Value of Systemic Staging in Asymptomatic Early Breast Cancer

Valor do estadiamento sistêmico no câncer de mama precoce assintomático

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Abstract

Objective Metastases are rare in early breast cancer (EBC), and international guidelines recommend against routine systemic staging for asymptomatic patients. However, imaging exams remain widely employed in the clinical practice. The aim of the present study is to evaluate the value of imaging for systemic staging in EBC.

Methods A retrospective analysis of newly-diagnosed breast cancer (BC) patients was performed. Clinical data including BC subtype, stage, presence of symptoms at diagnosis and instrumental procedures performed for staging were recorded.

Results A total of 753 patients were included, with a median age of 57 years. The majority of the patients underwent at least 1 imaging procedure (91%); had invasive ductal carcinoma (83.5%); histological grade 2 (51.4%); stage II (61.8%); and luminal subtype (67.9%). Among the 685 (91%) patients who underwent any radiologic staging, distant metastases (DMs) were detected in 32 (4.7%). In the univariate analyses, stage IIb and pathological lymph node involvement (pN1) showed a statistically significant association with the presence of DMs, versus only a trend for triple negative and human epidermal growth factor receptor 2 (Her2) positive subtype. In an exploratory analysis performed in this same subgroup, when unfavorable biology (triple negative or Her2 positive) was present, patients had a DM rate of 14.4%, one of the highest reported at this stage of the disease.

Conclusion Early breast cancer has a low prevalence of DM at the initial evaluation, and systemic staging of asymptomatic, unselected patients is not warranted as a routine practice. However, we have identified subgroups of patients to whom a full staging could be indicated.

Keywords

- breast neoplasms
- metastases
- neoplasm staging

Resumo

Objetivo Metástases são de ocorrência rara no câncer de mama precoce, e as diretrizes internacionais não recomendam o estadiamento sistêmico de rotina para pacientes assintomáticos. Apesar disso, exames de imagem continuam sendo

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largamente empregados na prática clínica. O objetivo do presente estudo é avaliar o valor do estadiamento por imagem no câncer de mama precoce.

Métodos Análise retrospectiva de pacientes recém-diagnosticados com câncer de mama. Foram registrados os dados clínicos dos pacientes, incluindo subtipo da neoplasia de mama, estadiamento, presença de sintomas no momento do diagnóstico e procedimentos de estadiamento.

Resultados Um total de 753 pacientes foram incluídos, com idade média de 57 anos. Grande parte deles se submeteu a pelo menos um exame de imagem (91%); tinha carcinoma ductal invasivo (83,5%); grau histológico 2 (51,4%); estádio II (61,8%); e subtipo luminal (67,9%). Entre os 685 (91%) pacientes que realizaram algum exame de imagem, metástases à distância foram detectadas em 32 (4,7%). Na análise univariada, estádio IIb e acometimento linfonodal (pN1) tiveram uma associação estatisticamente significativa com a presença de metástase, enquanto os subtipos triplo negativo e receptor tipo 2 do fator de crescimento epidérmico humano (Her2) positivo demonstraram apenas uma tendência para a identificação de metástases. Na análise exploratória deste mesmo subgrupo, diante da presença de biologia desfavorável (triplo negativo e Her2 positivo), os pacientes apresentaram uma taxa de metástase à distância de 14,4%, uma das mais altas relatadas nesse estádio.

Conclusão Neoplasia de mama precoce apresenta baixa prevalência de metástase à distância no momento do diagnóstico, e o estadiamento sistêmico de rotina de pacientes assintomáticos e não selecionados não é justificável. Contudo, identificamos subgrupos de pacientes para os quais o estadiamento completo poderia ser indicado.

