Volume 9 | Issue 3 | July - September 2019

e-Newsletter

ISCCP

Member International Federation of Cervical Pathology and Colposcopy

Newsletter of Indian Society of Colposcopy & Cervical Pathology (Reg.)

www.isccp.in

From the Editor's Pen

Dear All,

Greetings from ISCCP

After the two hectic issues full of research work, we are back with our sections of academic knowledge to update all the ISCCP members.

In this issue we have included a very interesting review article on "Guidelines for follow up in women treated (Curative intent) for cervical carcinoma" by Dr Nikhil S Parwate. As we all know, even if the patients are referred to a higher center for the treatment of cervical carcinoma, they generally get back to their practitioners for the follow-up. Most of the general gynecologists, after referring a patient to surgery/radiotherapy/chemotherapy for cervical carcinoma, are not aware of the follow up guidelines to detect early recurrences. This comprehensive review will update all the members about the current consensus on follow up guidelines.

This issue also contains the article by Dr Puneet Chandna on HPV infection and vaccination in males.

Journal scan coverage by Dr Deepti Goswami and the cervical cancer news from around the world by Dr Roopa Hariprasad will update all about what all is going on round the globe.

I once again request all the ISCCP members to contribute in the Newsletter in the form of review article/original articles/view point/case reports/images.

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Guidelines for Authors

All members of ISCCP are requested to send manuscripts pertaining to (but not exclusively limited to) to cervical cancer prevention/treatment for publication in the newsletter. The matter should be original and not published/under consideration for publication elsewhere.

This could be in one of following forms:

1. **Original Article:** Articles from original research (including aim, methods, results and discussion), should not exceed 5-6 typed pages, word limit of 1500 words and not more than 10 references. Tables and Figures could be included as per requirement.
2. **Review Article:** The article should not exceed 3-4 typed pages, word limit 2500 words with not more than 8 references.
3. **Case Report:** An interesting case report which has "take home message", word limit 800 words with not more than 3-5 references. Image should be sent separately in JPEG format
4. **Report of conferences/ CME? awareness/training camps:** up to 300 words with 2-3 images

References: References should be recent, relevant, indexed and in Vancouver style. References to literature cited should be numbered consecutively and placed at the end of the manuscript. In the text they should be indicated as superscript. All papers submitted are subject to review process. All accepted papers will be suitably edited before publication.

Submit to: Dr Aruna Nigam, praksharuna@hotmail.com

Forthcoming Conference

IMS ISCCP Colposcopy Workshop on 10th November, 2019 in Pune

ISCCP Workshop at IMS Chattisgarh State Conference Raipur on 14th December, 2019

Guidelines for Follow Up in Women Treated (Curative intent) for Cervical Carcinoma

Nikhil S Parwate
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For women with cervical cancer who have been treated with curative intent, follow-up includes identification of complications related to treatment and intervention in the event of recurrent disease. The concept of long-term surveillance of patients treated with curative intent is based on the premise that early detection will result in decreased morbidity and mortality. The assumptions are as following

1. Screening has adequate sensitivity and specificity and is resource-effective
2. Natural history of both the anatomic pattern and the timing of disease recurrence is known
3. The effective low-morbidity salvage therapy is available and can be applied.

Follow-up protocols in this population are variable, using a number of tests at a variety of intervals with questionable outcomes.

The specific components of such a program that need to be addressed include optimal intervals for follow-up, clinical utility of the surveillance tests currently available [history, physical exam, vaginal cytology, ultrasonography, magnetic resonance imaging (MRI), computed tomography (CT), positron-emission tomography (PET), or tumour markers], and modification of follow-up programs based on an individual patient's risk of recurrence and complications related to primary therapy.

Guideline Development

This practice guideline report was developed by the Gynecology Cancer Disease Site Group (DSG) of Cancer Care Ontario's Program in Evidence-Based Care (PEBC) using the methods of the practice guidelines development cycle[1,2,3]. The guideline is a convenient and up-to-date source of the best available evidence on the follow-up of patients with cervical cancer who are clinically disease-free after receiving primary treatment. It was developed through systematic review of the evidentiary base, evidence synthesis, and input from internal and external review participants in Ontario.

