ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at: www.ijmacr.com

Volume – 3, Issue – 1, January - February - 2020, Page No. : 24 - 31

Cervical cancer and its management

[1]Dr Mahhum Razzaq,[2]Dr Syeda Fouzia Basharat, [3]Dr Badshah Khan

[1]MBBS,Nawaz Sharif Medical College,Gujrat

[2]MBBS,Rawalpindi Medical College, Rawalpindi

[3]MBBS,Beihua University, China.

Corresponding Author: Dr Mahhum Razzaq**,** MBBS, Nawaz Sharif Medical College,Gujrat

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Introduction

The second most common cancer in women worldwide is cervical cancer [1]. The disease disproportionately affects the poorest regions above 80% of the cases are from well-developed countries.1 Cervical cancer is an important cause of early loss of life as it affects relatively young women. 90-95% women are curable at early stage (which include stage I and II) of disease by surgery or chemotherapy whereas women with stage III have 60% chances. Squamous cell carcinoma accounts for about two thirds of all cervical cancers. Whereas 15-25% of cases are found of adenocarcinoma and it has many variations and is found in. Tumor grade (well differentiated, moderately differentiated, and poorly differentiated), depth and width of invasion, and presence (or absence) of invasion of lymphovascular space are prognostic factors that should be adequately assessed. The main cause of cervical cancer is infection with high risk types of human papillomavirus. This has obvious implications for primary prevention (vaccination) and secondary prevention (screening) of this disease [2]. The International Federation of Gynecology and Obstetrics (FIGO) staging system is the most commonly used. It takes into account the results of the physical examination, colposcopy, histopathology (cervical biopsy or conisation), radiography (for example, chest radiography, intravenous pyelography, and barium enema), and endoscopy (for example, cystoscopy or sigmoidoscopy). Suspected invasion of the bladder or the rectum should be confirmed by biopsy.

Treatment of cervical cancer depends on the stage of disease. Currently used International Federation of Gynecology and Obstetrics system of staging (FIGO staging) is based on anatomical extent of the disease and on clinical evaluation and must not be changed because of subsequent surgical findings [3]. When there is doubt as to which stage a particular cancer should be allocated, the earlier stage is mandatory. In patients with histologically (biopsy, endo-cervical curettage and/or cone biopsy) confirmed cervical carcinoma, a staging procedure is required that involves colposcopy, vaginal and rectal examination, cystoscopy and rectosigmoidoscopy, to assess the extension to the surrounding structures (parametria, bladder and rectum). Suspected bladder and /or rectal involvement should be confirmed histologically. It is preferable to carry out this examination under general anesthesia. IVP is optional for stages >Ib2 cervical cancer. Computed tomography (CT) scanning and magnetic resonance imaging (MRI) are usually performed to determine lymphadenopathy and parametrial spread, respectively [4]. To rule out small nodal disease, particularly in para-aortic region where external radiation

may offer a survival advantage, Positron emission tomography (PET) scanning is the preferred approach. PET was shown to be significantly superior to CT/MRI (sensitivity: 92% vs. 60%) in identifying metastatic lesions. These diagnostic modalities are not technically included in the staging drawn up by FIGO, but should be performed whenever necessary. There is much debate as to whether cervical carcinoma should be staged surgically, because the current FIGO staging appears to be unreliable, especially for locally advanced disease. Among other factors this staging system ignores one of the most relevant prognostic indicatorsd lymph node metastases. Intraperitoneal laparotomy has not proven to be acceptable for surgical staging, due to high morbidity and mortality rates. Laparoscopic extra peritoneal approach is novel technique combining the benefits of laparoscopy with those of a retroperitoneal approach [5]. Some studies have suggested a benefit from laparoscopic surgical staging for patients with stage Ib2eIII disease, but overall, a few non-randomized studies comparing clinical with surgical staging, as well as the only randomized one published to date, have failed to demonstrate a survival benefit of surgical over clinical staging.

Stage IA microinvasive disease

The category of microinvasive cervical carcinoma (stage Ia) has been applied to certain early phases of invasive carcinoma that have limited metastatic potential and therefore are most likely curable by non-radical treatment. The diagnosis of stage Ia cervical squamous cell carcinoma should be based on cone biopsy, preferably using a technique that does not result in cauterized margins. Ideally, the management of microinvasive cancer should be planned in cooperation with an experienced pathologist. Histologic parameters are used to determine how extensive the operation should be and whether the regional lymph nodes should be treated. In general, the risk for nodal involvement in microinvasive disease is low. The patients most at risk of nodal metastases or central pelvic recurrence are those with definitive evidence of tumor emboli in lymph vascular spaces [6]. Each patient with microinvasive cancer should be evaluated individually. If distant spread is very unlikely, simple but complete excision of the lesion suffices.

