Emergency Embolization of Pelvic Vessels in Patients With Locally Advanced Cervical Cancer and Massive Vaginal Bleeding: A Case Series in a Latin American Oncological Center

Adriana Alméciga, MD1; Juliana Rodriguez, MD1,2; Julián Beltrán, MD3; James Sáenz, MD1,4; Abel Merchán, MD5; Jorge Egurrola, MD6; Javier Burbano, MD7; Lina Trujillo, MD1; Fernando Heredia, MD1,4; and René Pareja, MD1,9

abstract

PURPOSE Locally advanced cervical cancer may present with uncontrollable vaginal bleeding in up to 70% of cases. Pelvic vessel embolization has been used as an urgent maneuver for achieving fast hemostatic control. This report describes outcomes of selective pelvic vessel embolization in patients with severe bleeding due to a locally advanced cervical cancer.

METHODS In this retrospective study, technical aspects, clinical variables, and bleeding-related morbidity were described. The frequency of recurrent disease and the vital status at 1 year of follow-up were determined. Analysis was performed with statistical software R, version 3.6.2. The setting was Instituto Nacional de Cancerología- Bogotá, Colombia, between January 2009 and July 2017.

RESULTS A total of 47 patients were included. Median age was 44 years (range, 26-70 years). The pre-embolization median hemoglobin level was 7.9 g/dL (range, 5.0-11.3 g/dL). Blood transfusions were administered to 41 women (87.2%). Bleeding control was achieved in 95.7% of cases in the first 24 hours after the embolization. There were no major complications. In 17 cases (36.2%), minor complications were reported; the most common was pelvic pain. In 17.1% of cases, a second embolization was required. After 12 months of follow-up, 27.7% of patients were alive without disease, 44.7% were alive with disease, and 25.5% of them have died of cervical cancer progression.

CONCLUSION Selective pelvic vessel embolization is a useful alternative in patients with locally advanced cervical cancer and life-threatening bleeding. Its impact on recurrent disease and death due to oncologic cause is not clear.

INTRODUCTION

According to GLOBOCAN 2018, the burden of cervical cancer in Latin America is high, with an incidence of 1.6 and a mortality rate of 7.1 per 100,000 women. In Colombia, cervical cancer is the second most frequently occurring gynecologic cancer after breast carcinoma; its annual incidence and mortality are 12.7 and of 5.7 per 100,000 women, respectively. At diagnosis, more than two-thirds of patients present with advanced disease (International Federation of Gynecology and Obstetrics [FIGO] 2009 stage IB2-IVA). In this scenario, approximately 6% of patients will die of unstoppable cervicovaginal bleeding.

Ligation of the hypogastric artery is one method to stop bleeding due to cervical cancer, with a reported 85% decrease in blood flow from the bleeding area. Hypogastric artery ligation alone is not enough and might require concomitant ligation of the infundibulopelvic, round, and uterosacral ligaments. On the other hand, in these patients, surgical management can add intraoperative or anesthetic complications to the patient’s already critical condition. Arterial embolization was brought to our attention as an important tool in the control of massive hemorrhage due to gynecologic neoplasms, because it provides an exact visualization of the bleeding vessel and allows minimally invasive direct therapy to achieve hemostasis. This procedure, compared with surgical ligation, lowers the number of blood transfusions and surgical complications in almost all cases.

At Instituto Nacional de Cancerología, in Bogotá, Colombia, this procedure is offered to patients with cervical cancer and associated vaginal bleeding after conventional vaginal packing has failed and blood transfusion has been required. The objective of this
study was to describe the technique and the clinical results of a consecutive series of patients in whom selective embolization of pelvic vessels was used to control massive vaginal bleeding secondary to cervical cancer.

