INTRODUCTION

Breast cancer (BC) is a major oncological problem in developed countries and also an increasing problem in developing countries. In European Union countries, BC was diagnosed in over 330,000 women in 2008 and 89,000 women died due to BC. In Poland, approximately 16,000 women were diagnosed with breast cancer and over 5000 women died due to breast cancer in 2010. The incidence of breast cancer increases with age reaching its peak at 50-59 years. Eighty per cent of breast cancer occurs after the age of 50. The increase in mortality persisted in Poland until the mid-80s, followed by a stabilization of mortality rate at 15-16/105. Since the mid-90s of the last century there is a continuing decrease in mortality from breast cancer [1].

The recent decades have seen a rapid increase in the rate of diagnosed early breast cancer [2]. Despite improvement in BC diagnosis and treatment methods, occult breast cancer still remains a clinical problem. Occult breast cancer (OBC) is defined as isolated metastatic axillary lymphadenopathy with no palpable mass in the breast and no signs of primary breast cancer on mammography and no detected primary tumor outside the breast [3, 4]. It is classified by the American Joint Committee on Cancer as T0N1-3M0 stage II-III [5]. Breast cancer presenting as axillary adenopathy with clinically occult breast tumor was first described by Halsted in 1907 [6]. It is a rare presentation of the disease, accounting for 0.3-1% of all breast cancers [7]. On the other hand, less than 3% of metastases to the axillia originate from non-mammary sites [8]. The most common solid tumor is carcinoma (58%), followed by melanoma (22%) and sarcoma (20%). Among carcinomas, the most frequently encountered are lung, skin, stomach and ovary [9]. However, these metastases are rarely the first signs of disease [10]. The natural history of occult primary breast cancer remains unclear [11]. Prospective randomized trials have not been performed because of the scarcity of the patients [4]. National Comprehensive Cancer Network (NCCN) guidelines recommend magnetic resonance imaging (MRI) for...
these patients to identify neoplasms that are not identified on clinical examination or mammography. The current treatment options for T0N+ breast cancer conform to NCCN guidelines and include mastectomy with axillary lymph node dissections (ALND) with or without post-mastectomy radiation (BR) or ALND with whole-breast irradiation with or without lymph node irradiation [12].

With regard to non-occult breast cancer, the most important prognostic factors are: tumor size, histological type and grading, number of metastatic axillary lymph nodes, estrogen and progesterone receptor expression, infiltration of peritumoral lymphatic vessels and veins, HER2 status and assessment of the degree of proliferation based on Ki67 index [13]. However, there is no consensus regarding the prognostic factors of occult breast cancer [14].

DISCUSSION

Despite the improvement in investigative techniques, such as mammography, ultrasound and magnetic resonance imaging (MRI), occult breast cancer still poses a diagnostic and therapeutic challenge. Additionally, there is no consensus regarding the prognostic factors of OBC [14].

National Comprehensive Cancer Network guidelines recommend magnetic resonance imaging for identification of occult breast lesions that are not identified on clinical examination or mammography. MRI has high sensitivity for detection of cancer (range 94-100%) [15]. However, specificity has generally been lower and more variable and ranges from 37% to 97% [16]. In addition, magnetic resonance imaging is able to detect lesions that are not visible by conventional techniques, including mammography, ultrasonography, and physical examination, in 10-39% of cases [17]. Suspicious lesions detected by MRI must be confirmed histologically due to its low specificity [18].

NCCN guidelines recommend that women with T0N+ breast cancer receive the same treatment as patients with similarly staged cancer and an identified (T+) primary breast tumor [12]. Prospective randomized trials have not been performed because of the scarcity of the patients. Based on a retrospective study, overall survival (OS), disease-free survival (DFS) and cause-specific survival (CSS) among groups of patients who were treated with different methods has been compared. There have been reports that any treatment of the ipsilateral breast, including breast conserving therapy (BCT), mastectomy, or axillary lymph node dissection (ALND), can improve survival rates compared with nontreatment [4, 19, 20]. It was found that patients who underwent mastectomy had better OS and DFS compared with patients who had no local treatment [19]. However, mastectomy did not improve CSS compared with BCT [4].

Ping at al. [21] have compared the clinical characteristics between occult and non-occult breast cancer and observed that patients with OBC were significantly older than patients with non-OBC and estrogen receptors (ER) positive rate of OBC was lower. Furthermore, no significant difference was noticed in 5- and 10-year survival rate between OBC and stage III non-OBC patients.

Wang et al. [19] analyzed retrospectively 51 patients with OBC from 1990 to 2003 at a single institution. Among 51 patients, 38 patients received mastectomy and 13 patients had no local treatment of the breast. Disease-free survival was significantly increased in patients who had mastectomy compared with patients who had no local treatment of the breast (76 vs. 23 months, p<0.001). It was also found that patients who underwent mastectomy had better overall survival compared with patients who had no local treatment (p<0.001). The recurrence rate for breast cancer patients who had undergone a mastectomy and who had been only observed was 26% and 77%, respectively.

