

**Comparative Safety and Efficacy of Thermal Ablation Versus Cryotherapy for Treating Cervical Precancerous Lesions on Visual Inspection with Acetic Acid**

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**Abstract**

**Introduction:** Cervical cancer remains a significant global health challenge, particularly in low and middle-income countries (LMICs), where delayed diagnoses often result in advanced-stage disease. To alleviate this, effective and accessible screening and treatment methods are crucial, enabling early detection and intervention to reduce cervical cancer related morbidity and mortality.

**Objectives:** This study aims to evaluate the efficacy and safety of thermal ablation versus cryotherapy for treating cervical precancerous lesions in low-resource settings.

**Methods:** This study enrolled 60 women with cervical precancerous lesions confirmed by visual inspection with acetic acid (VIA test). Participants were randomly assigned to receive either thermal ablation (n=30) or cryotherapy (n=30). Safety outcomes, including adverse events and side effects, were assessed during and after treatment. Efficacy outcomes, including complete regression of lesions, were evaluated at 12 weeks post-treatment using VIA. Statistical analysis was performed

using Chi-square tests for categorical variables and independent sample t-tests for continuous variables, with a significance level set at  $p \leq 0.05$ .

**Results:** The mean age of participants was comparable between groups (Group A:  $38.43 \pm 6.82$  years; Group B:  $37.27 \pm 7.76$  years). The majority of patients in both groups (68.33% thermal ablation, 66.6% cryotherapy) reported no adverse events during treatment. Anxiety was most common side effect (30% thermal ablation, 33.3% cryotherapy). Pain levels and post-procedural complications were similar, with high patient satisfaction rates reported (90% cryotherapy; 96.7% in thermal ablation). Complete regression of lesions occurred in 96.7% of thermal ablation and 93.3% of cryotherapy at 12 weeks post-treatment with high satisfaction.

**Conclusion:** Thermal ablation is a safe and effective alternative to cryotherapy, with comparable efficacy and high patient satisfaction. Its portability and reduced operational costs make it particularly suitable for resource-limited settings, supporting efforts to eliminate

cervical cancer through single-visit screening and treatment strategies.

**Keywords:** Cervical cancer, thermal ablation, cryotherapy, cervical precancerous lesions, Visual Inspection with Acetic Acid (VIA).

### **Introduction**

Cervical cancer remains a significant global health challenge, with 604,100 new cases and 341,831 deaths reported in 2020. In India, it accounts for 9.4% of all cancers and is the second leading cause of cancer deaths among women in 12 states.<sup>1</sup> The burden is particularly severe in low and middle-income countries (LMICs), where nearly 90% of new cases are diagnosed. Late diagnoses in resource-constrained settings lead to advanced-stage presentations, exacerbated by barriers such as inadequate infrastructure for HPV vaccination and screening programs.<sup>2</sup>

In industrialized nations, the introduction of effective cytological screening has sharply reduced cervical cancer incidence; however, similar successes are lacking in developing regions. Evidence suggests that HPV vaccination is crucial in prevention but it cannot replace secondary prevention methods. Thus, the focus has shifted to developing novel, accessible screening approaches suitable for resource-poor settings. Early detection through routine screening and treatment of precancerous lesions can significantly reduce cervical cancer morbidity and mortality.<sup>3</sup>

Current screening modalities include Pap smears, liquid-based cytology, visual inspection with acetic acid (VIA), and HPV testing. While Pap smears require trained personnel and laboratory facilities, leading to challenges in LMICs, VIA offers a promising alternative. VIA involves swabbing the cervix with a 3-5% acetic acid solution, allowing abnormal cells to appear white upon visual inspection. This method is cost-effective, requires

fewer visits, and provides immediate results.<sup>3</sup> Studies indicate that VIA has comparable or superior diagnostic ability to cytology for high-grade precancerous lesions, with sensitivity, specificity, and positive predictive values often surpassing those of traditional methods.<sup>4</sup>

