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ORIGINAL ARTICLE

The contributory role of multidisciplinary meetings in the diagnosis and treatment of breast cancer

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Summary

Purpose: *The purpose of this study was to investigate the impact of multidisciplinary meetings (MDM) on breast cancer diagnosis and tailored treatment planning.*

Methods: *The data from 680 breast cancer patients diagnosed and treated at our hospital between January 2018 and December 2019 were analyzed according to which the decisions in regards to their treatment were made.*

Results: *The patient median age was 54 years (21-84) and stage distribution of 589 patients was as follows: stage 1-2 (86.62%), stage 3 35 patients (5.15%), and stage 4 56 patients (8.2%). 339 patients had luminal A (54%), 113 HER2 type (18%), 90 patients luminal B (14.4%), and 82 patients triple negative (TN) (13.2%). In 193 of the cases (28%) treatment decisions made as a result of MDM favored either a different sort of surgical technique or sequence of chemotherapy. The time between the initial diagnosis and the treatment decision was 5.8 weeks (1-20).*

Conclusions: *Determining whether the patient is in risk group, even at an early stage, or suspicious areas in other quadrants of the breast or axilla will change the treatment which may as well affect the survival of the patient. Those cases where additional examinations are necessary, patients can be subjected to additional work lists in order to enable faster decision making in MDMs.*

Key words: *breast cancer, magnetic resonance imaging, multidisciplinary, neoadjuvant chemotherapy, risk group*

Introduction

In breast cancer, which accounts for 25% of cancers in females worldwide, deaths have been decreasing [1]. In the current approach, staging based on tumor size and lymph node metastasis is not sufficient to make a treatment decision. Risk factors created according to the characteristics of the tumor also change the treatment approaches. Treatment approaches in breast cancer, whose survival results vary according to the stage and risk group, have revealed the need for tailored treatment. It has been reported since the early 2000s that breast cancer treatment should be planned with the MDM approach.

The ratio of hormone positive breast cancer is 70%. In this group of patients, reduction in relapse and improved survival were reported when hormonotherapy was added to the systemic therapy [2]. Luminal A is the best prognosis group that accounts for half of the group of breast cancer patients who are estrogen receptor (ER)+ and progesterone receptor (PR)+ and human epidermal growth factor (HER2) negative [3]. However, within luminal A group those with ER positive, HER2 negative, Ki67 index above 14% and PR below 20% and clinically poor prognosis were redefined as luminal B. In addi-

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tion to this group, HER2 positivity, if any, in ER and PR positive patients was also included in the luminal B group [4]. HER2 is associated with increase in HER2 oncogene expression and HER2 protein in the cell membrane [5] and associated with poor prognosis [6]. Approximately, 40% of all breast cancer patients are included in the luminal B group [7].

Breast cancers that do not have a hormone receptor present are called triple negative (TN), progress aggressively and survival is short. The BRCA gene has been shown to provide DNA stability. A new subgroup of TN patients with BRCA mutation, who has displayed platinum sensitivity has been identified [8]. In the light of this information, patients with TN, luminal B and HER2 type breast cancer should be evaluated as a risk group and treatment decisions should be made using this information.

It has been reported that treatment planning is carried out more quickly and easily with the help of MDM which is the gold standard in breast cancer treatment [9,10]. MDM is a comprehensive process that requires specific information and takes time to make critical patient-related treatment decisions. In this study we aimed to demonstrate the contribution of MDM in the diagnosis and treatment of breast cancer and to ensure its continuation.

Methods

Initiated 22 years ago in our tertiary referral hospital, mostly in order to encourage breast-conserving surgery and to identify patients who would be given neoadjuvant therapy, our MDMs are now indispensable in the process of decision making. All patients who have been admitted to our general surgery clinic and diagnosed with breast cancer are evaluated at MDM for the treatment plan.

The data of 680 patients who were diagnosed with breast cancer between January 2018 and December 2019 and who were decided to be treated according to multidisciplinary decisions in our hospital were evaluated retrospectively with the approval of the ethics committee of our hospital and in accordance with the 1975 Helsinki Declaration.