Results

Sixteen of the seventeen retrospective studies outlined the timing for follow-up visits[4-13,15-20]. Most studies used similar intervals: follow-up visits every 3–4 months within the first 2 years, every 6 months for the next 3 years, and annually thereafter or until year 10 or discharge at the discretion of the treating physician. All seventeen studies also reported that physical examinations with or without patient histories were performed at each follow-up visit[4-22].

Recurrence rates in most of the studies ranged from 8% to 26% of patients.[4-14,16,19,20] Overall, the median time to recurrence ranged from 7 months to 36 months after primary treatment.[4-20] Recurrences that were distant or detected at multiple sites occurred in 15%–61% of patients.[8-10,12,14,15,18-20] The timing of recurrences was inconsistently reported, and no observed differences in survival were reported by the timing of recurrence detection.

Thirteen of the seventeen studies reported mean or median survival after recurrence.[4-13,17,18,20] Five studies reported median overall survival after recurrence— a finding that ranged between 7 months and 12 months for the total patient population.[4,6-8,18] Eight studies reported results separately for patients who were symptomatic compared with those who were asymptomatic at the time of recurrence detection.[5,9-13,17,20] For patients who were symptomatic at the time of recurrence detection, median overall survival after recurrence ranged from 8 months to 38 months; for asymptomatic patients, the range was 8 months to unreached after 53 months of follow-up. No quality-of-life data were provided in any of the retrospective reviews identified in the literature search.

Practice Guideline

Patients need to be informed about symptoms of recurrence, because most women have signs or symptoms of recurrence that occur outside of scheduled follow-up visits.

Follow-up care after primary treatment should be conducted and coordinated by a physician experienced in the surveillance of cancer patients. Continuity of care and dialogue between the health care professional and the patient may well enhance and facilitate early detection of cancer recurrence and help to avoid duplication of surveillance testing and effort.

A reasonable follow-up strategy involves follow–up visits every 3–4 months in the first 2 years, and every 6–12 months in years 3–5.

After 5 years of recurrence-free follow-up, the patient should return to annual assessment with a history, general physical, and pelvic examination with cervical or vaginal cytology (or both) performed by the primary care physician.

At a minimum, follow-up visits should include a patient history and complete physical examination. Symptoms elicited during the patient history should include general performance status, lower back pain (especially if it radiates down one leg), vaginal bleeding, or unexplained weight loss. A physical examination should attempt to identify abnormal findings related to general health or those that suggest vaginal, pelvic sidewall, or distant recurrence. Because central pelvic recurrences are potentially curable, the physical examination should include a speculum exam with bimanual, pelvic, and rectal examination. The routine use of other investigations in asymptomatic patients is not advocated, because the roles of those investigations have yet to be evaluated in a definitive manner.

There is evidence to suggest that vaginal vault cytology adds significantly to the clinical exam in detecting early disease recurrence. If cytology is performed as part of routine follow-up after surgery for cervical cancer, its role would be to detect new precancerous conditions of the vagina, and it should be performed no more frequently than once annually. An abnormal cytology result that suggests the possibility of neoplasia warrants colposcopic evaluation and directed biopsy for histologic confirmation.

The role of abdominal or pelvic CT, MRI, PET or ultrasonography as part of routine follow-up has not been fully evaluated in prospective studies. Use of serum markers such as squamous cell carcinoma antigen or cancer antigen 125 has shown promise in predicting surgical findings or the post-radiotherapy course when disease is present; however, the role of such markers in the follow-up of patients post treatment is yet to be determined.

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Are HPV Related Diseases in Males and Female Alike?

Puneet Chandna
MD. PhD

HPV Acrimony may not just be Restricted to Cervical, Vulvar or Vaginal Cancer

HPV is spread from skin surface to skin surface, and cutaneous HPV infections are widespread throughout the general population.