Montagna et al. [22] reviewed information on 15 490 consecutive primary breast cancer patients, who underwent surgery at the European Institute of Oncology between 1997 and 2008. In this study, patients with OBC were compared with an equal number of patients with small invasive breast carcinomas (pT1) observed at the same institution during the same period, matched for year of surgery, age, nodal status and biological features. There was no significant difference in the disease-free survival (5-years DFS 66 vs. 68% p=0.91) and the overall survival (5-years OS 80 vs. 86% P = 0.99) between the OBC and control groups. A statistically significant worse outcome was observed within the group of OBC for patients with more than four involved lymph nodes (T0N2, T0N3) and with triple negative tumors. High risk of relapse and death was observed in OBC patients with triple negative tumors and extensive nodal involvement. Walker et al. [4] suggest that treatment with radiation and axillary lymph node dissection (ALND) may be an appropriate alternative to mastectomy for T0N+ breast cancer. The cause-specific survival (CSS) and overall survival (OS) of women with T0N+M0 ductal, lobular, or mixed breast cancer, who were treated between 1983 and 2006, were analyzed. The retrospective study included 750 out of 770 030 patients (incidence, 0.1%) with T0N+M0 disease. Of 750 patients, 276 patients underwent mastectomy (36.8%), 336 patients received radiation therapy (RT), and 220 patients received neither of these treatments (29.3%). In total, 596 patients underwent ALND (79.5%). In this group, 126 patients underwent ALND only (21.1%), 188 patients underwent mastectomy (31.5%), 202 patients received RT (33.9%), and 80 patients both underwent mastectomy and received RT (13.4%). Patients who received less than optimal locoregional therapy according to NCCN guidelines had worse outcomes. Specifically, the patients who
underwent breast conserving therapy or mastectomy had 10-year OS rate of 64.9% compared with 58.5% for patients who underwent ALND only (p=0.02) and 47.5% for patients who underwent observation (p=0.04). The 10-year CSS rate for patients who underwent breast conserving therapy or mastectomy was 74.6% compared with 71.2% for patients who underwent ALND only (p=0.09) and 71.9% for patients who underwent observation (p=0.69). In multivariate analysis of CSS for patients who underwent mastectomy or breast conserving therapy, the following factors were correlated with an unfavorable outcome: positive estrogen receptor status, ≥10 positive lymph nodes, and <10 resected lymph nodes. Mastectomy did not improve CSS when compared to breast conserving therapy (p=0.79).

He et al. [14] evaluated the treatment outcomes and prognostic factors in patients with occult breast cancer. The investigators retrospectively analyzed 95 patients with OBC who were treated between 1998 and 2010. Of the 95 patients, 64 underwent mastectomy plus ALND with or without post-mastectomy radiation (Mast + ALND group), 13 underwent ALND followed by ipsilateral breast radiotherapy (BR + ALND group) and the remaining 18 were treated with ALND (ALND only group). The median follow-up was 38.2 months (range: 4–160 months). Patients who underwent Mast + ALND or BR + ALND had significantly improved rates of locoregional recurrence-free survival (LRFS), recurrence/metastasis-free survival (RFS) than patients who only underwent ALND (p<0.05). There were no significant differences in the LRFS (p=0.718), RFS (p=0.935) and breast cancer-specific survival (BCSS) (p=0.991) rates between the patients who underwent Mast + ALND compared with those who received BR + ALND. Multivariate analysis revealed that patients with four or more involved lymph nodes had significantly worse outcomes (p=0.042 for BCSS and p=0.038 for RFS).

The overall survival (OS) and prognostic factors associated with OBC were evaluated in a study in Korea [23]. The retrospective study included 142 out of 85 733 patients (incidence, 0.17%) with T0/TxN1-1-N3M0 disease, who were treated between 1990 and 2009. Authors claim that it is the largest series published comparing the prognosis of OBC patients to that of patients with T1N1-3N3 disease. The median follow-up was 78 months (range, 15–198 moths). Overall, 32 patients (22.5%) underwent ALND only (ALND only group), 56 patients (39.4%) had breast conserving surgery (BCS) with ALND (BCS + ALND group) and 54 patients (38.0%) received mastectomy with ALND (Mast + ALND group). Of the 56 patients who underwent BCS with ALND, 83.9% received subsequent radiotherapy, and among 54 patients who underwent mastectomy with ALND, 38.9% received radiotherapy. No significant differences in OS were observed between patients undergoing ALND only (80.8%), BCS with ALND (98.0%), and mastectomy with ALND (92.5%). Nodal status was a significant prognostic factor (p=0.004) on univariate analysis. When compared with T1 patients group, T0/TxN1 patients showed better survival than T1N1 patients (HR=0.253; p=0.003), but T0/TxN2, T0/TxN3 patients showed similar survival to T1N2, T1N3 patients (HR=0.557 and HR=1.104, respectively; p=0.186 and p=0.822, respectively). In this series, the 10-year OS of OBC patients was 88.03%.

**CONCLUSIONS**

Occult breast cancer still remains a clinical problem. Patients who receive less than optimal locoregional therapy according to NCCN guidelines have worse outcomes. Definitive locoregional treatment with either mastectomy or breast conserving therapy improved outcome of patients with T0N+ breast cancer. Nodal status is a significant prognostic factor with regard to occult breast cancer.

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**BIBLIOGRAPHY**


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