The patient's anamnesis, pathology, radiological examination reports and findings from the examinations performed for diagnosis of the disease, genealogical background information of patients were sent to the Email addresses of the multidisciplinary treatment group by the first examining physician so that the participants could have the opportunity to evaluate the cases before the meeting.

Specialists from the surgery, radiation oncology, medical oncology, radiology, pathology, and nuclear medicine clinics met weekly to hold these MDM at the same place and time. Specialists from plastic reconstructive surgery and medical genetics were also invited when required.

The patient reports were read by an assistant doctor in MDM. The radiological images of the patient, which have been uploaded in the online system of our hospital, were viewed on the big screen in the meeting room. Patients to be decided at the meeting were examined by the doctors after a presentation is made.

Creating an algorithm

After the patient's data is presented, the patient is re-examined. Then, the experts provide evidence-based information according to the patient's risks, and thereby a treatment algorithm is created together with the consensus according to the priorities suitable for the patient. Patients who require additional examinations to make a decision are invited to the meeting again when new results are obtained. At the end of the meeting, all patients are provided by an in-depth explanation about decisions and options.

Statistics

In the present study, statistical analysis was conducted using the NumberCruncher Statistical System 2007 Statistical Software (Utah, USA) package program.

In addition to the descriptive statistical methods (mean, standard deviation, frequency and percentage distributions), independent t-test was used to compare binary groups and x^2 test to compare categorical data. The results were assessed based on the significance level of $p<0.05$.

Results

Histological and stage distribution are shown in Table 1 and 2. According to the risk groups, 339 patients were luminal A (54%), 113 patients HER2-type (18%), 82 patients luminal B (14.4%), and 90 patients TN (13.2%). At the diagnostic stage or information about tumor biology for 56 (8%) patients was not urgently needed to make a decision.

The median age was 54 years (21-84), 65 patients had a family history of cancer in 1st or 2nd degree relatives, while 81 patients had a history of cancer. Treatment decisions were made for 651 cancer patients for the first-time treatment, while 25 patients were admitted due to relapse or metastasis and 4 cancer patients for genetic counselling.

Mammography was performed on 672 patients at the diagnosis and USG was used as an additional examination method in 652 patients subsequent to mammography.

MRI was required in 465 patients to support mammography or ultrasound. False-positive lesions were confirmed by biopsy in 21 patients (3%). 106 lesions (15%) were evaluated with MRI as a third examination following mammography and ultrasound, which contributed significantly to the detection and treatment decisions of non-primary lesions, particularly in patients aged 50 and below (p=0.001) (Table 3). The contribution of the MRI

was found to be helpful in patients whose treatment decisions were postponed to the second meeting because additional examinations were required at MDM (p=0.009) (Table 4).

Data of the contribution of the MDM

In 193 of the cases (28.3%) decisions made through the MDM process resulted in either inclusion of a different surgical technique or sequence of chemotherapy. These changes were made for reasons such as starting the treatment of the patient in the risk group with neoadjuvant chemotherapy (NAC) even at an early stage or the decision of mastectomy in the patient who could not receive radiotherapy after breast conserving surgery or a second focus was detected in the breast. There were changes in the surgical methods to be employed in 54patients (7.9%) and in the order of adjuvant or neoadjuvant administration of chemotherapy in 139 patients (20.4%).

NAC application was performed in 35 patients at the locally advanced stage (19.5%) and 145 early-stage patients in the risk histological group (80.5%). In patients who could perform breast-conserving surgery, the tumor was marked prior to chemotherapy in case of tumor disappearance following chemotherapy administration, thereby keeping the area to be operated. For this purpose, the tumor on the breast of 94 patients (13.8%) was marked before NAC. In 19 patients who were not diagnosed with clinical and radiological axillary lymphadenopathy and in whom we decided to administered NAC, we also decided to perform sentinel lymph node biopsy (SLNB) after chemotherapy. The applied forms of surgery are shown in Table 5.

