

Resonance imaging on the surgical management of newly diagnosed breast cancer

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THE IMPACT OF PREOPERATIVE BREAST MAGNETIC RESONANCE IMAGING ON THE SURGICAL MANAGEMENT OF NEWLY DIAGNOSED BREAST CANCER

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Summary

Introduction: Breast cancer is the most commonly diagnosed malignancy in women and the leading cause of cancer death in women. Tumor size is a critical factor in determining the type and extent of surgical and oncologic treatment. It is accurately determined by imaging modalities such as mammography, ultrasound, and magnetic resonance imaging (MRI), which provide a more reliable determination of tumor size. The aim of our study was to investigate the impact of preoperative breast magnetic resonance imaging on surgical treatment of newly diagnosed breast cancer.

Material and Methods: The study retrospectively reviewed the records of 241 participants with newly diagnosed breast cancer who underwent preoperative mammography, breast ultrasound, and MRI between 2016 and 2020 at University Hospital Centre Rijeka. Patients were diagnosed with invasive ductal carcinoma, invasive lobular carcinoma, ductal carcinoma in situ, or a combination of the types. Surgical treatment included one of the following procedures: simple quadrantectomy, quadrantectomy and sentinel lymph node biopsy, quadrantectomy and axillary lymph node dissection, mastectomy and sentinel biopsy, or mastectomy and axillary dissection.

Results: Compared with histopathologic tumor size, breast MRI overestimated size in 10% of patients. T stage was underestimated in 5% of patients ($p > 0.050$). In comparison, breast ultrasound overestimated tumor size in 12% and underestimated it in 48% ($p < 0.001$). Similarly, mammography overestimated tumor size in 14% and underestimated it in 62% ($p < 0.001$).

Conclusion: In patients with newly diagnosed breast cancer, the use of preoperative breast MRI as an adjunct to mammography and ultrasound for locoregional staging significantly alters subsequent surgical treatment.

KEYWORDS: *breast cancer; breast surgery; magnetic resonance imaging; mastectomy.*

INTRODUCTION

Breast cancer is the most commonly diagnosed malignancy in women and the leading cause of cancer death in women, which has been

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recognized as a public health problem worldwide(1). Scientists have suggested renaming ductal carcinoma in situ (DCIS) as ductal intraepithelial neoplasia to emphasize its non-life-threatening nature(2). It is estimated that almost 70% of malignancies are caused by environmental factors. It takes 90-95% of breast cancer cases. Despite significant advances in breast cancer research, breast cancer remains the most common cancer in women worldwide, ahead of lung and cervical cancer. Incidence and mortality rates are expected to continue to increase in the coming years, and therefore represents a high priority for biomedical research(3-4).

Accurate tumor staging is essential for predicting prognosis and clinical outcome. The tumor, node, and metastasis (TNM) staging system is the most important classification for breast cancer, which includes anatomic and prognostic staging. Tumor size is a critical factor in determining the type and extent of subsequent surgical and oncologic treatment. Clinical tumor size is accurately determined by physical examination and imaging techniques such as mammography (MMG), ultrasound (US), or magnetic resonance imaging (MRI) (5-7). MMG and US are the most effective and important diagnostic tools for women with sparse and dense breast tissue(2). MMG is considered the mainstay of breast cancer screening and diagnosis. Along with ultrasound and MRI, it is used to detect and characterize lesions found during screening and to evaluate women with symptomatic disease. In addition to assessing the size and location of the

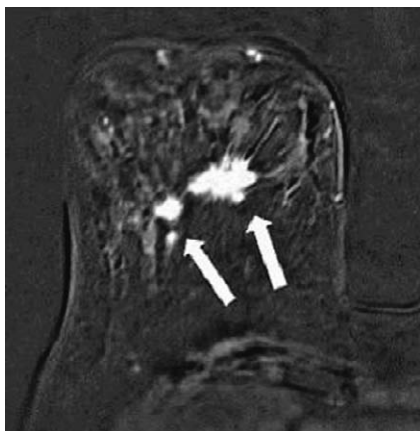


Figure 1. MRI of the right breast showing more than two enhancing mass lesions in a unique quadrant in a distance of ≤ 5 cm (arrow) (multifocal cancer).

