Original paper

An audit of uterine perforation and its effect on the final outcome in an academic research medical center: An optimized balance between overall treatment time and medical crisis

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Abstract

Purpose: Intra-cavitary brachytherapy is an integral component of cervical cancer management, and uterine perforation is the most significant complication, which may lead to prolonged overall treatment time and decreased local control in these patients.

Material and methods: A retrospective analysis of cervical cancer patients who completed radiotherapy (external beam radiotherapy and brachytherapy) in our department was conducted to determine the incidence, effect on overall treatment time, and final outcome in patients with uterine perforation during brachytherapy procedure.

Results: Among 55 women, of the 398 applications, 85 (21.36%) resulted in uterine perforation. Out of these 85 applications, treatment time was extended among 3 (3.5%) applications only, as re-insertion was done nearly after one week, while the remaining 82 (96.5%) applications were completed in time. At the time of analysis, the median follow-up was 12 months, and 32 patients were disease-free, 3 had distant metastatic disease, 2 had residual disease, and 18 were lost to follow-up.

Conclusions: In our study, uterine perforation incidence was found to be comparable with other centers worldwide. In asymptomatic and uncomplicated uterine perforation, treatment can be continued with computer-based optimized treatment plans without loading a specific dwell position and without affecting overall treatment time.

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Key words: brachytherapy, cervix carcinoma, uterine perforation.

Purpose

Cervical cancer is the most frequently diagnosed malignancy and the leading cause of cancer-related deaths in many low- and middle-income countries (LMIC), preceding breast cancer [1]. Most patients present with a locally advanced disease, which includes FIGO (the International Federation of Gynecology and Obstetrics) stages from IB3 to IVA. Concurrent chemoradiotherapy (CRT) is the standard treatment for these stages [2]. Radiation is delivered as external beam radiotherapy (EBRT) to gross cervical disease and pelvic nodes, followed by brachytherapy to localized disease only. Brachytherapy is an essential component in the treatment of cervical cancer, which helps to deliver a high radiation dose to localized target area in less time, without exceeding dose constraints of adjacent organs at risk (OARs), including the rectum, sigmoid, bladder, etc., and is known to improve both local control and overall survival [3].

According to the American Association of Physicists in Medicine (AAPM) Task Group 59 report recommendations, treating team should consist of a radiation oncologist and a medical physicist with expertise in brachytherapy. A treatment-unit operator who could be a physician, physicist, dosimetrist, or radiation therapist, is also required [4]. Moreover, the International Atomic Energy Agency (IAEA) indicates that nursing staff is among the minimum personnel required [5].

Intra-cavitary brachytherapy involves the insertion of a tandem into the cervix and uterus along with a pair of ovoids in vaginal fornices. Uterine perforation, vaginal laceration, and tumor hemorrhage are the reported complications of brachytherapy, out of which uterine

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perforation is the most feared. Brachytherapy procedures rely on imaging methods, such as portable X-ray, computed tomography (CT) scans, ultrasonography (USG), or magnetic resonance imaging (MRI) in addition to the clinical expertise of an oncologist. The availability of imaging modalities help in correct applicator placement and dose delivery and preventing complications [6]. In this study, we determined the incidence of uterine perforation during utero-vaginal brachytherapy application and its implications further.

Material and methods

The present study was conducted at a tertiary care academic hospital in India between January, 2021 to December, 2021. A retrospective analysis of cervical cancer patients who received external beam radiotherapy (EBRT) with a dose of 50 Gy in 25 fractions over five weeks, followed by intra-cavitary brachytherapy procedure using a modified Fletcher-Suit-Delcos (tandem and ovoid) applicator, was conducted to determine the incidence of uterine perforations during the procedure. Medical records and brachytherapy OT records of all patients were evaluated.

Results

Our study evaluated 398 brachytherapy applications in 126 patients with FIGO stage IIB-IVA cervical cancer. All the patients received three fractions of 7 Gray (Gy) each at weekly intervals. The dose was prescribed at point A.

