest on the study. During each enrollment, a quick reference guide was included with the device, in addition to the instructions for use. These served as real-time references and visual aides to clearly outline procedural steps. A second study-trained individual was present to re-review inclusion and exclusion criteria with the investigator before the procedure to ensure the patient still met eligibility before device placement and to collect required study data for each participant enrolled.

The primary effectiveness endpoint was the proportion of participants successfully treated for abnormal postpartum uterine bleeding and postpartum hemorrhage, defined as avoidance of other open surgical or nonsurgical interventions after intrauterine vacuum-induced hemorrhage-control device use in the setting of uterine atony. Nonsurgical, second-line treatment included uterine balloon tamponade therapy, uterine packing, or uterine artery embolization; open surgical interventions included exploratory laparotomy or re-operation, vascular ligation, uterine compression sutures, or hysterectomy. The primary safety endpoint was the incidence, severity, and seriousness of device-related adverse events. Adverse events were collected from enrollment to the 6-week follow-up visit, and all investigator reports of adverse events were reviewed by an independent obstetrician medical monitor. Secondary endpoints included time to control of hemorrhage, need for further nonsurgical treatment or surgical treatment after device placement for arrest of atony-related postpartum hemorrhage, treatment with blood transfusion after device placement and total units transfused, and assessment of usability at the conclusion of treatment as reported by the investigator placing the device based on a 5-point Likert scale (Strongly Agree, Agree, Neutral, Disagree, and Strongly Disagree).

Categorical data were summarized using frequency tables, presenting participant counts and relative percentages. Continuous variables were summarized as mean, SD, median, interquartile range, minimum, and maximum as appropriate. A 95% CI was calculated for the treatment success rate. Statistical analysis was performed by an independent statistician (Advanced Research Associates) using SAS 9.4. The study was performed under an Investigational Device Exemption from the U.S. Food and Drug Administration. Institutional review board approval was obtained at each clinical site before commencement of study enrollment.

Two analysis cohorts are presented in this article: an enrolled cohort (n=107) and an intention-to-treat (ITT) effectiveness cohort (n=106). The primary effectiveness analysis was performed on the ITT cohort, and the primary safety analysis was performed on the enrolled cohort.

## RESULTS

Of 107 participants enrolled with primary postpartum hemorrhage or abnormal postpartum uterine bleeding, 106 received any study treatment with the device connected to vacuum. The participant disposition chart is shown in Figure 3. Demographics, obstetric history, and delivery details are presented in Tables 1–3. The mean maternal age was 29.7±5.5 years. Race for the majority of participants was reported as White (57%) or Black or African American (24%). The majority of enrolled participants (64%) met criteria for obesity at admission (body mass index [BMI, calculated as weight in kilograms divided by height in meters squared] 30 or higher). Eighty-five percent of the deliveries were vaginal, with a mean gestational age of 38.1±2.0 weeks. Fifteen participants (14%) delivered neonates with macrosomia (4 kg or more), and 11 (10%) participants were enrolled after delivering twins. The primary cause of abnormal postpartum uterine bleeding or postpartum hemorrhage in all participants was uterine atony. Thirty-four participants (32%) also had delivery-associated lower genital tract lacerations that either had already been repaired or were repaired during treatment with the intrauterine vacuum-induced hemorrhage-control device. The median (interquartile range) estimated blood loss

