

12th Chapter of Surgeons Lecture: Shifting Paradigms in the Management of Breast Cancer—A Surgical Perspective[†]

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Introduction

The recorded history of breast cancer management spans four millennia. This story about breast cancer management is also one about change, about resistance to and acceptance of change. Breast cancer was, and still is, one of the most intensively studied diseases of all time. Treatment paradigm shifts have occurred throughout history, following major changes in understanding of the disease and its response to treatment modalities.¹

Early History

A review of the literature shows that from the time of the first documentation of the disease some 4000 years ago, there have been many theories about the disease, its aetiology and its treatment.² From the period of the ancient Egyptians, to that the ancient Greek civilisation, to the turn of the last century, and finally in the modern era, there have been major paradigm shifts in the understanding and management of breast cancer. The first description of breast cancer appeared in an ancient Egyptian papyrus housed in the British Museum, in which the condition is described as a cold bulging tumour of the breast. The ancient Egyptian doctors recognised the relentless growth of these breast tumours and noted the futility of any known treatment or intervention at that time. They wisely recommended that all treatments should be withheld, as their effects may be worse than the disease itself. The first paradigm for management of malignant breast tumours was to do nothing as all treatment proved futile, and often led to a more premature and painful death than the natural history of the disease itself. Galen transcribed the teachings of the ancient Greeks in AD 200. Their references to breast cancer treatment indicated that this disease was caused by a coagulum of black bile within the breast. This substance was a poison that was discharged from the body by the monthly menstrual flow. This point was used to explain

why breast cancer mainly occurred in women and was more commonly seen in postmenopausal women who had stopped menstruating. All therapy then was focused on getting rid of this black bile. The treatment paradigm of the ancient Greeks therefore was to remove the causative agent for breast cancer. The principle was sound, but we know today that this black bile is not the causative agent for breast cancer. As a result, there was little progress in the treatment of breast cancer and most of the time, the disease was left to run its natural course. A famous painting by the great artist Rembrandt entitled *Bathsheba* (1654) inadvertently captured the dark shadow of breast cancer in the left breast.³ It is believed that the model used by him for this painting died from breast cancer shortly thereafter, a fate common to all breast cancer patients at that time.

This Galenic doctrine was challenged by Miller in 1810 who described the cellular nature of breast cancer. He observed that cancer was caused by the abnormal and unregulated growth of cells. In addition, Virchow's studies about the morbid anatomy of breast cancer, published in 1840, added further information to support the new understanding that breast cancer resulted from the abnormal growth of cells in the mammary glands. Thus was established the theory of the cellular origin of breast cancer and its subsequent centrifugal method of spread from the breast to the regional lymph nodes and then to the distal regions of the body. This new concept led to the understanding that breast cancer was a local disease that spread outwards with time to invade adjacent tissues. The disease was believed to be curable if adequately excised by surgery and that more aggressive local excision would give better cure rates.

The Halstedian Era

Based on this new understanding, the paradigm that breast cancer was a disease that could be cured by surgical

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extirpation was established. The development of anaesthesia led to safer surgery and surgical treatment of breast cancer in the form of the Halsted radical mastectomy became established as the gold standard treatment of breast cancer in the late 19th century and early 20th century.⁴ The surgeon responsible for establishing the surgical treatment for breast cancer was Sir William Stewart Haldsted (1852–1922). He was the first surgeon-in-chief and first Professor of Surgery of the Johns Hopkins Hospital and University. A remarkable innovator, Haldsted introduced many new surgical procedures and techniques that have stood the test of time. These innovations included the aseptic technique for surgery, sensory nerve blocks, intestinal suture technique, the importance of gentle tissue handling, the silk suture, fine stitching, complete wound closures, and the ubiquitous surgical glove. The surgical operations developed by Haldsted included thyroid and parathyroid surgery, blood vessel surgery, hernia surgery and, of course, breast cancer surgery. Haldsted's landmark paper published in 1894 described the incision and dissection for the radical mastectomy procedure that subsequently took on his name and was known as the Haldsted radical mastectomy. In this operation, the entire breast was removed together with both ipsilateral pectoral muscles and axillary lymph nodes.

The Haldsted radical mastectomy remained the gold standard operation for breast cancer up to the late 1970s. This procedure gave the highest 3-year cure rates achievable at that time for breast cancer. He reported that 45% of his 50 patients treated by this method were disease-free at 3 years, with only 6% developing local recurrences. Prior to the Haldstedian era, cure rates by other forms of surgery were dismal. In Billroth's published series of 170 cases of breast cancer (1867–1876), there was a high recurrence rate of 82%, and a poor 3-year cure rate of 5%.