Brachytherapy dose delivery with four fractions of 7 Gy each has been a standard schedule, but leads to an increased bladder and rectal toxicities, as mostly, the optimal dose constraints for these organs at risk (OARs) are challenging to achieve. Delivering EBRT with 50 Gy in 25 fractions has EQD_2 of 50 Gy, whereas brachytherapy with three fractions of 7 Gy has EQD_2 of approximately 30 Gy. On combining EBRT and brachytherapy doses, EQD_2 of 80 Gy is achieved, which is optimal for tumor control along with respecting OARs dose constraints, thus balancing tumor control probability (TCP) and normal tissue complication probability (NTCP) as well.

Brachytherapy insertion was done under aseptic precautions, following proper bladder and bowel protocol with or without spinal anesthesia. A radiation oncology trainee inserted CT/MRI-compatible modified Fletcher-Suit-Delcos applicator under the supervision of a senior radiation oncologist. The applicator's position and orientation were confirmed on a post-insertion CT scan, and the obtained images were used for treatment planning partially.

Of the 398 applications, 85 (21.36%) cases of uterine perforations were seen in 55 women. Age distribution, disease stage, site of perforation, and uterus orientation details of these 55 patients are presented in Table 1. The mean tumor size at the first brachytherapy insertion was 4.24 cm.

In three out of the total of 85 applications with perforation (3.5%), there was a minor hemorrhage and these patients were managed symptomatically; for them, a re-insertion was done after one week. The rest (96.5%) of perforations were asymptomatic, and treatment was given with plan optimization, i.e., without loading at specific dwell portions corresponding with perforations.

Analysis was done at a median follow-up of 12 months for the 55 patients (85 applications), i.e., patients in whom perforation occurred during any insertion out of these applications. 18 out of the 55 patients (32.75%) were lost to follow-up. Out of the remaining 37 patients, three (5.45%) patients had distant metastatic disease, two (3.63%) patients had residual disease, and 32 (58.18%) patients were disease-free after the completion of treatment. Patients who were disease-free at the time of analysis, i.e., 32 out of 55, had no delay in the treatment due to perforation. Out of three patients with prolonged overall treatment time due to perforation, two had a residual disease, and one had metastatic disease during follow-up.

Discussion

Brachytherapy is an integral component of cervical cancer treatment. It requires proper placement of applicators in the vagina and uterine cavity for accurate radiation delivery to the target area. It should be done ideally by experienced oncologists, preferably under image guidance. Although complications related to the procedure, such as uterine perforation, can also occur by expert hands, the probability is very minimal. However, one can become an expert only after performing more procedures, as the learning curve is steep. In government academic hospitals/ tertiary centers in LMIC, due to the high

Table 1. Baseline characteristics, including site of perforation and orientation of uterus of patients with uterine perforation

Characteristics	Number	%
Age (years)	No. of patients = 55	
≤ 40	7	12.7
41-50	12	21.8
51-60	28	50.9
> 60	8	14.5
FIGO stage	No. of patients = 55	
IIB	25	45.5
IIIA	6	10.9
IIIB	11	20.0
IIIC1	11	20.0
IVA	2	3.6
Perforation	No. of applications = 85	
Through uterine fundus	23	27.1
Posterior wall	54	63.5
Lateral wall	8	9.4
Uterus orientation	No. of applications = 85	
Retroverted	25	29.4
Anteverted	23	27.1
Hyper-anteverted	15	17.7
Atrophic	22	25.8

patient workload, every procedure cannot be performed by experienced specialists. This is also because of the responsibility and a mandatory teaching-learning program for trainees at these institutions to provide learning and enough hand-on-experience to perform these procedures under experts. It is very much analogous to plotting a cell survival curve for fractionated radiotherapy, where with each fraction delivered and shoulder repeated, the curve ultimately becomes a straight line; similarly, with every procedure the trainee performs, the skills improve and become a part of a complete training. However, the analogy derived has a limited role in the real-world scenario, as new trainees join every year. These new students must be taught every time compared with other non-academic/non-teaching centers. In this case, the probability of occurring complications increases.

