Anesthesia for Intracavitary Brachytherapy: a 19-month Experience at the Philippine General Hospital during the COVID-19 Pandemic

Evangeline K. Villa, MD and Aaron Adolf R. Abad, MD

Department of Anesthesiology, Philippine General Hospital, University of the Philippines Manila

ABSTRACT

Background and Objective. Brachytherapy is the only demonstrated technique of delivering the high radiation dose required to control cervical cancer (>80 Gray [Gy]) without causing unwanted side effects. There is still limited data available in the Philippines regarding the anesthetic management of patients receiving intracavitary brachytherapy for cervical cancer. It is the aim of this study to present the anesthetic management of these procedures performed in a non-operating site remote from the main hospital during the first 1 ½ years of the COVID-19 pandemic.

Methods. A retrospective review of 446 eligible charts was made. Data collected included demographic variables, ASA physical status classification, anesthetic technique, anesthetic agents used, oxygen supplementation device, duration of procedure, intra-procedure complication, intra-procedure pain medications, post-procedure pain medications, recovery room (RR) rescue medications, time to fulfill discharge criteria, and patient disposition.

Results. Four hundred forty-six (446) anesthetic encounters involving 117 patients is presented. Charts from 46 patients were excluded as it cannot be located. Mean age of the patients was 49 years with majority having normal BMI. Spinal anesthesia (SA) was more frequently (75%) used compared to total intravenous anesthesia (TIVA). Less than 5% immediate anesthesia-related complications were recorded and all patients were discharged on the same day.

Conclusion. Spinal anesthesia and TIVA are safe and effective anesthetic techniques in patients with cervical cancer undergoing high dose intracavitary brachytherapy. Prospective studies to assess other aspects of their care as well as anesthesia-related long-term effects from repetitive anesthetic exposure is recommended.

Keywords: brachytherapy, uterine cervical neoplasm, spinal anesthesia, intravenous anesthesia

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Corresponding author: Evangeline K. Villa, MD
Department of Anesthesiology
Philippine General Hospital
University of the Philippines Manila
Taft Avenue, Ermita, Manila 1000, Philippines
Email: ekvilla@up.edu.ph
ORCiD: https://orcid.org/0000-0002-0399-7278

INTRODUCTION

Despite the ongoing COVID-19 pandemic, the top three leading causes of mortality in the Philippines for years 2020 and 2021 are ischemic heart disease, cerebrovascular disease, and neoplasm, respectively.[1] Among the neoplasms, cervical cancer ranks as the 2nd most common cancer among Filipino women.[2]

The discovery of radioactivity by Henri Becquerel in 1896 and the discovery of radium by Marie and Pierre Curie in 1898 paved the way for the use of radiation for treating cancers. In 1903, two patients with basal cell carcinoma received the first radium brachytherapy via skin irradiation. By 1910, "Stockholm technique", a brachytherapy method for treating cervical cancer was established in Stockholm by Gösta Forssell. Discovery of artificial radionuclides, development of remote afterloading devices as well as

advances in imaging technology has now even allowed individual treatment planning for brachytherapy.[3]

Brachytherapy is a form of radiation therapy that has been used for urogenital, intestinal, breast, retinal, and bronchial cancers. This entails implantation of a radioactive material sealed inside a seed, capsule, or pellet within a body cavity (intracavitary brachytherapy) or within tissues (interstitial brachytherapy).[4]

In brachytherapy, the radioactive source is applied directly or near the targeted tumor. Based on the inverse-square law, the delivered radiation dose is inversely proportional to the square of the distance from the source. This translates to delivery of a very high dose of radiation to the tumor leading to therapeutic irradiation while at the same time sparing the nearby normal structures.[5]

Brachytherapy may constitute part of a multimodal cancer treatment plan or given as a single treatment either with curative or palliative intent and can be used in cases unfit for major surgery or chemotherapy. To date, brachytherapy is the only demonstrated technique of delivering the high radiation dose required to control cervical cancer (>80 Gray [Gy]) without causing unwanted side effects.[6] A locally conducted study likewise showed that brachytherapy led to significant improvement on tumor control and overall survival among patients with locally advanced cervical cancer.[7]

Neuraxial and general anesthesia have both been used for pelvic brachytherapy.[3,8-11] There is still limited data available in the Philippines regarding the anesthetic management of patients receiving intracavitary brachytherapy for cervical cancer.

