



vacuum aspiration is the predominant technique but is not available uniformly throughout the world. In Brazil, manual vacuum aspiration is used in 70% of gestational trophoblastic disease reference centers.<sup>5</sup> This likely reflects the legal restrictions on the use of electric vacuum aspiration devices related to the criminalization of elective termination of pregnancy in Brazil, as in many parts of Latin America.<sup>3-5</sup>

The optimal method of molar uterine evacuation is uncertain and many factors such as the urgency of the procedure, uterine size, availability of electric or manual vacuum suction equipment, and the costs of the materials needed for evacuation may influence the choice.<sup>5,10,14,15</sup> There are limited data comparing the different techniques of molar evacuation.<sup>11-15</sup>

The aim of this article is to evaluate our experience with molar uterine evacuation, comparing the two most commonly used techniques for suction evacuation in Brazil: electric compared with manual vacuum aspiration. We particularly wanted to evaluate and report our experience with the use of manual vacuum aspiration in the treatment of women with molar pregnancy, which may be of particular interest and value to clinicians in regions where electric vacuum aspiration is not routinely available.

## MATERIALS AND METHODS

This is a retrospective cohort study of patients with molar pregnancy followed at the Rio de Janeiro Trophoblastic Disease Center (Maternity Ward of Santa Casa da Misericórdia do Rio de Janeiro, Maternity School of Rio de Janeiro Federal University, and Antonio Pedro University Hospital of Fluminense Federal University) from January 2007 to December 2016.

The patients who participated in this study comprised all patients who had been diagnosed with molar pregnancy and underwent uterine aspiration in one of the hospitals associated with the Rio de Janeiro Trophoblastic Disease Center. The diagnosis of molar pregnancy was confirmed by histopathology using the morphologic criteria described by Sebire et al<sup>16</sup> as well as p57<sup>KIP2</sup> immunohistochemical analysis to confirm the diagnosis of the type of hydatidiform mole (complete or partial hydatidiform mole).<sup>17</sup> All patients included in this study were in complete human chorionic gonadotropin (hCG) remission after either benign molar pregnancy or postmolar gestational trophoblastic neoplasia, defined as normal hCG levels for at least 6 or 12 months, respectively. Patients whose medical records were incomplete, who discontinued follow-up, or who underwent uterine evacuation using misoprostol or sharp curettage as the sole method of evacuation were excluded from this study.

Before uterine aspiration, the patients with molar pregnancy underwent a clinical and preanesthetic evaluation, including a complete metabolic profile, complete blood count, chest radiograph, and serum quantitative hCG. Pelvic-transvaginal ultrasonography was performed in all patients. For patients with a uterus larger than 20 cm measured suprapubic-fundus on physical examination (confirmed by ultrasonography), thyroid-stimulating hormone, free thyroxine, and electrocardiogram were also obtained to assess thyroid and cardiac function. In all patients, two units of packed red blood cells were reserved.

For uterine evacuation, preparation of the cervix with misoprostol was not performed. If necessary, cervical dilators were used. Most patients treated at the Maternity Ward of Santa Casa da Misericórdia do Rio de Janeiro and Maternity School of Rio de Janeiro Federal University underwent electric vacuum aspiration. Electric vacuum aspiration was the procedure of choice unless the machine was unavailable (there being one machine for the facility). Patients treated at Antonio Pedro University Hospital of Fluminense Federal University underwent only manual vacuum aspiration (Appendix 1, available online at <http://links.lww.com/AOG/B75>) because an electric device is not available at this institution. In cases of an enlarged uterus for gestational age (defined as a uterus measuring at least 4 cm more than expected for gestational age), or by clinical decision, the uterine vacuum aspiration procedure was guided by transabdominal ultrasonography. After molar uterine vacuum aspiration, either with electric or manual vacuum aspiration, gentle sharp curettage was performed to ensure complete uterine evacuation.