Palavras-chave
- neoplasia de mama
- metástases
- estadiamento de neoplasia

Introduction

Breast cancer (BC) is the second most frequent cancer worldwide, and the most common amongst women.[1] Distant metastases (DMs) are found in ~ 4% of newly-diagnosed patients with early breast cancer (EBC)—defined as stage I-II by the American Joint Committee on Cancer (AJCC) Cancer Staging Manual, Seventh Edition (2010)[2]—when they undergo imaging procedures for initial staging.[3] Because DMs are uncommon in this setting,[4–7] international guidelines advise against routine imaging of asymptomatic EBC patients.[8,9] The National Comprehensive Cancer Network (NCCN) only recommends imaging procedures in cases of EBC when guided by symptoms (such as bone, respiratory or abdominal pain), or laboratory abnormalities (such as elevated alkaline phosphatase, abnormal liver function), but recommends staging for all stage III patients[2] due to the higher prevalence of occult DMs in this population.[10]

Recently, the American Society of Clinical Oncology (ASCO) published recommendations advising against the use of baseline staging in EBC patients. Actually, it was considered one of the "top five" opportunities for improvement in cancer care and cost reduction.[11] Simos et al[12] evaluated the impact of this recommendation in their clinical practice; however, no significant change was observed after the ASCO's statement, which indicates a certain "addiction" of the oncology community to comprehensive staging – often reinforced by strong demands by the patients to be comprehensively staged.

Imaging procedures are not harmless. Previous research show that significant proportions of patients require further procedures to clarify equivocal scan results,[7,12] which could increase the risk of iatrogenic events. For instance, a study evaluating staging in EBC observed abnormal scan findings in 86% of patients. However, only 12% were eventually diagnosed with DM.[13] Furthermore, this approach may lead to delays in the treatment delivery, have negative impact on the cost of care, and cause unnecessary psychological distress to patients. On the other hand, failure to properly diagnose DMs during the initial workup may also lead to an inappropriate treatment, such as unnecessary local surgery and/or radiation and adjuvant chemotherapy.

The aim of the present study is to assess the value of systemic staging through imaging procedures in asymptomatic patients with EBC in a tertiary, high-demand public institution and help to establish a more cost-effective approach for budget-constricted public health services.

Methods

We have performed a retrospective review of all newly-diagnosed BC cases registered between 2010 and 2012 at the Instituto do Câncer do Estado de São Paulo. The expression EBC was used to define specifically stage I-II tumors according to the AJCC Cancer Staging Manual, Seventh Edition.[2] Stage III-IV patients were excluded, but we were careful as not to exclude patients with apparent stage I-II who subsequently had DMs detected by imaging procedures. Patients who underwent imaging procedures for other conditions (such as concurrent cancer diagnosis, surveillance for other cancers) were also excluded. Patients who underwent either neoadjuvant or adjuvant therapy were included; for the neoadjuvant

cases, the most advanced stage (clinical or pathological) was considered for analysis.

The molecular subtypes of BC were defined according to immunohistochemical (IHC) parameters: luminal A (estrogen receptor [ER] > 1% and/or progesterone receptor [PR] > 1%, human epidermal growth factor receptor 2 (Her2) negative and Ki67 index < 15%); luminal B (ER > 1% and/or PR > 1%, Her2 negative and Ki67 index ≥ 15%); triple positive (Her2 positive [Her2 score 3 and/or FISH positive] and hormonal receptor [HR] positive [ER and/or PR >1%); Her2 positive and HR negative (ER and PR <1%); Her2 positive and hormonal receptor negative (Her2 positive; HR negative; ER and PR negative, Her2 score 3 and/or FISH positive); and triple negative (TN) (ER, PR and Her2 negative).

The characteristics of the patients were summarized by descriptive statistics. The categorical parameters were compared by sided Pearson X2-test or Fisher exact test, as appropriate, and the *t*-test was used for the continuous variables. The Shapiro-Wilk test was used to test for normality of the variable age, which was analyzed by applying the *t*-test or the Mann-Whitney test, as appropriate. For all analyses, a two-sided p-value < 0.05 was considered as statistically significant. The analyses were performed using the Statistical Package for the Social Sciences (SPSS, IBM Corp., Armonk, NY, US) software, version 20.0. Approval by the institutional ethics in research committee was obtained before the beginning of the present study.

Results

We have identified 753 patients with EBC, with a median age at diagnosis of 57 years (range: 26–93). Most patients (629) had invasive ductal carcinoma (83.5%), histological grade 2 (51.4%), stage II disease (61.8%), no pathological lymph node involvement (pN0) (67.1%), and luminal A or B subtypes (67.9%). At least one imaging procedure for systemic staging was performed in 685 patients (91%) (►**Table 1**). The patients who underwent high-quality diagnostic procedures (computed tomography [CT], magnetic resonance imaging [MRI] or bone scan [BS]) directed to the most common sites of DMs (bone, lung and liver) were defined as the "completely" staged group (CSG) and represent 29.8% of all staged patients (204 of 685) (►**Table 2**).

