

# 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

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**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.

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## INTRODUCTION

According to GLOBOCAN 2018, the burden of cervical cancer in Latin America is high, with an incidence of 14.6 and a mortality rate of 7.1 per 100,000 women.<sup>1</sup> 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.<sup>1</sup> At diagnosis, more than two-thirds of patients present with advanced disease (International Federation of Gynecology and Obstetrics [FIGO] 2009 stage IB2-IVA).<sup>2</sup> In this scenario, approximately 6% of patients will die of unstoppable cervicovaginal bleeding.<sup>3</sup>

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.<sup>4</sup> However, due to the frequent recurrence of revascularization hemorrhage, it has been shown that

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.<sup>4</sup>

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.<sup>5,6</sup>

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

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## 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.

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, 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).

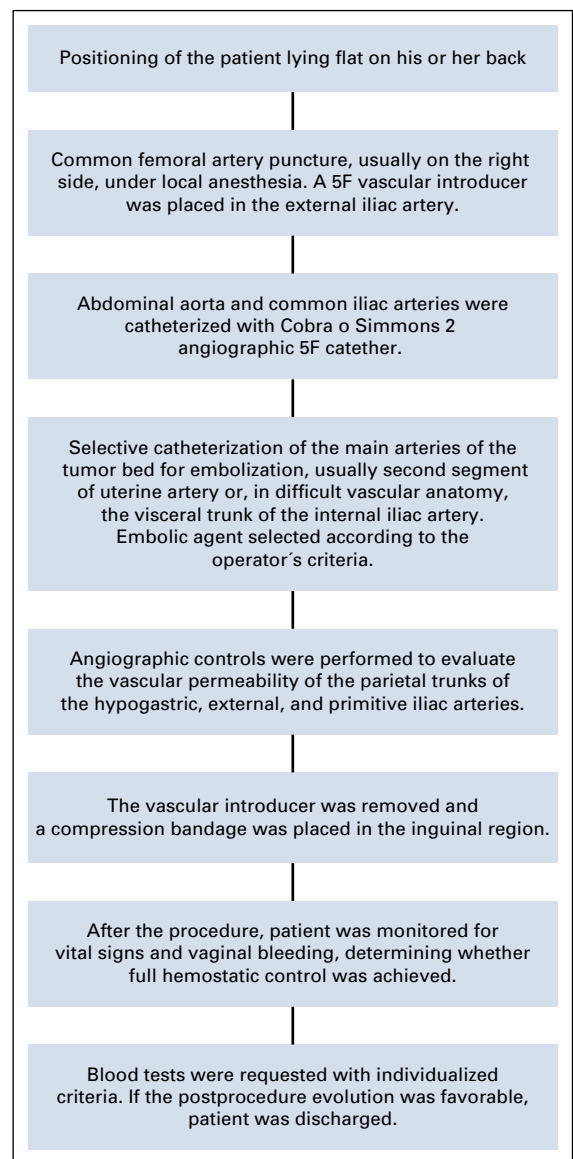
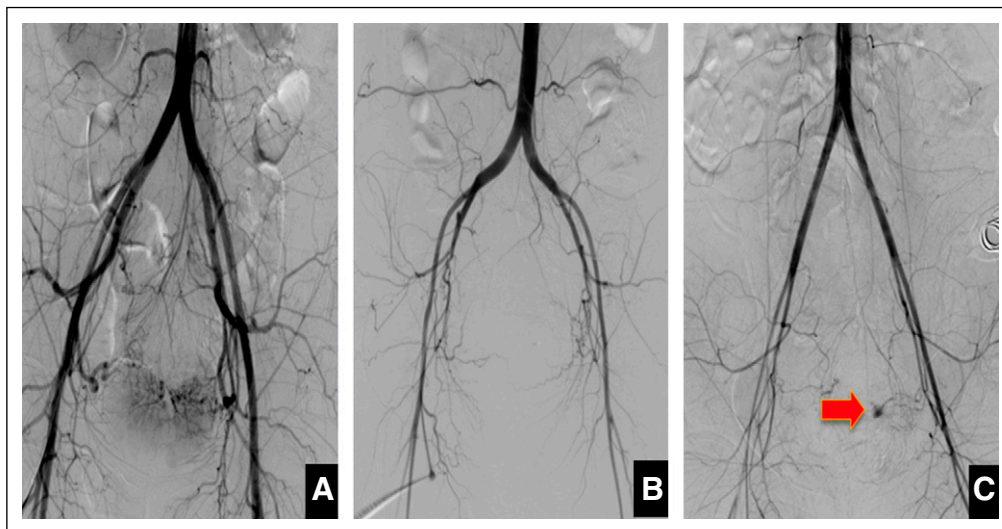