Surgical procedures were performed by a stable team of physicians who were experienced in the uterine aspiration procedures. The choice of uterine evacuation technique as noted previously was dictated primarily by the availability of techniques at the treating facility. All patients received the same anesthetic care, including total intravenous anesthesia with a propofol infusion and fentanyl boluses as needed. Oxytocin was not routinely administered during the surgery and was reserved for patients with an enlarged uterine size for gestational age, with poor uterine tone, or in patients in whom there was copious hemorrhage during the procedure. It is worth noting that the three reference centers in gestational trophoblastic disease have adopted the same criteria for blood transfusion: hematocrit less than 21%, hemoglobin less than 7.0 g/dL with signs of hypovolemia or aggravating medical factors such as cardiovascular disease, or acute bleeding. Prophylactic antibiotic therapy was not routinely administered. Once the surgery



was finished, all patients were transferred to the postoperative care unit with continuous monitoring and with the following minimal prescription: 1,000 mL saline with 10 units of oxytocin intravenously for infusion over 6 hours, 500 mg paracetamol intravenously every 8 hours, and 20 mg tenoxicam (a nonsteroidal antiinflammatory drug) once daily. In case of pain reported by the patient, the frequency of paracetamol was increased to every 4 or 6 hours (maximum of 3 g per day).

All patients were hospitalized for at least 24 hours. Before discharge, they underwent a complete medical evaluation, had a new complete blood count, received prescriptions (which included hormonal contraception and usually a nonopioid analgesic), and the schedule for the postmolar follow-up. The patients started contraception at discharge after uterine evacuation for treatment of molar pregnancy. Hormonal contraception was given free to all patients who wished to use this form of contraception.<sup>18</sup>

Follow-up was performed with weekly measurement of serum hCG using the Siemens Diagnostic Products Corporation Immulite assay. Remission was defined as three consecutive weekly hCG values below 5 international units/L.<sup>4,5</sup> After that, medical visits and measurement of hCG levels continued monthly for 6 months in the case of spontaneous remission and 12 months after completion of chemotherapy in the cases of gestational trophoblastic neoplasia. When patients did not attend the scheduled visits, a social worker and hospital psychologist actively tried to contact them by phone and telegram to identify what was hindering compliance and to motivate them to return for follow-up.

Progression to postmolar gestational trophoblastic neoplasia was diagnosed using the criteria established by the International Federation of Gynecology and Obstetrics 2000, presented in Appendix 2, available online at <http://links.lww.com/AOG/B75>.<sup>19</sup> Before chemotherapy was started, all patients were evaluated for metastatic disease with physical examination, including a pelvic examination, uterine Doppler ultrasonography, and chest radiograph. In case of metastasis, the investigation was complemented by brain, abdominal, and pelvic magnetic resonance imaging and chest computed tomography. Prognostic scoring for resistance to chemotherapy followed the International Federation of Gynecology and Obstetrics and World Health Organization Prognostic Scoring System, as shown in Appendix 2 (<http://links.lww.com/AOG/B75>).<sup>2</sup>

The 8-day methotrexate and folinic acid (leucovorin) rescue regimen with 1 mg/kg methotrexate intramuscularly on days 1, 3, 5, and 7 alternating with 0.1 mg/kg folinic acid orally on days 2, 4, 6, and 8 was

used as a first-line treatment in all cases of low-risk gestational trophoblastic neoplasia. In cases of chemoresistance, second-line chemotherapy was initiated with 1.25 mg/m<sup>2</sup> actinomycin-D intravenous pulse every 15 days. The third-line chemotherapy treatment was etoposide, methotrexate, actinomycin-D, cyclophosphamide, and vincristine, reserving etoposide, cisplatin, methotrexate, actinomycin-D for the fourth line. Additional lines of therapy were selected at treating physician discretion.

Preoperative demographic and clinical information was collected from the medical charts, including age at diagnosis, reproductive history, gestational age at diagnosis, preoperative hCG, and medical complications on presentation (anemia—hemoglobin less than 9 g/dL, bleeding, enlarged uterus for gestational age, theca lutein cysts—ovarian cysts 6 cm or greater as assessed by ultrasonography, preeclampsia, hyperthyroidism, and acute respiratory distress syndrome). Details of the procedure, including the selection of evacuation method, administration of oxytocin, and use of ultrasonography, were abstracted from the operative notes. Postoperative variables included final surgical pathology, postevacuation hCG, in cases of gestational trophoblastic neoplasia, Prognostic Risk Score,<sup>19</sup> selection and duration of chemotherapy treatment, and use of adjuvant procedures. The individual primary study outcomes were incomplete uterine evacuation (determined by clinical, hormonal, and ultrasonography evaluation and in cases of doubt by hysteroscopic evaluation), uterine perforation, development of symptomatic uterine synechia (suspected as a result of amenorrhea and confirmed by hysteroscopy in all cases), and development of postmolar gestational trophoblastic neoplasia. Secondary endpoints were other perioperative outcomes (operative time, rate of transfusion, hemoglobin change, length of stay) and the clinical course of neoplasia (Prognostic Risk Score, presence of metastases, time to remission, and need for multiagent chemotherapy).

