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Review

Breast cancer: Actual methods of treatment and future trends



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ABSTRACT

The recent ten to twenty years have seen a substantial progress in the diagnosis and treatment of breast cancer. A rapid development of various curative options has led to the improvement of treatment outcomes, while paying more and more attention to the aspects of quality of life and cosmetic effect. In our publication, we wish to outline certain trends in the development of modern treatment of breast cancer. Among topics discussed are new forms of molecular diagnostics, new approach to the idea of sentinel node biopsy, as well as new techniques for delivery of medical procedures, the increasing use of nomograms, progress in the techniques of breast conservative treatment, modern approach to occult breast lesions, the increasing use of neoadjuvant treatment and intraoperative radiotherapy.

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1. Introduction

In Poland, over 14,000 women are diagnosed with breast cancer (BC) each year (48/100,000), with mortality of 5000 (14.5/100,000). The incidence of BC increases with age reaching its peak at 50–59 years (approximately 32% of all cases). The disease occurs particularly in post-menopausal women (78%), with only 22% of patients below 50 years of age. BC below 35 years occurs rarely, representing just 3% of all cases, and exceptionally in women below 25 years.^{1–5}

Notably, the breast cancer mortality rate in Poland shows a declining trend, which may indicate an improvement in BC diagnosis and treatment methods (0.64 in 1963, 0.38 in 2005).^{1,6} The novelties in BC diagnosis and treatment are presented in this report.

The last decades have witnessed profound transformations in BC therapy. The prognosis has improved considerably

and patient's quality of life has become a matter of concern for both medical professionals involved in the diagnostic and therapeutic process and scientists developing new approaches and treatment modalities which determine progress in this area. Only a few decades ago, women with diagnosed BC were treated with radical mastectomy including axillary lymph node dissection (ALND) to achieve a proper locoregional control and enable full recovery. While this treatment goal has remained valid up to the date, the surgical approach has come to be more conserving and selective both with regard to the breast and axillary lymph nodes. The impact of surgery on patient's quality of life is manifested with less mutilating procedures or the application of novel techniques which allow to deliver satisfactory cosmetic effect on the appearance of the breast.

It is now believed that patients with diagnosed BC should be referred to specialised breast units which are able to ensure diagnosis and therapy adequate for that disease. Decisions

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regarding individual treatment are from the very beginning taken by a multidisciplinary team composed of a surgeon, clinical oncologist, radiation therapist, psychologist, physical therapist, nurse, and social worker. Such a system makes it possible to plan an optimal treatment being a resultant of available treatment methods for each stage of the disease, patient's expectations, logistics, costs, as well as possible complications and distant treatment outcomes.

It is estimated that around 30–50% of patients referred to breast units have their treatment plans changed after re-assessment of their examination results, mainly regarding surgery, but also the interpretation of imaging and histopathology test results,⁷ hence a significant need for such units to be established.

The European Society of Breast Cancer Specialists (EUSOMA) has defined a set of criteria to be met by a breast unit and conditions of eligibility for accreditation and European Cancer Care Certification. They are aimed to raise the quality of diagnosis, treatment and care of breast cancer patients across Europe. Soon, as it seems, each diagnosis of breast cancer will lead to patient being referred to a specialised breast unit.

2. Fundamental science

Recently, apart from the standard determination of cancer stage according to the TNM classification, expression of oestrogen and progesterone receptors and HER2 receptor, the genetic profile of cancer has increasingly been determined.^{8–12} The molecular profile of a tumour helps in taking therapeutic decisions and establishing more precise prognosis of oncology patients. There are several tests available at the moment. The first of them, a 21-gene recurrence score assay Oncotype DX[®]. The result, referred to as recurrence score (RS) evaluates the response to hormonal therapy and chemotherapy in oestrogen positive BC. Another commercially available test is a 70-gene MammaPrint assay.¹³ That test allows to evaluate the risk of distant metastases in patients with early BC. Tests are performed on a fresh tissue collected from the tumour by biopsy or during surgery.

Yet another test to help differentiate BC subtypes is the division proposed by Perou into the following subgroups: luminal A, luminal B, basal, HER-2 over-expressing, and normal-like.¹⁴ The basal type of BC is the one with negative oestrogen and progesterone receptors, and HER2 protein. This excludes hormonal and trastuzumab-based treatment. The division helps in determining the response to chemotherapy and evaluating prognosis. Soon, owing to the molecular cancer evaluation, treatment personalisation will become a basic tool to identify treatment method and patient prognosis.

3. Sentinel node biopsy

The publication of the report by Veronesi et al. marked the beginning of a new approach to surgical treatment of BC where efforts are made to limit the extent of procedure as much as possible.¹⁵ However, the removal of the axillary lymph system remains an integral part of treatment. Why ALND? First, it is important to remove cancerous tissue, that is metastasis, in

axillary lymph nodes. It has been proved that lymphadenectomy in that group of patients reduces the number of relapses and has a favourable impact on long-term survival. Second, and very importantly, pathology results of dissected lymph nodes provide full information on the stage of disease. It is a main factor determining the inclusion and extent of adjuvant treatment.

For all the above benefits, lymphadenectomy also involves a number of complications, the most common of them including: lymphatic oedema of the upper limb, movement and sensory disorders of the shoulder, pain or prolonged chylothorax. Those complications may occur in up to 80% of post-surgery patients. It is a great number considering that around 60% of patients are not found to have metastases to the lymph nodes. For them, lymphadenectomy is of no therapeutic but merely of a diagnostic value. Therefore, a method has been sought for years to safely evaluate the lymphatic system, while causing a limited number of consequences and complications¹⁶.

The application of sentinel lymph node biopsy (SLNB) in BC was first tested in the early 1990s. Numerous randomised studies confirmed its value and efficacy in the evaluation of axillary lymph node status. Researchers agree, however, that full consequences of dropping ALND in patients with negative SLNB may only be assessed after results of prospective studies are known on large groups of patients with long-term follow-up. At present, there are nine studies of that kind being conducted in the world.^{16,5,17}

Since the 1990s, when Giuliano¹⁸ proposed the use of blue dye to identify the sentinel node, markers have mostly been based on radiocolloids or, more recently, on indocyanine green.^{17–20}

As in the case of breast conserving therapy, SLNB has been found to have its indications and contraindications. Whenever possible, axillary lymphadenectomy in BC patients should be replaced with SNLB. That technique is also advisable in patients with the regional lymph node status established as N0. SNLB can be applied with lymph nodes which are palpable or visible by imaging if the clinician finds them to be clear of cancer (small, soft). For that group of patients, however, a fine-needle lymph node biopsy is recommended before the decision to perform SLNB is taken.

Excluded from SLNB are patients with metastases to regional lymph nodes (clinical or cytology confirmed) or with distant metastases; patients who do not agree for the procedure or those who report allergy to colloidal markers or methylene dye. Breast-feeding women are recommended to stop feeding before the administration of the marker and not to resume until 24 h thereafter.¹⁶ Another issue that has been discussed recently in relation to SLNB is whether it should be used in pregnant women, especially that women tend to start their motherhood at an increasing older age.²¹ Due to teratogenic properties of methylene blue being and potential anaphylactic activity of Lymphazurin,^{22,23} Tc99-m has been proved to be safe in use and of very little effect to the foetus.^{24,25}

The analysis of the lymph node collected by SLNB being more detailed as compared to ALND, a problem of clinical evaluation of micro metastases appeared.²⁶ In the NSABP B-32 study, the impact of micro metastases on five-year survival

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