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Optimizing the Indication for Breast-Conservative Surgery (BCS) in Patients with Locally-Advanced Breast Cancer

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Rezumat

Optimizarea indicației de chirurgie conservatorie a sânului la pacientele cu cancer mamar local-avansat

Introducere: Principalul beneficiu al chimioterapiei neoadjuvante este reducerea dimensiunilor tumorale, ceea ce permite efectuarea de intervenții chirurgicale conservatorii (BCS) la paciente cu indicație de mastectomie radicală. RMN mamar a fost propusă pentru evaluarea dimensiunilor tumorale post-chimioterapie neoadjuvantă, pentru a stabili categoria de paciente care au devenit eligibile pentru BCS.
Scop: Scopul studiului nostru a fost de a determina modul în care asocierea RMN la evaluarea de rutină, clinică și radiologică a tumorii la prezentarea inițială, şi postchimioterapie, afectează decizia chirurgicală.
Material și metodă: 54 de paciente cu cancer mamar stadiile IIB-IIIB au fost înrolate într-un studiu prospectiv, care a investigat efectele RMN asupra deciziei chirurgicale.
Rezultate: Planul chirurgical a fost modificat, de la BCS la mastectomie radicală, în 6 cazuri (13,04%). Ca urmare a utilizării RMN, un procent de 21,73% de date importante au fost adăugate în procesul de evaluare a extensiei bolii (invazia marelui pectoral şi tegumentului, boală multifocală/multicentrică). Datorită utilizării RMN, 28 (60.86%) dintre pacientele cu cancer mamar reconvertit la operabilitate, postchimioterapie neoadjuvantă, au fost considerate eligibile pentru BCS.
Concluzii: Studiul nostru demonstrează că RMN mamar se impune ca o metodă cu o mare acuratețe în evaluarea extensiei tumorale, precum și în stabilirea eligibilității pentru BCS.

Cuvinte cheie. chimioterapie neoadjuvantă, cancer mamar, RMN, chirurgie conservatorie

Abstract

Background: The main benefit of neoadjuvant chemotherapy is a reduction in tumor size, which allows breast-conserving surgery (BCS) in patients who otherwise would have required a mastectomy. Breast magnetic resonance (MRI) has been proposed to evaluate tumor extent after neoadjuvant chemotherapy, to determine which patients have become eligible for BCS.
Aim: The aim of our study was to determine how the association of breast MRI to routine clinical and radiologic assessment of the tumor at initial presentation, and after chemotherapy, affects the overall surgical decision process.
Material and Methods: 54 women with stage IIB-IIIB breast cancer were prospectively enrolled in a study investigating the effects of MRI on the surgical decision.
Results: Surgical plan was changed from BCS to radical mastectomy in 6 cases (13.04%). As a result of using MRI in evaluating disease extent, 21.73% of valuable data were added by MRI (pectoralis major muscle and skin invasion, multifocal /multicentric disease). Due to MRI examination 28 (60.86%) of the patients with operable breast cancer after neoadjuvant chemotherapy, were eligible for BCS.

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Conclusions: Our study demonstrates that MRI is the most accurate in determination of tumor size and extent, and in establishing eligibility for BCS.

Key words: neoadjuvant chemotherapy, breast cancer, MRI, breast-conserving surgery

Introduction

Neoadjuvant chemotherapy is used for the treatment of locally advanced breast cancer and enables more breast-conserving surgeries (BCS) to be performed, by shrinking larger tumors (1). Breast MRI is increasingly being used and is potentially valuable in ruling out multicentric/multifocal disease, and in defining the extent of a primary breast cancer (2,3).

Aim

The aim of our study was to determine the impact of adding MRI assessment of the tumor to standard non-MRI evaluation, on breast surgical planning.

Material and Methods

We prospectively studied 54 patients (age range, 37-69; mean 52.43±9.47), diagnosed with locally advanced breast cancer between 2004-2012, admitted to the Oncology Department of the Clinical Emergency Hospital of Constanta. Of the 54 patients, 46 have completed the protocol.