Cryotherapy is a common ablative technique used to treat cervical intraepithelial neoplasia (CIN) lesions.<sup>5</sup> Its advantages include a lack of serious side effects, ease of delivery in remote areas, and a favorable risk profile for future pregnancies. However, logistical challenges, such as refrigerant availability and equipment failure, hinder its implementation in LMICs.<sup>6</sup> In contrast, thermal ablation (TA), an alternative ablative method developed in 1966, utilizes electricity to destroy premalignant cervical lesions. This technique is potentially better suited for low-resource settings due to its reliance on battery power instead of refrigerants gases like CO<sub>2</sub> and N<sub>2</sub>O, smaller device size, and shorter treatment times.<sup>7</sup> WHO recommends thermal ablation as a viable option in “screen and treat” settings. However, there is limited randomized evidence evaluating its efficacy and safety compared to cryotherapy. This study aims to analyse thermal ablation as a treatment modality for women with cervical precancerous lesions, comparing its effectiveness and safety against cryotherapy.

### **Materials & Methods**

This randomized interventional study was a prospective, comparative analysis conducted in the Department of Obstetrics and Gynecology at SMS Medical College and Attached Hospital, Jaipur. The study commenced from March 2023 to April 2024. The sample Size calculation, with a 0.05 alpha error and 80% power, required at least 30 participants per group to compare success rates of 43% vs. 79%, leading to a total of 60 subjects for the study.

### Inclusion criteria

1. women aged 25-54 years.
2. Positive VIA test (visual inspection with acetic acid).
3. who provided written informed consent
4. Type 1 TZ

### Exclusion criteria

1. Those with lesions too large for a 25 mm cryotherapy probe.
2. Pregnant women
3. Women with history of cervical treatment.
4. Active genital infections or bleeding
5. Genital tract cancer
6. Lesions covering >75% of the ectocervix
7. Lesions extending to the cervical canal or vagina

### Statistical Analysis

Women with VIA-positive cervical lesions were randomly assigned to two groups using block randomization: Group A (30 patients) for cryotherapy and Group B (30 patients) for thermal ablation.

Data were compiled in an MS Excel spreadsheet and presented as tables and charts. Nominal and categorical variables were analyzed using Chi-square or Fisher's Exact test, while continuous variables were summarized as mean and standard deviation and compared with independent sample t-tests. A p-value of  $\leq 0.05$  was deemed significant, with analyses performed using Epi Info version 7.2.1.0.

### Methodology

Eligible women aged 25-54 years provided informed consent and completed a socio-demographic questionnaire. Urine pregnancy tests were conducted; those testing positive were excluded. Participants underwent a speculum examination for a pap smear and the Visual Inspection with Acetic Acid (VIA) test. A 5% acetic acid solution was applied, and VIA was positive if distinct aceto-white lesions were observed near the

transformation zone. 30 VIA positive women were treated with cryotherapy and thermal ablation treatment each (Total 60 patients). Post procedure, participants reported their pain and satisfaction levels using VAS score, ranging from 0 (happy) to 10 (crying). Safety assessment were conducted immediately after treatment and 12 weeks, with participants self-reporting any discomfort or problems experienced. All participants received antibiotic and counselling on abstinence for 6 weeks atleast and follow up visits were scheduled at 12 weeks. Treatment efficacy was evaluated at 12 weeks through complete regression of lesions on VIA test and overall participant satisfaction.

### Results and Observations

In this study, the mean age of women in Group A was  $38.43 \pm 6.82$  years, compared to  $37.27 \pm 7.76$  years in Group B ( $p=0.539$ ). Residence was also comparable: 51.7% from rural areas and 48.3% from urban areas ( $p=0.301$ ). Socioeconomic status differed significantly, with 53.3% low middle SES and 35% low SES ( $p=0.028$ ). Smoking status was similar, with 10% smokers and 90% non-smokers ( $p=0.671$ ).

