New Concept in Management of Breast Cancer –
The Multidisciplinary Approach

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Surgery has been the mainstay of treatment of breast cancer for almost a whole century since Halsted popularised his radical mastectomy in 1894. He believed that breast cancer metastasised by local spread, and therefore en bloc resection of the affected breast with the overlying skin, pectoral muscles and the entire axillary contents was necessary. In those days, breast cancer often presented as a fungating or ulcerating mass, with satellite nodules and massive axillary lymphadenopathy. Survival was poor despite such radical surgery with 13% survival.

In 1970s, when breast cancer was diagnosed at an earlier stage without massive axillary metastasis, distant metastasis still occurred despite radical surgery. Modified radical mastectomy with preservation of pectoral muscles was developed by Patey. Results from randomised trials showed no difference in survival compared to radical mastectomy and it had since become the standard procedure for breast cancer.

Breast conserving surgery

Increased awareness of breast cancer among women and availability of breast screening programmes in many countries had enabled detection of smaller size breast cancers. A wide local excision of the cancer with histological proven clear margins, and preserving the rest of the breast without jeopardising the overall breast cosmesis was developed. Together with the refinement in radiotherapy techniques, these had led to the introduction of randomised trials on breast conserving surgery in breast cancer treatment. Lumpectomy was followed by whole breast irradiation which aimed to eradicate any residual subclinical tumour foci in the affected breast.

Prospective randomised trials showed no difference in local recurrence, disease-free interval and long term survival between modified radical mastectomy and breast conserving surgery followed by whole breast irradiation. This has marked the development of an integrated approach in the management of breast cancer.

Sentinel lymph node biopsy

Axillary lymph node dissection has long been part of a standard treatment of invasive breast cancer. The aim is to provide an accurate staging of the cancer which bears important prognostic information, to guide subsequent adjuvant therapy, and to achieve regional control of the cancer. With increasing detection of smaller size cancers through mammography screening, which are associated with low risk of nodal involvement, efforts are made to discover ways of predicting axillary node involvement, without removing “normal” lymph nodes. This effort hopefully can avoid unnecessary axillary dissection, which is associated with morbidity of numbness, paraesthesia of upper arm, and lymphedema.

Lymphatic mapping and sentinel node biopsy was developed by Morton for melanoma and subsequently developed by Giuliano for breast cancer. Sentinel node is defined as the first node to receive lymphatic drainage from the cancer and logically should predict the status of the remaining nodal basin. The combination technique using both radioisotope and blue dye injection has matured and produced consistent results of sentinel node identification and high accuracy in predicting axillary nodal status. The technique of sentinel node biopsy has also made possible a more accurate staging of the axilla. Pathologists can examine closely one or a few of these important nodes which are most likely to harbour metastasis, by serial sectioning and to perform immunohistochemical staining. Serial sectioning was found to detect more metastasis and upstage the cancer by almost 30%. Occult metastases were detected by immunohistochemical staining and its clinical significance is still to be worked out by accumulating more data.

Nationwide randomised trials are currently conducted in UK, many European countries, USA, Australia and New Zealand. Individual medical centres in the world with vast experience in sentinel node biopsy have omitted routine axillary dissection after negative sentinel node biopsy and followup did not show increase risk of axillary recurrences. Recent data from the UK ALMANAC trial showed a significant reduction in morbidity comparing sentinel node biopsy and conventional axillary dissection.

At present, sentinel node biopsy could be performed for clinically early stage breast cancer, where the percentage of actual nodal involvement has been known to be low using conventional methods. The current indications are for clinically node negative T1 and 2 invasive cancers. For centres starting to go into sentinel node biopsy, training in the technique and validation of accuracy are recommended.

Image-guided wide local excision for nonpalpable cancer

With the widespread use of screening mammography, increasing number of clinically occult malignancy has
Breast reconstruction following mastectomy

Breast cancer patients are often faced with double anxiety due to the life-threatening nature of the disease and the disfigurement from surgical therapy. With earlier staging of breast cancer and improvement in treatment outcome, quality of life becomes an important issue in long-term survivors. Breast reconstruction has become possible in the last 30 years with the development of autogenous tissue flaps and improvement in implant safety and designs. The previous fear of masking local recurrences and delaying adjuvant therapy has been solved by cumulative evidence indicating the safety of reconstruction. Immediate reconstruction is favoured over delayed procedure because of the better cosmetic outcome and the greater psychological benefit to the woman without having to go through a phase of breast loss.

The commonly performed breast reconstruction includes placement of expander/implant in subpectoral muscle pocket, latissimus dorsi myocutaneous flap with implant, transverse rectus abdominis myocutaneous (TRAM) flap, free or pedicled, and deep inferior epigastric perforator (DIEP) flap.

Virtually all patients undergoing mastectomy are potential candidates for breast reconstruction. Advanced staging of the disease is not a contraindication to reconstruction. The decision to reconstruct or not is a complex issue involving the patient's concern of her own image, social habits, and the psychological stress of cancer diagnosis. The choice between various procedures depend on the expectation of the patient, the physical built of the patient and her medical history. The pros and cons of each option and its suitability for that particular individual should be fully explained and discussed before reaching a final decision.

Nipple-areolar complex represents the visual focal point of a breast form, distracting one’s attention from scars. Reconstruction is possible as a second stage after breast reconstruction, usually 2 to 3 months later, or after completion of chemotherapy. It could be performed in conjunction with any necessary breast mound revision. Local skin flaps for creating nipple and areolar tattooing has been made simple enough to appeal to patients who want to complete this part of the reconstruction.