METHODS
Descriptive, retrospective research was conducted including all patients with a confirmed histopathological diagnosis of locally advanced cervical cancer (according to FIGO 2009: IB2, IIA2, IIB, IIA, IIIA, IIIB, and IVA), complicated with uncontrolled vaginal bleeding, who underwent embolization of pelvic vessels at the Instituto Nacional de Cancerología during the period from January 2009 to July 2017.

The procedure was conducted in our institution by an expert interventional radiologist, as described in Figure 1. Conventional angiographic acquisitions of the abdominal aorta, aortoiliac bifurcation, and the internal iliac arteries were conducted to evaluate the tumor’s main blood supply and surrounding circulation. We proceeded with selective catheterization of the main tumors arteries to introduce the embolizing agent. Subsequently, angiographic controls were conducted to evaluate the vascular permeability of the posterior hypogastric branches and external and primitive iliac arteries (Fig 2).

A review of the medical records was performed by two researchers. The inclusion criterion was selective pelvic vessel embolization due to uncontrollable bleeding cervical cancer leading to secondary anemia (hemoglobin concentration, < 12 g/dL), with clinical signs of orthostatic hypotension. Cases of procedures performed at another institution or patients with incomplete data on the technique and associated morbidity were excluded. The following characteristics of the population were collected: age, FIGO stage, status of cancer treatment at the time of embolization, variables related to hemorrhagic morbidity (eg, preprocedure hemoglobin level, prior bleeding management, need for transfusion, readmission due to bleeding), and the embolization technique (eg, embolizing agent, occluded blood vessel, among others).

CONTEXT
Key Objective
To determine if emergency embolization of pelvic vessels can be used to treat uncontrollable bleeding in locally advanced cervical cancer.

Knowledge Generated
The success rate of first embolization in bleeding control is 95.7%. Some patients had transient pelvic pain after the procedure (31.9%); no major complications or deaths were reported in this case series.

Relevance
In countries with a high prevalence of cervical cancer and limited resources, as in Latin American countries, arterial embolization is a lifesaving strategy for uncontrollable tumoral bleeding with low morbidity.

FIG 1. Procedure of embolization of pelvic vessels.
Postembolization complications were classified on the basis of the Society of Interventional Radiology Classification System into minor and major complications. In addition, status of disease (ie, alive without disease, alive with disease, death) at 12 months was described.

A univariate analysis was conducted. Categorical variables were expressed in absolute numbers or frequencies and percentage. Normal distribution was verified for continuous variables by the Shapiro-Wilk test. The data were then expressed in median and range (difference of minimum and maximum values). R, version 3.6.2, was used for the database analysis. This project was approved by local institutional review board. The informed consent of a patient was obtained for the publication of images; the confidentiality of her data was guaranteed.

**RESULTS**

A total of 52 patients with locally advanced cervical cancer were scheduled to undergo embolization of pelvic vessels. Four cases in which information about complications related to the procedure was unavailable and one patient who received embolization outside the institution were excluded. For the final analysis, 47 patients were included.

Median age was 44 years (range, 26-70 years). More than half the patients (51.1%) were diagnosed with stage IIIB cancer. The majority of women underwent embolization at the time of initial diagnosis (n = 38, 80.8%), and 34 patients (72.3%) had not started oncologic treatment at embolization. The main prescribed treatment modality in this population was concurrent chemoradiotherapy (Table 1).

All patients’ main complaint was vaginal bleeding. In 37 cases (78.7%), a prior vaginal packing was performed without success. In the remaining 10 cases, primary embolization was indicated because of massive bleeding. Forty-one women (87.2%) received blood transfusions, with a median of 3 units of packed red blood cells (range, 1-8 units). The pretransfusion median hemoglobin level was 7.9 g/dL (range, 5-11.3 g/dL). None of the patients required surgical ligation of hypogastric arteries after embolization.