A thorough clinical examination to determine the orientation of uterus, including size, direction, angle of anteflexion, residual disease after EBRT, measuring the length of uterine canal by uterine sound, and using TRUS (transrectal ultrasound) to ensure placement of uterine tandem into uterine cavity, helps in decreasing the risk of uterine perforations further other than clinical expertise [7]. On average, the incidence of uterine perforation, even with surety of an oncologist of correct placement, is around 8-10% [8, 9]. According to the available literature, the average incidence of uterine perforation during brachytherapy ranges from 1.75% to 13.7% [2, 4]. In our study, uterine perforation was observed in 21.3% of insertions. Young trainees performed all the applicator placements, which can be the reason for a higher than average incidence in our study, other than various modifiable/unavoidable reasons, such as USG/MRI guidance or a more anteflexed uterus. Barnes *et al*. showed that advanced patient age (> 60 years) and tumor size are significant predictors of uterine perforation [9]. Other reported risk factors included anatomical distortion of the cervix due to advanced disease, cervical stenosis, radiation fibrosis, previous cone biopsy, etc. [10-12]. The commercially available uterine tandems have fixed angulations, thereby increasing the risk in the markedly retroverted or anteverted uterus [13]. Segedin *et al*. showed that the most common site of uterine perforation is the posterior uterine wall, followed by the fundus and anterior wall due to the anatomy of the uterus/cervix and vagina [14].

In the case of uterine perforation, if radiation treatment is delivered, there is a risk of damage to surrounding pelvic organs, resulting in necrosis, strictures, or fistula formation. Therefore, if the procedure is performed blindly without the help of image-guided or computer-based planning, there is a consensus to abort the treatment in the event of perforation, manage the patient symptomatically, and consider re-insertion. But this practice has led to an increase in the overall treatment time (OTT), which significantly compromised oncological outcomes in terms of increasing local recurrence [15]. Hence, nowadays, with image-guided and computer-based planning, optimization is possible by manipulating dwell-time and positions. In case of a perforation, a part of the tandem outside the uterus does not get any dwell position, and the rest of optimized radiotherapy dose is delivered. Therefore, we can proceed with the treatment safely, except in case of significant hemorrhage or very few other situations where medical management needs to be prioritized. Also, complications of uterine perforation, such as infections, sepsis, and other medical risks, have become less frequent with the rational use of antibiotics/coverage during brachytherapy procedures [12, 16]. In a study, Small *et al*. reported that it might be safe to proceed with brachytherapy treatment without delay or need for prophylactic antibiotics in the event of perforation, if there is no excessive hemorrhage [17].

As every time the applicator is inserted, there is a risk of perforation, strategies have been tried to reduce the risk. Using a Smit sleeve before brachytherapy is a technique that facilitates accurate tandem placement, and eliminates the risk of malposition of tandem in subsequent insertions, thus reducing the risk of complications [18]. More important is imaging before and after the procedure, which helps to detect inaccurate placement of applicators and aids in dose optimization during computer-based planning process [19, 20].

Conclusions

Uterine perforations during intra-cavitary brachytherapy can be reduced but not eliminated owing to various physician, procedure, and patient-related factors. It is imperative to use image guidance during the procedure. If perforation occurs, it is safe to proceed with the treatment in the image-guided and computer-based optimized treatment era after excluding significant hemorrhage, where the need for medical management is crucial and dominant over OTT.

Disclosure

The authors report no conflict of interest.