OBJECTIVES

The general objective of this study is to determine the anesthetic technique and immediate anesthesia-related outcomes among patients with cervical cancer who underwent high dose intracavitary brachytherapy at Philippine General Hospital (PGH) Cancer Institute (CI) during the first 1 ½ years of the COVID-19 pandemic. The specific objectives include describing the demographic profile of the patients, anesthetic technique and management, periprocedural anesthesia-related complication, immediate anesthesia-related outcomes, and patient disposition.

METHODS

Upon approval by the University of the Philippines Manila Review and Ethics Board, this retrospective chart review study was conducted in PGH CI brachytherapy unit.

The study population comprised of gynecologic patients who underwent high dose brachytherapy in PGH CI under the care of an anesthesiologist from March 1, 2020 until September 30, 2021. Those who underwent brachytherapy without an anesthesiologist, i.e., under local anesthesia were excluded.

Eligible charts were manually identified through inspection of the CI brachytherapy unit logbook. Eligibility was based on the presence of an attending anesthesiologist for the procedure. The retrieved paper charts were endorsed to a trained independent data abstractor for data collection in a designated area in the CI brachytherapy unit.

Data collected included demographic variables, ASA physical status classification, anesthetic technique, anesthetic agents used, oxygen supplementation, duration of procedure, intra-procedure complication, intra-operative pain medications, post-operative pain medications, CI brachytherapy recovery room (RR) rescue medications, time to fulfill discharge criteria, and patient disposition.

Data collected were encoded using MS Excel (Microsoft 2016) and was analyzed using STATA 15 (Statacorp, College Stattion, Texas, USA). An all cell-wise data analysis was done. Summary statistics such as means and standard deviations was used for summarizing all normally distributed data Frequencies and percentages were used for reporting categorical variables.

RESULTS

Demographic Profile of Patients

There were 163 patients identified to have fulfilled the inclusion criteria within the designated study period. Among the 163 patients, the charts of 46 patients cannot be located, hence, only 117 patient charts were reviewed. Each patient chart can have 1 to 4 documentation of anesthesia encounters depending on how may fractions of intracavitary brachytherapy the patient has received. A total of 446 anesthesia encounters for high dose intracavitary brachytherapy involving 117 cervical cancer patients done at PGH from March 2020 - September 2021 were reviewed.

The mean age is 49.1 years. Slightly more than half had a normal BMI. Most (96.6%) were classified as ASA 2. Only four patients had information on obstetric history. Majority of the patients had already four anesthesia requiring brachytherapy encounters. (Table 1)

Anesthetic Technique

Among the 446 high dose intracavitary brachytherapy procedures done, almost 75% were conducted under SA and the rest were performed under TIVA.

Hyperbaric bupivacaine was the only local anesthetic used for SA. Use of epinephrine as an adjunct was done for only one encounter. Different doses of hyperbaric bupivacaine with or without epinephrine were employed wherein the most common was 10 mg (43.1%).

Among those who received TIVA, various combinations of sedative agents were used ranging from 1 to 4 agents with or without a non-sedative adjunct. Majority (78%) were given midazolam, fentanyl, and propofol. (Table 2)

Table 1. Demographic Profile of Patients[a] (n=117)

	n (%)
Age (mean, SD)	49.1 ± 11.7
BMI category[b]	
Underweight	12 (10.3)
Normal	55 (47.0)
Overweight	32 (27.3)
Obese	6 (5.1)
Cannot be computed[c]	12 (10.3)
ASA physical status classification[d]	
ASA I	0 (0)
ASA 2	113 (96.6)
ASA 3	4 (3.4)
Obstetric history	
Multigravida	4 (3.4)
Not recorded	113 (96.6)
Number of high-dose intracavitary brachytherapy encounter(s)	
One	1 (0.8)
Two	5 (4.3)
Three	9 (7.7)
Four	102 (87.2)

[a] *Values are presented as mean + standard deviation or as frequency (percentage)*
[b] *Body Mass Index classification: Underweight: BMI <18.5, Normal: BMI 18.5–24.9, Overweight: BMI 25.0–29.9, Obese: BMI of 30 and above*
[c] *No data on height*
[d] *ASA physical status classification: ASA I – healthy patient, no systemic disease, ASA II – patient with mild systemic disease, ASA III – patient with severe systemic disease*