Stage Ia1 cervical cancer

Several studies have suggested that FIGO stage Ia1 disease, defined as minimal microscopic invasion have the risk of nodal disease of approximately 7%9 and accordingly, unless there are strong reasons for conservative treatment, the patient can be treated by primary radical hysterectomy, modified radical hysterectomy with pelvic lymphadenectomy or primary radiotherapy. Radical vaginal trachelectomy and laparoscopic pelvic lymphadenectomy may be an option where preservation of fertility is desired. More recent studies suggested that the rate of lymph node involvement in this group of patients (Ia2) who do not have lymph vascular invasion may be much lower and questioned whether conservative therapy might be adequate for patients believed to have no residual disease following colonization [7]. Stage Ia2 with no lymphovascular invasion can be treated effectively by complete excision (conization or extrafascial hysterectomy) though radical trachelectomy/hysterectomy may be warranted. Pelvic node dissection is disputable in this group of patients. Recommended treatment for Stage Ia2 cases with unfavorable pathologic characteristics (lymphovascular invasion) is: Radical hysterectomy with pelvic node dissection, Radical trachelectomy with laparoscopic pelvic node dissection, in young women if pregnancy is desired Early invasive carcinoma of the cervix can be treated with intracavitary radioactive sources alone, and this should be

considered in patients who are at increased risk of operative mortality because of age or medical status.

Stage IbeIIa cervical cancer

There is no standard management of stage IbeIIa cervical carcinoma. Most patients are treated by either radical surgery or radical radiotherapy. Both treatment modalities have proven to be equally effective, but differ in associated morbidity [8]. With radical surgery, however, ovarian function can be preserved and vaginal stenosis secondary to radiation avoided, which is of great advantage especially for younger patients. In addition, surgery avoids the possible chronic radiation damage to other surrounding structures (bladder, small and large bowel), which is difficult to manage. Combinations of surgery and radiotherapy are also used, although specific protocols vary considerably. Treatment decisions for each patient are based on multiple factors including the age, medical condition of the patient, tumor-related factors and treatment preferences, to yield the best cure with minimum complications. Stage Ib1 and early stage IIa disease the standard surgical procedure in stage Ib and IIa cervical cancer is radical hysterectomy with pelvic lymphadenectomy. Primary surgery has the advantage of removing the primary disease and allowing accurate surgical staging, thereby allowing any adjuvant therapy to be more accurately targeted. The operation involves removal of the uterus and the paracervical tissues surrounding cervix and the upper 2 cm of vagina. The ovaries may be conserved, particularly if the patient has squamous pathology in order to avoid the effects of early menopause in younger women [9]. A randomized study comparing survival, relapse and morbidity between type II and type III radical hysterectomy in stage IbeIIa cervical cancer has found both to be equally effective; the latter being associated with a higher degree of late complications [10]. To overcome serious morbidity and voiding dysfunction related to the extent of radical hysterectomy, specific nerve-sparing techniques have been introduced. Recent studies have shown that early cervical cancer can be treated successfully with laparoscopic assisted radical vaginal hysterectomy (LARVH), with similar efficacy and recurrence rates to radical hysterectomy. Finally, radical vaginal trachelectomy and laparoscopic pelvic lymphadenectomy may be an option in small cervical cancer where preservation of fertility is desired. Several studies have reported recurrence rates comparable to radical hysterectomy (approximately 4%), and encouraging live-born pregnancy rates. Alternatively, radical trachelectomy may be performed via an abdominal route. These procedures are still considered investigational and appropriate cases should be referred to specialized gynecological cancer centers. A standard part of surgical treatment of stage IbeIIa cervical cancer is pelvic lymphadenectomy. Pelvic lymph nodes are carefully dissected to remove as many of the nodes as possible [11]. The average number of lymph nodes removed is 23e28. It was well documented that the percentage of nodal involvement is increasing from 10.5% positive nodes when less of 20 nodes are removed, to 26.5% when more than 50 nodes are removed. During the last few years several pilot studies on the feasibility of lymphatic mapping/ sentinel node biopsy in cervical cancer have yielded promising results. However, the findings of a high percentage of patients with bilateral and/or more than one sentinel lymph node demands improvements in the detection rate prior to consider the sentinel node biopsy a routine procedure in cervical cancer patients [12]. Much has been written about the prognostic significance of lymph node metastases in cervical carcinoma. Lymph node has been shown to be the only significant independent predictor for overall survival. Overall 5-year survival of lymph node negative patients is 90% after