All patients underwent clinical exam, mammography, breast ultrasound, and breast MRI, before and after administration of 4 cycles of chemotherapy. A standard bilateral mammogram was obtained using the conventional mammography unit (Senographe DMR). Breast ultrasound was performed using Logic 500, with a broadband linear array transducer (7.5 MHz). High-resolution MRI of both breasts was performed on a 1.0-T scanner, with a dedicated breast coil (Signa Horizon, GE).

The size of the tumor was measured by its longest diameter. Tumor response after neoadjuvant chemotherapy was categorized as described by clinical exam, mammography, ultrasound, and MRI. Each patient was also evaluated for the potential impact of MRI on surgical treatment plan. Suspicion of multicentric (the presence of one or more suspicious enhancing foci in a quadrant different from that in which the index tumor was found), or multifocal (coexistence of two or more distinct foci in the same quadrant) disease was noted.

Statistical analysis used GraphPad Prism 4 software.

Results

According to TNM stage at diagnosis (4), 26 (48.18%) patients were staged IIB, 20 (37.03%) patients were staged IIIA, and 8 (14.81%) patients were staged IIIB. Invasion of pectoralis major muscle was diagnosed in 7 patients, all staged IIIB disease (*Table 1*).

MRI diagnosed pectoralis major invasion in 3 cases in which clinical exam, mammography, and ultrasound were negative, adding valuable data in diagnosing the extent of the disease in 5.55% of the patients studied, and in 37.50% of patients with stage IIIB disease. Differences in the diagnostic sensibility of pectoralis major invasion were statistically significant between clinical exam and MRI (p=0.0253), mammography and MRI (p=0.0090), and ultrasound and MRI (p=0.0026).

Skin invasion was diagnosed in 8 patients, also all staged IIIB disease (*Table 2, Fig. 1*).

MRI diagnosed skin invasion in 1 case in which clinical exam, mammography, and ultrasound were negative, adding valuable data in diagnosing the extent of the disease in patients with stage IIIB disease. Differences in the diagnostic sensibility of skin invasion were statistically significant between clinical exam and MRI (p=0.0105), mammography and MRI (p = 0.0273), and ultrasound and MRI (p=0.0035).

Table 3 illustrates patient distribution according to the response to neoadjuvant chemotherapy (5), as shown by clinical exam, mammography, ultrasound, and MRI. The highest percentage of PR was associated with MRI examination (59.25%).

All 8 patients staged IIIB disease performed also neoadjuvant radiotherapy. For the rest of 46 patients with down-staged disease after chemotherapy, the presence of multifocality and multicentricity was evaluated after completion of chemo-

Table 1. *Performance of all methods used in diagnosing invasion of pectoralis major muscle*

Invasion of pectoralis major	Clinical Exam	Mammography	Ultrasound	MRI
Positive	4	3	2	7
Negative	3	4	5	0

Table 2. *Performance of all methods used in diagnosing skin invasion*

Skin invasion	Clinical exam	Mammography	Ultrasound	MRI
Positive	4	5	3	8
Negative	4	3	5	0

Table 3. *Response to chemotherapy*

Response to chemotherapy	Clinical exam	Mammography*	Ultrasound**	MRI
Complete response (CR)	0	0	0	0
Partial response (PR)	21	22	19	32
Stable disease (SD)	33	25	33	22
Progressive disease (PD)	0	0	0	0

*7 false-negative results in patients with dense breasts;
**2 false-negative results in patients with dense breasts.