This study was approved by the Maternity School of Rio de Janeiro Federal University institutional review board under protocol number 2.092.118.

From prior studies comparing manual with electric vacuum aspiration for nonmolar gestations, we assumed a baseline 2.5% risk for complications in the electric vacuum aspiration group.<sup>14</sup> With our sample size, this gave us 80% power with a 95% two-sided CI to detect differences with the use of manual evacuation corresponding to a reduction in a complication to 0.5% or less or an increase in a complication to 5.5% or greater using the Fleiss method with continuity correction.



The distributions of qualitative variables were evaluated using the  $\chi^2$  statistic. For continuous variables, the Shapiro-Wilk test was used to verify the normality of the distribution. The differences of means were evaluated with a Student *t* test for variables with normal distributions and nonparametric Kruskal-Wallis test when data were not normally distributed. To analyze uterine evacuation in relation to the qualitative variables, the  $\chi^2$  test or, when appropriate, the Fisher exact test was used.

For outcomes of interest, crude and adjusted odds ratios with 95% CIs were calculated using the Wald test for logistic regression. Variables were selected for inclusion into the multivariate model by the Akaike Information Criteria. Corrections for multiple testing were performed using the Holm-Šidák test. All statistical analyses were carried out using the R statistical package.

## RESULTS

Figure 1 presents a flow diagram showing the selection of the study population. Among 2,563 patients with molar pregnancy followed during the study period, 1,950 women underwent uterine aspiration at the Rio de Janeiro Gestational Trophoblastic Disease Reference Center. We excluded 53 patients with incomplete medical records, 87 patients who discontinued follow-up, 45 cases of partial hydatidiform mole of more than 13 weeks of gestation that had undergone uterine evacuation using misoprostol, and 38 cases of uterine evacuation done by sharp curettage as a result of suspicion of early abortion and diagnosed later by histopathology as molar pregnancy. These exclusion criteria did not differ among the three specialized services of the Rio de Janeiro Gestational Trophoblastic Disease Reference Center, as shown in Appendix 3, available online at <http://links.lww.com/AOG/B75>. Thus, among the 1,727 patients with molar pregnancy included in this study, 1,206 underwent electric and 521 underwent manual vacuum aspiration.

As indicated in Table 1, patients undergoing electric or manual vacuum aspiration were similar with regard to demographics, clinical presentation, final diagnosis, use of ultrasonography to monitor the evacuation and oxytocin during the uterine evacuation, and major perioperative complications. The only significant difference was the reference center, which as noted in the methods was expected as a result of the study design.

There was incomplete uterine evacuation in approximately 13% of all patients with molar pregnancy, regardless of the method for uterine aspiration

