The inherent value of staging in the management of gynaecological cancers

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Introduction

Staging can be defined as assessing the anatomical extent of the tumour. Stages are an artificial subdivision of the ongoing disease process based on the applicable anatomical landmarks.[1] The main goals in treating patients with cancer are to improve cure rates, increase survival time and enhance quality of life.[2] The most crucial factor pertaining to cancer outcome is the disease extent at the time of presentation.[3] The stage of the disease is used to indicate this extent. This is essential to optimally manage the cancer patient.[4]

Presently there are three groups involved in gynaecological cancer staging, which include the International Federation of Gynaecology and Obstetrics (FIGO), the American Joint Commission on Cancer (AJCC) and the International Union against Cancer (UICC). Each of these organizations has developed their own staging system. Because most cancers are now staged surgically instead of clinically, pathologists also play a vital role, not only in determining diagnosis but also in predicting prognosis. Most surgical pathology reports are based on the College of American Pathologists' 2009 staging guidelines.[5]

Gynaecological malignancies are generally divided into four stages: Stage 1 – extend of tumour limited to organ of origin; Stage 2 – local extension past the original primary organ of origin; Stage 3 – more extensive infiltration of neighbouring organs or structures; Stage 4 – Metastatic disease distant from primary site of origin.[6] The main objectives of the staging systems include the mechanism to facilitate comparing patients between different centres and to provide a prognostic factor in predicting the outcome of disease.[6,7] Subsequent to constant changes in diagnostic medicine and new publications on prognostic information, the staging systems for cancer need to continuously evolve.[7]

The history of staging gynaecological cancers

Staging systems for gynaecological cancers have been a tradition of gynaecologists with the first staging system for cancer of the cervix published in 1920.[4] In 1923 the German Gynaecological Society was the first institution to stage cervical cancer by differentiating between operable and inoperable tumours.[8]

The League of Nations Classifition for Cervical Cancer was published in 1929 after the Radiological Sub-Commission assigned a group of experts to examine the likelihood of producing uniform statistical information on the outcome of radio-therapeutic methods used in the treatment of cervical cancer. These experts, Prof G. Heyman (Radiumhemmet, Stockholm, Sweden), Dr A. Lacassagne (Radium Institute of the University of Paris, France) and Prof F. Voltz (Munich, Germany) recommended that different institutions need to report statistical information in a consistent fashion in order to analyse and interpret findings. Clinical examination and anatomical extent of the disease formed the basis of an international system classifying patients with cervical cancer.[6,8]

Due to a lack of success of the 1929 classification an Annual Report on the outcome on radiotherapy treatment for cervical cancer after five years of observations, was recommended at the Health Organization conference in 1934.[6,8] Under guidance of Heyman (see above) the first Annual report was published in 1937 and contained guidelines on operability. The second and third editions were published before World War II in 1938 and 1939 and the fourth edition published in 1941.[8] The second Annual Report contained the first recorded modifications to the staging system, including wording and definition changes.[6] In 1938, Heyman and Strandquist also published a pocket-sized atlas on cervical cancer staging with English, French and German text and contained definitions and diagrams on staging.[6,9]

A new classification called ''The International Classification of the Stages of Carcinoma of the Uterine Cervix'' was agreed upon at the International Gynaecological Congress and Fourth American Congress of Obstetrics and Gynaecology, held in New York in 1950. Results on the treatment of cancer of the uterine copus were published in the 8th volume (1953) of the Annual Report. Subsequently, similar treatment outcomes were published for vaginal cancer (Volume 13, 1964), ovarian cancer (Volume 15, 1973) and vulvar cancer (Volume 17, 1979).[6]

The International Federation of Gynaecology and Obstetrics (FIGO) assumed guardianship of the Annual Report in 1958. Volume 12, published in 1961, was the first issue under its backing. Publication of the report relied on