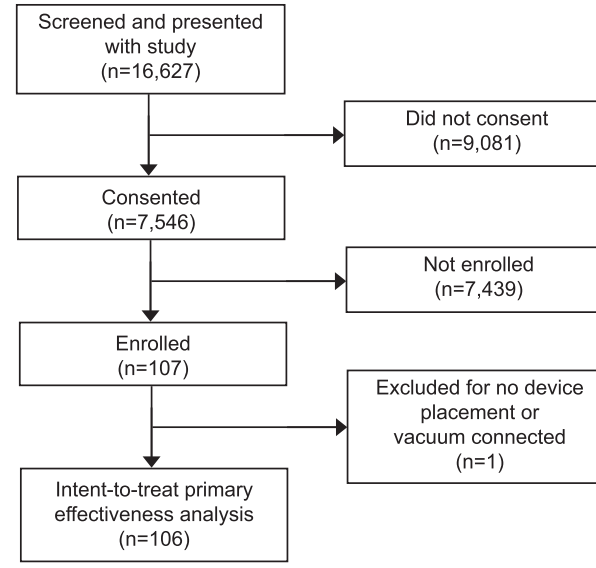


**Fig. 3.** Participant disposition.

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**Table 1. Demographics**

| Characteristic | Enrollment Cohort (N=107) |
|---|---|
| Age (y) | 29.7±5.5 |
| Ethnicity* | |
| Non-Hispanic | 82 (88) |
| Hispanic | 15 (16) |
| Refused | 2 (2) |
| Other | 1 (1) |
| Race* | |
| White | 57 (61) |
| Black or African American | 24 (26) |
| Asian | 8 (9) |
| Other | 8 (8) |
| Refused | 2 (2) |
| American Indian or Alaskan Native | 1 (1) |
| Native Hawaiian or Pacific Islander | 0 (0) |
| Admission BMI (kg/m$^2$)† | 35.2±9.7 |
| Admission BMI category (kg/m$^2$) | |
| Underweight (less than 18.5) | 1 (1) |
| Normal weight (18.5–25) | 6 (6) |
| Overweight or preobesity (25.0–29.9) | 28 (30) |
| Obese class I (30.0–34.9) | 21 (22) |
| Obese class II (35.0–39.9) | 18 (19) |
| Obese class III (40 or higher) | 25 (27) |
| Missing | 2 (2) |

BMI, body mass index.
Data are mean±SD or % (n).
* Race and ethnicity categories were collected according to National Institutes of Health standards. "Other" as a category was included by patient self-report.
† Two participants were missing a height or weight for calculation of BMI and are excluded from this analysis.

**Table 2. Obstetric and Medical History**

| History | Enrollment Cohort (N=107) |
|---|---|
| No. of prior pregnancies | |
| 0 | 33 (35) |
| 1 | 25 (27) |
| 2 | 18 (19) |
| 3 or more | 24 (26) |
| No. of prior vaginal births | |
| 0 | 51 (54) |
| 1 | 25 (27) |
| 2 | 11 (12) |
| 3 or more | 13 (14) |
| No. of prior cesarean births | |
| 0 | 91 (98) |
| 1 | 5 (5) |
| 2 | 3 (3) |
| 3 or more | 1 (1) |
| PPH at previous delivery* | 16 (9/57) |
| Baseline anemia† | 36 (39) |
| Chronic anemia† | 9 (10) |
| Sickle cell | 1 (1) |
| Antepartum hemorrhage, this pregnancy | 4 (4) |
| Preeclampsia, this pregnancy | 23 (25) |
| Macrosomia (birth weight 4 kg or more), this pregnancy | 14 (15) |

PPH, postpartum hemorrhage.
Data are % (n) or % (n/N).
* Includes participants with a previous delivery in the denominator.
† Baseline and chronic anemia are defined by site-specific protocol and diagnosis.

before treatment was 870 mL (700–1,000 mL) for vaginal delivery and 1,300 mL (1,050–1,425 mL) for cesarean delivery.

A 6-week postpartum health assessment was obtained for 103 of the 107 (96%) enrolled participants. A total of eight device- or procedure-related adverse events were reported in the study. These events included endometritis (n=4), disruption of a vaginal laceration repair (n=1), presumed endometritis (n=1), bacterial vaginosis (n=1), and vaginal candidiasis (n=1). All of the events resolved with treatment and without serious adverse sequelae. No cases of uterine rupture, lower genital tract laceration, or uterine incision dehiscence related to device use were reported.