Table 2. Anesthetic Technique used on the Patients[a] (n=446)

	n (%)
Spinal Anesthesia	334 (74.9)
Hyperbaric bupivacaine	333 (99.7)
5.0 mg	3 (0.9)
6.0 mg	4 (1.2)
7.0 mg	6 (1.8)
7.5 mg	106 (31.7)
8.0 mg	48 (14.4)
10.0 mg	143 (42.8)
12.0 mg	5 (1.5)
12.5 mg	2 (0.6)
15.0 mg	4 (1.2)
No data	12 (3.6)
Hyperbaric bupivacaine + epinephrine	
10 mg + 1:200,000	1 (0.3)
Total Intravenous Anesthesia	112 (25.1)
Midazolam, propofol	1 (0.89)
Midazolam, fentanyl, propofol	87 (77.68)
Midazolam, fentanyl, dexmedetomidine	2 (1.79)
Midazolam, fentanyl, ketamine, propofol	4 (3.57)
Midazolam, fentanyl, ketamine, propofol, atropine	3 (2.68)
Midazolam, fentanyl, dexmedetomidine, propofol	1 (0.89)
Midazolam, ketamine, propofol	3 (2.68)
Midazolam, ketamine, propofol, atropine	1 (0.89)
Propofol	6 (5.36)
Propofol, fentanyl	4 (3.57)

[a] *Values are presented as frequency (percentage)*

Periprocedural Anesthetic Management

For providing oxygen supplementation, a Hudson face mask was most commonly used. Majority of patients did not receive supplemental intraoperative pain medication. Mefenamic acid was the most commonly prescribed post-operative analgesic. (Table 3)

Intraprocedural Anesthesia-related Complications

Overall, less than 5% of the patients manifested with intraprocedural anesthesia-related complications. Among those who received SA, hypertension (2.4%) and hypotension (2.1%) mainly comprised the observed complications. Similar occurrence was noted among those who had TIVA but in a comparatively negligible extent (1.8%). Pain, however, was only noted on the TIVA group. (Table 4)

Course and Disposition

The duration of the procedure was comparable for both anesthetic techniques. Less than 5% in both groups required rescue medications to address hypertension, post-operative nausea and vomiting (PONV), and pain. Patients who received TIVA had a slightly shorter time to fulfill the discharge criteria. All patients from both groups satisfied the discharge criteria and were sent home. (Table 5)

A higher proportion of patients under SA group did not require any postoperative rescue medication. PONV and hypertension were more commonly reported among those who received SA while pain and hypertension was more likely to be reported by patients who underwent TIVA.

DISCUSSION

Cancer remains a significant cause of morbidity and mortality in the Philippines together with cardiovascular diseases.[2] Among Filipino women, cervical cancer is the second most frequent malignancy and is the 4th leading cause of cancer-related mortality. It is estimated that annually in the Philippines, 7,897 women will be diagnosed with cervical cancer and 4,052 will die from it.[12]

The continued burden of cervical cancer among patients has also expanded the role of the anesthesiologist who now play a vital role in enabling safe and optimal radioactive source placement while ensuring patient safety and comfort during brachytherapy.

While only 117 patients were included in the review, the initially identified eligible 176 patients show that despite the COVID-19 pandemic, efforts were made to provide this much needed treatment modality for cervical cancer patients. As brachytherapy involves placement of radioactive sources within or close to the tumor, it is able to deliver adequate doses to the central and peripheral portions of the tumor leading to improved primary tumor remission rate, recurrence rate, and overall survival rate.[13]

Table 3. Intraprocedural Anesthetic Management[a]

	Spinal Anesthesia (n=334)	TIVA (n=112)
Oxygen supplementation		
Nasal cannula	57 (17.07)	10 (8.93)
Hudson face mask	192 (57.49)	90 (80.36)
Anesthesia face mask	4 (1.20)	2 (1.79)
No data	81 (24.25)	10 (8.93)
Intraprocedural pain medications[b]		
None	323 (96.70)	102 (91.07)
Paracetamol	8 (2.40)	2 (1.79)
Ketorolac	1 (0.30)	0 (0.0)
Paracetamol + ketorolac	1 (0.30)	0 (0.0)
Paracetamol + tramadol	1 (0.30)	0 (0.0)
Butorphanol	0 (0.0)	0 (0.0)
Fentanyl	0 (0.0)	5 (4.46)
Tramadol	0 (0.0)	1 (0.89)
Ketamine	0 (0.0)	2 (1.79)
Postprocedural pain medications[c]		
None	29 (8.68)	14 (12.50)
Mefenamic Acid	110 (32.93)	42 (37.50)
Paracetamol	97 (29.04)	26 (23.21)
Ibuprofen	2 (0.60)	2 (1.79)
Celecoxib	62 (18.56)	10 (8.93)
Tramadol	0 (0.0)	1 (0.89)
Tramadol + paracetamol	29 (8.68)	12 (10.71)
Celecoxib, tramadol + paracetamol	2 (0.60)	0 (0.0)
Mefenamic Acid, tramadol + paracetamol	0 (0.0)	5 (4.46)
Paracetamol, celecoxib	3 (0.90)	0 (0.0)