radical hysterectomy and pelvic node dissection. Patients with positive pelvic lymph nodes have a 5-year survival at 59.5% and are at risk for both pelvic and distant recurrences. Postoperative pelvic radiation in patients with nodal metastases has been the standard approach. It increases local control, but there are no controlled studies showing an impact on survival, due to inability of adjuvant pelvic irradiation to influence distant metastases [13]. The finding of enlarged and involved para-aortic lymph nodes (PALN) raises a number of questions regarding the best approach to management. Extended-field radiotherapy is the standard part of treatment achieving the long-term survival of 30e40% for stage Ib patients with positive PALN. The results of randomized trial have found a consistent benefit to concurrent chemo-radiation with cisplatin-based chemotherapy incorporated in extended field irradiation of women with positive PALN. With the combination of surgery and radiation therapy, however, the rates and types of complications increase resulting in greater subsequent morbidity than for either modality alone [14]. In order to reduce the morbidity caused by combined treatment, the options differ on the management of patients with positive lymph nodes detected at the time of radical hysterectomy. Frozen section of lower para-aortic nodes as the initial operative step and abandoning surgical approach if these lymph nodes are positive has been advocated by some authors. More recently, laparoscopic lymphadenectomy has been performed to identify lymph node metastases in order to avoid radical surgery. In contrast to the above approaches, some authors identify and resect all bulky, positive nodes, even when radiation therapy is planned as primary treatment, believing that although capable of sterilizing small lymph node metastases, radiotherapy is unlikely to be successful against bulky nodal disease. Surgical removal of bulky lymph nodes has proven safe with no excessive morbidity nor enhanced systemic spread of the disease [15].The survival of patients who had bulky nodes removed is significantly higher compared to those who did not (31% vs. 6%). Other factors such as large tumor volume, deep stromal invasion, unfavorable histological type of the tumor, lymphovascular invasion, as well as parametria or surgical margins close to the tumor or involved by the tumor have unfavorable prognostic effects in patients with stage Ib and IIa cervical cancer. Most studies indicate that adjuvant radiation therapy in these cases could improve prognosis even if lymph-node negative [16]. To identify the group of lymph node negative patients who are at high risk of recurrence, the clinico-pathologic risk of recurrence following radical hysterectomy was quantified by the GOG scoring system, which identifies the group of lymph node negative patients who are at high risk of recurrence, so that the others can be spared adjuvant therapy. To overcome the problem of morbidity without compromising survival, the small-field technique was designed which has shown a decrease of pelvic recurrence and significant improvement in 5-year disease-free period of patients with high-risk node-negative stage Ib cervical cancer. On the other hand, the evaluation of adverse prognostic factors before selecting the surgical approach has enabled less radical surgery in stages Ia2eIb1. Tailoring parametrectomy has been shown to be feasible and safe. Median follow up for 30 months had shown 5-year overall survival of 95% for node-negative patients at frozen section and submitted to modified radical hysterectomy, compared with 74% in patients who were found having nodal metastases intraoperative and submitted to classical radical hysterectomy. Stage Ib2 disease Treatment of bulky stage Ib tumors (primary tumors greater than 4 cm) is difficult and whatever primary treatment is chosen, the recurrence rate is higher when compared to stage Ib1 disease. While

some centers are performing primary surgery as for stage Ib1 disease followed by tailored postoperative radiation with or without chemotherapy, others are in favor of primary radiation therapy [17]. However, the rate of pelvic relapse is significantly higher among patients with stage Ib2 disease who had radiation alone (30%) compared to those who had surgery plus adjuvant radiation (20%). Neoadjuvant chemotherapy is possible alternative in treatment of bulky Ib2eIIa cervical cancer. The rationale for use of neoadjuvant chemotherapy is that apart from eradicating micro metastases, it would debulk the tumor and thus improve the outcome of subsequent surgery or radiotherapy. However, several randomized phase III studies have failed to demonstrate a survival benefit over conventional radiotherapy alone. Neoadjuvant chemotherapy followed by radical surgery has emerged as a possible alternative to conventional chemo-radiation, which may improve a survival in patients with stage Ib2 disease. The latter approach offers the advantages of surgery, and the neoadjuvant chemotherapy will keep to a minimum the risk of extra cervical spread of the tumor without combining surgery and radiotherapy.