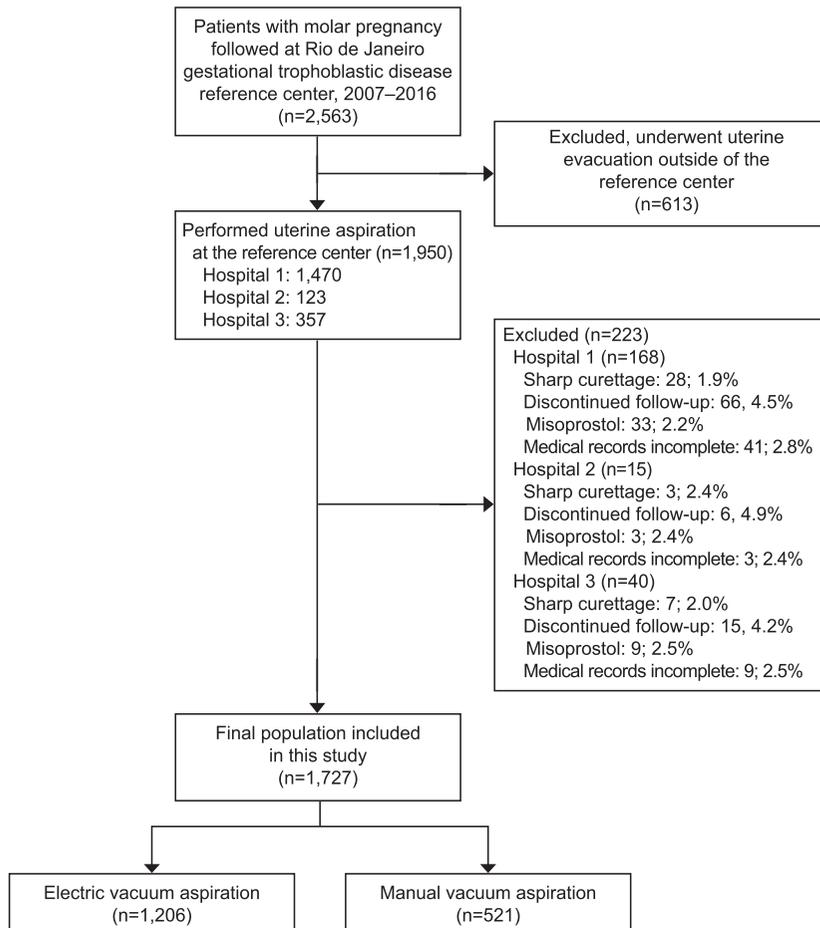
(Table 2;  $P=.949$ ). Patients undergoing uterine electric vacuum aspiration had significantly greater changes in the hemoglobin levels after evacuation ( $-0.3$  vs  $-0.19$  g/dL,  $P<.001$ ) and shorter operative times for uterine evacuation (25.3 vs 34.2 minutes,  $P<.001$ ) when compared with patients who underwent manual vacuum aspiration (Table 2). The uterine evacuation technique was not associated with the development of postmolar gestational trophoblastic neoplasia (14.2% vs 17.3%,  $P=.074$ ) or its aggressiveness (metastatic disease: 19.9% vs 17.8%,  $P=.082$ ; high-risk prognostic score: 22.8% vs 23.3%,  $P=.082$ ; need for multiagent chemotherapy: 24.0% vs 24.4%,  $P=.096$ ). The most notable difference between electric and manual vacuum aspiration was the risk of uterine synechia after the procedure (5.2% vs 1.2%,  $P<.001$ ). Although there was no clinical diagnosis of uterine perforation among the patients undergoing manual vacuum aspiration, there were nine cases of uterine perforations among those undergoing electric vacuum aspiration (0.7%); however, our study was not adequately powered to assess this outcome.

Multivariate logistic regression was performed to identify the variables associated with early or late complications (Appendices 4 and 5, available online at <http://links.lww.com/AOG/B75>). The odds ratios were adjusted for age, medical complication on presentation, gestational age at diagnosis, pre-evacuation hCG level, histology of molar pregnancy, use of ultrasonography to monitor the uterine evacuation, use of oxytocin during the uterine evacuation, and setting of the study. After adjustment, manual vacuum aspiration was associated with a lower risk of blood transfusion (adjusted odds ratio [OR] 0.63, 95% CI 0.44–0.83,  $P<.001$ ), but the adjusted OR was relatively weak and falls within the zone of potential bias for a cohort study.<sup>20</sup> More notably, uterine synechia developed less frequently after manual vacuum aspiration than after electric vacuum aspiration, 6 of 521 vs 63 of 1,206 (adjusted OR 0.21, 95% CI 0.09–0.49,  $P<.001$ ) despite no differences in the occurrence of incomplete uterine evacuation, 65 of 521 vs 161 of 1,206 (adjusted OR 0.93, 95% CI 0.69–1.27), development of postmolar gestational trophoblastic neoplasia, 90 of 521 vs 171 of 1,206 (adjusted OR 1.26, 95% CI 0.96–1.67), or the need for multiagent chemotherapy, 22 of 521 vs 41 of 1,206 (adjusted OR 0.81, 95% CI 0.73–1.28) (Table 3).

## DISCUSSION

Since the introduction of uterine vacuum aspiration techniques,<sup>21,22</sup> manual vacuum aspiration has been less widely used than electric worldwide, because





**Fig. 1.** Flow diagram summarizing the derivation of the study population. Hospital 1, Maternity Ward of Santa Casa da Misericórdia do Rio de Janeiro; Hospital 2, Maternity School of Rio de Janeiro Federal University; Hospital 3, Antonio Pedro University Hospital of Fluminense Federal University.

*Padrón. Manual Vacuum Aspiration for Molar Pregnancy. Obstet Gynecol 2018.*

there is more limited evidence to support its safety, efficacy, and acceptability among women with an indication of termination of pregnancy.<sup>10–15</sup> When we consider the comparison of these techniques with molar uterine vacuum aspiration, the studies are even smaller and less conclusive.<sup>10,13,23,24</sup>

In this study of 1,727 patients with molar pregnancy, manual vacuum aspiration seems to be as acceptable and effective a method for molar uterine evacuation as electric. In addition, manual vacuum aspiration appears to be associated with less development of symptomatic synechia.