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financial support from various cancer institutes and organisations resulting in irregular intervals of Annual Report publications. The ''Annual Report on the Results of Treatment in Gynaecological Cancer'' has been published once every three years since 1973. The reports correspond with the FIGO World Congress under the auspices of the FIGO Committee on Gynaecologic Oncology.[6] The Annual Report was recently retitled the ''FIGO Cancer Report ''with the latest edition launched in Rome 2012.[10] The report focusses on updating staging and management guidelines and different gynaecological cancers.[10]

The most recent changes made to the FIGO staging system was published in 2009 and included changes to staging of cancer of the vulva, cervix, endometrium and sarcomas.[7]

Other organizations involved in the staging of gynaecological malignancies include the International Union Against Cancer (UICC) and the American Joint Committee on Cancer (AJCC). AJCC was renamed in 1980 and before then was known as the American Joint Committee for Cancer Staging.[6,11] The AJCC has been involved in the development of staging systems for cancer since 1959 and accepted the FIGO staging systems in 1976.[6] In 1966, a committee, appointed by UICC, introduced a well known tumour-node-metastasis (TNM) staging system to classify cervical cancer.[6] The TNM system is a double staging system comprising of a pre-treatment (clinical) classification and a post-surgical (histo-pathological) classification, resulting in clinical and pathological staging of each patient. In the FIGO classification, with the exception of cervical cancer and gestational trophoblastic neoplasia, a single surgical or pathological staging is performed.[11,12]

Despite certain past differences, the UICC, AJCC and FIGO have changed their gynaecological cancer staging systems so that all three systems at present are essentially the same and annual meetings are held to guarantee comparability of the staging systems.[6]

Recent developments in the staging of gynaecological malignancies

Cervical cancer

Amongst South African woman, cancer of the cervix remains the most common malignancy representing about 23% of all reported cancers.[13] Cervical cancer is staged clinically and not surgically due to epidemiological reasons.[12] Although surgical staging might be more quantitative and accurate than clinical staging, 80% of cervical cancers are diagnosed in developing countries with limited recourses, making clinical staging more applicable.[7] The FIGO staging system is used more widely in comparison to the TNM system.[14] The ''T'' stage of the clinical TNM (cTNM) staging system is similar to the FIGO stages except for carcinoma in situ which has been removed from the FIGO classification in 2009.[7,14] The pathological staging system (pTNM) is reserved for patients treated surgically or after incidental findings of cervical cancer following a hysterectomy.[14]

Since 1950, the systems used to stage cervical cancer have been revised eight times with the latest changes made by FIGO in 2009. The main controversies arising from these changes include: the same criteria are now used to stage both microinvasive adenocarcinoma and squamous cell carcinoma of the cervix; and examination of patients under anaesthesia, utilizing cystoscopy, sigmoidoscopy and IVP are not compulsory. Although lymphovascular space involvement (LVSI) was excluded from the staging system, this finding needs to be reported together with other surgical-pathological findings.[7] LVSI is also not included in the AJCC/UICC staging system despite literature indicating that it is a negative prognostic indicator.[5] Although the FIGO staging is not dependent on the use of imaging studies, a meta-analysis found MRI superior to CT scan for evaluating the involvement of the parametria.[15] FIGO requested that recorded findings of tumour size and parametrial involvement on MRI/CT scanning be sent through for data entry for the Annual Report.[7]

Distinguishing between FIGO stage IB1 (tumour < 4cm) and FIGO stage IB2 (tumour > 4cm) is important. Although this could be clinically challenging there is a considerable difference between the sub-stages with regards to 5-year survival (89.1% versus 75.7%).[16] The FIGO staging system does not include reporting of the cervical tumour extending into the corpus of the uterus. There appears to be an increase chance of nodal metastasis if the uterine corpus is involved and therefore potentially worsen the outcome for all stages.[5] Due to a lack of a grading system used for squamous cell carcinoma, it is not compulsory to report it, however, some literature support grading of adenocarcinoma of the cervix due to the prognostic value.[5]

Endometrial cancer

Endometrial cancer is one of the most prevalent gynaecological cancers in the developed world with the incidence expected to rise due to an aging population and the obesity epidemic.[17] The majority of patients present with post-menopausal bleeding and the 5-year relative survival for stage1 disease is as high as 97%.[17]