Uterine artery embolization was performed in 34 cases (72.4%) and hypogastric artery embolization in 13 (27.6%), according to radiologist decision. Forty-two patients (89.3%) underwent bilateral selective and five (10.7%) underwent unilateral selective embolization. The embolic agents used were calibrated particles in 35 cases (74.5%) and other agents in 12 cases (25.5%). These other agents were Spongostan gelatin sponges (Ferrosan, Copenhagen, Denmark) in 5 cases; Gelfoam (Pharmacia & Upjohn Company, New York, NY) in 4 cases; and Gelfoam (Pharmacia & Upjohn Company, New York, NY) plus silk in three cases.

The bleeding control after embolization was achieved in 95.7% of cases in the first 24 hours. Two patients (4.3%) required new vaginal packaging with hemostatic solution (Monsel’s solution) on the tumor and bleeding control was achieved in both between 24 and 48 hours after the procedure.

There were no major complications related to embolization. In 17 cases (36.1%), minor complications were reported; pelvic pain was the most common complication (31.9% of
the total population). One patient had fever, leukocytosis, and nausea, considered to be postembolization syndrome. All patients received opioid analgesics and acetaminophen according to medical criteria, achieving analgesic response in the first 48 hours after the procedure, and were discharged within this period, with the same analgesic treatment (Table 2).

During follow-up, 18 patients (38.3%) had bleeding episodes in the first 3 months after the procedure. Of these, only 8 (17.1%) required a second embolization for uncontrollable bleeding and secondary anemia (median hemoglobin level, 6.7 g/dL; range, 6.2-8.9 g/dL) despite vaginal packing. The median number of transfusions in this group was 2 units of packed red blood cells (range, 1-5 units). There were no major nor minor complications. In all patients, hemostatic control was achieved within the first 24 hours.

Finally, the vital status was described at 12 months follow-up and showing that 44.7% of the patients were alive with disease (n = 21 cases), 27.6% were alive without disease (n = 13 cases), and 25.5% died of disease (n = 12 cases). Information about oncologic outcome was not retrievable for one patient.

**DISCUSSION**

We have presented data from 47 cases of pelvic vessel embolization in patients with locally advanced cervical cancer and uncontrollable vaginal bleeding, in whom control was achieved in 95.7% of cases in the first 24 hours, with minor morbidity reported, and no major complications.

Approximately 85% of cases of cervical cancer occur in developing countries. This is especially due to limited access to health services, screening, and treatment of pre-invasive lesions. In our study, > 70% of our patients had not yet received treatment when they presented with a hemorrhagic episode. The median time in months from initial diagnosis to embolization was 2.5 months (range, 0-40.2 months).

In locally advanced stages of cervical cancer, fragility of tumoral neoformation vessels results in frequent hemorrhagic morbidity. Massive vaginal bleeding in patients with cervical cancer progresses rapidly and could lead to death from hemorrhagic shock in a few hours. This complication can be managed with quite simple measures such as vaginal packing and administration of hemoderivatives. When this fails to control hemorrhage, surgical ligation of the hypogastric artery or with arterial embolization are the only remaining alternatives. In this series, most patients presented with vaginal bleeding and moderate anemia, and although more than one-third of the patients received blood transfusion and/or vaginal tamponade as initial management, it was necessary to perform a pelvic vessel embolization procedure as additional therapy.

Even though surgical methods have high efficacy in the control of massive bleeding, arterial embolization has become a feasible therapy in untreatable hemorrhage that does not respond to initial management in gynecologic and obstetric conditions involving massive and uncontrollable bleeding. Its first reported use was in patients with gynecologic malignancies in the mid-1970s; transcatheter arterial embolization of the internal iliac arteries was first described by Ring in 1972 and 1973. Miller et al in 1976 performed selective gelatin sponge embolization to control bleeding in two patients with gynecologic cancer. There are multiple studies that have shown the role of selective pelvic-vessels embolization in cervical cancer (Table 3).