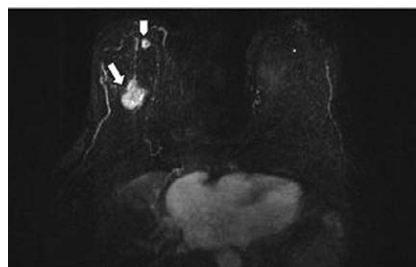


Figure 2. Axial maximum-intensity projections (MIP) reconstructions show the enhancing mass (arrow) in the centre of the right breast, with irregular shape, lobulated margins. Anteriorly, at the distance > 5 cm there is another enhancing mass lesion in a different quadrant – multicentric disease. Pathohistological findings revealed invasive mucinous tumor measuring 2,3 cm (G1, ER 95.1%, PR 9.3 %, Ki67 3.3%) and a small luminal B, HER-2 negative cancer.

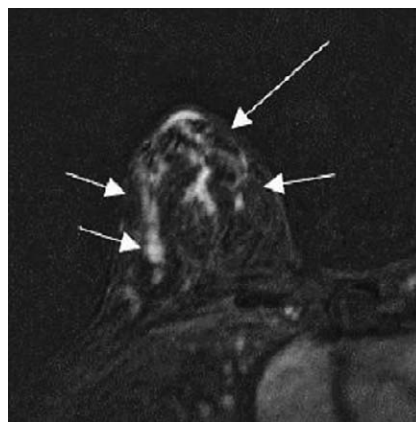


Figure 3. Axial subtraction images of the right breast show area of non-mass enhancement in the right breast (arrows) that correlates with mammography detected microcalcifications (not shown). Biopsy proved ductal carcinoma in situ (DCIS). Mastectomy with reconstruction and sentinel lymph node biopsy (SNLB) was performed and final pathohistological exam confirmed diffuse DCIS (Van Nuys prognostic index 6, ER 30%, PR 14%, Ki67 2%), without SNL metastasis.

tumor, MMG in conjunction with special views is considered useful for examining surrounding tissues, and ultrasound is the method of choice for assessing axillary lymph nodes(4). Breast MRI is used as an additional diagnostic tool in the preoperative evaluation of breast cancer patients, usually after abnormal MMG and US findings are obtained. Compared with MMG or US, MRI is considered more reliable in determining tumor size(5). Histopathological findings are the gold standard for accurate determination of tumor size on surgical specimens(5,6). For assessing disease extension and

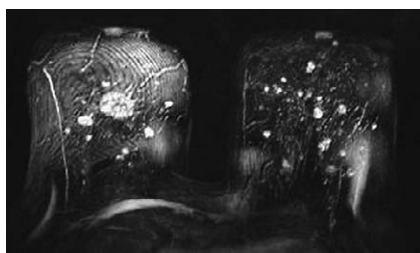


Figure 4. Axial maximum-intensity projection (MIP) shows synchronous invasive lobular cancer (ILC). The MRI was performed for staging multifocal right ILC (luminal A, ER 8%, PR 44%, Ki67 15%, G2 and luminal B; HER-2 negative, G2, ER 19%, PR 18%, Ki67 15%). In the axilla 24/44 lymph nodes were infiltrated (N3). Additional suspicious areal of non-mass enhancements were found in the left breast. Ultrasound guided biopsy was performed and additional ILC was proven (luminal B; HER-2 negative, ER 4%, PR 2%, Ki67 11%). The initial surgical plan after MRI was changed.

detecting additional tumor lesions, breast MRI is more efficient than MMG and US, especially for the purpose of staging multifocal and multicentric disease or in the presence of DCIS (Figs. 1-3).