Stage IIbeIVa cervical cancer

Radiotherapy has long played a major role in the treatment of locally advanced cervical cancer. Standard treatment for advanced cervical cancer is radical external-beam radiation therapy plus brachytherapy. It is important that appropriate dosing is administered to the central tumor and the pelvic side wall nodes. Modern approach to management of cervical cancer is changing the traditional role of radiotherapy as a single treatment modality of advanced cervical cancer. Nowadays, treatment of advanced cervical cancer will depend on the findings of locally advanced disease or bulky nodes on preoperative CT scan. There is strong evidence that chemotherapy should be incorporated into radiation treatment of patients with advanced cervical cancer. Today, concurrent cisplatin-based chemo-radiation is considered the treatment of choice in locally advanced, metastatic and recurrent cervical cancer. A significant benefit of concomitant chemo-radiotherapy over radiation therapy alone was shown for local and distant recurrence. The addition of chemotherapy has significantly improved cumulative rates of survival at 8 years (67% vs. 41%) [18]. By concurrent chemotherapy the delay in starting the radiation treatment and prolongation of overall treatment time is avoided. Hematological and gastrointestinal toxicities were significantly more frequent in the chemotherapy group, but acute side effects were generally of short duration and resolved with medical treatment. Late toxicity was rare and no increase of late complication rate was documented. Patients shown to have metastatic disease present on pre-treatment assessment have been found to have a poor prognosis. An investigational approach to perform a preirradiation therapy extra peritoneal surgical debulking of all macroscopic lymph nodes, followed by extended-field radiation therapy and brachytherapy, has shown encouraging results in improving prognosis of these patients. Survival for patients with completely resected bulky pelvic and common iliac nodes was comparable to that for patients with micrometastases. Recurrent cervical cancer the recurrence rate of cervical cancer is between 10% and 20% for FIGO stages IbeIIa and 50e70% in locally advanced cases (stages IIbeIVa). Both persistent and locally recurrent pelvic tumors are characterized by an advanced malignant progression and often exhibit an anatomically complex topography rendering curative treatment very difficult and rarely successful. Treatment of recurrent disease depends on previous treatment, site or extent of recurrence, disease-free interval and patient's performance status. According to the present consensus,

patients after surgical therapy should be treated with chemo-radiation and central pelvic relapses following primary or adjuvant radiation should undergo surgery. Radical hysterectomy may be adequate for small lesions, but most patients will need pelvic exenteration. Pelvic exenteration may be considered in selected cases of central pelvic recurrence after radiotherapy, when there is no evidence of distant metastases. In all cases of tumor involvement of pelvic wall, exenteration is abandoned. Pelvic exenteration, originally described by Brunschwig, consists of removal of the bladder, urethra, genital organs (including vulva/vagina), parts of the perineum and anus/ rectum. Later modifications were anatomically defined with respect to the caudal extension and with the regard to one pelvic organ to be left in situ (anterior or posterior exenteration), in order to maximize survivability and minimize anatomical distortion [19]. The 5-year survival after this type of operation has improved significantly over the time, reaching 30e60% for anterior and 20e40% for posterior exenteration. Although with curative intent, this extensive procedure results in comprehensive changes to the patients, requiring extensive psychosocial counseling to prepare them for the changes in body image and lifestyle. Novel surgical salvage therapy to a selected subset of patients with locally advanced and recurrent cervical carcinoma involving the pelvic wall, including pre-irradiated patients for whom treatment with long-term survival prospects has been beyond the scope of current therapeutic options, is performed in the form of laterally extended endopelvic resection (LLER). LLER includes the internal iliac vessel system, endopelvic part of the obturator internus muscle, coccygeus, iliococcygeus and pubococcygeus muscles into the exenteration specimen. Complication, disease-free and overall survival rates and postoperative quality of life scores of patients with mesenteric side wall disease are comparable to those with central disease treated with standard exenteration. The role of chemotherapy in patients with recurrent or metastatic disease is merely palliative. There is no standard, but when chemotherapy is indicated, cisplatin administered in dosage of 50e100 mg/m every 3 weeks seems to be a reasonable option [20]. Randomized trials of cisplatin versus various cisplatin-containing combinations have indicated that these combinations induce higher response rates, sometimes a small benefit in progression-free survival, but no major impact on overall survival and in all cases more toxicity. As an overall conclusion, it should be remembered that despite all screening modalities, the incidence of invasive cervical cancer remains stable or has even increased. The advances in treatment, particularly systemic therapies, have improved outcomes for cervical cancer but have not changed much the stage-related prognosis. Surgery and radiotherapy have already proven to be effective in treatment of invasive cervical cancer. Chemotherapy is now accepted as an integral component of the treatment, not only in palliative therapeutic situations, but also in patients presenting with principally curable disease.