For patients undergoing chest imaging, chest X-ray (CXR) was more frequently performed (57.8%), followed by CT (42.2%). Regarding abdominal imaging, abdominal ultrasonography (AUS) was the preferred method (59.8%), and bone scan (BS) was the procedure of choice for skeleton staging (96.3%). Additional staging modalities required for confirmation of metastatic disease—including biopsy, imaging or both—were performed in 19 patients (2.8%).

Among those who underwent any radiologic staging, DMs were detected in 32 patients (4.7%). The bones were the most frequent site of metastases in 20 (62.5%) patients, and all of the cases were identified by conventional BS. Despite CXR and AUS being the most frequently used methods, only one case of DM was diagnosed by these means. The CT scan was responsible for the detection of all cases of lung (10 cases) and the majority of liver metastases (10 in 11 cases). Metastases were found in 9.3% of the CSG versus 2.7% of the patients not submitted to a "complete" staging.

In the population of staged patients ($n = 685$), disease stage ($p < 0.001$) and pathological lymph node involvement

Table 1 Patient and tumor characteristics

Variables	Patients (%)	At least one imaging procedure for staging perfomed (%)	Systemic staging not perfomed (%)
	753 (100)	685 (91)	68 (9)
Age (years)			
< 40	52 (6.9)	48 (92.3)	4 (7.7)
40–59	351 (46.6)	327 (92.9)	24 (7.1)
60–69	181 (24.0)	160 (88.4)	21 (11.6)
≥ 70	169 (22.5)	150 (88.8)	19 (11.2)
Stage (TNM)			
I	288 (38.2)	241 (83.7)	47 (16.3)
II	465 (61.8)	444 (95.5)	21 (4.5)
Treatment			
Neoadjuvant	64 (8.5)	63 (98.4)	1 (1.6)
Adjuvant	661 (87.8)	596 (90.2)	65 (9.8)
Definitive*	28 (3.7)	26 (92.9)	2 (7.1)
Histology			
Ductal	629 (83.5)	575 (91.4)	54 (8.6)
Lobular	49 (6.5)	42 (85.7)	7 (14.3)
Mixed	11 (1.5)	10 (90.9)	1 (9.1)
Other	62 (8.2)	56 (90.3)	6 (9.7)
Unknown	2 (0.3)	2 (100)	0 (0)
Histologic grade			
Grade 1	147 (19.5)	130 (88.4)	17 (11.6)
Grade 2	387 (51.4)	351 (90.7)	36 (9.3)
Grade 3	195 (25.9)	181 (92.8)	14 (7.2)
Unknown	24 (3.2)	23 (95.8)	1 (4.2)
Molecular subtype			
Luminal A	240 (31.8)	213 (88.8)	27 (11.2)
Luminal B	272 (36.1)	246 (90.4)	26 (9.6)
Her2 + HR-	39 (5.2)	34 (87.2)	5 (12.8)
Her2 + HR+	84 (11.2)	78 (92.9)	6 (7.1)
Triple negative	80 (10.6)	76 (95)	4 (5)
Unknown	38 (5.1)	38 (100)	0 (0)
Nodal Stage			
pN0	505 (67.1)	446 (88.3)	59 (11.7)
pN1mic	38 (5.0)	36 (94.7)	2 (5.3)
pN1	183 (24.4)	178 (97.3)	5 (2.7)
Unknown*	27 (3.5)	25 (92.3)	2 (7.7)

Abbreviations: Her2 + HR + , human epidermal growth factor receptor 2 positive and hormonal receptor positive; Her2 + HR-, human epidermal growth factor receptor 2 positive and hormonal receptor negative; pN0, no pathological nodal invasion; pN1, macrometastatic nodal invasion; pN1mic, micrometastatic nodal invasion; TNM, TNM staging system.
Note: *Patients who did not undergo surgery