MRI is thought to improve surgical planning and the likelihood of complete tumor excision on the first attempt. In up to 10% of patients with newly diagnosed breast cancer who have undergone preoperative MRI, the synchronous tumor is occult on US and MMG (Fig. 4), so preoperative MRI may help patients avoid additional secondary surgery or a second course of chemotherapy(7,8). The aim of our study was to evaluate the impact of preoperative breast MRI on surgical treatment of newly diagnosed breast cancer (9). Cancer early detection currently plays a key role in the fight against this disease. Another important part of breast cancer detection is the number of women undergoing diagnostic tests, which remain unsatisfactory.

MATERIALS AND METHODS

Our retrospective study evaluated the records of 241 patients with newly diagnosed breast cancer who underwent preoperative diagnostic evaluation by MMG, US, and MRI. The study was conducted from January 2016 to January 2020 in the Department of General Medicine and Oncological Surgery in collaboration with the Department of Radiology, Clinical Hospital Center Rijeka, Croatia. Patients were divided into four groups accord-

ing to breast cancer type: invasive ductal carcinoma (IDC), invasive lobular carcinoma (ILC), ductal carcinoma in situ (DCIS) and a combination of invasive carcinoma and DCIS. Surgical treatment included one of the following procedures: mastectomy and axillary lymph node dissection (ALND); mastectomy and sentinel lymph node biopsy (SLNB); quadrantectomy and ALND; quadrantectomy and SLNB; or simple quadrantectomy. Some of the patients were treated with chemotherapy and/or radiotherapy before surgery.

MRI scans were performed using a 1.5 Tesla MRI scanner (Aera, Siemens, Erlangen, Germany) and a four-channel phased array breast coil. Dynamic breast imaging was performed before and after intravenous contrast injection (Gadovist, Bayer Schering Pharma AG, Germany or Dotarem, Guerbert, Villepinte, France) through the antecubital vein at a dose of 0.1 mmol/kg using a power injector (Medrad, Bayer HealthCare, The Netherlands). Axial T2, DWI, and T1 non-contrast images were acquired as ADC maps, and values were obtained from DWI images. A kinetic curve was generated for each lesion and classified into one of three categories: persistent (type 1), plateau (type 2), and washout (type 3) in terms of difference in signal intensity. Tumor size was measured and recorded using the first post-contrast subtraction images in the longest plane.

Data were analyzed using MedCalc version 19.1.7. (MedCalc Software, Ostend, Belgium). Results are reported as total frequency and relative frequency. Chi-square test and T-test for proportions were used to analyze differences between variables. P value <0.05 was considered statistically significant. Our study was conducted retrospectively using the medical records of the patients who underwent surgery. The institutional ethics committee approved the study, but informed consent was waived because of the retrospective design of the study.

RESULTS

The mean age was 55 years (range 25 to 82 years). Patients underwent MMG, US and breast MRI as part of the preoperative diagnostic work-up prior to surgical treatment. In addition, 17% of them received chemotherapy, 5% received radiotherapy and 69% received both chemotherapy and radiotherapy (Table 1).

Table 1.

Oncological management

Cancer treatment	Numbers	Percentages
Chemotherapy and radiotherapy	166	69%
Chemotherapy	40	17%
Radiotherapy	13	5%
Untreated patients	22	9%
Total	241	100%
<i>P</i>	<0.001	

Invasive ductal carcinoma (IDC) was diagnosed in 123 (51%) of the participants, invasive lobular carcinoma (ILC) in 39 (16%), ductal carcinoma in situ (DCIS) in 24 (10%), and both invasive carcinoma and DCIS in 55 (23%) (Table 2). All of the patients with synchronous tumor had bilateral IDC.

Table 2.