- Non-Genital Warts occur in 10 percent of children, with a peak incidence between the ages of 12 and 16.
- Genital WartsThe peak prevalence occurs in persons between the ages of 17 and 33 years of age, and the peak incidence is in those aged 20 to 24 years.
- HPV types 16 and 18 cause nearly 90 percent of anal cancers and precancerous anal lesions.
- Oropharyngeal cancer — HPV infection plays a role in the pathogenesis of squamous cell carcinomas of the head and neck.
- Recurrent respiratory papillomatosis is the most common benign laryngeal tumor in children and is thought to be caused by HPV acquired during passage through the birth canal of an infected mother.

Males: Routine HPV immunization is recommended in many countries for adolescents and young adults but not in India.

Vaccination Boys

HPV vaccination provides a direct benefit to male recipients by safely protecting against cancers that can result from persistent HPV infection.

Vaccination with 9-valent or quadrivalent vaccine also protects against anogenital warts (90 percent of which are caused by HPV types 6 and 11).

Despite a smaller direct absolute benefit of HPV vaccination in males compared with females, the overall benefit of vaccinating males outweighs its potential risks because of additional population benefits from herd immunity and the documented safety of HPV vaccines.

Boys: In many countries, HPV vaccine is recommended at 11 to 12 years. It can be administered as starting at 9 years of age, and catch-up vaccination is recommended for males aged 13 to 21 years who have not been previously vaccinated or who have not completed the vaccine series.

Models and studies indicate a possibility of lesser herd protection (Community immunity or Herd Immunity) from female vaccination, and thus males would have more direct benefit from vaccination.

Although it is not clear that greater HPV-type coverage by vaccinating males with the 9-valent rather than quadrivalent vaccine would substantially improve male cancer prevention, it would likely further reduce the risk of cervical cancer in women indirectly through herd immunity.

Cervical Cancer News from Around the World

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In 2019, WHO will Ramp Up Work to Eliminate Cervical Cancer Worldwide by Increasing Coverage of the HPV Vaccine, Among Other Interventions

WHO News: 21 March 2019

The world is facing multiple health challenges. These range from outbreaks of vaccine-preventable diseases like measles and diphtheria, increasing reports of drug-resistant pathogens, growing rates of obesity and physical inactivity to the health impacts of environmental pollution and climate change and multiple humanitarian crises.

In 2019, WHO will ramp up work to eliminate cervical cancerworldwide by increasing coverage of the HPV vaccine, among other interventions. 2019 may also be the year when transmission of wild poliovirus is stopped in Afghanistan and Pakistan. Last year, less than 30 cases were reported in both countries. WHO and partners are committed to supporting these countries to vaccinate every last child to eradicate this crippling disease for good.

For more, read:
https://www.who.int/vietnam/news/feature-stories/detail/ten-threats-to-global-health-in-2019

AI-powered, Cloud-Based Cervical Cancer Screening Platform Launched in China

Mobile Health News: April 05, 2019

Increasing the cervical cancer screening coverage rate of rural women in China is a priority and the new screening platform could potentially address some of these gaps.

China Maternal and Child Health Care Association and Wuhan University Landing AI Cytology Diagnostic Centre recently launched a cervical cancer screening AI cloud diagnostic platform. The platform can be accessed worldwide as of April 1, 2019 and women, especially those from countries along Belt and Road Initiative, will be able to benefit from a high-quality, low-cost cervical cancer screening services.

For more, read:
https://www.mobihealthnews.com/content/ai-powered-cloud-based-cervical-cancer-screening-platform-launched-china

Screening also Prevents Rare Types of Cervical Cancer

April 4, 2019

Rare types of cervical cancer can be effectively prevented with screening, a comprehensive study of identified cases of rare cervical cancer over a 10-year period in Sweden concludes. This has now been investigated by researchers at Karolinska Institute in a study published in the BMJ, in which they investigated all Swedish cases of invasive cervical cancer from 2002 to 2011, identified using the National Swedish Cancer Registry. Of these over 4,200 cases, 338 were identified as not belonging to the most common types of cervical cancer (squamous epithelial cancer and adenocarcinoma).

