Cryotherapy has No Place in Colposcopy Practice Con

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Four points about Cryotherapy

- Efficacious
- Safe
- Viable alternative to surveillance for CIN 2
- High-value option







Cryotherapy: Efficacy

12-month cure rates for CIN 2 or CIN 3

| Cryotherapy (%) | Loop excision (%) | Reference |
|-----------------|-------------------|---------------------|
| 93-94 | 91-99 | Martin-Hirsch, 2013 |
| 94.7 | 94.7 | Santesso, 2016 |
| 92.0 | 97.6 | Chirenje, 2001 |

WHO Recommendation, 2016, Santesso: "For all screen-and-treat recommendations, cryotherapy is first choice of treatment for women who are screened positive and eligible for cryotherapy."







Cryotherapy: Safety, peri-procedure outcomes

| Outcome | | Cryotherapy (%) | Loop excision (%) | Reference |
|----------------|-----|-----------------|-------------------|----------------|
| Major bleeding | | 0.03 | 0.23 | Santesso, 2016 |
| | RCT | 0.5 | 2.0 | Chirenje, 2001 |
| Severe pain | | 3.6 | 0.7 | Chamot, 2010 |
| | RCT | 1.0 | 1.0 | Chirenje, 2001 |

Santesso, 2016: "Generally, there were more adverse events with... LEEP than with cryotherapy."







Cryotherapy: Safety, short-term outcomes

| Outcome | Cryotherapy (%) | Loop excision (%) | Reference |
|----------------------------------|-----------------|-------------------|----------------|
| Pain, longer term to next menses | 9.0 | 66.8 | Chamot, 2010 |
| RCT, 2-week | 44 | 46 | Chirenje, 2001 |
| Vaginal discharge, watery | 65.0 | "most" | Chamot, 2010 |
| RCT, 2-week | 92.4 | 78.5 | Chirenje, 2001 |
| Vaginal discharge, offensive | 2.0 | 3.2 | Chamot, 2010 |
| RCT, 2-week | 68.2 | 79.0 | Chirenje, 2001 |
| Acceptability, 2-weeks | 91 | 96 | и |

Cochrane, 2013: "The evidence suggests that there is no obvious superior surgical technique for treating cervical intraepithelial neoplasia in terms of treatment failures or operative morbidity."





Cryotherapy: Safety, longer-term outcomes

| Outcome | Cryotherapy | Large loop excision of TZ | Reference |
|------------------|------------------|---------------------------|---------------|
| Pre-term birth | | | |
| <37 weeks | 1.02 (0.22-1.77) | 1.56 (1.36-1.79) | Kyrgiou, 2016 |
| <32-34 weeks | 1.86 (0.08-43.9) | 2.13 (1.66-2.74) | u |
| <28-30 weeks | 1.38 (0.81-2.36) | 2.57 (1.97-3.35) | u |
| Repeat treatment | | | |
| <37 weeks | | 2.81 (2.33-3.39) | u |
| Depth ≤10-12 mm | | 2.01 (1.28-3.15) | u |

Observational evidence mixed. No randomized trials.







Cryotherapy: Safety, longer-term outcomes

ASCCP, 2012: "Studies of the effect of treatment on future pregnancy are conflicting... Nevertheless, because pregnancy complications can be devastating, the potential benefits of treatment should be balanced against the risk to future pregnancies."

ACOG, 2016: "Avoiding unnecessary excision or ablation of the cervix in young women clearly is advisable even though the association between LEEP and preterm birth has been challenged."

Santesso, 2016: "The quality of the evidence for all outcomes was low to very low."







HPV-based strategies -> increased diagnoses of CIN 2
HPV triage of ASC-US (ALTS 2003)
Primary HPV testing (Patanwala 2013)

CIN 2 has high spontaneous regression rates: 38-44% in 6-12 months (ALTS 2003; Moscicki 2010; Helm 2013)







ASCCP, 2012: CIN 2, 2/3 management

CIN2,3 in Young Women Management of Young Women with Biopsy-confirmed Cervical Intraepithelial Neoplasia - Grade 2,3 (CIN2,3) in Special Circumstances Young Women with CIN2,3 Either treatment or observation is acceptable, provided colposcopy is adequate. When CIN2 is specified. observation is preferred. When CIN3 is specified, or colposcopy is inadequate, treatment is preferred. Treatment using Excision Observation — Colposcopy & Cytology @ 6 month intervals for 12 months or Ablation of T-zone 2x Cytology Negative Colposcopy worsens or and Normal Colposcopy High-grade Cytology or Colposcopy CIN3 or CIN2,3 persists for 24 months persists for 1 year Either test Cotest in 1 year -> abnormal Repeat Colposcopy/Biopsy Treatment Recommended Both tests negative Recommended © Copyright, 2013, American Society for Colposcopy and Cervical Pathology. All rights reserved. ASCP Cotest in 3 years





Problems with surveillance

- Conversion to inadequate colposcopy -> excision
- ASCCP 2012 regarding surveillance: "Treatment is recommended if colposcopy is inadequate, if CIN 3 is specified, or if CIN 2 or CIN 2,3 persists for 24 months."
- Resource intensive
- Adverse psychological effects (Sharp 2014)
- High default rates (Kyrgiou 2007, 2016)







Candidacy for cryotherapy as per WHO 2011 Guidelines

- adequate colposcopy
- lesion(s) completely visible
- lesion(s) not covering more than 75% of the ectocervix
- lesion(s) can be covered entirely with the cryoprobe

http://www.who.int/reproductivehealth/publications/cancers/9789241502856/en/







12-month cure with surveillance: ~40%

12-month cure with cryotherapy: ~90%

Number needed to treat for benefit: 1/0.50 = 2

For every 2 women treated with cryotherapy compared with surveillance, 1 will be cured.





Cryotherapy: a High-Value option

- Systems perspective: flexible, relatively inexpensive
- Patient perspective: highly acceptable, efficient





Conclusion

Cryotherapy has an important place in colposcopy practice

- Efficacious
- Safe
- Viable alternative to surveillance for CIN 2
- High-value option





Conclusion

Cryotherapy has an important place in patient-centered care

Cryotherapy should at least be offered to women who are appropriate candidates

- as an alternative to loop excision
- as an alternative to surveillance for CIN 2, CIN 2/3