Since FIGO changed the staging of endometrial cancer from clinical to surgical in 1988, surgical evaluation and staging have been the mainstay of treatment.[17] The standard surgical procedures performed for a patient with endometrial cancer include a total extrafascial hysterectomy (vaginal, laparoscopic or robotic-assisted approaches also possible), bilateral salpingo-oophorectomy with pelvic and para-aortic lymph node dissection together with biopsies of suspicious areas, further cytoreduction if applicable and omentectomy (mostly patients with clear cell or serous histology).[12]

The main changes made in 2009 to the 1989 surgical staging system were as follows: in women without myometrial involvement and those with no more than 50% invasion, the survival was similar if no lymph node metastases were present; these groups were therefore combined.[7] *Before, FIGO stage IIA indicated cervical infiltration with only endocervical glands involved, but because of a lack of prognostic importance it was removed from the FIGO staging system. Stage II is currently defined as invasion of the cervical stroma by the tumour. There is clear evidence that cervical stromal involvement influences prognosis of the patient.*[5] Woman with parametrial improvement are staged as IIIB. Collecting peritoneal washings for cytology as part of the staging criteria was removed. The reasons for differentiating between positive pelvic nodes and para-aortic nodes are because of survival difference and to assess prognosis better.[7]

Determining how deep the myometrium is infiltrated is subjective and the junction between the endometrium and myometrium is frequently irregular. Difficulty may arise to evaluate true invasion when adenomyosis or metaplasia of the endometrial stroma is present. The change, in FIGO stage 1 classification, to myometrial infiltration less than 50% (IA) and 50% or more (IB) may help to decrease confusion.[5]

Lewin et al.[18] compared the old and new FIGO staging system for endometrial cancer and concluded that by reducing sub stages with stage I and distinguishing between pelvic and para-aortic lymph node involvement clarified prognostic factors and guide treatment concepts. *Another study*[19] *compared the prognostic value between the 1988 and 2009 FIGO staging system and concluded that the 1988 system was still superior to the new classification system. The reason for this conclusion was because the new staging system removed the old IA which has the best overall survival. Findings from both studies are likely to be true because of the difference in study groups and patient data between the two studies.*[20]

Uterine Sarcomas

Before the changes made in 2009, uterine sarcomas were staged the same as endometrial carcinoma.[5,7] Because this staging system was poorly indicative of survival, a new staging system was proposed based on the other soft tissue sarcomas.[7] Continued data collection on these cancers is needed to improve this staging system, which, at best, is less than ideal.

Carcinosarcomas (previously known as MMMT) should be staged using the same staging system as for cancer of the uterine corpus.[7] *Uterine sarcomas consist of leiomyosarcomas (LMS), endometrial stromal sarcomas (ESS) and adenosarcomas.*[7] *FIGO has introduced two separate staging systems for uterine sarcomas, one for staging of LMS and one for ESS and adenosarcomas. Because these sarcomas behave differently, staging of LMS focuses on the tumour size whereas staging of the other two sarcomas focus on myometrial invasion. Comparing ESS to LMS, ESS is generally not as aggressive as LMS and has a better prognosis.*[5] *The AJCC also have two staging categories for uterine sarcomas but adenosarcomas are separate from LMS and ESS.*[5]

Predicting the overall survival in patients with uterine leiomyosarcomas by comparing the old to the new FIGO staging system, Lim and colleagues[21] concluded that neither of the staging systems were ideal in dividing patients in significant stages predictive of overall survival and that other options should be explored.