The treatment success rate for the intrauterine vacuum-induced hemorrhage-control device was 94% (100/106, 95% CI 88–98%) in the ITT cohort. Five participants in the ITT cohort required additional surgical or nonsurgical treatment for atony-related bleeding; one participant did not require additional treatment for atony-related bleeding and instead received a suture for an initially unrecognized cervical laceration. The five participants requiring additional atony-related treatment included a participant treated with uterine balloon tamponade for recurrence of atony with bleeding 2.5 hours after device treatment had ended, when re-treatment with the device was not allowed per protocol (n=1); a participant with intraoperative B-Lynch compression suture treatment added in conjunction with the study treatment (n=1); uterine balloon tamponade used after the vacuum regulator was determined to be dysfunctional (n=1); a B-Lynch compression suture followed by hysterectomy (n=1); and a hysterectomy (n=1). In the other 100 participants in the ITT analysis cohort, the device successfully controlled the hemorrhage.

To objectively measure both the procedure performance and the use of resources for treatment, analyses were performed on time to uterine cavity collapse, time to hemorrhage control, and total procedure time (Table 4 and Fig. 4). In successful use of the

**Table 3. Delivery Characteristics**

| Characteristic | Enrollment Cohort (N=107) |
|---|---|
| Vaginal delivery | 85 (91/107) |
| Spontaneous | 90 (82/91) |
| Assisted | 10 (9/91)* |
| Cesarean delivery | 15 (16/107) |
| Emergent | 56 (9/16) |
| Planned | 44 (7/16) |
| Multiple births (twins) | 10 (11/107)† |
| Anesthesia | |
| Epidural | 76 (81) |
| Other‡ | 15 (16) |
| Spinal | 6 (6) |
| None | 3 (3) |
| Systemic | 1 (1) |
| Type of labor | |
| Induced | 67 (72) |
| Augmented | 17 (19) |
| Spontaneous | 8 (8) |
| No labor cesarean | 8 (8) |
| Gestational age (wk) | 38.1±2.0 |
| Birth weight (kg) (n=118)§ | 3.2±0.7 |

Data are mean±SD, % (n/N), or % (n).
* Type of assisted delivery includes forceps (6) and vacuum-assisted (3).
† Ten of the multiple births were vaginal deliveries, and one multiple birth was a cesarean delivery.
‡ Other type of anesthesia includes combined spinal epidural (11), epidural or general (2), nitrous oxide (2), and nalbuphine (1).
§ One hundred eighteen neonates were delivered to the 107 participants, including 11 sets of twins and 96 singletons.

intrauterine vacuum-induced hemorrhage-control device to control hemorrhage, the initial collapse of the uterus reported by investigators occurred in a median of 1 minute (interquartile range 1–2) from the time of vacuum connection, which was either palpated abdominally, demonstrated on ultrasound scan, or visualized intraoperatively (at cesarean delivery). In 82% of participants in whom the device controlled abnormal bleeding, the control occurred within 5 minutes, with a median time of 3 minutes (interquartile range 2–5). Including the required minimums of 60 minutes for vacuum treatment time and 30 minutes of observation without the vacuum connected, the median time of vacuum treatment was 144.0 minutes (interquartile range 85.8–295.8), with total device in-dwelling median time of 191.0 minutes (interquartile range 132.8–365.8). The duration of hospital stay from delivery to discharge was similar to standard delivery hospitalization lengths of stay, with a median stay of 2.2 days (interquartile range 2.0–2.7), with 73% of participants staying 2 days or less. The median length of stay for cesarean birth was higher at 3.0 days (interquartile range 3.1–4.4) compared with 2.0 days (interquartile range 1.9–2.4) for vaginal birth, a difference that is consistent with expected longer stays after cesarean birth.