TIVA – Total intravenous anesthesia
[a] *Values are presented as frequency (percentage)*
[b] *Intraprocedural pain medication refers to supplemental analgesic medication given during the procedure.*
[c] *Postprocedural pain medication refers to supplemental analgesic medication given as take-home analgesic.*

Table 4. Intraprocedural anesthesia-related complications[a]

	Spinal Anesthesia (n=334)	TIVA (n=112)	Total no. of Patients
None	318 (95.21)	107 (96.40)	425 (95.3%)
Hypotension[b]	7 (2.10)	2 (1.80)	9 (2.0%)
Hypertension[c]	8 (2.40)	1 (0.90)	9 (2.0%)
PVC	1 (0.30)	0 (0.0)	1 (0.2%)
Hypotension + pain[d]	0 (0.0)	1 (0.90)	1 (0.2%)
Hypertension + pain	0 (0.0)	1 (0.90)	1 (0.2%)

TIVA – Total intravenous anesthesia
PVC – Premature ventricular contraction
[a] *Values are presented as frequency (percentage)*
[b] *Hypotension - blood pressure <20% of patient's baseline blood pressure*
[c] *Hypertension - blood pressure >20% of patient's baseline blood pressure*
[d] *Pain was deduced from the need to add supplemental analgesic or to increase the ongoing propofol infusion based on the patient's vital signs*

Demographic Profile of Patients

The mean age (49.1) of patients with cervical cancer undergoing brachytherapy in this series was relatively younger compared to the series of Rodriguez et al. with a median age of 55.8 years.[14] This can either be due to earlier onset of disease or earlier diagnosis. A study conducted a decade ago identified that risk factors for cervical cancer including young age at first intercourse, low socioeconomic status, high parity, smoking, use of oral contraceptives, and risky sexual behaviors are more prevalent among Filipino women compared to those belonging in other countries.[15] On the other hand, active cancer programs advocated by the Department of Health and gynecological societies may have contributed to increased awareness of gynecologic cancer among Filipino women.[2] No comparison can be made in terms of BMI and ASA physical status classification as current published literature describe these parameters collectively among brachytherapy patients instead of per malignancy location.

Table 5. Course and Disposition[a]

	Spinal Anesthesia (n=334)	TIVA (n=112)	P value*
Duration of procedure (mins)	81.96 (19.67)	79.80 (21.94)	0.21
Rescue meds given in recovery room			
None	324 (97)	107 (95.5)	
Ondansetron	1 (0.30)	0 (0.0)	
Metoclopramide	1 (0.30)	0 (0.0)	
Celecoxib	1 (0.30)	0 (0.0)	
Clonidine	1 (0.30)	0 (0.0)	
Nicardipine	1 (0.30)	0 (0.0)	
Losartan	5 (1.5)	1 (0.89)	
Losartan, Tramadol + Paracetamol	0 (0.0)	2 (1.79)	
Carvedilol	0 (0.0)	2 (1.79)	
Indication for rescue meds in recovery room			
Not applicable[b]	324 (97%)	107 (95.5)	<0.0001
Pain	1 (0.30)	0 (0.0)	<0.0001
PONV	2 (0.60)	0 (0.0)	<0.0001
Hypertension	10 (2.99)	2 (1.79)	<0.0001
Pain and hypertension	0 (0.0)	3 (2.68)	<0.0001
Length of time to fulfill discharge criteria	70.77 ± 36.84	61.09 ± 31.54	0.0005
Sent home	334 (100)	112 (100)	

PONV – Post-operative nausea and vomiting
[a] Values are presented as frequency (percentage)
[b] No rescue medications were given
** Mann-Whitney test*

Anesthetic Technique

A trend favoring neuraxial anesthesia compared to total intravenous anesthesia was observed in this study which is similar to published literature.[3,8,11,16] This can be attributed to spinal anesthesia's rapid onset, predictable duration of action, and capacity to provide sufficient analgesia and immobilization.[3] Another plausible reason for its popularity in light of the COVID-19 pandemic situation is the absence of aerosol generation in regional anesthesia techniques.[16,17]

Hyperbaric bupivacaine is the preferred local anesthetic for spinal anesthesia. Being denser than CSF, it will flow by gravity to the dependent areas of the spine.[17,18] This characteristic allows anesthesiologists to control the spread of spinal blockade.