For more, read:
https://medicalxpress.com/news/2019-04-screening-rare-cervical-cancer.html

HPV Vaccine Linked to 'Dramatic' Drop in Cervical Disease

BBC News: 4 April 2019

The routine vaccination of girls with the HPV vaccine in Scotland has led to a "dramatic" drop in cervical disease in later life, new research suggests.

Human papilomavirus (HPV) is a sexually transmitted infection and some types are linked to cervical cancer.

Researchers said the vaccine has nearly wiped out cases of cervical pre-cancer in young women since an immunisation programme was introduced 10 years ago.

For more, read:
https://www.bbc.com/news/uk-scotland-47803975

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Undurraga M, Catarino R, Navarria I, Ibrahim Y, Puget E, Royannez Drevard I, Pache JC, Tille JC, Petignat P.

User Perception of Endocervical Sampling: A randomized comparison of endocervical evaluation with the curette vs. cytobrush

PLoS One. 2017 Nov 6; 12(11): e0186812.

This study was conducted at the colposcopy clinic of the University Hospital of Geneva and involved 200 patients who were randomized into two groups, according to technique:

ECC group = 89

ECB group =101

Excluded =10 (incomplete information or cervical stenosis).

Patients and physicians' preference regarding the technique as well as the quality of samples were assessed. ECB samples were analyzed using both cytological (cell block) and histologic analysis, while ECC samples were analyzed using standard histologic analysis.

Results

- Physicians preferred ECB against ECC, classifying it more frequently as an easy technique (94.1% vs.61.4%, p<0.001).
- Physicians more frequently evaluated the ECB as little or not uncomfortable for patients (28.7% vs.10.2%, p<0.001).
- Patients themselves didn't express a preference for either technique.
- Brush allowed for a better quality of samples, with a lower rate of inadequate samples (2.0% vs. 14.3%, p = 0.002) and greater amount of material.

Authors concluded that endocervical sampling using ECB seems to be easier to perform and provides better quality samples. ECB can therefore be an acceptable alternative to ECC in standard practice.

Leeman A, Del Pino M, Molijn A, Rodriguez A, Torné A, De Koning M, Ordi J, Van Kemenade F, Jenkins D, Quint W.

HPV Testing in First-void Urine Provides Sensitivity for CIN2+ Detection Comparable with A Smear taken by a Clinician or a Brush-based Self-sample: Cross-sectional data from a triage population

BJOG. 2017 Aug; 124(9): 1356-1363.

This cross-sectional study was conducted at a colposcopy clinic in Spain and involved 113 women referred for colposcopy after an abnormal Pap smear.

They were sent a device (Colli-Pee™, Novosanis, Wijnegem, Belgium) to collect urine samples on the morning of colposcopy (U1). A later urine sample (U2), clinician-taken smears (CTS), and brush-based self-samples (SS) (Evalyn brush™, Rovers Medical Devices B.V., Oss, the Netherlands) were also analyzed.

All samples were tested for HPV DNA using the analytically sensitive SPF10-DEIA-LiPA25 assay and the clinically validated GP5+/6+-EIA-LMNX. The main outcome measures were histologically confirmed CIN2+ and hrHPV positivity for 14 high-risk HPV types.

Results

- Samples from 91 patients were analyzed.
- All CIN3 cases (n = 6) tested positive for hrHPV in CTS, SS, U1, and U2 with both HPV assays.
- Sensitivity for CIN2+ with the SPF10 system was 100, 100, 95, and 100%, respectively. With the GP5+/6+ assay, sensitivity was 95% in all sample types. The sensitivities and specificities for both tests on each of the sample types did not significantly differ.
- There was 10-14% discordance on hrHPV genotype.