One concern regarding manual vacuum aspiration has been incomplete uterine evacuation. Both manual and electric vacuum aspiration have high complete abortion rates (97.9% vs 97.5%) in cases of first-trimester nonmolar abortion.<sup>11</sup> In our sample, formed exclusively by patients with molar pregnancy, the rate of complete uterine emptying did not reach 90% with either technique. This may reflect not only the greater amount of molar trophoblastic tissue compared with an

abortion, but also the invasiveness of molar trophoblastic cells into the maternal decidua.<sup>25</sup>

Another concern with evacuation of a molar pregnancy is the risk of uterine perforation because uteri with molar pregnancy are generally softer and larger than at the time of a first-trimester abortion.<sup>26,27</sup> However, we did not observe a significantly increased risk of uterine perforation with either manual or electric vacuum aspiration. Although differences in rates of uterine perforation as well as prolonged length of stay were not statistically different between the groups, both of these were rare events, and we lacked sufficient power to detect differences in rare outcomes.

Although the pressure exerted by the manual vacuum aspiration is advertised as similar to an electric device,<sup>28</sup> in fact, the vacuum pressure of the electric vacuum aspiration is approximately 100 mm Hg higher than manual.<sup>29,30</sup> Perhaps, the increased suction pressure is responsible not only for faster uterine evacuation with the electric device, but also for more intense decidual detachment, trauma, and greater risk of synechia.



**Table 1. Demographic Characteristics of Patients With Molar Pregnancy Followed at the Rio de Janeiro Gestational Trophoblastic Disease Reference Center According to the Technique of Uterine Evacuation**

Variable	EVA (n=1,206)	MVA (n=521)	P
Age (y)	24.8 (13–57)	28.9 (12–55)	.067*
Gravidity	2.1 (1–3)	1.9 (1–3)	.071*
Parity	0.8 [0–3]	0.7 [0–4]	.170*
Gestational age at diagnosis (wk)	11.4 (5–14)	10.8 (6–15)	.198*
Reference center			
Maternity Ward of Santa Casa	1,103 (91.5)	199 (38.2)	<.001 <sup>†</sup>
Antonio Pedro University Hospital of Fluminense Federal University	0	317 (60.8)	
Maternity School of Rio De Janeiro Federal University	103 (8.5)	5 (1.0)	
Medical complication on presentation			
Bleeding	892 (74.0)	375 (72.0)	.225 <sup>†</sup>
Anemia	87 (7.2)	46 (8.8)	.109 <sup>†</sup>
Enlarged uterus for gestational age	395 (32.8)	136 (26.1)	.098 <sup>†</sup>
Theca lutein cysts	321 (26.6)	125 (24.0)	.187 <sup>†</sup>
Preeclampsia	26 (2.2)	19 (3.6)	.091 <sup>†</sup>
Hyperemesis	144 (11.9)	52 (10.0)	.112 <sup>†</sup>
Hyperthyroidism	36 (3.0)	19 (3.6)	.151 <sup>†</sup>
Acute respiratory distress syndrome	32 (2.7)	20 (3.8)	.093 <sup>†</sup>
hCG pre-evacuation level (international units/L)	175,994 (323–4,168,000)	131,715 (5,736–3,793,000)	.381*
Histology of molar pregnancy			
Complete hydatidiform mole	984 (81.6)	397 (76.2)	.084 <sup>†</sup>
Partial hydatidiform mole	222 (18.4)	124 (23.8)	
Use of ultrasonography to monitor the evacuation	621 (51.5)	260 (49.8)	.174 <sup>†</sup>
Use of oxytocin during the uterine evacuation	699 (58.0)	290 (55.7)	.187 <sup>‡</sup>

EVA, electric vacuum aspiration; MVA, manual vacuum aspiration; hCG, human chorionic gonadotropin.

Data are median (range), mean [interquartile range], or n (%) unless otherwise specified.

\* Nonparametric Kruskal-Wallis test.

<sup>†</sup> Chi-squared test.

<sup>‡</sup> Fisher exact test.