FIG 1. Procedure of embolization of pelvic vessels.



**FIG 2.** Aortograms. (A) A moderately vascularized mass is seen in the central pelvic region, with arterial contributions derived from uterine arteries. (B) There is a generalized decrease in the caliber of the pelvic vessels and external iliac arteries, related to hemorrhagic shock in a patient with cervical neoplasia without evidence of active bleeding prior to embolization. (C) Similar to (B), there is a marked decrease in the caliber of all visualized arteries, with contrast accumulation dependent on the left uterine artery. This is a pseudoaneurysm (red arrow) with active bleeding due to tumor infiltration and rupture of the vascular wall.

Postembolization complications were classified on the basis of the Society of Interventional Radiology Classification System into minor and major complications.<sup>7</sup> 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 four 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

**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.

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.<sup>8</sup> 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 neofunction 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.<sup>9</sup> 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.<sup>3</sup> 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.<sup>10,11</sup> 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<sup>11a</sup> in 1972 and 1973. Miller et al in 1976<sup>12</sup> 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).<sup>4,9,11-17</sup>

The procedure is performed if an interventional radiologist is available. The treatment has an efficacy of 69%-100% in the first 24 hours.<sup>15</sup> 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

**TABLE 2.** Technical Aspects of Embolization and Morbidity (N = 47)

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)

new bleeding episodes compared with surgical ligation. It also improves the patient's general condition to continue oncologic therapy.<sup>18</sup>

Different reports rate overall complication rates for obstetric and gynecologic cases between 6% and 9%.<sup>19</sup> 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.<sup>20</sup> 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.<sup>21</sup>

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.<sup>22</sup> 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<sup>14</sup> 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.<sup>14</sup> 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.<sup>23</sup> 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.

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 <sup>12</sup>	1976	2	IIIB	Internal iliac	Absorbable	4	100
			Relapse	Upper hemorrhoidal	Gelfoam	5	
Yahvac et al <sup>13</sup>	2002	8	IIB	Uterine	Polyvinyl alcohol	1 (n = 3)	100
						6 (n = 1)	
						11 (n = 1)	
						12 (n = 1)	
						50 (n = 1)	
Kapp et al <sup>14</sup>	2004	24	IB (n = 1)	Uterine	Polyvinyl alcohol	Not described	Not described
			II (8)	Internal iliac			
			III B (n = 12)				
			IV (n = 3)				
Karaman et al <sup>4</sup>	2010	1	IIIB	Internal iliac bilateral	Coil	Not described	Not described
Albu et al <sup>15</sup>	2011	1	IIB	Uterine	Embolospheres	Not described	24 hours
Nogueira-García et al <sup>16</sup>	2015	6	IV	Uterine bilateral			
Çaypınar et al <sup>9</sup>	2016	1	IVA	Internal iliac bilateral	Not described	2	12 hours
			IV	Internal iliac artery (n = 2), external iliac artery (n = 2), uterine artery (n = 1), superior rectal artery (n = 1)	Gelatin sponge particle (n = 1)	3.5	80
Chen et al <sup>11</sup>	2018	6	IV		Polyvinyl alcohol (n = 1)	10	
					n-Butyl-2-cyanoacrylate (n = 2)	34	
					Stent graft (n = 2)	5	
						3	
						2.5	
Matyevich et al <sup>17</sup>	2018	81	IIB (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)			

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## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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