Reference

1. Pecorelli S, Beller U, Heintz PA, Benedet LJ, Creasman WT, Peterson F. The 25th FIGO Annual Report on the Results of Treatment in Gynecologic Cancer. Int J Gynaecol Obstet 2003;83(Suppl. 1): 1–229.
2. Lai CH, Huang KG, See LC, et al. Restaging of recurrent cervical carcinoma with dual-phase [18F]fluoro-2-deoxy-D-glucose positron emission tomography. Cancer 2004;100:544–52.
3. Sonoda Y, Leblanc E, Querleu D, et al. Prospective evaluation of surgical staging of advanced cervical cancer via a laparoscopic extraperitoneal approach. Gynecol Oncol 2003;91:326–31.

4. Vergote I, Amant F, Berteloot P, Van Gramberen M. Laparoscopic lower para-aortic staging lymphadenectomy in stage Ib2 and III cervical cancer. Int J Gynecol Cancer 2002;12:22–6.
5. Lai CH, Huang KG, Hong JH, Lee CL, Chou HH, et Chang TC. Randomized trial of surgical staging (extraperitoneal or laparoscopic) versus clinical staging in locally advanced cervical cancer. Gynecol Oncol 2003;89:160–7.
6. Winter R. Conservative surgery for microinvasive carcinoma of the cervix. J Obstet Gynaecol Res 1998;24(6):433–6.
7. Nam J-H, Kim S-H, Kim J-H, Kim Y-T, Mok J-E. Nonradical treatment is as effective as radical surgery in the management of cervical cancer stage Ia1. Int J Gynecol Cancer 2002;12:480–4.
8. Lu KH, Burke TW. Early cervical cancer. Curr Treat Options Oncol 2000;1:147–55.
9. Hacker NF. Cervical cancer. In: Berek JS, Hacker NF, editors. Practical gynecological oncology. 3rd ed. Sydney: Lippincott Williams Wilkins; 2000. p. 345–405.
10. Creasman WT, Zaino RJ, Major FJ, DiSaia PJ, Hatch KD, Homesley HP. Early invasive carcinoma of the cervix (3 to 5 mm invasion): risk factors and prognosis. A Gynecologic Oncology Group study. Am J Obstet Gynecol 1998;178(1 Pt 1):62–5.
11. Landoni F, Maneo A, Colombo A, et al. Randomized study of radical surgery versus radiotherapy for stage Ib-IIa cervical cancer. Lancet 1997;350:535–40. 836 V. Kesic / EJSO 32 (2006) 832e837
12. Landoni F, Maneo A, Cormio G, et al. Class II versus Class III radical hysterectomy in stage Ib-IIa cervical cancer: a prospective randomized study. Gynecol Oncol 2001;80:3–12.
13. Selman TJ, Luesley DM, Murphy DJ, Mann CH. Is radical hysterectomy for early stage cervical cancer an outdated operation? Br J Gynaecol 2005;112:363.
14. Hoffman MS. Extent of radical hysterectomy: evolving emphasis. Gynecol Oncol 2004;94:1–9.
15. Steed H, Rosen B, Murphy J, Laframboise S, De Petrillo D, Covens A. A comparison of laparoscopic-assisted radical vaginal hysterectomy and radical abdominal hysterectomy in the treatment of cervical cancer. Gynecol Oncol 2004;93:588–93.
16. Plante M, Renaud MC, Francois H, Roy M. Vaginal radical trachelectomy: an oncologically safe fertility-preserving surgery. An updated series of 72 cases and review of the literature. Gynecol Oncol 2004; 94:614–23.
17. Angioli R, Estape R, Salom E, et al. Radical hysterectomy for cervical cancer: hysterectomy before pelvic lymphadenectomy or vice versa? Int J Gynecol Cancer 1999;9:307–11.
18. Sedlis A, Bundy BN, Rotman MZ. A randomized trial of pelvic radiation versus no further therapy in selected patients with stage Ib cancer of the cervix after radical hysterectomy and pelvic lymphadenectomy. Gynecol Oncol 1999;73:177–83.
19. Torne A, Puig-Tintore LM. The use of sentinel lymph nodes in gynaecological malignancies. Curr Opin Obstet Gynecol 2004;16: 57–64.
20. Angioli R, Palaia I, Cipriani C, et al. Role of sentinel lymph node biopsy procedure in cervical cancer: a critical point of view. Gynecol Oncol 2005;96:504–9

How to citation this article: Dr Mahhum Razzaq, Dr Syeda Fouzia Basharat, Dr Badshah Khan, "Cervical cancer and its management", ijmacr- January – February - 2020, Vol – 3, Issue -1, P. No. 24 - 31