showed amplification or deletions in many but not all lymph node samples. Surprisingly, one IMS EpCam positive sample that was negative for all other markers, and also by IHC, showed distinct amplifications and deletions proving the malignant nature of the cells. Together the results suggest the existence of heterogenic micrometastatic tumor cell populations with a complex gene and protein expression pattern, including differences between cells obtained from different. The data raises questions on the accuracy of the methods used for identification of micrometastatic tumour cells, and also suggest the presence of tumour cells in the two tissue types without the capacity to give rise to relapse.

Special Session (Wed, 23 Sep, 17:00−18:00)
Case-based: leadership and management

295 INVITED

Measuring quality at a local level

D. Doran[1]. [1]*Lawrence Bloomberg Faculty of Nursing -, Nursing, Toronto, Canada*

Background: At no time in the history of health care has the growth in knowledge and technologies been so profound. However despite rapid advances in science and technology, the health care system has struggled in its ability to provide consistently high-quality care to all who require health care services.
Purpose: This paper explores how we can utilize quality measurement at the local level to transform care at the bedside. It embraces the vision set out in the United Kingdom National Health System Next Stage Review report that quality improvement should be the organising principle of everything we do. The local level refers to the unit of care such as a hospital unit, team, patient care programme, or community centre.
Methodology: The paper draws on the health care quality literature and the results of three studies to discuss approaches to local quality measurement and strategies for the continuous improvement of patient care. The three studies utilized quasi-experimental research designs to evaluate the feasibility and impact of providing clinicians with access to real-time feedback about patient outcomes data along with access to research evidence to support the continuous improvement of patient care.
Results: High quality care is conceptualized as having three dimensions: (1) ensuring that care is safe, (2) effective, and (3) provides patients with the most positive experience possible. All staff must be active participants and leaders in transforming the quality of care. Providing clinicians with access to real-time feedback about quality indicators along with access to research evidence promotes reflective practice and encourages the uptake of evidence-based practice guidelines. However in order to promote effective utilization of local quality measurements it is important to create a favourable context for evidence-based practice.
Conclusion: It is recommended that we provide clinicians with access to quality measurement indicator data in real time along with access to information resources to support the continuous improvement of patient-centred care.

296 INVITED

Encouraging innovation in clinical practice

M. Krishnasamy[1]. [1]*Peter MacCallum Cancer Centre, Department of Nursing and Supportive Care Research, Melbourne Victoria, Australia*

This paper will present an overview of essential components of innovative health care. Consideration will be given to the characteristics of inspiring health care teams and to the features of novel systems of health care. The audience will be invited to think about how these characteristics and philosophies can be assimilated into clinical practice in order to optimise patient-reported outcomes. The benefits of innovative clinical practice as a means of practice advancement for the individual practitioner will also be explored. Two practice models currently in place at the Peter MacCallum Cancer Centre in Melbourne, Australia, will be presented as pragmatic examples of how innovations in practice can be achieved through utilising the skills and expertise of the multidisciplinary team.

Thursday 24 September 2009

Scientific Symposium (Thu, 24 Sep, 09:00−11:00)
Optimising therapy of young women with early breast cancer

297 INVITED

Epidemiology and prognosis of breast cancer in very young population

P. Tai[1]. [1]*University of Saskatchewan, Department of Oncology Allan Blair Cancer Center, Regina, Canada*

Background: Very young women aged less than 35 with breast cancer are regarded as high-risk patients in the literature. This study examines the relationship between age and mortality for breast cancer patients. This may have important prognostic and therapeutic implications.
Material and Methods: Data of 83,804 pT1−2M0 patients from 9 registries of the Surveillance, Epidemiology, and End Results Program (SEER) of the United States were used. This study employed proportional hazards to model mortality in women with T1−2 breast cancers. The martingale residuals of the model were used to examine the effect of age on mortality. This procedure was applied to node-negative (N0) and node-positive (N+) patients. All causes mortality and breast cancer specific mortality were evaluated. The analysis was applied first to node-negative cases ("training set") in order to find an expression of the functional form which relates age to mortality. The functional form obtained from node-negative cases was then applied to node-positive cases ("validation set"). In addition to the validation with the same transformation which was obtained for node-negative patients, a further iterative search was performed in order to improve the fit for node-positive patients. We also studied the German Breast Cancer Study Group GBSG-2 dataset, a separate prospective database of 686 node-positive patients.
Results: The relationship between age and mortality is biphasic. This results in a U-shaped curve. For both N0 and N+ patients among the T1−2 group, the analysis suggested two age components. One component is linear and corresponds to a natural increase of mortality with each year of age. The other component is quasi-quadratic and is centered around age 50. This component contributes to an increased risk of mortality as age departs from 50. It suggests a hormonally related process: the farther from menopause in either direction, the more prognosis is adversely influenced by the quasi-quadratic component. Younger patients experience the same relative mortality risk from all causes as do older patients. A 30-year old patient has a risk of death almost equal to a 60-year old patient.
There is a complex relationship between hormone receptor status and other prognostic factors, like age. Very young patients tend to develop hormone receptor negative tumors. They have poorer survival explained in part by presentation with later stage disease and more aggressive tumors, in terms of grade and receptor status. They are more likely treated with conservative surgery than older patients.
The German Breast Cancer Study Group GBSG-2 dataset showed similar findings, confirming the poor prognosis of very young breast cancer patients.
Conclusions: The present analysis confirms the findings of many epidemiological and clinical trials that the relationship between age and mortality is biphasic. Compared with older patients, young women experience an abnormally high risk of death. These facts are important in the discussion of options for adjuvant treatment with breast cancer patients.