Ovarian cancer

The last modified FIGO staging system was published in 1988. *FIGO aims to update the staging system for ovarian cancer in the near future.*[12] The objectives of ovarian cancer staging are as follows: make the correct diagnosis; determine the extent of the disease; assess the prognosis; choose the (neo-) adjuvant treatment most suitable for the patient.[22,23]

The primary treatment for woman with ovarian cancer remains surgery. A large number of women, especially in early stage disease, still receive sub-optimal treatment and surgical staging. Studies have shown a survival benefit when women with ovarian cancer are operated by gynaecologic oncologists.[24]

The majority of patients present with advanced disease where the cancer has spread throughout the peritoneal cavity and/or regional and para-aortic lymph nodes.[22,25] Initial surgical staging and treatment potentially followed by systemic platinum-based chemotherapy is indicated for all ovarian cancer patients except: if an extra ovarian tumour has not been excluded in a woman with a complex ovarian cyst; for poor surgical candidates secondary to comorbidities; or where there is inability to perform optimal cytoreduction due to tumour bulk.[26]

Factors that inversely correlate with surgical management include disease stage, tumour grade differentiation and the volume of disease left behind after cytoreductive surgery. This again highlights the need for a surgeon to be experienced in this type of surgery.[22,26]

Vulvar cancer

Vulvar cancers form around 5% of gynaecological cancers and following uterine, ovarian and cervical cancer, it is thus the fourth most common cancer affecting the female genital tract.[23] Before 1988, vulvar cancer was staged clinically.[7] The main prognostic indicator predicting overall survival is the presence or absence of inguinofemoral lymph node metastasis. Around 20% of patients with normal inguinal lymph nodes on clinical examination will have metastasis and around 30% with enlarged lymph nodes will have negative nodes on histological examination.[27] Because of the poor ability to predict positive lymph nodes on clinical examination, a surgical staging system was adopted.[7]

Major changes were made in 2009 to the previous FIGO staging system after a global debate.[12] In order to better reflect prognosis in certain groups, prognostic factors including lesion size and extent of nodal involvement were included in the new staging system.[7,12]

A few significant changes were made and described below. Lesions with less than 1mm invasion are now staged as IA. In the event of negative lymph nodes, the size of the lesion does not seem to influence survival. Because of the prognostic value, the number and size of lymph node metastasis have been divided.[7] *In comparison to the TNM staging system, the FIGO staging system combines the T and N categories. This may cause confusion and unreliable reporting. FIGO stages IA, IB, II and IVA directly compare to pTNM categories T1, T2, T3 and T4 correspondingly, and FIGO stage III with category pN.*[5]

Tan et al.[28] compared the 1988 FIGO vulva staging system to the 2009 staging system and showed a survival difference between stage I and II in the new system for relapse-free and disease-specific survival, but not for overall survival. Different survival periods were observed when separating stage III into three substages. This validated the effect of the number and extend of nodal involvement on survival even further.

The value of staging gynaecological cancers

The prognosis of a patient diagnosed with cancer depends on a variety of factors including the tumour, the patient and the environment.[29] Any patient where a malignancy is suspected requires staging by their clinician. The gynaecological oncologist, trained appropriately, is in the best position to stage the patient based on clinical findings, imaging studies and biochemical markers, as applicable.[30]

A staging system should have three aspects. Firstly it should be accurate and evidence-based, which implies adapting to significant scientific changes. Secondly it should be trustworthy and guarantee that identical cases are consistently allocated to the same stage group. Lastly it should be practical and easy to use, without requiring special diagnostic investigations or exceptional expertise.[6]

The main aim of staging is to classify the extent of the malignancy, providing an overall picture of the impact of the tumour on the patient.[4,30] In certain cancers, like ovarian cancer for example, the clinical management of the patient relies on the correct surgical staging and it is essential to make the correct diagnosis and determining the magnitude of the disease.[22] After the correct diagnosis is made and the extent of the disease is determined, staging of the cancer assist the clinician in formulating the prognosis of the patient.[4,30]

One of the major objectives of staging agreed upon internationally is to indicate and establish the prognosis of the individual, which is generally expressed as the 5-year survival.[1,3,4,22,30,31] Cancer staging is also structured in such a way to act as a prognostic factor in predicting the outcome of the disease and giving order to the complicated behaviour of the malignancy.[6]