Final histopathological findings of the breast cancer

Breast cancer type	Numbers	Percentages
Invasive ductal carcinoma (IDC)	123	51%
Invasive lobular carcinoma (ILC)	39	16%
Ductal carcinoma in situ (DCIS)	24	10%
Invasive carcinoma and DCIS	55	23%
Total	241	100%
<i>P</i>	<0.001	

Regarding molecular subtypes, 81 (34%) patients had luminal A subtype, 127 (53%) had luminal B subtype, 12 (5%) had triple-negative breast cancer subtype, 9 (4%) had HER-2 enriched breast cancer subtype, while in 12 (4%) patients the subtype was undetermined (Table 3).

Table 3.

Molecular subtypes of breast cancer

Breast cancer subtype	Numbers	Percentages
Luminal A	81	34%
Luminal B	127	53%
Triple-negative	12	5%
HER2	9	4%
Undetermined	12	4%
Total	241	100%
<i>P</i>	<0.001	

Compared with histopathologically determined tumor size, breast MRI overestimated tumor size in 10% of patients. MRI underestimated T stage in 5% of patients. In comparison, ultra-

sound overestimated tumour size in 12% and underestimated it in 48%, while mammography overestimated and underestimated tumor size in 14% and 62% of patients, respectively (Table 4).

Size estimation of ILC on MRI and MMG showed a statistically significant difference ($p=0.002$) with a mean tumor size of ILC of 37.08 ± 25.12 mm on MRI and 21.85 ± 15.21 mm on mammography, respectively. Tumor size was underestimated in 62% of patients on MMG and 48% on US (both $p<0.001$). With MMG, tumor was overestimated in 14% of patients and with US in 12%. In contrast, overestimation occurred in only 10% of cases and underestimation in 5% of cases on MRI ($p>0.050$), suggesting that the frequency of assessment, i.e., overestimation and underestimation in breast cancer cases, is the same. It is important to emphasize that underestimation of tumor size by MRI is significantly lower ($p>0.050$) than underestimation by ultrasound and mammography, making breast MRI the best option for assessing the size and extent of breast cancer.

Breast MRI showed tumor mass in 65% of patients, and 35% of lesions showed area without mass enhancement (Table 5). Regarding axillary lymph node involvement, MRI findings were negative in 141 (59%) patients and positive in 76 (32%) patients. Final pathological examination of axillary lymph nodes revealed negative findings in 138 (57%) patients and positive findings in 103 (43%) patients (N1 23%, N2 8%, N3 12%). Compared to histopathology, MRI results were false positive in 18 patients (7.5%) and false negative in 6 (2.5%) patients (Table 6). There was no difference in the number of positive and negative axillary lymph nodes found with MRI and final histopathology (all $P>0.05$) (Table 6).

When comparing the accuracy of MRI and pathology size, there was no statistically significant difference between mass and non-mass lesion. In 22 (56%) of the 39 patients with ILC, MRI showed a mass lesion with a mean tumor size of 27.5 ± 19.98 mm; in the other 17 (44%), ILC presented as a non-mass area of enhancement with a mean tumor size of 49.47 ± 26.19 mm. However, there was no statistically significant difference between the mean tumor size on histopathological findings and both subgroup ($p=0.78$ and $p=0.38$, respectively). Pure DCIS (22 cases in total) presented as a mass lesion with a mean diameter of 26.76 ± 17.85 mm in 13 cases, and a non-mass le-

Table 4.

Tumour size on different imaging tools in comparison to histopathological tumour size

Tumour size in comparison to histopathological tumour size	Overestimation		Underestimation		P value
	Numbers	Percentages	Numbers	Percentages	
Mammography	34	14%	149	62%	<0.001
Ultrasound	29	12%	116	48%	< 0.001
Magnetic resonance	23	10%	11	5%	> 0.050
T-test of proportion	all P values > 0.05		a P > 0.05; b P<0.001; c P = 0.006		

^a difference between mammography and ultrasound

^b difference between mammography and magnetic resonance

^c difference between ultrasound and magnetic resonance

Table 5.