Table 2 Patient and tumor characteristics according to radiologic staging

Variables	"Incompletely" staged patients	"Completely" staged patients	*p*-value
	481	**204**	
Mean age (years)	58.7	56.4	0.45
Stage			
I	214 (44.5%)	27 (13.2%)	
IIa	159 (33.1%)	66 (32.4%)	
IIb	108 (22.5%)	111 (54.4%)	< 0.001
Treatment			
Neoadjuvant	26 (5.4%)	37 (18.1%)	
Adjuvant	441 (91.7%)	155 (76%)	
Definitive*	14 (2.9%)	12 (5.9%)	< 0.001
Histology			
Ductal	400 (83.2%)	175 (85.8%)	
Lobular	32 (6.7%)	10 (4.9%)	
Mixed	9 (1.9%)	1 (0.5%)	
Other	38 (7.9%)	18 (8.8%)	
Unknown	2 (0.4%)	0	0.54
Histologic grade			
Grade 1	105 (21.8%)	25 (12.3%)	
Grade 2	254 (52.8%)	97 (47.5%)	
Grade 3	103 (21.4%)	78 (38.2%)	
Unknown	19 (4%)	4 (2%)	< 0.001
Estrogen receptor			
Negative	60 (12.5%)	52 (25.5%)	
Positive	420 (87.3%)	151 (74%)	
Unknown	1 (0.2%)	1 (0.5%)	< 0.001
Progesterone receptor			
Negative	105 (21.8%)	67 (32.8%)	
Positive	372 (77.3%)	136 (66.7%)	
Unknown	4 (0.8%)	1 (0.5%)	0.01
Her-2			
Negative	409 (85%)	160 (78.4%)	
Positive	69 (14.3%)	44 (21.6%)	
Unknown	3 (0.6%)	0	0.05
Molecular subtype			
Luminal A	172 (35.8%)	41 (20.1%)	
Luminal B	167 (34.7%)	79 (38.7%)	
Her2 + HR-	19 (4%)	15 (7.4%)	
Her2 + HR+	50 (10.4%)	28 (13.7%)	
Triple negative	40 (8.3%)	36 (17.6%)	
Unknown	33 (6.9%)	5 (2.5%)	< 0.001
Nodal stage			
pN0	348 (72.3%)	98 (48%)	
pN1mic	24 (5%)	12 (5.9%)	
pN1	95 (19.8%)	83 (40.7%)	
Unknown*	14 (2.9%)	11 (5.4%)	< 0.001

Abbreviations: Her2, human epidermal growth factor receptor 2; Her2 + HR + , human epidermal growth factor receptor 2 positive and hormonal receptor positive; Her2 + HR-, human epidermal growth factor receptor 2 positive and hormonal receptor negative; pN0, no pathological nodal invasion; pN1, macrometastatic nodal invasion; pN1mic, micrometastatic nodal invasion.
Notes: "Completely" staged are patients who underwent high-quality diagnostic exams (computed tomography, magnetic resonance imaging or bone scan) directed to the most common sites for breast cancer metastases (the bones, the lungs and the liver). "Incompletely" staged are patients with any imaging studied but who did not meet the "completely" criteria. *Patients who did not undergo surgery.

($p < 0.001$) were identified as risk factors by univariate analysis. Metastatic disease was proportionally more frequent in patients with Her2 positive or TN molecular subtypes, but these findings did not achieve statistical significance (►**Table 3**).

In an exploratory analysis, the combination of CSG and unfavorable biology (TN or Her2 positive) resulted in a DM rate of 14.4%.

Discussion

In a review of data from prospective and retrospective studies evaluating the role of staging by imaging in cases of EBC (7 studies for stage I and 11 studies for stage II), the presence of occult DMs was rare, with a reported median prevalence of 0.2% (range 0–5.1%) in stage I BC after conventional imaging tests (excluding positron emission tomography [PET]/CT), and 1.2% (range 0–34.3%) in stage II BC after imaging tests that included PET/CT. Conversely, DMs were found in ~ 14% of all stage III BCs.[5]

Interestingly, our results suggest that the prevalence of occult metastases (4.7%) is slightly higher than in previous studies; however, the rate remains low. Potential explanations for our findings include: 1) the retrospective nature of most studies could lead to biases caused by poor data quality (such as difficulties in classifying apparent EBC patients who were identified as metastatic by imaging staging but were registered simply as stage IV); 2) heterogeneity between study populations and tumor features (such as when information about BC subtypes is not reported in older studies); 3) heterogeneity of the imaging methods employed, because the accuracy of imaging methods has improved over time, and might influence the diagnostic ability to detect small metastatic lesions.