During the first MDM, no decision could be made for 45 of the 680 patients due to the need for additional examinations. The time that elapsed from the first diagnosis until the treatment decision was 5.8 weeks (1-20).

Table 1. Histologic distribution

Histology	*Number*	*%*
Invasive ductal	516	79.72
In situ	44	6.81
Invasive lobular	40	6.19
Mucinous	16	2.48
Paget	7	1.08
Papillary malignant	4	0.62
Mesenchymal	3	0.46
Invasive ductal+mucinous	2	0.31
Tubular	2	0.31
Phylloid	1	0.15
Sarcoma	1	0.15
Lymphoma	1	0.15
Metaplastic carcinoma	1	0.15
Solid papillary carcinoma	1	0.15
Poorly differentiated carcinoma	1	0.15
Neuroendocrine	1	0.15
Malignant cells	39	0.05
Total	680	100

Table 2. Stage distribution

Stages	*Number*	*%*
1-2	589	86.62
3	35	5.15
4	56	8.24
Total	680	100

Table 3. The number of radiological examinations required until decision

Exams until decision	*Contribution to diagnosis of MRI*		
	No *n (%)*	*Yes* *n (%)*	*p*
1 exam	64 (95.52)	3 (4.48)	
2 exam	214 (86.99)	32 (13.01)	
3 exam	263 (79.22)	69 (20.78)	0.001

1 exam: Diagnosis with one examination only (mammography or ultrasonography or MRI); 2 exam: Two of mammography or ultrasonography or MRI; 3 exam: Mammography and ultrasonography and MRI.

Table 4. Contribution of MRI to decision-making in the second meeting in those who could not be decided

	Contribution of MRI in diagnosis		
	No *n (%)*	*Yes* *n (%)*	*p*
Decisions on first meeting	544 (94.44)	91 (87.50)	0.009
Decisions on second meeting	32 (5.56)	13 (12.50)	

Table 5. Surgical applications

	Number	*%*
Breast-conserving surgery	339	57.15
Mastectomy	254	42.82
Bilateral skin-sparing mastectomy	2	0.03

Discussion

In MDM, which has been going on for 22 years in our hospital, we aimed to evaluate the consistency between the decisions we made in diagnosis and treatment with the literature and the contribution of MDM in practice.

Although NAC could not be proven to have contributed to survival at locally advanced stage, it contributed to survival in patients that responded to chemotherapy. Relapse was lower in patients that fully responded to NAC while HER2 and TN patients were the groups of patients with the best response rates, where benefits can be seen due to high proliferation [11]. NeoALLTO and CHER-LOB studies support this data, showing that NAC improves disease-free survival and survival when complete response is achieved [12,13]. The HER2 subgroup, which accounts for 18% of breast cancers in our hospital, is slightly less than that reported in the literature [14]. Accordingly, 70 of the 100 HER2-type patients to be treated with NAC were in early stage.

The best response to NAC was achieved in the group of TN patients regardless of the cytotoxic drugs used (22% versus 11%; p=0.034) [15]. The data presented at the San Antonio Breast Cancer Symposium (SABCS) 2016 confirms how a higher rate of full response could be achieved in BL1 tumors compared to other TNBC subtypes (20% versus 38%, p = 0.015) [16]. The rate of our patients with TN was 13.2% and the decision of NAC was made for 40 of these patients with consensus. Genetic counseling was recommended to detect the BRCA 1 mutation, which is a guide in determining the platinum-responsive group during MDM, and time loss during the treatment phase was prevented.

By giving genetic counseling in patients with a family history, protective recommendations for secondary cancers other than molecular studies were obtained for the response to systemic treatment in patients with TN disease. For this purpose, genetic counseling was recommended to 44 patients by MDM.

With the contribution of MDM, NAC could be applied to patients with risky groups, even at an early stage, as they will benefit from systemic treatment. Without the MDM procedure, the patient who applies to clinics that are not experienced in the treatment of breast cancer can be operated because they are at an early stage. However, after performing the necessary examinations in the clinics, these patients may as well receive NAC if seen beneficial by MDM.