Breast magnetic resonance imaging

MRI findings	Numbers	Percentages
Mass	156	65%
Non-mass enhancement	85	35%
P	<0.001	

sion with a mean diameter of 48.90 ± 18.39 mm in 9 cases on MRI. When comparing the accuracy of the size of DCIS on MRI and pathology there was no statistically significant difference (p>0.05).

Table 6.

Axillary lymph node involvement

Axillary lymph nodes	MRI findings		Final pathological findings		P
	Numbers	Percentages	Numbers	Percentages	
Negative	141	59%	138	57%	0.736
Positive	76	32%	103	43%	0.136

All patients underwent surgical treatment planned based on tumor size and extent of regional lymph node involvement: 10 (4%) patients underwent quadrantectomy; 71 (30%) quadrantectomy and sentinel lymph node biopsy (SLNB); 30 (12%) quadrantectomy and axillary lymph node dissection (ALND); 43 (18%) mastectomy and SLNB, and 87 (36%) mastectomy and ALND (Table 7).

Of the total number of patients, 130 underwent mastectomy, while 111 underwent breast-conserving surgery. MRI findings showed a non-mass enhancement lesion in 84 women, while a mass lesion was found in 157 women. (Table 8).

Table 7.

Surgical management

Surgery	Numbers	Percentages
Quadrantectomy	10	4%
Quadrantectomy + SLNB	71	30%
Quadrantectomy + ALND	30	12%
Mastectomy + SLNB	43	18%
Mastectomy + ALND	87	36%
Total	241	100%
P	<0.001	

Table 8.

According to MRI findings

Surgery	Numbers	Percentages
Non-mass lesion	84	35%
Mass lesion	157	65%
Total	241	100%
P	<0.001	

Due to the extensive intraductal component (EIC) found on MRI in 55 cases with non-mass lesion, total mastectomy was performed.

In each case, the biopsy was performed before the surgical plan. In the cases underestimated by MRI, re-excision was performed in 55 cases (especially due to tumor at the surgical margins in ductal carcinoma in situ and EIC). (Table 9).

Table 9.

Number of total mastectomies

Surgery	Numbers	Percentages
Extensive intraductal component on MRI	55	65%
Without extensive intraductal component	29	35%
Total	84	100%
P	0.009	

In 22% of patients in this study, preoperative MRI changed the course of surgical treatment. In newly diagnosed patients with breast cancer, preoperative MRI is recommended regardless of the type, size, and location of the tumor. Thanks to this treatment method, total mastectomy indicated after preoperative MRI, most women have a good prognosis and a better quality of life.

DISCUSSION

Hlubocky et al. studied the impact of preoperative breast MRI on the treatment of 1352 breast cancer patients and in 17.8% surgical treatment was changed based on the results of preoperative breast MRI. They recommend the use of preoperative breast MRI in the majority of newly diagnosed breast cancer patients, larger tumours, invasive lobular carcinoma and tumours in the lower inner quadrant(10). Surgical management was changed in 55 patients based on preoperative breast MRI, representing a total of 22% of participants.

Preoperative breast MRI is associated with an increased likelihood of ipsilateral mastectomy and contralateral prophylactic mastectomy as surgical management for newly diagnosed breast cancer(11). Digital breast tomosynthesis improves diagnostic accuracy for additional ipsilateral and contralateral breast cancer in women with dense breasts. Breast MRI was significantly associated with more extensive surgery. The results suggest that the correct indications for breast MRI should be applied and that widespread use should be discouraged(12). Our results are consistent with previous studies reporting that preoperative breast MRI is associated with more mastectomies, contralateral prophylactic mastectomies and reconstructive surgeries in patients with invasive early breast cancer and ductal carcinoma in situ. Preoperative breast MRI was associated with major surgical intervention. One study showed that premenopausal patients with high breast density and patients with invasive lobular carcinoma benefited most from preoperative breast MRI(13,14). It had no effect on the overall rate of incomplete tumour excision, but resulted in a significantly lower rate of incompletely excised invasive ductal carcinoma(15-17). Preoperative MRI could reduce the likelihood of reoperation in 25% of patients with primary breast cancer(15), especially in patients