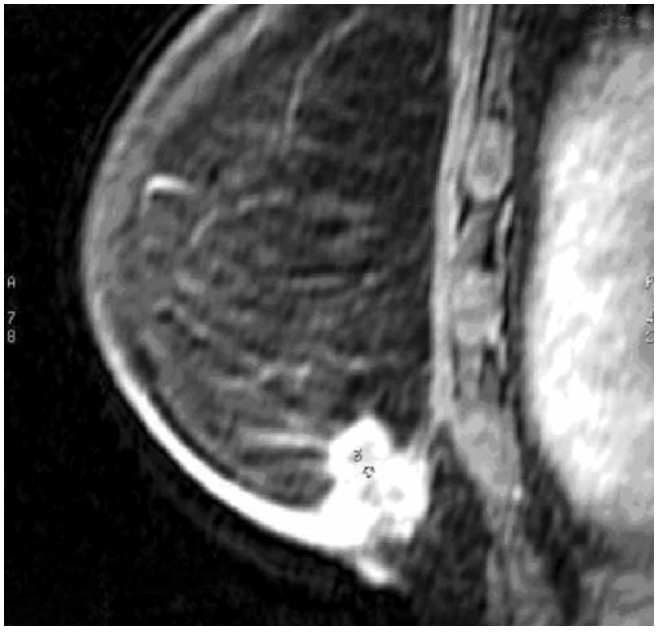

Figure 1. *56 year-old patient, diagnosed with left breast cancer. Breast MRI shows 4 nodular masses (8-19 mm). The tumor located in the lower quadrants is relative to the chest wall, and we can also notice increased skin contrast*

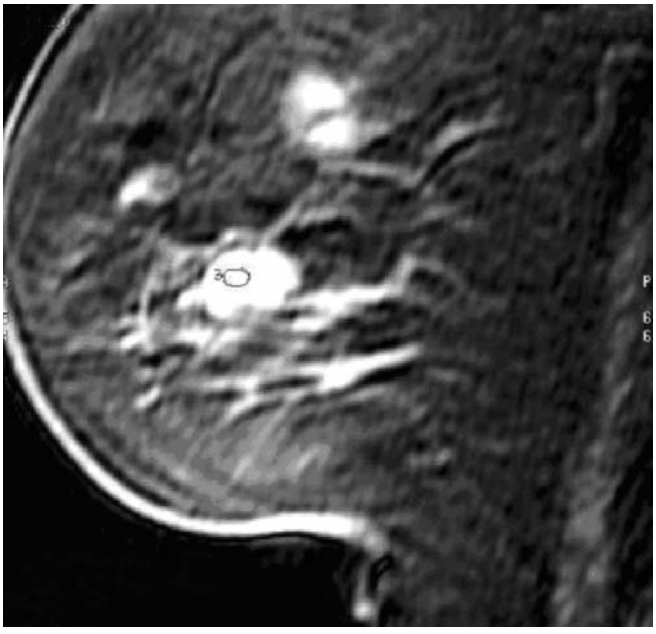

Figure 2. *56 year-old patient, diagnosed with left breast cancer. Breast MRI shows 4 nodular masses (8-19 mm)*

therapy. For 8 patients, 5 with stage IIB, and 3 with stage IIIA, the methods used in the study indicated the presence of multifocal/multicentric disease (*Table 4, Fig. 2*).

None of the patients with multifocal/multicentric disease was diagnosed by clinical exam. Differences in diagnostic sensibility of multifocal/multicentric disease were statistically significant between clinical exam and MRI ($p < 0.0001$), mammography and MRI ($p = 0.001$), and ultrasound and MRI ($p = 0.0002$).

MRI diagnosed multifocal/multicentric disease in 6 cases that were negative on clinical exam, mammography, and ultrasound, adding valuable data in establishing disease extent in 13.04% of the cases. Also, surgical plan was changed to radical mastectomy for the same percentage of patients.

As a result of using MRI in evaluating disease extent, a percentage of 21.73% of valuable data were added by MRI (pectoralis major muscle invasion, skin invasion, and multifocal/multicentric disease).