For the patient who was decided to receive NAC, it was decided to insert a mark in the tumor to prevent the loss of the primary tumor site before breast conserving surgery. For this purpose, the tumor on the breast of 94 patients (13.8%) was marked by the radiologist before NAC.Increasing NAC indication in the risky patient group will increase the need for this procedure.This process requires additional appointments in the radiology departments. however, patient treatment is not delayed thanks to MDM additional work lists in our hospital. In clinics where this procedure cannot be performed, breast conserving surgery may not be performed, where the tumor may disappear after NAC.

In the diagnosis of breast cancer, MRI is used as an additional examination method because of the limitations of mammography and ultrasonography and the success rate in diagnosis reaches 99% [17]. However, its low specificity (72%) requires more tests and biopsies to distinguish the presence of malignancy, which can cause additional workload and time loss [18]. In the prospective POMB study, with preoperative MRI performed in addition to preoperative mammography and ultrasonography, 15% of the patients initially planned for breast conserving surgery were decided to undergo mastectomy [19]. A metanalysis involving 19 studies reports that preoperative MRI increases the number of mastectomies [20].In our meetings, one or more lesions were detected in 127 patients in MRI, and these findings changed the initial decision of surgical procedure to be performed in 106 patients (15%). However, false positivity was detected in 21 patients (3%) in the biopsies run on these new lesions. The difference that MRI made in the diagnosis as a third test was found to be statistically significant in the group of patients aged 50 and below (p=0.001). The MRI performed on the patients that had to be assessed during the second meeting to make a decision on their treatment was also found statistically significant (p=0.009). It may be necessary to request additional examinations for the diagnosis of the patient. Thus, the presence of foci other than the primary tumor changed the type of surgery and contributed to local control.

As reported in a metanalysis in 2019, post-NAC SLNB was found to be safe in patients who did not have lymphadenopathy clinically and radiologically only when at least 3 lymph nodes had been removed [21].With the decision taken by MDM, in 19 of our patients who did not have axillary pathology clinically and radiologically and who were going to be administered NAC, breast surgery and SLNB were performed after the systemic therapy. With the help of the decision taken in MDM, this approach helped the patients to receive the right treatment with a less morbid approach without receiving anesthesia twice.

Because non-compliance to treatment was associated with worse disease outcome, we tried to obtain tailored treatment profits that the patient can adapt [22]. In the context of MDM compliance with treatment may be prevented in cases such as mental problems, difficulty in accessing the radiotherapy center, excessively sagging breasts, obese patients, patients with pacemakers, breast conserving surgery or in patients who had previously received radiotherapy in that area, were also evaluated.

The average time from the first diagnosis to the treatment decision was 5.8 weeks (1-20), and this period is reported as 30 days in developed multidisciplinary clinics [23]. Additional examinations were required due to insufficient fine-needle biopsy for immuno-staining or unnecessary radiological examinations, which were referred from hospitals with little experience in breast cancer treatment, therefore, diagnosis was delayed. Special appointment lists were prepared for MDM patients in pathology and radiology for additional examinations to speed up the procedures.

The minutes of the multidisciplinary meetings held in our hospital in 2018-2019 and the hospital's database have been used in the present single-centered study, which has some limitations. The data concerning the resection rates after breast-conserving surgery and the tumor response rates of patients who were administered NAC could not be obtained.

Conclusion

Our data show that MDM contributes to treatment change in approximately one (28.3%) of 3 patients. Determining that the patient is in the risky group even at an early stage,

increasing breast-conserving surgery rates or detecting suspicious areas in other quadrants of the breast or in axilla will change the treatment in favor of the patient's survival when supported by the MDMs.

It will be beneficial for the patient to refer the patient to centers that are experienced in the diagnosis and treatment of breast cancer and make decisions with MDM in order to avoid loss of time in diagnosis.

The minutes prepared at the end of the meeting support the decisions taken against the patient complaining about the treatment.

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Conflict of interests

The authors declare no conflict of interests.

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