Staging assists the clinician and the patient in making an informed decision regarding the treatment options available, whether curative or palliative.[30] The stage of the disease plays an important role in making this critical decision to plan treatment, which could include surgery, radiotherapy, chemotherapy, hormonal therapy, systemic agents and/or image guided local therapy.[3,9,30] Different combinations can be used for curative or palliative treatment.[30] Apart from guiding the clinician to select the best treatment option, staging also provides a method of evaluating the effect of the therapy or treatment.[4] Staging helps to evaluate outcome, compare different modalities of treatment and to decide on the ideal therapy.[1,22] This objective was one of the main reasons for the initial development of a staging system for cervical cancer, which compared the results of surgery to radiotherapy.[8]

One of the fundamental objectives of staging gynaecological cancers is to facilitate communication between different treatment centres and oncology units.[1,9] Staging provides a common language for information exchange with regards to results and treatment, as well as clinical experience without ambiguity.[1,4,9,31] This enables and promotes standardization of communication between different centres caring and managing cancer patients.[7] Cancer staging systems contribute to the continuous investigation into the understanding of cancers.[9] Staging gynaecological cancers facilitate stratification of patients into subgroups and identifies ideal candidates for clinical studies.[21] Apart from identifying and selecting appropriate candidates for clinical trials, staging serves as a method of evaluating results and treatment outcomes of such trials and therefore help with knowledge creation.[4]

Indirectly, staging plays a vital role in improving the quality of care given to the cancer patient and contribute to individual patient care.[3,8] Staging enhances good clinical practice in oncology units and facilities treating oncology patients and assures the quality of clinical classification systems.[3,11]

The role of the gynaecologic oncologist

The American Board of Obstetrics and Gynaecology in 1969 was the first to recognise the need for a sub-speciality in gynaecologic oncology. Later, in 1982, the Royal College of Obstetrics and Gynaecology (RCOG) followed with formulating guidelines and prerequisites for training in the sub-speciality.[32] In South Africa, training of sub-specialists in gynaecological oncology is still a fairly recent development, with the first candidate fulfilling the criteria in 2008.[33] The requirements for the College of Obstetricians and Gynaecologists of South Africa's sub-speciality certificate in gynaecologic oncology specify that a training period of at least 24 months should be spend in an accredited unit, together with completion of a surgery logbook and research project and passing the written and oral exit examination.[33]

In many countries, gynaecologic oncology is not yet recognised as a sub-speciality.[32] Medicine is becoming more sub-specialised because of the progress made in recent decades. Patient outcomes are better when treated by multidisciplinary teams. Patients with gynaecological cancers often require multidiscipline treatment with surgery and/or chemotherapy and/or radiotherapy. Evidence support better outcome if patients with gynaecological cancers are treated by a gynaecologic oncology sub-specialist.[32,34] These findings were confirmed in a recent Cochrane review which showed that there is also a better outcome for patients with gynaecological cancers when they are treated in a specialist centre.[35] Possible reasons why the prognosis improve when patients are treated by a gynaecologic oncologist might be because the sub-specialist is better equipped to deal with challenging surgery. Apart from developing surgical skills to meet technical challenges including management of complications, training programs in gynaecological oncology give the sub-specialist the knowledge and understanding of where surgery fits into the multidisciplinary approach.[34] Sub-speciality training further equips the gynaecologic oncologist with the necessary skills and proficiency in medical and radiation oncology, palliative care, cancer genetics and cancer research.[32]

Primary debulking surgery directly compares to the overall survival of gynaecological cancer patients, especially for ovarian cancer as well as cervical and vulva cancer.[33] A number of studies have shown that gynaecological oncologists are more likely to optimally debulk patients with ovarian cancer than general gynaecologists.[34] The same positive effect can be seen in patients with vulvar cancer. Optimal surgery has a high impact on survival and when surgery is performed by a sub-specialist it leads to better lymphadenectomy rates and improved disease survival.[34] Due to a number of factors, including better healthcare, people live for longer and the proportion of older people are getting bigger. Gynaecological cancers and other diseases frequently seen among elderly patients are also expected to rise in years to come. The need to train more gynaecologic oncologists might need to increase in order to fulfil the needs of a growing population and to insure good quality care and optimal patient outcomes.[36]

Conclusion

Gynaecologists have been involved in developing and revising cancer staging systems for almost a century now. Cancer staging adds value to the holistic management of

cancer patients and enables clinicians to communicate clinical expertise and improve treatment methods.[4] Staging may also add therapeutic value, for example by performing a lymphadenectomy for the purpose of staging may remove metastatic lymph nodes that would otherwise not be sterilized by radiotherapy.