References

1. Sung H, Ferlay J, Siegel RL et al. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021; 71: 209-249.
2. Green JA, Kirwan JJ, Tierney J et al. Concomitant chemotherapy and radiation therapy for cancer of the uterine cervix. *Cochrane Database Syst Rev* 2005; 20: CD002225.
3. Lanciano RM, Won M, Coia LR et al. Pretreatment and treatment factors associated with improved outcome in squamous cell carcinoma of the uterine cervix: A final report of the 1973 and 1978 patterns of care studies. *Int J Radiat Oncol Biol Phys* 1991; 20: 667-676.
4. Kubo HD, Glasgow GP, Pethel TD et al. High dose-rate brachytherapy treatment delivery: report of the AAPM Radiation Therapy Committee Task Group No. 59. *Med Phys* 1998; 25: 375-403.
5. IAEA. IAEA HUMAN HEALTH SERIES No. 30 Implementation of High Dose Rate Brachytherapy in Limited Resource Settings.
6. Viswanathan AN, Thomadsen B. American Brachytherapy Society consensus guidelines for locally advanced carcinoma of the cervix. Part I: General principles. *Brachytherapy* 2012; 11: 33-46.

7. Irvin W, Rice L, Taylor P et al. Uterine perforation at the time of brachytherapy for carcinoma of the cervix. *Gynecol Oncol* 2003; 90: 113-122.
8. Granai CO, Doherty F, Allee P et al. Ultrasound for diagnosing and preventing malplacement of intrauterine tandems. *Obstet Gynecol* 1990; 75: 110-113.
9. Barnes EA, Thomas G, Ackerman I et al. Prospective comparison of clinical and computed tomography assessment in detecting uterine perforation with intracavitary brachytherapy for carcinoma of the cervix. *Int J Gynecol Cancer* 2007; 17: 821-826.
10. Kim RY, Levy DS, Brascho DJ et al. Uterine perforation during intracavitary application. Prognostic significance in carcinoma of the cervix. *Radiology* 1983; 147: 249-251.
11. Jhingran A, Eifel PJ. Perioperative and postoperative complications of intracavitary radiation for FIGO stage I-III carcinoma of the cervix. *Int J Radiat Oncol Biol Phys* 2000; 46: 1177-1183.
12. Corn BW, Shaktman BD, Lanciano RM et al. Intra- and perioperative complications associated with tandem and colpostat application for cervix cancer. *Gynecol Oncol* 1997; 64: 224-229.
13. Mayr NA, Montebello JF, Sorosky JI et al. Brachytherapy management of the retroverted uterus using ultrasound-guided implant applicator placement. *Brachytherapy* 2005; 4: 24-29.
14. Segedin B, Gugic J, Petric P. Uterine perforation – 5-year experience in 3-D image guided gynaecological brachytherapy at Institute of Oncology Ljubljana. *Radiol Oncol* 2013; 47: 154-160.
15. Perez CA, Grigsby PW, Castro-Vita H et al. Carcinoma of the uterine cervix. I. Impact of prolongation of overall treatment time and timing of brachytherapy on outcome of radiation therapy. *Int J Radiat Oncol Biol Phys* 1995; 32: 1275-1288.
16. Small W, Strauss JB, Hwang CS et al. Should uterine tandem applicators ever be placed without ultrasound guidance? No: a brief report and review of the literature. *Int J Gynecol Cancer* 2011; 21: 941-944.
17. Small W, Kim YS, Joyce C et al. Uterine perforation during brachytherapy for cervical cancer: Complications, outcomes, and best practices for forward treatment planning and management. *Brachytherapy* 2021; 20: 557-564.
18. Bayrak M, Abakay CD. Prevention of uterine perforation during intracavitary brachytherapy of cervical cancer. *J Contemp Brachytherapy* 2021; 13: 167-171.
19. Al-Hammadi NM, Chandramouli SH, Hammoud R et al. Off-line magnetic resonance imaging navigation of cervix cancer brachytherapy in patients with risk factors for uterine perforation. *J Contemp Brachytherapy* 2017; 9: 519-526.
20. Bahadur YA, Eltaher MM, Hassouna AH et al. Uterine perforation and its dosimetric implications in cervical cancer high-dose-rate brachytherapy. *J Contemp Brachytherapy* 2015; 7: 41-47.