Table 3 Association between clinical characteristics and metastases between all patients staged and only "completely" staged patients

	All staged patients	Metastases	*p*-value	"Completely" staged patients	Metastases	*p*-value
Variables	**685**	**32 (4.7%)**		**204**	**19 (9.3%)**	
Age (mean)	58.1	56.3	0.47	56.4	54.2	0.31
Stage (TNM)						
I	241	3 (1.2%)	< 0.001	27	1 (3.7%)	
IIa	225	7 (3.1%)		66	2 (3.0%)	
IIb	219	22 (10.0%)		111	16 (14.4%)	0.02
Histology						
Ductal	575	28 (4.9%)	0.61	175	17 (9.7%)	
Lobular	42	3 (7.1%)		10	1 (10.0%)	
Mixed	10	0		1	0	
Other	56	1 (1.8%)		18	1 (5.6%)	1.0
Histologic grade						
Grade 1	130	5 (3.8%)	0.83	25	3 (12.0%)	
Grade 2	351	17 (4.8%)		97	9 (9.3%)	
Grade 3	181	10 (5.5%)		78	7 (9.0%)	0.89
Molecular subtype						
Luminal A	213	9 (4.2%)	0.46	41	5 (12.2%)	
Luminal B	246	9 (3.7%)		79	5 (6.3%)	
Her2 + HR-	34	2 (5.9%)		15	1 (6.7%)	
Her2 + HR+	78	5 (6.4%)		28	3 (10.7%)	
Triple negative	76	6 (7.9%)		36	5 (13.9%)	0.64
Nodal stage						
pN0	446	6 (1.3%)	< 0.001	98	3 (3.1%)	
pN1mic	36	1 (2.8%)		12	1 (8.3%)	
pN1	178	13 (7.3%)		83	8 (9.6%)	0.13

Abbreviations: Her2 + HR + , human epidermal growth factor receptor 2 positive and hormonal receptor positive; Her2 + HR-, human epidermal growth factor receptor 2 positive and hormonal receptor negative; pN0, no pathological nodal invasion; pN1, macrometastatic nodal invasion; pN1mic, micrometastatic nodal invasion; TNM, TNM staging system.
Note: "Completely" staged are patients underwent high-quality diagnostic exams (computed tomography, magnetic resonance imaging or bone scan) directed to the most common sites for breast cancer metastases (the bones, the lungs and the liver).

From another perspective, Simos et al[14] found that most BC patients would not feel comfortable if they were not referred to systemic staging to rule out metastatic diseases, even if the physician recommendation was in compliance with evidence-based guidelines. However, in the same study, when patients were asked about the ranges of chances of detecting metastatic disease, 57.1% chose the range between 6–10%,[14] an expectation that is clearly in conflict with the data from the literature.[7,15] In fact, no single cut-off point has ever been established to define when and which methods of imaging should be employed as a function of the clinical impact and cost-effectiveness. Cancer Care Ontario (CCO) subjectively established, during the development of its guidelines, that methods for BC staging should be able to detect DMs in at least 1% of all patients.[15] Modern methods such as CT and PET/CT have an enhanced performance for the detection of DMs, being more likely to achieve this goal. However, they also have higher costs and are not easily available everywhere.

Few studies directly discussed the financial aspects of EBC staging. A recently published retrospective population-based cohort study from Ontario, Canada, assessing the cost of unwarranted imaging in cases of EBC, based on ASCO and CCO recommendations, reported a substantial cost implication. Among 26,547 stage I-II BC patients, around half of them underwent at least 1 imaging test, resulting in an excess cost of 6.8 million Canadian dollars (CA$258.6 per capita). In the present study, isotopic BS represented the number one cost driver.[8]

While it is important to consider the cost of unnecessary image staging, it is also important to consider the consequences of underdiagnosing metastatic diseases at the initial workup. Metastatic BC is indeed an incurable disease, as supported by numerous studies. In a recent Indian study, resection of the primary tumor failed to improve outcomes in metastatic BC patients.[16] Therefore, the detection of metastatic diseases—even if in a small fraction of the EBC population—could spare futile surgery and/or radiation therapy for the primary tumor as well as other aggressive treatments, such as adjuvant chemotherapy (especially for luminal subtypes, as Her2 positive and triple negative breast cancer [TNBC] would need chemotherapy with or without the addition of targeted therapies anyway). This would help cutting costs and avoid unnecessary side effects. Therefore, an accurate estimation of the risk of occult DMs in cases of EBC is critically important. With the risk being negligible, the adherence to the ASCO guidelines and to the guidelines of other societies will likely be enhanced.