The Post-Halstedian Era

In spite of reasonably good local control, the Haldsted radical mastectomy could not prevent the occurrence of distant metastases, and this was the reason why the other 50% of his patients eventually succumbed to the disease. The earlier teachings of Virchow were then challenged with new concepts. These newer ideas considered the role of vascular invasion and subsequent spread of cancer cells as another way in which breast cancer could spread and metastasize.⁵ With this hypothesis came the discovery that breast cancer does in fact spread via the vascular route in addition to lymphatic spread and direct spread. This can result in distant metastases even during early stages of the disease. This concept provided the explanation why good local control did not always lead to cure. Thus a new paradigm was established, that breast cancer requires systemic treatment in addition to good local control by

surgery. With this new understanding came the era of adjuvant chemotherapy, adjuvant hormonal therapy, and less radical surgery in the form of the modified radical mastectomy (sparing the pectoral muscles), skin sparing mastectomy, and the breast conserving operations (quadrantectomy, segmental mastectomy, and lumpectomy). The idea of conservation of the breast became fully established following the publication of two landmark clinical trials in the *New England Journal of Medicine* by Veronisi (1981) and Fisher (1985), where less radical surgery in the form of segmental resections or lumpectomies were shown to have no significant survival disadvantage as compared with the classical total mastectomy procedure provided certain conditions were met.^{6–9}

Management of the Axillary Lymph Nodes

The paradigm governing the management of the axillary lymph nodes in breast cancer has also undergone changes.¹⁰ The gold standard 3 level axillary lymph node dissection gave way to lesser procedures following the publication of clinical trials like the NSABP B-4 trial. The realisation of the morbidities following radical axillary clearance and a better understanding about how lymphatic spread takes place has led to adoption of lesser procedures and eventually to the new era of sentinel lymph node biopsy. The major concerns following formal axillary dissection include seroma formation, shoulder dysfunction, intercosto-brachial nerve anaesthesia, lymphoedema of the ipsilateral arm and hand, infections (cellulitis) of the ipsilateral hand and arm, preclusion of future invasive procedures on the ipsilateral arm, and cosmetic deformities of the axilla. Thus, sentinel lymph node dissection was welcomed by surgeons as a method of selecting out a group of patients that would be spared unnecessary morbidity.¹¹ Sentinel lymph node dissection is currently being evaluated by clinical trials in many centres for T1 primary breast cancer. This new approach uses a special blue dye and/or a radioisotope to help identify the first or sentinel lymph node in the axilla that breast cancer would spread to. If this node is found to be negative for metastases, then the formal axillary dissection procedure (done for staging and prognosis) can be omitted, thus obviating unnecessary morbidity to the axilla and upper limb.

Multidisciplinary Team Management

In summary, breast cancer is considered as a complex local and systemic disease with several treatment options. The initial planning requires consideration of the many different prognostic factors including the size of the tumour, stage of disease, tumour grade, lymph node status and hormone receptor status. The complexities of treatment options for the modern management of breast cancer have

necessitated the acceptance of a new paradigm that breast cancer is best managed by a multidisciplinary team of specialists rather than by a medical specialist acting alone and using only his own judgement. This multidisciplinary approach, incorporating the opinions of the surgical oncologist, medical oncologist, radiation oncologist, reconstructive plastic surgeon, radiologist, pathologist, physiotherapist, and breast care nurse, would be able to plan and execute standardised and best practice options for the breast cancer patient. In spite of this multidisciplinary team approach, new challenges continue to surface and intrigue us. In order to assist the teams, international established guidelines are available for reference. There are currently several well-accepted international guidelines for breast cancer management, including the BASO Guidelines (1995), DBCG Guidelines (1977), Italian Breast Cancer Task Force Guidelines (1977), ASCO Guidelines (1997), and for Singapore, the MOH Breast Cancer treatment guidelines (1995). The controversies regarding management of screen detected microscopic cancers, ductal carcinoma *in situ*, lobular carcinoma *in situ*, atypical ductal hyperplasia, immuno-histochemistry (IHC) detected lymph node micrometastases, and the BRCA1 and BRCA1 germline mutations continue to stimulate and challenge us to think further and deeper, always looking for more answers as to what is the correct approach.

Breast Reconstruction After Mastectomy

The concept of breast reconstruction has also undergone major paradigm shifts. From an era of no reconstruction, we have moved to delayed reconstruction, and finally to immediate reconstruction, this field of reconstructive plastic surgery has also seen unprecedented developments and advancements. The techniques of breast reconstruction have also evolved from the use of simple breast implants, to tissue expansion followed by implants, to expandable implants, and finally to the use of autologous musculocutaneous flaps and fascio-cutaneous flaps.¹²⁻¹⁴ The autologous flaps can be applied as vascular pattern pedicled flaps or as free flaps. We have seen the developments of the latissimus dorsi flap, the transverse rectus abdominis myocutaneous (TRAM) flap, and the deep inferior epigastric perforator flap (DIEP), as the more commonly used flaps in breast reconstruction today.

Conclusion

In conclusion, breast cancer still remains the leading cancer among females all over the world. Although we know much more about the disease today, we are unable to stop it from occurring and the incidence of the disease continues to rise at a rate of 3% to 5% per annum. In America and some Western countries, 1 in 10 women will

suffer the disease during their lifetime. In Singapore, this risk is 1 in 20. Even though we know more than ever about the disease, and are beginning to diagnose the condition earlier, we are still unable to prevent it from occurring in the general population. Today, we see major advances in diagnostic radiology, histo/cyto-chemistry, and molecular genetics. Likewise, the major therapeutic modalities (surgery, medical oncology, radiotherapy and hormonal therapy) of breast cancer have seen unprecedented advances. With the early success of the first chemoprevention trial, we are now set for yet another paradigm shift in the management of this very common cancer.

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