298 INVITED

Adjuvant therapy of very young women with early breast cancer

O. Pagani[1]. [1]*Oncology Institute of Southern Switzerland, Division of Research, Bellinzona, Switzerland*

Approximately 7% of women with breast cancer (BC) are diagnosed before the age of 40 years, and this disease accounts for more than 40% of all cancer in women in this age group.
Women under 35 or 40 with primary BC have historically been considered at poor prognosis, independently of other factors, but in some recent studies age is not independent in multivariate analyses, which include gene signatures.
Treatment choices on the contrary are dependent on BC biology (receptor status) as well as patient factors (ovarian function and desire for future fertility).
Trial results of adjuvant treatments for premenopausal women largely reflect outcomes for patients in their 40 s. Thus, findings from studies that consider these average results may not be directly applicable to younger patients.

Today, positive estrogen receptors (ER+) identify women who require endocrine therapy, and HER2/neu positivity those who require trastuzumab and also benefit most from anthracyclines.
Tamoxifen (T) plus ovarian ablation or suppression (OA) or T alone are currently accepted as standard adjuvant endocrine therapies (ET) in young women with ER+ early BC.
The additional benefit of chemotherapy (CT) for premenopausal patients with endocrine-responsive BC who receive combined ET with OA and T (or an aromatase inhibitor) remains an open question.
In the future more sophisticated molecular factors may identify those patients who require ET alone, CT alone, newer biologic therapies, or combinations of these approaches.
CT, ET, and local therapies have the potential to significantly impact both the physiologic health-including future fertility, premature menopause, and bone health-and the psychological health of young women as they face a diagnosis of BC. Better tools and strategies to manage these long-term consequences of the disease and related treatments need to be implemented and monitored and health care professional should systematically address in advance these issues when dealing with young patients.
As many unanswered questions remain, it is also important to increase the accrual of young women with early BC in clinical trials focused on this important patient population.

299 INVITED

Strategies to preserve fertility in young breast cancer patients

B. Gerber[1], H. Mueller[2]. [1]*University of Rostock, Ob/Gyn, Rostock, Germany;* [2]*Fertility-Center Rostock, Ob/Gyn, Rostock, Germany*

Abstract: Approximately 10% of all breast cancers appeared in women under 39 years. Improved treatment of breast cancer in premenopausal patients increased survival rates, but the therapy may influence fertility and ovarian function. Currently there is a big public and individual interest of breast cancer affected women in preservation of ovarian function and fertility. Chemotherapy induced amenorrhea (CIA) has many objective (osteoporosis, cardiovascular, urogenital atrophy, cognitive etc.) and subjective (hot flushes, sleep disturbances, change of mood etc.) consequences. In patients with breast cancer who wish to avoid a CIA and to preserve their fertility ovarian protection by GnRH agonists, cryopreservation of operative sampled ovarian tissue or obtained fertilized or non-fertilized eggs after stimulation and puncture or embryos after in vitro fertilization are technically possible. However there are no evidence-based recommendations for preservation of fertility or ovarian function in breast cancer patients. Except the cryopreservation of embryos all other procedures are experimental. It is also undefined who is going to carry the costs. Moreover, there are recent data that the reappearance of ovarian hormones may stimulate occult tumor cells in hormone sensitive breast cancer. Therefore it seems necessary to inform breast cancer patients about the possible negative effects of preservation of ovarian function.