Forty participants (38%) in the ITT analysis cohort received any blood product. Thirty-five participants (33%) received 1–3 units, and five (5%) received 4 or more units of red blood cells. No participant developed coagulopathy. Although there was clinically significant blood loss before use of the use of the intrauterine vacuum-induced hemorrhage-control device, blood evacuation or loss during treatment was measurable in the tubing or canister and low at a median of 110 mL (interquartile range 75–200).

Investigators who used the device for the study provided an independent assessment of device usability as a part of data collection during each case. Almost all users recommend the device for the treatment of postpartum hemorrhage (97%) and reported that the device was easy to use (98%) (Fig. 5).

## DISCUSSION

In this single-arm observational study, we have shown that the intrauterine vacuum-induced hemorrhage-control device has the potential to be used to rapidly and effectively control abnormal postpartum uterine bleeding and postpartum hemorrhage. In this

**Table 4. Procedure Timing**

| Procedure Timing Analysis | n | Median (IQR) |
|---|---|---|
| Delivery to abnormal bleeding diagnosis (min) | 107 | 23 (9.0–68.5) |
| Peel pack open to insertion (min) | 102* | 2.0 (1.0–3.8) |
| Vacuum connected to uterine collapse (min) | 100† | 1.0 (1.0–2.0) |
| Vacuum connected to bleeding control (min) | 100† | 3.0 (2.0–5.0) |
| Duration of vacuum treatment (min) | 100† | 144.0 (85.8–295.8) |
| Total in-dwelling time (min) | 100† | 191.0 (132.8–365.8) |
| Admission to discharge (d) | 107 | 3.0 (2.6–3.8) |
| Delivery to discharge (d) | 107 | 2.2 (2.0–2.7) |

IQR, interquartile range.
* Five participants missing time of peel pack open to insertion.
† Data available for participants in whom device treatment was successful.

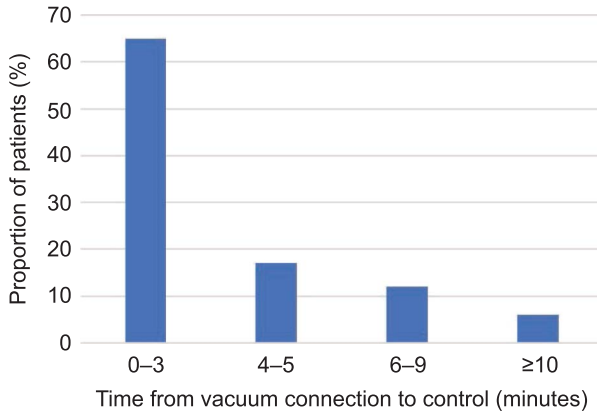


**Fig. 4.** Time to control abnormal bleeding or postpartum hemorrhage (minutes).

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cohort, control occurred within minutes, the indwelling time for the device was short, and treatment was definitive for the majority of patients. The device had a low rate of adverse events during this study, all of which were expected risks and resolved with treatment without serious clinical sequelae. Investigators, all first-time users of the device, found the system easy to use, which suggests that, after device education and with availability of a quick reference guide outlining steps, there is a minimal learning curve for use.

The intrauterine vacuum-induced hemorrhage-control device demonstrates the potential to mechanically achieve the goals of normal uterine physiology or pharmaceutical uterotonics when they are not working alone, contracting the uterus when this does not occur spontaneously immediately postpartum. The use of low-level vacuum (70–90 mm Hg) to contract the myometrium and decrease uterine size is in contrast to traditional mechanical methods used for tamponade, which work by creating outward pressure, causing uterine distention. With tamponade systems there can be complexities to effective placement and maintenance of treatment, because the balloon can rupture if overfilled; therefore, it is recommended to use the minimal amount of uterine distension to accomplish control of bleeding.[14] Tamponade commonly requires the use of vaginal packing to keep the balloon in place, but, when used, a positive tamponade test must first be performed to ensure that packing does not obscure ongoing bleeding.[14] The active nature of intrauterine vacuum treatment and the mechanism of action creates immediate observability and allows for monitoring of any ongoing blood loss, controlling hemorrhage in a definitive manner. Effectiveness is initially observed by the palpable change in uterine tone and visible cessation of blood flow. The ongoing active evacuation of any blood and clot from the uterine cavity using low-level vacuum allows real-time quantification of blood loss throughout treatment, and vaginal packing is not required. Blood collected during treatment can be used in resuscitation efforts through cell salvage.[23]