The procedure is performed if an interventional radiologist is available. The treatment has an efficacy of 69%-100% in the first 24 hours. Similarly, bleeding control 24 hours after embolization was successful in 95.7% of patients in our study. The procedure decreases the need for transfusion and the incidence of

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**TABLE 1. Clinical Characteristics (N = 47)**

| Characteristic                        | No. of Patients, (%) |
|--------------------------------------|----------------------|
| Mean age, years (range)              | 44 (26-70)           |
| FIGO stage                           |                      |
| IB2                                  | 1 (2.1)              |
| IIB                                  | 13 (27.6)            |
| IIIA                                 | 1 (2.13)             |
| IIIB                                 | 24 (51.1)            |
| IVA                                  | 2 (4.3)              |
| IVB                                  | 6 (12.8)             |
| Clinical course                      |                      |
| Initial diagnosis                    | 38 (80.8)            |
| Progression                          | 7 (14.9)             |
| Relapse                              | 2 (4.3)              |
| Status of cancer treatment at the time of embolization | |
| Not received yet                     | 34 (72.3)            |
| In active treatment                  | 2 (4.3)              |
| Already received                     | 11 (23.4)            |
| Primary cancer treatment             |                      |
| Concomitant chemotherapy and teletherapy | 9 (19.1)          |
| Concomitant chemotherapy and teletherapy plus brachytherapy | 23 (48.9)          |
| Exclusive radiation therapy          | 4 (8.5)              |
| Palliative treatment                 | 2 (4.3)              |
| None                                 | 9 (19.1)             |
| Duration of primary cancer treatment, days, median (range), | 66.5 (12-130) |

Abbreviation: FIGO, International Federation of Gynecology and Obstetrics.
new bleeding episodes compared with surgical ligation. It also improves the patient’s general condition to continue oncologic therapy. Different reports rate overall complication rates for obstetric and gynecologic cases between 6% and 9%. Complications described are related to the angiographic procedure (eg, groin puncture site hematoma, catheter-induced vessel dissection, contrast medium–associated allergy or nephrotoxic effect) and complications secondary to embolization such as postembolization syndrome (ie, pain, fever, nausea, and leukocytosis) in up to 50% of patients. Other infrequent complications are uterine, bladder, or rectal necrosis; abscess and sepsis; ischemia of adjacent tissue; and sexual dysfunction. No major complications were reported in our patients. Minor complications were reported in 17 women. The risks of such complications are reduced by knowledge of the vascular anatomy and meticulous attention to embolization technique.

Finally, an interesting aspect that has been discussed is the oncologic outcome of this procedure. The role of tumor oxygenation and its impact on treatment is well known. Tumor hypoxia is an adverse factor in this neoplasm and is related to poor outcome regardless of management modality. In addition, tumor hypoxia has also been observed to promote genetic changes associated with metastatic disease. Embolization could be related to a state of chronic hypoxia by occluding the main vessels supplying the tumor and, thus, its sensitivity to kill cells could be affected. In our study, 34 patients (72.3%) had not received oncologic treatment at the time of embolization. They had been recommended to undergo embolization before a massive vaginal bleeding that put their life at risk. Because of the type of study, the oncologic impact of the procedure is unknown. However, Kapp et al evaluated 24 patients with cervical cancer who underwent bilateral embolization before definitive radiotherapy compared with 230 patients who did not undergo embolization. With a median follow-up of 49.5 months, the authors reported a trend toward poorer disease-specific survival and pelvic control in patients who had undergone embolization, even though no impact on radiocurability could be demonstrated in multivariate analysis after controlling for the major tumor characteristics and hemoglobin level during the treatment. Additional evidence on this aspect is necessary.

A strength of this study is that, to our knowledge, it is the largest published series about pelvic vessels embolization in locally advanced cervical cancer in Latin America. Taking into account that cervical cancer is a high-prevalence disease in countries with low resources, it can be proposed as a lifesaving strategy for uncontrollable vaginal bleeding with less morbidity compared with traditional surgical treatment. Among the study limitations, we can mention the low number of patients included, the retrospective nature of the study, a heterogeneous population with different stages of the disease, the lack of evaluation of the oncologic impact of the procedure, and its external validity, because not all the cancer centers in developing countries have an interventional radiology service.