Skin and/or nipple-sparing total mastectomy with immediate breast reconstruction

With the aim to restore the body image to its natural shape as much as possible after mastectomy, skin-sparing mastectomy has evolved in the treatment of early breast cancer, removing the skin at risk for local recurrence, namely skin overlying the tumour, biopsy scars, and nipple-areolar complex. This has gained wide acceptance especially in the treatment of extensive ductal carcinoma in situ (DCIS), which is basically a parenchymal disease without skin involvement. Nipple-sparing total mastectomy is currently being studied concerning its oncological safety and may prove to be feasible in selected cases.

Radiotherapy

Radiotherapy has been used in the treatment of breast cancer since the early 1900s. It was mainly used for chest wall recurrence or primary treatment of inoperable breast cancer. Over the decades, its use has shifted to being an integral part of breast conserving therapy, and as adjuvant treatment after mastectomy in cases with high risk for local or regional recurrence such as close deep resection margin, large tumour size, or extensive lymph node metastasis. This development owes itself to the availability of sophisticated machines, providing supervoltage irradiation; and refinement in radiation techniques such as fractionation of dose, protraction of treatment duration. All these resulted in less side effects especially on the lungs and heart. Current trials on partial breast irradiation and intraoperative radiotherapy after lumpectomy may lead us to another breakthrough in breast cancer management.

Adjuvant systemic therapy

The presence of micrometastasis at the time of diagnosis of primary tumour predetermines the possibility of distant failure, leading to cancer death. Adjuvant systemic therapy was established in the 1950s in animal models to improve survival. Its rationale was to administer cytotoxic drugs or endocrine therapy to kill or inhibit clinically occult metastasis, when the tumour burden was low and when growth kinetics were most favourable. Randomised trials were initiated in 1970s. Tamoxifen was introduced in 1970s, doxorubicin-based chemotherapy in 1980s, taxanes in the 1990s into adjuvant regimens. Currently more than 100 trials has matured with prolonged followup of 15-20 years. Results from metanalysis showed the overall reduction in breast cancer mortality in the last decade both in UK and USA. This was attributed partly to the detection of earlier cancers due to screening programmes, as well as the more aggressive use of postoperative adjuvant systemic therapy, even for tumour size >1cm without lymph node involvement. At present, adjuvant chemo and/or endocrine therapy is offered to patients with >10% chance of recurrence. Analysis of data from the Hong Kong Sanatorium & Hospital Multidisciplinary Breast Conference showed that >50% of all breast cancers treated would benefit from postoperative adjuvant chemotherapy; about two-thirds would require radiotherapy and hormonal therapy as adjuvant treatment from today’s standard of care.

Dose-dense adjuvant chemotherapy

Dose intensification can be achieved by increasing the dose of chemotherapy (dose intensity) or by increasing the frequency of chemotherapy administration (dose density)
which is possible with the support of G-CSF administration. Numerous randomised trials have failed to confirm any overall survival advantage with dose intensity regimens. In contrast, dose-dense regimens have recently been shown to improve both overall and disease-free survival, and have thus been considered as a breakthrough in chemotherapy.

Hormonal therapy
Tamoxifen is the first-line endocrine therapy for breast cancer since the 1970s. It inhibits the growth of ER-positive tumours and new contralateral lesions by competitive antagonism of oestradiol binding to the oestrogen receptor of the cancer cells. Aromatase inhibitors are a new class of oestrogen inhibitors. It suppresses plasma oestrogen levels in postmenopausal women by inactivating aromatase, the enzyme responsible for oestrogen synthesis from androgenic substrates. Commonly used aromatase inhibitors include nonsteroidal drugs, anastrozole and letrozole, and steroidal drug, exemestane. They have been used with good response as second line hormonal therapy especially in metastatic setting. Recent drug trials have shown reduction in recurrences using aromatase inhibitors compared to tamoxifen. This group of drugs therefore form an alternative to tamoxifen as first line adjuvant therapy in postmenopausal women. However, the long term safety as regards to osteoporosis and bone fracture are still being studied. The choice of hormonal therapy needs to be tailored in individual patients according to the tumour characteristics.

Targeted drug therapy
The best characterised targeted drug is the monoclonal antibody trastuzumab which binds directly to the extracellular domain of the ErbB2 (HER2/neu) gene product - an unliganded sister molecule to the epidermal growth factor receptor (EGFR). Tumours overexpressing ErbB2 tend to have a more refractory clinical course and such patients now can be offered trastuzumab, either in the metastatic or neoadjuvant setting, as monotherapy or as chemosensitizer in combination with cytotoxic agents such as taxanes or vinorelbine.

Neoadjuvant therapy
Neoadjuvant chemotherapy, or preoperative chemotherapy, has been used to reduce tumour size in locally advanced otherwise inoperable cancer, to facilitate surgery or radiotherapy. However, it has not been shown to improve survival. It is now used with increasing popularity to downsize the tumour to allow for breast conserving surgery. This sequencing strategy in the multidisciplinary management is individualised for a particular patient and requires collective opinion from the surgeon, medical and radiation oncologists, radiologist and pathologist.

Conclusions
The extent of breast cancer surgery has become less mutilating as more cancers are detected at a smaller size.

Reconstructive surgery has allowed a fuller recovery of the patient even if total mastectomy is required. The increasing use of systemic therapy in early stage breast cancer has led to a reduction in mortality of breast cancer as a whole. A better understanding of the tumour characteristics allow us to tailor the treatment of each individual patient to get maximum response.

Multidisciplinary approach to breast cancer management is the way forward in this evolution. Specialists from different disciplines now work as a team, either in form of multidisciplinary breast conference, or multidisciplinary breast clinics, in sharing their knowledge and designing the best management plan for individual patient in terms of long term survival and quality of life.

References