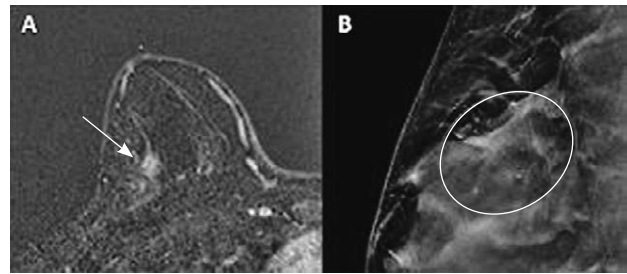


Figure 5. (A) Axial subtraction image of the right breast showing an oval mass (arrow) and an area of non-mass enhancement in the posterior region (asterisk), representing an extensive intraductal component. (B) Calcification on the mediolateral oblique projection of the right breast (circle), but the extent is better seen with MRI. Final pathologic examination revealed a luminal B, HER-2 positive breast carcinoma pT1c pN0 (ER 100 %, PR 90 %, Ki67 15 %) with an in situ component

with extensive intraductal components, which sometimes can only be seen with MRI (Fig. 5). It provides higher accuracy in 30% of patients undergoing preoperative MMG and US(16). The incidence of synchronous breast carcinoma reported in the literature ranges from 0.3% to 12%. Detection is very important as it affects the prognosis of the patients. During preoperative examination MR in patients with recently diagnosed breast cancer, synchronous contralateral malignancy is detected in up to 4.1% of cases. These tumors are usually small and are not detected on mammography, so early detection means better outcomes and less aggressive treatment. In the last two years, MRI has been increasingly used as the gold standard for preoperative management of breast cancer patients in Croatia as it reduces the rate of surgical complications and leads to faster postoperative recovery, but it is still not performed in all breast cancer patients.

We are aware of some drawbacks of our study as the number of patients included is relatively small and it is a retrospective analysis. We emphasise that all diagnostic procedures were performed at the same hospital for each patient. Breast MRI is the most sensitive option for detecting breast cancer and is superior to MMG and US in assessing the extent of disease and detecting additional lesions. It is more useful than conventional imaging for staging breast cancer in multicentric disease or noncalcified DCIS(18,19).

Extensive intraductal component refers to intraductal carcinoma, which may manifest as ex-

tension of primary breast carcinoma into surrounding tissues and is sometimes detected as pathological calcifications on mammography. EIC is an important risk factor for re-excision rate after breast-conserving surgery and for local recurrence after surgery(20).

Indications for axillary dissection were ultrasound-suspicious axillary lymph nodes with a clinically positive axilla and malignant cells in the cytological findings of lymph node puncture in patients who did not undergo neoadjuvant chemotherapy (luminal A). We have had cases of patients with axillary lymphadenopathy, suspicious UTZ lymph nodes, unclear cytological puncture results who underwent axillary dissection and in the final pathological examination they had a negative axilla. The cause of lymphadenopathy in these patients was collagenosis (SLE, scleroderma and dermatomyositis). One patient had lymphadenopathy within cat scratch disease. After the first operation and pathological examination of sentinel lymph nodes patients with three or more positive sentinel lymph nodes underwent axillary dissection as did those with two positive sentinel lymph nodes with capsule breakthrough and extranodal infiltrate in fatty tissue. In the cases of patients with one or two positive sentinel lymph nodes without capsule breakthrough, we did not indicate axillary dissection. This explains the large number of axillary dissections that can be observed in this manuscript.