Cancer control needs not only the integration of prevention, screening, and a high-quality diagnosis and treatment structure but also the full range of other services, including rehabilitation, survivorship, and palliative care. Selective pelvic-vessel embolization as a hemostatic strategy in this study was a useful tool in patients with locally advanced cervical cancer with life-threatening bleeding. Embolization achieved adequate early hemostatic control in most patients with low morbidity and no deaths. The methodology used in this study did not allow us to determine the oncologic impact of this technique.

| Characteristic                                      | No. of Patients, (%) |
|----------------------------------------------------|-----------------------|
| Hemoglobin level, median (range), g/dL             | 7.9 (5-12.3)          |
| Maneuvers to manage bleeding                       |                       |
| Vaginal packing and blood transfusion              | 33 (70.2)             |
| Vaginal packing                                     | 4 (8.5)               |
| Blood transfusion                                   | 8 (17.0)              |
| None                                               | 2 (4.3)               |
| Embolizing agent                                    |                       |
| Calibrated particles                                | 35 (61.7)             |
| Other                                              | 12 (38.3)             |
| Occluded blood vessel                               |                       |
| Hypogastric artery                                  | 13 (27.6)             |
| Uterine artery                                      | 34 (72.4)             |
| Occluded vessel laterality                          |                       |
| Bilateral                                           | 42 (89.3)             |
| Right                                              | 3 (6.4)               |
| Left                                               | 2 (4.3)               |
| Complications associated with embolization          |                       |
| Pelvic pain                                         | 15 (31.9)             |
| Fever                                              | 1 (2.1)               |
| Other                                               | 1 (2.1)               |
| None                                               | 30 (63.8)             |
| Readmission for bleeding within 3 months            |                       |
| Yes                                                 | 18 (38.3)             |
| No                                                  | 29 (61.7)             |
| Second embolization requirement                     |                       |
| Yes                                                 | 8 (17.1)              |
| No                                                  | 39 (82.9)             |
### TABLE 3. Studies of Embolization in Cervical Cancer