A review of available treatment options for postpartum hemorrhage reveals a significant unmet need. Atony-related postpartum hemorrhage that is nonresponsive to available uterotonics will require additional treatment. The intrauterine vacuum-induced hemorrhage-control device reported herein offers an additional treatment option, with the potential to be

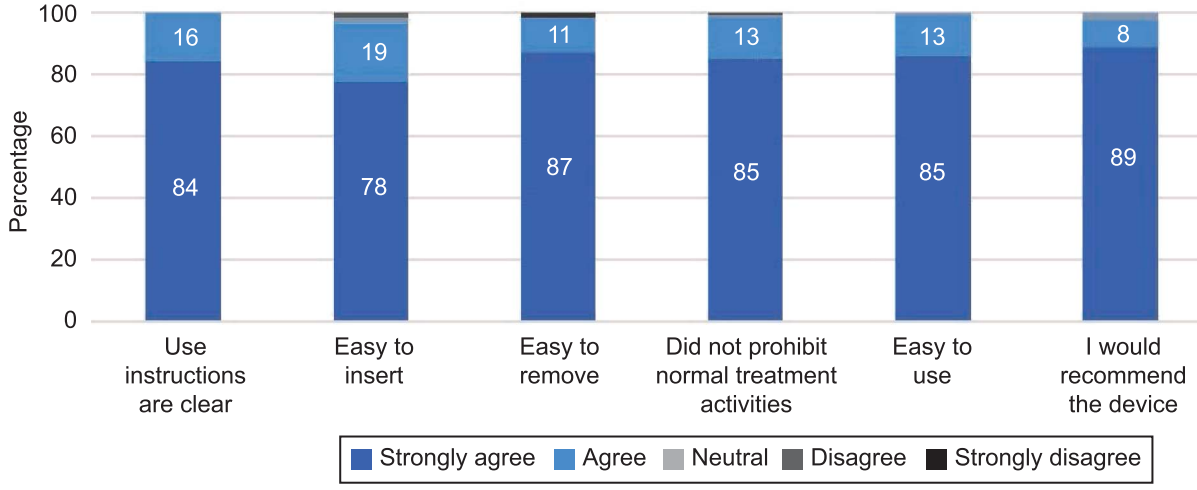


**Fig. 5.** Device usability assessment.

*D'Alton. Vacuum Device for Postpartum Hemorrhage. Obstet Gynecol 2020.*

used early in ongoing bleeding, that is rapid, easy to deploy, effective, and has a reassuring safety profile without serious complications. With 87% effectiveness reported for balloon tamponade devices in a recent meta-analysis,[15] the 94% effectiveness of the vacuum device observed in this single-arm treatment study is promising. Treatment with more invasive procedures, such as uterine artery embolization and surgical interventions, which may not be available in all obstetric units and which carry more risk and cost, may potentially be avoided in a significant number of women when health care professionals have access to more treatment options.

This study has multiple strengths, including the prospective design with a rigorously defined protocol, analysis powered to evaluate effectiveness in the included cohort and safety for common adverse outcomes, and training for investigators and research staff. However, the study is not without limitations, which include that this study was not randomized by design. There are challenges, although not insurmountable, to a randomized controlled trial for atony-related abnormal postpartum bleeding and postpartum hemorrhage. Such a design should be considered in the future, with careful evaluation of the most appropriate comparator for the device and optimal timing for device use within treatment algorithms. As the first large study of this device, enrollment was limited to participants with 1,500 mL or less estimated blood loss for safety reasons, so further study is needed in more severe postpartum hemorrhage cases. Additionally, the majority of cases described herein were vaginal deliveries, which could limit the generalizability of the results. With additional research on this device, safety will be further assessed in a greater number of cases. Finally, patient-reported satisfaction or family-reported outcomes were absent from this study. For example, the majority of participants included had some form of neuraxial labor analgesia, which raises the question of how the procedure will be tolerated in patients without analgesia.