A good quality staging system should be current, consistent and easy to apply.[6] Staging is a marker of anatomical extent and one of the prognostic indicators. By including too many prognostic factors in a staging system, it could render it impractical1. It is imperative that women with gynaecological malignancies undergo complete staging, preferable by a gynaecologic oncologist, and that patients receive evidence-based care to improve quality of life and overall survival.

References

1. *Bösze P. Prognostic factors and staging: the role of molecular markers. CME J Gynecol Oncol. 2001;6:232-4.*
2. *Penson RT, Wenzel LB, Vergote I, Cella D. Quality of life considerations in gynecologic cancer. Int J Gynaecol Obstet. 2006;95:S247-57.*
3. *Benedet JL. Introduction. CME J Gynecol Oncol. 2001;6:229.*
4. *Benedet JL, Pecorelli S. Why cancer staging? Int J Gynecol Obstet. 2006;95(Suppl 1):S3.*
5. *Cole L, Stoler MH. Issues and inconsistencies in the revised gynecologic staging systems. Semin Diagn Pathol. 2012;29(3):167-73.*
6. *Odicino F, Pecorelli S, Zigliani L, Creasman WT. History of the FIGO cancer staging system. Int J Gynaecol Obstet. 2008;101(2):205-10.*
7. *Mutch DG. The new FIGO staging system for cancers of the vulva, cervix, endometrium and sarcomas. Gynec Oncol. 2009;115:325-28.*
8. *Di Paola GR. History of and rational for staging gynaecological cancers. CME J Gynecol Oncol. 2001;6:230-1.*
9. *Benedet JL. Conclusions. CME J Gynecol Oncol. 2001;6:270-3.*
10. *International Federation of Gynecology and Obstetrics [homepage on the Internet]. No date [cited 2013 March 20]. Available from: http://www.figo.org.*
11. *Hermanek P. Why TNM system for staging of gynaecologic tumours? CME J Gynecol Oncol. 2001;6:267-9.*
12. *Pecorelli S. Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. Int J Gynaecol Obstet. 2009;105:103-4.*
13. *South African Human Papillomavirus Advisory Board. Prophylactic human papillomavirus vaccination against cervical cancer: a summarised resource for clinicians. South Afr J Gynaecol Oncol. 2011;3(1):39-42.*
14. *Frumovitz M. Invasive cervical cancer: Staging and evaluation of lymph nodes. In: UpToDate, Basow, DS (Ed). UpToDate, Waltham, MA, 2013.*
15. *Bipat S, Glas AS, van der Velden J, Zwinderman AH, Bossuyt PM, Stoker J. Computed tomography and magnetic resonance imaging in staging of uterine cervical carcinoma: a systematic review. Gynecol Oncol. 2003;91(1):59-66.*
16. *Quinn MA, Benedet JL, Odicino F, Maisonneuve P, Beller U, Creasman WT, et al. Carcinoma of the cervix uteri. FIGO 26th Annual Report on the Results of Treatment in Gynecological Cancer. Int J Gynaecol Obstet. 2006;95(1):S43-103.*
17. *Frederick PJ, Straughn JM Jr. The role of comprehensive surgical staging in patients with endometrial cancer. Cancer Control. 2009;16(1):23-9.*
18. *Lewin S, Herzog T, Barrena Medel N, Deutsch I, Sun X, Burke W, et al. Comparative performance of the new versus old FIGO staging system for endometrial cancer. Gynecol Oncol. 2010;116:S6-7.*
19. *Abu-Rustum NR, Zhou Q, Iasonos A, Alektiar KM, Leitao MM Jr, Chi DS, et al. The revised 2009 FIGO staging system for endometrial cancer: should the 1988 FIGO stages IA and IB be altered? Int J Gynecol Cancer. 2011;21(3):511-6.*