In Group A, 27 (90%) patients had discharge, compared to 26 (86.7%) in Group B ( $p=1.000$ ). Foul-smelling discharge occurred in 2 (6.7%) of Group A and 6 (20%) of Group B ( $p=0.255$ ). Lower abdominal pain was reported by 24 (80%) in Group A and 19 (63.3%) in Group B ( $p=0.252$ ). Most females (88.3%) had aceto-white areas <50% of the TZ, with 7 (11.7%) having areas >50% but <75%. Group A had 93.3% and Group B had 83.3% with areas <50%, showing no significant difference ( $p=0.421$ ).

Table 1: Comparison of mean procedure time (min) of study groups

Group	N	Procedure time in min (Mean ± SD)	P value
Group A (Cryo)	30	10.6 ± 1.69	<0.001 (S)
Group B (Thermal)	30	1.09 ± 0.24	

The mean procedure time was much less in Group A cryotherapy (10.6 ± 1.69 min), as compared to Group B thermal ablation (1.09 ± 0.24 min), this difference was found to be statistically significant (p<0.001).

Table 2: Comparison of safety of procedures using Pain (VAS score\*) during treatment

Pain (VAS score)	Group A (Cryo)		Group B (Thermal)		Total	
	N	%	N	%	N	%
1 (no pain)	12	40	14	46.7	26	43.3

Table 3: comparison of safety profile between two groups in terms of side effects or complications over 12 weeks:

Side effects or complications	Group A(cryo)		Group B (thermal)		Total		P value
	N (30)	%	N (30)	%	N (60)	%	
1. During or immediately after treatment							
No complaints	20	66.6	21	70	41	68.33	1.000
Anxiety	10	33.33	9	30	19	31.66	1.000
Post procedural pain	2	6.66	1	3.33	3	5	1.000
Spotting per vaginum	2	6.66	0	0	2	3.33	0.472
Dizziness	2	6.66	1	3.33	3	5	1.000
Vasovagal reaction	1	3.33	0	0	1	1.66	1.000
2. Side effect or complications at 12 weeks							
No complaints	28	93.33	29	96.66	57	95	1.000
Pain abdomen	1	3.33	1	3.33	2	3.33	1.000
Watery vaginal discharge	1	3.33	0	0	1	1.66	1.000

Post-procedural complications like pain, anxiety, dizziness, and spotting are minimal and showed no significant differences between groups (p value-1.000). At 12 weeks, post procedure complications like pain, watery discharge were similarly reported with no serious

2-3 (mild)	18	60	15	50	34	51.7
4-6 (moderate)	0	0	1	3.3	1	1.7
7-10 (Severe)	0	0	0	0	0	0
Total	30	100	30	100	60	100
Chi-square = 1.427 with 2 degrees of freedom; P = 0.490						

Pain levels during the procedure were comparable between group A and group B, with 40% and 46.6% of participants reporting no pain, 60% and 50% participants reporting mild pain respectively (p= 0.906). Only 1 patient had moderate pain in thermal group. Severe pain not reported in either groups.

In both Group A and Group B, the majority of patients reported high satisfaction with the procedure: 90% in Group A and 96.7% in Group B indicating better safety profile of thermal ablation group than cryotherapy group.

side effects like severe abdomen pain, heavy bleeding, malodorous discharge, PID, hospital admission are not found in either group indicating good safety profile of both procedures.

Table 4: Comparison of assessment for efficacy after 12 weeks (3 months) follow up with visual inspection with acetic acid (VIA) between two groups

Lesion regression	Group A (Cryo)		Group B (Thermal)		Total	
	N	%	N	%	N	%
Complete (VIA negative)	28	93.3	29	96.7	57	95
Incomplete (VIA positive)	2	6.7	1	3.3	3	5
Total	30	100	30	100	60	100

Chi-square = 0.000 with 1 degree of freedom; P = 1.000

At 3 months, complete regression of aceto-white areas occurred in 28 (93.3%) of Group A and 29 (96.7%) of Group B, with no significant difference in treatment efficacy (p=1.000).

At 3 months follow up, majority of the patients in both Group A (93.37%) as well as Group B (96.7%) were highly satisfied. No significant difference was seen in patient satisfaction between the two groups (p=1.000).