Additional potential benefits of this approach include that using a definitive treatment as soon as it is determined that uterotonics and massage alone are not working, with subsequent rapid cessation of bleeding, may decrease overall blood loss and associated need for blood transfusion or quantity of transfused product. The short duration of time the device is in-dwelling may limit rates of device-related complications such as infection while also reducing resource utilization and cost by decreasing time spent in the labor and delivery unit. Finally, we can reasonably assume that this short duration and more physiologic approach to treatment with the device may be better aligned with shared postpartum treatment goals, including enhancing maternal recovery and facilitating maternal–newborn bonding.

In conclusion, the intrauterine vacuum-induced hemorrhage-control device offers a therapeutic modality that may be considered early in the treatment of abnormal postpartum uterine bleeding or postpartum hemorrhage. Given the speed with which the device has been demonstrated to control abnormal bleeding and postpartum hemorrhage, it is likely to offer benefit to the patient and family, the clinical team, and the health care system overall. This study demonstrates that the intrauterine vacuum-induced hemorrhage-control device might fill an essential treatment need as we strive to decrease rates of severe maternal morbidity and mortality and improve maternal outcomes.

## REFERENCES


1. Gülmezoglu AM, Lawrie TA, Hezelgrave N, Oladapo OT, Souza JP, Gielen M, et al. Interventions to reduce maternal and newborn morbidity and mortality. In: Black RE, Laxminarayan R, Temmerman M, Walker N, editors. Reproductive, maternal, newborn, and child health: disease control priorities, 3rd ed. Washington, DC: The International Bank for Reconstruction and Development/The World Bank; 2016.
2. Bateman BT, Berman MF, Riley LE, Leffert LR. The epidemiology of postpartum hemorrhage in a large, nationwide sample of deliveries. Anesthesia Analgesia 2010;110:1368–73.
3. Goffman D, Friedman AM, Sheen JJ, Kessler A, Vawdrey D, Green R, et al. A framework for improving characterization of obstetric hemorrhage using informatics data. Obstet Gynecol 2019;134:1317–25.
4. Main EK, Goffman D, Scavone BM, Low LK, Bingham D, Fontaine PL, et al. National partnership for maternal safety, Obstet Gynecol 2015;126:155–62.
5. Dena G, Ananth CV, Fleischer A, D'Alton M, Lavery JA, Smiley R, et al. The New York State Safe Motherhood Initiative: early impact of obstetric hemorrhage bundle implementation. Am J Perinatology 2019;36:1344–50.
6. Shields LE, Wiesner S, Fulton J, Pelletreau B. Comprehensive maternal hemorrhage protocols reduce the use of blood products and improve patient safety. Am J Obstet Gynecol 2015; 212:272–80.
7. Callaghan WM, Kuklina EV, Berg CV. Trends in postpartum hemorrhage: United States, 1994–2006. Am J Obstet Gynecol 2010;202:353.e1–6.
8. Mulic-Lutvica A, Bekuretsion M, Bakos O, Axelsson O. Ultrasonic evaluation of the uterus and uterine cavity after normal, vaginal delivery: ultrasound in puerperium. Ultrasound Obstet Gynecol 2001;18:491–8.
9. Andersen HF, Hopkins MP. Chapter 80: postpartum hemorrhage. In: Sciarra JJ, editor. Gynecology and obstetrics, volume 2. Philadelphia, PA: Lippincott Williams & Wilkins; 2004.