20. *Gebhart F. FIGO Revision Sparks Endometrial Cancer Controversy. DocGuide.com [Internet]. 2010 March 19 [cited 2013 March 11]. Available from: www.docguide.com/figo-revision-sparks-endometrial-cancer-controversy*
21. *Lim D, Wang WL, Lee CH, Dodge T, Gilks B, Oliva E. Old versus new FIGO staging systems in predicting overall survival in patients with uterine leiomyosarcoma: a study of 86 cases. Gynecol Oncol. 2013;128(2):322-6.*
22. *Van Trappen PO, Jacobs IJ. Controversies and new trends in staging ovarian and Fallopian tube carcinoma. CME J Gynecol Oncol. 2001;6:260-6.*
23. *Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. A Cancer J Clin. 2013;63(1):11-30.*
24. *Goff BA, Matthews BJ, Larson EH, Andrilla CH, Wynn M, Lishner DM, et al. Predictors of comprehensive surgical treatment in patients with ovarian cancer. Cancer. 2007;109(10):2031-42.*
25. *Cannistra, SA. Cancer of the ovary. N Engl J Med. 2004;351:2519-29.*
26. *Mann WJ Jr, Chalas E, Valea FA. Epithelial ovarian cancer: Initial surgical management. In: UpToDate, Basow, DS (Ed). UpToDate, Waltham, MA, 2013.*
27. *Gonzalez Bosquet J, Magrina JF, Magtibay PM, Gaffey TA, Cha SS, Jones MB, et al. Patterns of inguinal groin metastases in squamous cell carcinoma of the vulva. Gynecol Oncol. 2007;105(3):742-6.*
28. *Tan J, Chetty N, Kondalsamy-Chennakesavan S, Crandon A, Garrett A, Land R, et al. Validation of the FIGO 2009 staging system for carcinoma of the vulva. Int J Gynecol Cancer. 2012;22(3):498-502.*
29. *Greene FL. A cancer staging perspective: the value of anatomical staging. J Surg Oncol. 2007;95(1):6-7.*
30. *Smith BA. The importance of staging in oncology. AORTIC [Internet]. No date [cited 2013 March 11]. Available from: www.aortic-africa.org/images/.../The_Importance_of_Staging.doc*
31. *Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A (Eds.). AJCC Cancer Staging Handbook. 7th ed. Springer. 2010. www.suttermedicalfoundation.org/remoteaccess/ajcc/files/01%20Purpose%20and%20Principles%20of%20Cancer%20Staging.pdf (Accessed 2013 March 11).*
32. *Manchanda R, Godfrey M, Wong-Taylor LA, Halaska MJ, Burnell M, Grabowski JP, et al. The need for accredited training in gynaecological oncology: a report from the European Network of Young Gynaecological Oncologists (ENYGO). Ann Oncol. 2013;24(4):944-52.*
33. *Snyman LC. Meeting future requirements in gynaecological oncology subspecialty training. South Afr J Gynaecol Oncol. 2012;4(2):48-9.*
34. *Morrison J. Improving outcomes in gynaecological cancer: the benefits of subspecialisation [editorial]. Cochrane Database Syst Rev. 2012;4:ED000040. http://www.thecochranelibrary.com/details/editorial/1501421/Improving- outcomes-in-gynaecological-cancer-the-benefits-of-subspecialisation.html.*
35. *Woo YL, Kyrgiou M, Bryant A, Everett T, Dickinson HO. Centralisation of services for gynaecological cancer. Cochrane Database Syst Rev. 2012;3:CD007945. DOI: 10.1002/14651858.CD007945.pub2.*
36. *Wallace AH, Havrilesky LJ, Valea FA, Barnett JC, Berchuck A, Myers ER. Projecting the need for gynecologic oncologists for the next 40 years. Obstet Gynecol. 2010;116(6):1366-72.*