The authors concluded that CIN2+ detection using HPV testing of U1 shows sensitivity similar to that of CTS or brush-based SS, and is convenient. There was substantial to almost excellent agreement between all samples on genotype with both hrHPV assays. There was no advantage in testing U1 compared with U2 samples.

Elfgren K, Elfström KM, Naucler P, Arnheim-Dahlström L, Dillner J.

Management of Women with Human Papillomavirus Persistence: Long-term follow-up of a randomized clinical trial

Am J Obstet Gynecol. 2017 Mar; 216(3): 264.e1-264.e7.

Optimal clinical management of HPV-positive but cytology-negative women is unclear. This study provides some insight on the long-term outcome of this subset of women.

Among 12,527 women aged 32-38 years enrolled in a double blind, randomized clinical trial of human papillomavirus (HPV) screening in Sweden, authors followed up the 195 women who attended the colposcopy screening who were cytologically normal but persistently HPV positive (at least 12 months later; median, 19 months) in the HPV testing arm (n = 100) or were randomly selected from the control arm (n = 95).

Women in the HPV testing arm were followed up with repeated HPV testing, cytologies, and colposcopies if persistently HPV-positive without CIN 2 or worse.

A similar number of random colposcopies and tests were carried out in the control arm. Women were followed up over 13 years for the main outcome measures: cumulative incidence of CIN 2 or worse and CIN 3 or worse.

Results

- Among women who continued to attend and had continuous HPV persistence, all (40 of 40, 100% [95% confidence interval, 91-100%]) developed CIN 2 or worse.
- There were no cases among women who cleared their HPV persistence (0 of 35, 0% (95% confidence interval, 0-10%) ($P < .001$).
- Among women who had had HPV persistence but did not continue with repeated HPV tests (unknown persistence status), 56% (15 of 27 women) developed CIN 2 or worse. Almost all cases occurred within 6 years.
- The intensive clinical management in the trial appeared to result in diagnoses of earlier CIN 2 or worse but apparently did not prevent CIN2 or worse.

The authors concluded that women with HPV persistence will, in general, either become HPV negative or develop CIN 2 or worse within 6 years, even with intensive clinical follow-up.

ISCCP Activities

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ISCCP-NARCHI Camp on Cervical Screening & Public Awareness Session

A public awareness session along with screening for cervical cancer was conducted by Dr Sujata Das and her team of young doctors from ISCCP-NARCHI on 16th June, 2019 at Shiv temple, Shalimar Bagh, Delhi. There were 52 women who attended the interactive session, of which 29 underwent screening.

Health Camp Organized by ISCCP and Narchi in Association with MCD South Delhi

IMS +ISCCP Colposcopy Workshop Agra-on 28th July 2019, organized by Dr Savita Tyagi

Vaccination Camp in Government School in VIZAG – on 22nd August 2019 organized by Dr Leela Digurmati with the theme to Vaccinate Daughters and Screen Mothers. Vaccination was done for class 10 students.

ISCCP Colposcopy Workshop, Karnal on 1st September 2019 organized by Dr Ragini Agarwal and Dr Mitra Saxena

2nd Dose Cervical Cancer Vaccination at Sant Parmanand Hospital 13th September 2019 organized by Inner Wheel – 250 girls below 14 were vaccinated

Workshop on Colposcopy Cryotherapy and LEEP, 15th September, 2019 at Lucknow

Full-day Workshop on Colposcopy, Cryotherapy and LEEP was organized at Atal Bihari Vajpayee Scientific Convention Centre, Lucknow on 15th September 2019 by Prof Nisha Singh, Department of Obstetrics & Gynaecology, KGMU Lucknow. About 200 delegates registered for the workshop from Lucknow & surrounding cities.

Cervical Cancer Awareness Camp was organized by Dr Anita Sabharwal at Lady Irwin College on 20th September, 2019

AOGD Preconference Preventive Oncology Workshop was Organized on 26th September, 2019 at Safdarjung Hospital by Dr Saritha Shamsunder