In the time when the study was performed, we had different criteria for surgical margins (safety margins are 3mm free of tumor for IDC and 5mm for DCIS). According to literature new criteria are surgical margins free of lesion for IDC and 2 mm margins for DCIS(21). This was the reason for the increased number of reexcisions in the study. Today, the number of reexcisions would certainly be less. We conclude that in newly diagnosed breast cancer patients MRI may suggest more extensive surgery, but it can never be said that the tumor is not at the surgical margin in the pathohistological findings. Thus, MRI does not reduce the number of reexcisions, but assists the surgeon in planning the operation by suggesting a more extensive excision. The criteria for breast conserving surgery did not depend on the location of the tumor in the breast, but on the size of the tumor compared to the breast volume. The difference in treatment depending on tumor location

was only in the surgical approach. For tumor localization in the middle, an omega incision or a periareolar incision was performed and for tumor localization in the lower inner quadrant, a radial incision was performed.

Preoperative MRI is not mandatory in every case of newly diagnosed breast cancer, but we recommend it for all younger patients (< 50 years) diagnosed with breast cancer, for all patients with dense breasts, regardless of age, and for patients with a family history of breast cancer and patients with BRCA mutations(22). Due MRI is the most sensitive method for staging breast cancer, it should be used as a problem-solving method when the results of mammography and ultrasound cases are equivocal. We strongly advise preoperative MRI in all cases where tumour delineation, identification of satellite lesion, and evidence of intraductal extension by MMG and US are equivocal. Our study confirms the above facts and encourages the use of MRI for surgical planning in the vast majority of patients diagnosed with breast cancer.

CONCLUSION

In patients with newly diagnosed breast cancer, preoperative breast MRI as an adjunct to mammography and ultrasound for locoregional staging can significantly alter subsequent surgical management.

The authors declare no conflict of interest.

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Sažetak

UTJECAJ PREOPERACIJSKE MAGNETSKE REZONANCIJE DOJKI NA KIRURŠKO LIJEČENJE
NOVODIJAGNOSTICIRANOG RAKA DOJKE

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Uvod: Rak dojke je najčešće dijagnosticirana zloćudna bolest u žena i vodeći uzrok smrti od raka u žena. Veličina tumora je ključan čimbenik u određivanju vrste i opsega kirurškog i onkološkog liječenja. Točno se utvrđuje slikovnim modalitetima poput mamografije, ultrazvuka i magnetske rezonancije (MRI) koja omogućuje najpouzdanije određivanje veličine tumora. Cilj našeg istraživanja bio je istražiti utjecaj preoperativne magnetske rezonancije dojke na kirurško liječenje novodijagnosticiranog raka dojke.

Materijal i metode: U studiju su bile retrospektivno uključene 241 bolesnica s novodijagnosticiranim karcinomom dojke koje su podvrgnute preoperativnoj mamografiji, ultrazvuku dojke i magnetskoj rezonanci između 2016. i 2020. godine u KBC-u Rijeka. Pacijentima je dijagnosticiran invazivni duktalni karcinom, invazivni lobularni karcinom, duktalni karcinom in situ ili kombinacija tipova. Kirurško liječenje uključivalo je jedan od sljedećih zahvata: kvadrantektomiju, kvadrantektomiju i biopsiju sentinel limfnog čvora, kvadrantektomiju i disekciju pazuha, mastektomiju i sentinel biopsiju ili mastektomiju i disekciju pazuha.

Rezultati: U usporedbi s histopatološkom veličinom tumora, MRI dojke je precijenio veličinu u 10% bolesnica. T stadij je podcijenjen u 5% bolesnica ($p>0,050$). Za usporedbu, ultrazvuk dojke precijenio je veličinu tumora u 12%, a podcijenio u 48% slučajeva ($p<0,001$). Slično, mamografija je precijenila veličinu tumora u 14%, a podcijenila u 62% slučajeva ($p<0,001$).

Zaključak: U bolesnica s novodijagnosticiranim rakom dojke, primjena preoperativne MRI dojke kao dopune mamografiji i ultrazvuku za lokoregionalno određivanje stadija značajno mijenja naknadno odluku kirurškog liječenja raka dojke. KLJUČNE RIJEČI: rak dojke; kirurgija dojke; magnetska rezonancija; mastektomija.