Although the secondary outcomes of need for transfusion and need for extra analgesia postoperatively were statistically different between the electric and manual vacuum aspiration groups, we note that the adjusted ORs were relatively weak, falling within the zone of potential bias for a cohort study.<sup>20</sup> In contrast, the effect size for reduction in uterine synechia is likely of greatest clinical relevance. In addition, we wish to emphasize that for the primary outcomes of incomplete evacuation and development of postmolar gestational trophoblastic neoplasia, the two evacuation techniques appear to be comparable. Importantly, our study demonstrates that neither of these vacuum aspiration methods influences the progression of hydatidiform mole into gestational trophoblastic neoplasia or its severity. In fact, these data are very similar to those in the literature<sup>2,4,7,9,10</sup> and did not differ between patients who underwent electric or manual vacuum aspiration.

Our study does have important limitations. The main limitation of this study was its retrospective design and nonrandomization of treatments. However, Table 1

shows that the population undergoing electric or manual vacuum aspiration had very similar demographic and presentation characteristics. The patients all came from roughly the same geographic area. Although the data were collected from different databases of three different hospitals, the maintenance of these databases as well as the insertion of the data is the responsibility of the same researcher (A.B.), who also guarantees that they use the same protocols and medical records for patients with molar pregnancy. A major strength of this study is the substantial number of patients evaluated undergoing molar evacuation and the depth and completeness of its data collection.

In conclusion, our article represents the experience of molar uterine evacuation at the Rio de Janeiro Trophoblastic Disease Center, the largest trophoblastic reference center in the Americas, which manages more than 300 new patients with gestational trophoblastic disease per year. Despite being simple, inexpensive, and easy to handle, manual vacuum aspiration use in most hospitals is limited as a result



**Table 2. Clinical Outcomes for Patients With Molar Pregnancy According to the Technique of Uterine Evacuation**

Variable	EVA (n=1,206)	MVA (n=521)	P
Complete uterine evacuation	1,045 (86.7)	456 (87.5)	.949*
Uterine perforation	9 (0.7)	0 (0)	.051 <sup>†</sup>
Preoperative hemoglobin (g/dL)	11 [6–13]	10 [5–13]	.089*
Postoperative hemoglobin (g/dL)	10 [3–13]	10 [3–13]	.056 <sup>‡</sup>
Change in the hemoglobin levels after uterine evacuation (g/dL)	−0.3 (−5.1 to −0.1)	−0.19 (−4.9 to −0.1)	<.001 <sup>‡</sup>
Need for blood transfusion	76 (6.3)	45 (8.6)	.714 <sup>†</sup>
Duration of surgery (min)	25.3 (16–31)	34.2 (26–41)	<.001 <sup>‡</sup>
Need for extra postoperative analgesia	160 (13.3)	92 (17.7)	.071*
Postoperative infection	11 (0.9)	7 (1.3)	.509 <sup>†</sup>
Hospital stay (d)	1 [1–5]	1 [1–5]	.512 <sup>‡</sup>
Patients had length of stay greater than 3 d	112 (9.3)	49 (9.4)	.982 <sup>†</sup>
Occurrence of postmolar GTN	171 (14.2)	90 (17.3)	.074*
Presence of metastatic disease	34 (19.9)	16 (17.8)	.082 <sup>†</sup>
WHO-FIGO <sup>§</sup> Prognostic Risk Score of GTN 7 or greater	3 (1–12)	2 (1–11)	.081 <sup>‡</sup>
Need for chemotherapy with multiagent regimen	39 (22.8)	21 (23.3)	.082*
Need for chemotherapy with multiagent regimen	41 (24.0)	22 (24.4)	.096 <sup>†</sup>
Occurrence of synechia	63 (5.2)	6 (1.2)	<.001 <sup>†</sup>

EVA, electric vacuum aspiration; MVA, manual vacuum aspiration; GTN, gestational trophoblastic neoplasia; WHO, World Health Organization; FIGO, International Federation of Gynecology and Obstetrics.

Data are median (range), mean [range], or n (%) unless otherwise specified.

\*  $\chi^2$  test.

<sup>†</sup> Fisher exact test.

<sup>‡</sup> Nonparametric Kruskal-Wallis test.

<sup>§</sup> The WHO prognostic scoring system as adapted by FIGO.

of unfamiliarity of the clinicians with its use.<sup>13</sup> Our results showed that manual vacuum aspiration appears to be similar to electric vacuum aspiration for treatment of molar pregnancy and may be associated

with less development of uterine synechia.<sup>10</sup> Manual vacuum aspiration therefore appears to be a reasonable effective substitute to electric vacuum aspiration in the treatment of molar pregnancy.