300 INVITED

Child-bearing in breast cancer survivors

N. Kroman[1]. [1]*Rigshospitalet, Breast Surgery, Copenhagen, Denmark*

Over the last decades time of childbearing has been steadily postponed in the western world. Therefore, an increasing number of women are seeking medical advice concerning pregnancy after treatment of breast cancer. Since oestrogen is an established growth factor in breast cancer, it has been discussed whether women should be advised against pregnancy subsequent to breast cancer treatment because of the fear of a negative prognostic effect of the high oestrogen levels associated with pregnancy.
The literature on the subject has been sparse, and the majority of the studies is small and methodological insufficient. Lately some harder evidence has appeared indicating that pregnancy after breast cancer treatment does not worsen prognosis. In the latest update on material from Danish Breast Cancer Coopertive Group, DBCG, 371 women experienced pregnancy after treatment of breast cancer (1). In a multivariate analysis that included age at diagnosis, stage of disease, and pregnancy history prior to diagnosis, women who had a full-term pregnancy subsequent to breast cancer treatment were found to have a reduced risk of dying (relative risk: 0.73; 95% confidence interval: 0.54−0.99) compared with other women with breast cancer. The effect was not significantly modified by age at diagnosis, tumour size, nodal status, or pregnancy history before diagnosis of breast cancer. Furthermore, neither spontaneous abortions nor induced abortions subsequent to breast cancer treatment seem to influence the prognosis. Overall, the fertility rate is reduced to one third, and the incidence of induced abortion is significantly increased among women treated for breast cancer.
Breast cancer is potential life-threatening disease, but many women do get cured. On the basis of the present knowledge women believed to be cured from breast cancer should not be advised from getting pregnant.

References

[1] Kroman N, Jensen MB, Wohlfahrt J, Ejlertsen B. Pregnancy after treatment of breast cancer – a population-based study on behalf of Danish Breast Cancer Cooperative Group. Acta Oncol 2008;47(4):545−9.

Scientific Symposium (Thu, 24 Sep, 09:00−11:00)
New directions in the treatment of gastric cancer

301 INVITED

Changing epidemiology of gastric cancer – influence on treatment strategies and outcome

Y.-K. Kang. *Asan Medical Center, Division of Oncology, Korea*

In spite of the decreasing trend worldwide, gastric cancer is still the 4th most common malignancy in incidence and the 2nd most common cause of cancer death. The most remarkable change in gastric cancer epidemiology in recent decades is shift of the primary tumor location from distal to proximal, which was the most dramatic in Western countries like Europe and US. So, the incidence of lower esophageal (EA) and esophagogastric junction adenocarcinoma (EGJA) has increased rapidly in Western countries, while the incidence of gastric non-cardiac adenocarcinoma (GA) has decreased. This shift of primary tumor site can be attributed to several factors; increasing gastroesophageal reflux disease related to obesity, decreased H. pylori infection, and increased consumption of fresh fruits and vegetables with decreased consumption of salt or salted foods. In contrast, such a change has not been so apparent in East Asian countries like Korea and Japan. There is a minimal tendency of decreasing incidence of gastric cancer in this region as well. But, the incidence of gastric cancer is still very high and no change is noticed in the incidence of EA and EGJA. Because of this change in epidemiology of gastric cancer worldwide, issues have been raised for the proper management of gastric cancer.
Among the issues, the most critical question would be 'could EA and/or EGJA be managed in the same principle as GA?' In etiology, EA is known to be associated with gastroesophageal reflux, while GA develops associated with H. pylori infection. EA also shows different clinical behavior from GA. Because of lack of serosal envelope and the rich submucosal lymphatic network, esophageal cancer can easily develop extensive local infiltration and lymph node involvement. So, the TNM staging classification for GA cannot be applied to EA. For localized tumors, treatment of EA is different from GA. Esophagectomy, either transthoracic or transhiatal, is necessary for EA, but not for GA. Since EGJA develops between esophagus and stomach, both staging systems for EA and GA have been used for EGJA. But, recent studies suggest that EGJA is etiologically and clinically closer to EA than GA. For metastatic or recurrent tumors, systemic chemotherapy is indicated in both EA and GA. Chemotherapeutic agents active for both EA and GA were not so different. So, in many UK clinical trials of systemic chemotherapy for GA mostly include EA as well as EGJA. And, inclusion of two tumor types different in etiology and biology in a clinical trial was justified with a recent UK study showing no difference in outcome with conventional cytotoxic chemotherapy among EA, EGJA, and GA. But, recent studies of targeted agents suggest that there may be difference in response to targeted agents among these tumors. For instance, Dragovich et al. reported that erlotinib was active in EGJA, but inactive in GA. Recent ToGA study also suggested that efficacy of HER2 targeting therapy would not be the same between EGJA and GA because HER2 overexpression was more frequently found in EGJA than in GA. These indicate that EA would be better treated separately from GA or EGJA. And, for the global phase III trials of cytotoxic or targeted therapy on gastric cancer, either location of the primary gastric tumor (EGJA vs GA) or geographical region (Western vs East Asia) should be included in stratification factors for randomization.

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