In establishing eligibility for BCS, from the 46 downstaged patients we excluded: 6 patients with multifocal/multicentric disease (3 with stage IIB, and 3 with stage IIIA), 15 patients with centrally located tumors (central quadrant – from which 2 patients with concomitant multifocal/multicentric disease, and 4 patients with microcalcifications), and the remaining 3 patients with microcalcifications (*Table 5*).

As a result of MRI use in breast cancer management, 28 (60.86%) of patients studied were considered eligible for BCS. In only 9 cases out of 28 (32.14%) eligible cases, surgeons and patients agreed for BCS.

Pathology confirmed that multifocality/multicentricity was correct in 5 (83.33%) of the 6 cases diagnosed by MRI. One case diagnosed by MRI with multifocal/multicentric disease was a false-positive result, and it was due to atypical ductal hyperplasia. Pathology confirmed that BCS indication was correct in 27 (96.42%) of the 28 cases. Also, pathology confirmed that radical mastectomy indication was correct in 17 (94.44%) of 18 cases.

Table 4. *Performance of all methods used in diagnosing multifocality/multicentricity*

Multifocal/ multicentric disease	Clinical exam	Mammography	Ultrasound	MRI
Positive	0	2	1	8
Negative	8	6	7	0

Table 5. *Patients with radical mastectomy indication*

	Stage/No. of patients (N)	
	IIB	IIIA
Multifocal/multicentric disease	3	3
Centrally located tumors	8	7
Microcalcifications	4	3

Discussions

A high accuracy presurgical evaluation of residual disease, has a major impact on the clinical outcome of breast cancer patients undergoing neoadjuvant chemotherapy, and the

maximum benefit of therapy is reduction of tumor size, which allows BCS. Studies have shown that the use of MRI in the evaluation of response to neoadjuvant chemotherapy changes the breast cancer surgical decision (6-8).

Out of the 54 patients studied, 46 were converted to operability after neoadjuvant chemotherapy, and BCS was indicated for 28 (60.86%) patients, due to MRI data. The percentage of 60.86% patients with BCS indication is similar to a study performed by Gentilini et al (9), which reported a rate of 63.10% cases with BCS indication after neoadjuvant chemotherapy.

Breast MRI has brought additional data to the therapeutic surgical plan, changing the theoretical indication of a BCS to radical mastectomy in 6 patients (13.04%) diagnosed with multifocal/multicentric disease. Our results are consistent with the results of other studies, which show an average of 20% of cases with modified surgical behaviour due to the use of preoperative MRI (7,8).

The percentage of BCS performed in our study is similar to data found in the literature. An Italian study published in 2003 (10) reported BCS variability rates from 33% to 41.1%, depending on age at diagnosis, geographic area of residence, and level of education, the percentages being higher in patients from urban area, of young ages (<40 years), and increased educational level. The results of the italian study are similar to NCI (National Cancer Institute) reports, which showed a low frequency of BCS use in the USA, ranging between 10% and 45% (11,12).

BCS represents a safe treatment option for breast cancer, and in 1999 was declared, in the NCI consensus (14), as the preferred treatment option. Consensus was adopted after a large number of clinical trials which showed a similar survival for mastectomy and BCS (13-15).

The results of recent studies (16,17) suggest that BCS is feasible even in patients with locally-advanced breast cancers, with a reasonable rate of local relapse.

Conclusions

BCS is now well established as an oncologically safe treatment for primary breast cancer (5). The high staging accuracy of breast MRI makes it an attractive method for assessing tumor response to preoperative chemotherapy. Although breast MRI is not a perfect method, overestimating or underestimating residual disease in some cases, since MRI appears to provide a more accurate determination of tumor size and extent, comparing with routine clinical and radiologic tumor assessment, it is likely that MRI would be more accurate in determining eligibility for BCS.

Using MRI staging results in association with standard clinical and radiologic staging for presurgical planning would lead to an improvement in net health outcome by increasing the use of BCS and avoiding the need for re-excision surgery when BCS is not appropriate.

Conflicts of interest

None to declare.

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