**Table 3. Multivariate Logistic Regression Analyzing the Influence of Manual Vacuum Aspiration for Treatment of Molar Pregnancy in Relation to Electric Vacuum Aspiration on the Occurrence of Early or Late Complications**

Variable	Manual vs Electric Vacuum Aspiration for Treatment of Molar Pregnancy		P
	Crude OR (95% CI)*	Adjusted OR (95% CI)*	
Early complication			
Uterine perforation	0 (0)	0 (0)	.993
Need for extra postoperative analgesia	0.65 (0.48–0.81)	0.78 (0.54–0.92)	.018
Need for blood transfusion	0.58 (0.28–0.92)	0.63 (0.44–0.83)	<.001
Length of hospital stay 3 d or greater	1.09 (0.76–2.09)	1.37 (0.87–2.14)	.171
Late complication			
Incomplete evacuation	0.86 (0.61–1.23)	0.93 (0.69–1.27)	.661
Development of postmolar gestational trophoblastic neoplasia	0.91 (0.72–1.20)	1.26 (0.96–1.67)	.102
WHO-FIGO <sup>†</sup> Prognostic Risk Score of GTN 7 or greater	0.60 (0.35–2.01)	0.71 (0.23–2.19)	.550
Need for chemotherapy with multiagent regimen for postmolar GTN	0.76 (0.69–1.25)	0.81 (0.73–1.28)	.673
Occurrence of synechia	0.19 (0.07–0.46)	0.21 (0.09–0.49)	<.001

OR, odds ratio; GTN, gestational trophoblastic neoplasia.

\* Wald test for logistic regression adjusted by age, gestational age at diagnosis, medical complication, pre-evacuation human chorionic gonadotropin, histology of molar pregnancy, use of ultrasonography to monitor the uterine evacuation, use of oxytocin during the uterine evacuation, and setting of the study.

<sup>†</sup> The WHO prognostic scoring system as adapted by FIGO.