| Author          | Year | No. of Patients | Stage (No. of patients) | Artery Embolized (No. of patients) | Material                        | Survival, Months (No. of patients) | Effectiveness (%) |
|-----------------|------|----------------|-------------------------|------------------------------------|---------------------------------|-----------------------------------|-------------------|
| Miller et al    | 1976 | 2              | IIIB                    | Internal iliac                     | Absorbable                      | 4                                 | 100               |
|                 |      |                |                         | Relapse                            | Upper hemorrhoidal               | Gelfoam                           | 5                 |
| Yalvac et al    | 2002 | 8              | IIB                     | Uterine                            | Polyvinyl alcohol               |                                   | 100               |
|                 |      |                |                         |                                    |                                 | 1 (n = 3)                         |                   |
|                 |      |                |                         |                                    |                                 | 6 (n = 1)                         |                   |
|                 |      |                |                         |                                    |                                 | 11 (n = 1)                        |                   |
|                 |      |                |                         |                                    |                                 | 12 (n = 1)                        |                   |
|                 |      |                |                         |                                    |                                 | 50 (n = 1)                        |                   |
| Kapp et al      | 2004 | 24             | IB (n = 1)              | Uterine                            | Polyvinyl alcohol               | Not described                     | Not described     |
|                 |      |                |                         |                                    |                                 | II (8)                            |                                 |
|                 |      |                |                         |                                    |                                 | Internal iliac                    |                                 |
|                 |      |                |                         |                                    |                                 | IIB (n = 12)                      |                                 |
|                 |      |                |                         |                                    |                                 | IV (n = 3)                        |                                 |
| Karaman et al   | 2010 | 1              | IIIB                    | Internal iliac bilateral           | Coil                             | Not described                     | Not described     |
| Albu et al      | 2011 | 1              | IIB                     | Uterine                            | Embolospheres                    | Not described                     | 24 hours          |
| Nogueira-García | 2015 | 6              | IV                      | Uterine bilateral                  | Microcoils                       | Not described                     | 100               |
| Çaypinar et al  | 2016 | 1              | IVA                     | Internal iliac bilateral           | Not described                    | 2                                 | 12 hours          |
| Chen et al      | 2018 | 6              | IV                      | Internal iliac artery (n = 2),     | Gelatin sponge particle (n = 1)  | 3.5                               | 80                |
|                 |      |                |                         | external iliac artery (n = 2),     | Polyvinyl alcohol (n = 1)        |                                   |                   |
|                 |      |                |                         | uterine artery (n = 1),            | n-Butyl-2-cyanoacrylate (n = 2)  |                                   |                   |
|                 |      |                |                         | superior rectal artery (n = 1)     | Stent graft (n = 2)              |                                   |                   |
|                 |      |                |                         |                                    | Other (n = 5)                    |                                   |                   |
| Matylevich et al| 2018 | 81             | IIIB (n = 4)            | Uterine bilateral (n = 45)         | Not described                    | Median, 8.4                       | 94                |
|                 |      |                |                         |                                    |                                 | IIIB (44)                         |                                 |
|                 |      |                |                         |                                    |                                 | Uterine unilateral and internal   |                                 |
|                 |      |                |                         |                                    |                                 | iliac unilateral (n = 6),         |                                 |
|                 |      |                |                         |                                    |                                 | internal iliac bilateral (n = 18) |                                 |
|                 |      |                |                         |                                    |                                 | IV (n = 20)                       |                                 |
|                 |      |                |                         |                                    |                                 | Other (n = 5)                     |                                 |
AFFILIATIONS
1 Department of Gynecology Oncology, Instituto Nacional de Cancerología, Bogotá, Colombia
2 Department of Gynecology and Obstetrics, Section of Gynecology Oncology, Fundación Santa Fe de Bogotá, Bogotá, Colombia
3 Department of Radiology, Instituto Nacional de Cancerología, Bogotá, Colombia
4 Universidad Militar Nueva Granada, Bogotá, Colombia
5 Centro de Investigaciones Oncológicas Clínica San Diego, Bogotá, Colombia
6 Faculty of Health Science, Program of Medicine, Universidad de Magdalena, Magdalena, Colombia
7 Fundación Valle de Lili, Cali, Colombia
8 Department of Gynecology and Obstetrics, School of Medicine, Universidad de Concepción, Concepción, Chile
9 Clínica de Oncología Astorga, Corporación Universitaria Remington, Universidad Pontificia Bolivariana, Medellín, Colombia

CORRESPONDING AUTHOR
René Pareja, MD, Calle 1 #9-85, Bogotá, Colombia; e-mail: ajerapener@gmail.com

AUTHOR CONTRIBUTIONS
Conception and design: Julián Beltrán, Abel Merchán, Jorge Egurrola, Fernando Heredia, René Pareja
Administrative support: René Pareja

Provision of study material or patients: Julián Beltrán, Abel Merchán, Jorge Egurrola

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Collection and assembly of data: Adriana Alméciga, Juliana Rodriguez, Julián Beltrán, Abel Merchán, Javier Burbano, Fernando Heredia
Data analysis and interpretation: James Sáenz, Jorge Egurrola, Lina Trujillo, Fernando Heredia
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST
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Juliana Rodriguez
Honoraria: Johnson & Johnson
Travel, Accommodations, Expenses: AstraZeneca
Abel Merchán
Travel, Accommodations, Expenses: AstraZeneca, Johnson & Johnson

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