The heterogeneity of the dosages of local anesthetic used in this study can be a reflection of the anesthesiologist's preference and estimated duration of the procedure which is influenced by patient-related factors and provider-related factors. It is worth noting that a minimum of T10 block is required for this procedure. The applicator insertion causes distension of the cervix and upper vagina leading to stimulation of parasympathetic autonomic afferents from the S2 - S4 while the presence of the applicator rod in the uterine body stimulates the sympathetic autonomic afferents which enter the spinal cord at T10 - L1 level.[9] Vaginal packing with a radiopaque two-inch gauze is done to stabilize the applicator while simultaneously ensuring that the rectum and urinary bladder are displaced from the applicator as much as possible.[6] This is another source of pain as it stimulates somatic afferents via the pudendal nerves S2 - S4.[9]

Among those who received TIVA, the most common combination composed of midazolam, fentanyl, and propofol. To date, various sedation regimens for brachytherapy among cervical cancer patients have been published including propofol infusion + fentanyl or remifentanil, midazolam + propofol infusion + fentanyl + oxycodone as well as promethazine + tramadol infusion.[14,19,20] This can be attributed to the institution's resources and anesthesiologist's preference. It is worth emphasizing that among the different sedation regimens listed, it consistently included a short-acting sedative and an analgesic in the form of an opioid.

Periprocedural Anesthetic Management

No comparison in terms of oxygen supplementation device can be made since existing literature compare other form of airway devices (face mask, endotracheal tube, supraglottic airway) for non-neuraxial technique and does not analyze this component of anesthetic care for neuraxial technique.[8]

Most patients for both anesthetic techniques did not receive additional intraprocedural pain medication. For the SA group, these consisted of non-opioid analgesics while for the TIVA group, these consisted of an opioid or NMDA antagonist. This is similar to the findings of Frankart et al. wherein patients under the general anesthesia group required significantly greater amounts of narcotics compared to those under the SA group.[11] This highlights the need for analgesia as there are multiple sources of pain for this procedure.[6,9] Spinal anesthesia provides analgesia and immobility via blockade of sensory and motor nerves of the spinal cord. Non-opioid analgesics were administered in this group as

part of preventive analgesia. On the other hand, opioids had to be incorporated and added during the procedure in the TIVA group to achieve adequate degree of analgesia. Mefenamic acid was the most commonly used post-operative analgesic as the procedural pain is mostly associated with the presence and manipulation of the applicator.[9]

Intraprocedural Anesthesia-related Complications

Minimal intraprocedural anesthesia-related complications were noted for both anesthetic techniques which is similar with existing literature.[8,10] The SA group had alterations in the blood pressure which is either due to sympathetic blockade or sense of distress once the loss of sensation is felt by the patient. The TIVA group had a few episodes primarily related to pain sensation.

Course and Disposition

The statistically significant slightly faster recovery of the TIVA group compared to the SA group shows that the duration of action of intravenous anesthetic agents is more predictable compared to the time to two-segment regression of local anesthetic in the CSF. This can also be due to the heterogeneity of the local anesthetic dosages used in the study.

Few patients required intervention in the recovery room that were readily addressed with pharmacologic symptomatic management. Risk stratification for PONV will help identify patients who will benefit from prophylactic antiemetic. Emphasis on the appropriate number of fasting hours should be done as prolonged fasting is a predisposing factor to PONV development.[21] Appropriate use of multimodal preventive analgesia serves as a bridge to address pain post-procedurally.

Regardless of anesthetic technique, all patients fulfilled the discharge criteria and were sent home after the high dose intracavitary brachytherapy procedure. This can be attributed to an adequate preanesthetic evaluation that is part of the routine practice which allows identification and optimization of modifiable factors before their scheduled brachytherapy session.[22]

CONCLUSION AND RECOMMENDATIONS

Spinal anesthesia and total intravenous anesthesia are both safe and effective anesthetic techniques for patients with cervical cancer undergoing high dose intracavitary brachytherapy in an ambulatory basis. There were minimal periprocedural anesthesia-related complications for both techniques that can be addressed readily.

Future prospective studies can be performed that will explore other aspects of care including choice of local anesthetic, spinal anesthesia adjuvant medication, spinal anesthesia dosage regimen, sedation regimen, incidence of postdural puncture headache, patient satisfaction, provider satisfaction, cost effectiveness, and workflow efficiency. Results of these studies can aid in developing guidelines and quality improvement projects for cervical patients who will undergo high dose brachytherapy in the PGH Cancer Institute.

Statement of Authorship

Both authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

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