## REFERENCES

1. Berkowitz RS, Goldstein DP. Clinical practice. Molar pregnancy. *N Engl J Med* 2009;360:1639-45.
2. Ngan HY, Seckl MJ, Berkowitz RS, Xiang Y, Golfier F, Sekharan PK, et al. Update on the diagnosis and management of gestational trophoblastic disease. *Int J Gynaecol Obstet* 2015;131(suppl 2):S123-6.
3. Maestá I, Braga A. [Challenges of the treatment of patients with gestational trophoblastic disease] [in Portuguese]. *Rev Bras Ginecol Obstet* 2012;34:143-6.
4. Braga A, Uberti EM, Fajardo MC, Viggiano M, Sun SY, Grillo BM, et al. Epidemiological report on the treatment of patients with gestational trophoblastic disease in 10 Brazilian referral centers: results after 12 years since International FIGO 2000 Consensus. *J Reprod Med* 2014;59:241-7.
5. Braga A, Burlá M, Freitas F, Uberti E, Viggiano M, Sun SY, et al. Centralized coordination of decentralized assistance for patients with gestational trophoblastic disease in Brazil: a viable strategy for developing countries. *J Reprod Med* 2016;61:224-9.
6. Lurain JR. Gestational trophoblastic disease I: epidemiology, pathology, clinical presentation and diagnosis of gestational trophoblastic disease, and management of hydatidiform mole. *Am J Obstet Gynecol* 2010;203:531-9.
7. Biscaro A, Braga A, Berkowitz RS. Diagnosis, classification and treatment of gestational trophoblastic neoplasia. *Rev Bras Ginecol Obstet* 2015;37:42-51.
8. Dantas PR, Maestá I, Cortés-Charry R, Growdon WB, Braga A, Rudge MV, et al. Influence of hydatidiform mole follow-up setting on postmolar gestational trophoblastic neoplasia outcomes: a cohort study. *J Reprod Med* 2012;57:305-9.
9. Kohorn EI. Worldwide survey of the results of treating gestational trophoblastic disease. *J Reprod Med* 2014;59:145-53.
10. Tidy JA, Gillespie AM, Bright N, Radstone CR, Coleman RE, Hancock BW. Gestational trophoblastic disease: a study of mode of evacuation and subsequent need for treatment with chemotherapy. *Gynecol Oncol* 2000;78:309-12.
11. Wen J, Cai QY, Deng F, Li YP. Manual versus electric vacuum aspiration for first-trimester abortion: a systematic review. *BJOG* 2008;115:5-13.
12. Milingos DS, Mathur M, Smith NC, Ashok PW. Manual vacuum aspiration: a safe alternative for the surgical management of early pregnancy loss. *BJOG* 2009;116:1268-71.
13. Tasnim N, Mahmud G, Fatima S, Sultana M. Manual vacuum aspiration: a safe and cost-effective substitute of electric vacuum aspiration for the surgical management of early pregnancy loss. *J Pak Med Assoc* 2011;61:149-53.
14. Goldberg AB, Dean G, Kang MS, Youssof S, Darney PD. Manual versus electric vacuum aspiration for early first-trimester abortion: a controlled study of complications rates. *Obstet Gynecol* 2004;103:101-7.
15. Rausch M, Lorch S, Chung K, Frederick M, Zhang J, Barnhart K. A cost-effectiveness analysis of surgical versus medical management of early pregnancy loss. *Fertil Steril* 2012;97:355-60.
16. Sebire NJ, Makrydimas G, Agnantis NJ, Zagorianakou N, Rees H, Fisher RA. Updated diagnostic criteria for partial and complete hydatidiform moles in early pregnancy. *Anticancer Res* 2003;23:1723-8.
17. Madi JM, Braga A, Paganella MP, Litvin IE, Da Ros Wendland EM. Accuracy of p57KIP2 compared with genotyping for the diagnosis of complete hydatidiform mole: protocol for a systematic review and meta-analysis. *Syst Rev* 2016;5:169.
18. Dantas PRS, Maestá I, Filho JR, Junior JA, Elias KM, Horowitz N, et al. Does hormonal contraception during molar pregnancy follow-up influence the risk and clinical aggressiveness of gestational trophoblastic neoplasia after controlling for risk factors? *Gynecol Oncol* 2017;147:364-70.
19. FIGO Oncology Committee. FIGO staging for gestational trophoblastic neoplasia 2000. FIGO Oncology Committee. *Int J Gynecol Obstet* 2002;77:285-7.
20. Grimes DA, Schulz KF. False alarms and pseudo-epidemics: the limitations of observational epidemiology. *Obstet Gynecol* 2012;120:920-7.
21. Wu Y, Wu X. A report of 300 cases using vacuum aspiration for the termination of pregnancy. *Chin J Obstet Gynaecol* 1958:447-9.
22. Karman H, Potts M. Very early abortion using syringe and vacuum source. *Lancet* 1972;1:1051-2.
23. Lara-Ricalde R, Rodríguez-Bosch M, de la Jara-Díaz J, Tovar-Calleros G, Ahued-Ahued JR. Manual intrauterine aspiration on the treatment of molar pregnancy [in Spanish]. *Ginecol Obstet Mex* 1999;67:438-41.
24. Braga A, Moraes V, Maestá I, Amim Júnior J, Rezende-Filho J, Elias K, et al. Changing trends in the clinical presentation and management of complete hydatidiform mole among Brazilian women. *Int J Gynecol Cancer* 2016;26:984-90.
25. Candelier JJ, Frappart L, Diatta AL, Yadaden T, Cissé ML, Afoutou JM, et al. Differential expression of E-cadherin,  $\beta$ -catenin, and Lewis x between invasive hydatidiform moles and post-molar choriocarcinomas. *Virchows Arch* 2013;462:653-63.
26. Hemlin J, Möller B. Manual vacuum aspiration, a safe and effective alternative in early pregnancy termination. *Acta Obstet Gynecol Scand* 2001;80:563-7.
27. Yin LH. Efficacy assessment of terminating pregnancy by different methods of induced abortion. *J Huaihai Med* 2005;2:115-6.
28. Yonke N, Leeman LM. First-trimester surgical abortion technique. *Obstet Gynecol Clin North Am* 2013;40:647-70.
29. Berkeley synevac system 10 vacuum curettage. Available at: <https://cdn.shopify.com/s/files/1/1046/1086/files/ACMI-Berkeley-VC-10-Vacuum-Curettage-System-Instructions-for-Use-and-Technical-Manual.pdf>. Retrieved February 10, 2018.
30. Frankel N. Performing uterine evacuation with the Ipas MVA Plus® aspirator and Ipas EasyGrip® cannulae: instructional CD-ROM. Chapel Hill (NC): Ipas; 2004.