**Discussion**

Cervical cancer is a major health issue in India, contributing significantly to cancer-related morbidity and mortality. Regular screening and timely treatment of precancerous lesions can prevent this disease. However, challenges such as inadequate screening programs, limited resources, and high costs of advanced methods like HPV DNA testing hinder prevention efforts, particularly in Low-Middle-Income Countries (LMICs).

To address these issues, the World Health Organization (WHO) advocates a 'screen and treat' approach. While traditional cryotherapy relies on gas supplies, thermal ablation, recently endorsed by the WHO, offers a viable alternative that doesn't require gas and is effective for treating Cervical Intraepithelial Neoplasia (CIN) lesions. Studies show success rates of 97.6% for thermal ablation and 92.9% for cryotherapy, making thermal ablation a promising option in resource-constrained settings.

In our study, the mean age of women in Group A (cryotherapy) was 38.43±6.82 years and in Group B

(thermal ablation) was 37.2±7.76 years. The majority (38.3%) of patients in both groups were aged 35-44 years, with 36.7% under 35 years and 25% aged 45-54 years; this difference was not statistically significant. These findings align with previous studies, such as those by Dipanwita Banerjee et al. (2020)<sup>8</sup> and Manju Lata Verma (2023)<sup>9</sup>, which reported mean ages of 37 and 38 years for cryotherapy and thermal ablation, respectively.

Patient satisfaction, assessed using a Visual Analog Scale (VAS), showed high satisfaction rates immediately after the procedure: 90% in the cryotherapy group and 96.7% in the thermal ablation group, with no significant difference (p=0.612). This is consistent with studies by Manju Lata Verma et al. (2022)<sup>9</sup>, Tania Metaxas et al. (2022)<sup>10</sup>, and Leeya F. Pinder et al. (2020)<sup>11</sup> which also reported high satisfaction rates for both treatments.

Our study found minimal intraoperative pain during cryotherapy (60%) and thermal ablation (50%), align with previous studies Randall et al 2019<sup>12</sup>; Banerjee et al,<sup>8</sup> 2020, showing lower rates of severe adverse events. The low pain levels may be attributed to the quick and simple nature of both treatments.

The majority (66.6% in cryotherapy arm and 70% in thermal therapy arm) of patients reported no adverse effects, 30 in cryotherapy group & 33.33% in thermal ablation group had minimal complications. Notably, no severe side effects were reported. These findings align with previous studies Thomas C. Randall et al<sup>12</sup> 2019 and

Hurtado Roca Y et al<sup>13</sup> 2020 suggesting that severe adverse events are rare, while mild to moderate side effects are more common.

Both treatments demonstrated high success rates, with 93.33% of cryotherapy and 96.7% of thermal ablation patients showing complete regression of lesions (VIA negative) at 12 weeks consistent with previous research Marlieke de Fouw et al<sup>14</sup>;2019 (93.8% for cryotherapy and 91.4% for thermal ablation; Manju Lata Verma<sup>9</sup>, 2023 (92.7% for cryotherapy and 97.6% for TA) confirming the effectiveness of both treatments.

At 12 weeks post-treatment, satisfaction remained high, with 93.37% in the cryotherapy group and 96.7% in the thermal ablation group, and no significant difference ( $p=1.000$ ). Previous studies, including those by Leeya F. Pinder et al. (2020)<sup>11</sup> and Dipanwita Banerjee et al. (2020)<sup>8</sup>, also reported high satisfaction rates and cure rates for CIN 1+ lesions, at 74.1% for cryotherapy and 81.0% for thermal ablation ( $p=0.57$ ).

### Conclusion

Thermal ablation has demonstrated a favorable safety profile and effectiveness comparable to cryotherapy, resulting in high patient satisfaction rates. The cordless and portable nature of the thermal ablation device makes it more user-friendly and less time-consuming. Unlike cryotherapy devices, it does not require a gas supply, which lowers operating costs and makes it a more viable alternative, particularly in low-resource settings. This method could facilitate a single-visit screening and treatment approach, thereby optimizing initiatives aimed at eliminating cervical cancer.

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