10. Lyon DS. Chapter 90: postpartum care. In: Sciarra JJ, editor. Gynecology and obstetrics, volume 2. Philadelphia, PA: Lippincott Williams & Wilkins; 2004.

11. Baskett TF. A flux of the reds: evolution of active management of the third stage of labour. J R Soc Med 2000;93:489–93.

12. Grönvall M, Tikkanen M, Tallberg E, Paavonen J, Stefanovic V. Use of Bakri balloon tamponade in the treatment of postpartum hemorrhage: a series of 50 cases from a tertiary teaching hospital. Acta Obstet Gynecol Scand 2013;92:433–8.

13. Yoong W, Ridout A, Memtsa M, Stavroulis A, Aref-Adib M, Ramsay-Marcelle Z, et al. Application of uterine compression suture in association with intrauterine balloon tamponade ("uterine sandwich") for postpartum hemorrhage. Acta Obstet Gynecol Scand 2012;91:147–51.

14. Georgiou C. Balloon tamponade in the management of postpartum haemorrhage: a review. BJOG 2009;116:748–57.

15. Suarez S, Conde-Agudelo A, Borovac-Pinheiro A, Suarez-Rebling D, Eckardt M, Theron G, et al. Uterine balloon tamponade for the treatment of postpartum hemorrhage: a systematic review and meta-analysis. Am J Obstet Gynecol 2020;222:293.e1–52.

16. Grange J, Chatellier M, Chevé MT, Paumier A, Launay-Bourillon C, Legendre G, et al. Predictors of failed intrauterine balloon tamponade for persistent postpartum hemorrhage after vaginal delivery. edited by David N. Hackney. PLoS One 2018;13:e0206663.

17. Rani PR. Recent advances in the management of major postpartum haemorrhage–a review. J Clin Diagn Res 2017;11:QE01–5.

18. American College of Obstetricians and Gynecologists, Safe Motherhood Initiative. Obstetric hemorrhage checklist. Available at: https://www.acog.org/-/media/project/acog/acogorg/files/forms/districts/smi-ob-hemorrhage-bundle-hemorrhage-checklist.pdf. Retrieved August 4, 2020.

19. California Maternal Quality Care Collaborative. OB hemorrhage toolkit v 2.0. Available at: https://www.cmqcc.org/resources-tool-kits/toolkits/ob-hemorrhage-toolkit. Retrieved August 4, 2020.

20. Purwosunu Y, Sarkoen W, Arulkumaran S, Segnitz J. Control of postpartum hemorrhage using vacuum-induced uterine tamponade. Obstet Gynecol 2016;128:33–6.

21. American College of Obstetricians and Gynecologists. reVITALize obstetric data definitions (version 1.0). Available at: https://www.acog.org/-/media/project/acog/acogorg/files/pdfs/publications/revitalize-ob.pdf?la=en&hash=D9ECE1577C2A0B535F42C1B8DC492070. Retrieved August 4, 2020.

22. Postpartum hemorrhage. Practice Bulletin No. 183. American College of Obstetricians and Gynecologists. Obstet Gynecol 2017;130:e168–86.

23. Sullivan IJ, Ralph CJ. Obstetric intra-operative cell salvage: a review of an established cell salvage service with 1170 reinfused cases. Anaesthesia 2019;74:976–83.

**Authors' Data Sharing Statement**

Will individual participant data be available (including data dictionaries)? *Yes.*

What data in particular will be shared? *Individual participant data that underlie the results reported in this article, after deidentification. Only summary tables, figures, and text will be available.*

What other documents will be available? *None.*

When will data be available (start and end dates)? *Beginning 6 months and ending 36 months after article publication.*

By what access criteria will data be shared (including with whom, for what types of analyses, and by what mechanism)? *Investigators who provide a methodologically sound proposal and whose proposed use of the data has been approved by an independent review committee. For meta-analysis. Proposals and requests should be directed to kathryn@alydiahealth.com*

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