As compared with CXR, CT has a higher capacity to detect small nodules. The American College of Radiology (ACR) recommends CT scans for tumor types with higher propensity for lung metastases, such as BC, even in the presence of a normal CXR.[17] Regarding the detection of liver metastases, the sensitivity of AUS ranges from 50 to 76%, versus 68 to 85% for CT.[18] In the present study, many patients with presumed stage I or II BC did not undergo CT, which may be a problem due to the low accuracy of AUS and CXR. Our results are in line with these recommendations, with all cases of lung metastases identified by CT, and only 1 out of 11 liver metastases identified by AUS (10 were identified by CT).

Nodal involvement is a strong and independent negative prognostic factor. In a recent study, the 5-year survival rate of non-metastatic patients was 85%, and, for patients with or without lymph node involvement, 99%.[1] Even tumors smaller than 2 cm have a worse prognosis if there is lymph node involvement; in 1 series of 24,740 patients, the 5-year survival rate was 96%, 86% and 66% with none, 1–3 and more than 4 nodes involved respectively.[19] The prognostic significance of micrometastatic nodal invasion (pathological lymph node involvement [pN1] micromestatasis; invasive component > 0.2 mm and/or involving more than 200 cells, but not < 2.0 mm) remains under investigation, but it has been suggested by some studies.[20–22] Our results are in line with these data, indicating a higher risk of occult DMs in cases of EBC with nodal involvement (1.3% in no regional lymph node metastasis [pN0], 2.8% in pN1 micrometastasis, and 7.3% in pN1). In the present study, pathological involvement of lymph nodes (pN +) outperformed cancer stage as a risk factor for the presence of DM (1.3% for stage I and 6.5% for stage II).

Limited data are currently available about the molecular classification of BC and the prevalence of occult DMs in cases of EBC. A Chinese retrospective study with information on molecular subtype in 3,411 patients with stage I–III BC showed that luminal a, luminal b, luminal B plus Her2, Her2 overexpression, and basal-like have a statistically different risk for bone (1.4%, 0.7%, 2.5%, 2.7%, and 0.9% respectively; $p < 0.05$), liver (0.1%, 0.1%, 1.0%, 1.1%, and 0.9% respectively; $p < 0.01$) and lung metastases (0.2%, 0%, 0%, 0.27%, and 0.9% respectively; $p < 0.05$); however, the risk of occult metastases was generally low for all subtypes.[6] Conversely, we report a numerically, non-statistically significant higher rate of DM in Her2 positive and TN disease (6.4% in Her2 positive and HR positive; 5.9% in Her2 positive and HR negative, and 7.9% in TN). The lack of statistical significance could simply be due the small sample size for subgroup analyses.

We speculated that the combination of unfavorable biology and lymph node involvement could indicate a group of EBC patients at a higher risk of having DM, and performed exploratory analyses combining high-risk tumors (higher pretest value) with high-sensitivity imaging (►**Table 3**). In this group, we detected an occult DM rate of 14.4%. Due to the heterogeneity between the "completely" and "incompletely" staged population and to the small relative size of the CSG (►**Table 2**), it was difficult to establish the relative contribution of each factor (tumor features and radiologic methods).

Despite the small sample of metastatic patients in our work, the results clearly indicate the futility of AUS and CXR as tools to identify DMs in cases of EBC, probably because these methods have a lower accuracy, and patients at a very early stage of BC might have a lower volume of disease than patients at a more advanced stage of the disease. The observational character of our study could also produce a selection bias, with patients at increased risk for DM more likely to be submitted to more accurate studies. It is

conceivable that a large, prospective, randomized clinical trial would definitively clarify the role of modern imaging studies in this setting. However, due to competing funding priorities, it is unlikely that such a trial will ever be performed. Finally, radiological evaluation with CT, MRI or PET-CT are certainly more accurate, but the expenses related to these procedures also need to be measured in a cost-effectiveness study before they are implemented into the routine practice. Despite these limitations, our results strongly suggest that, should an imaging staging be required in EBC patients, BS and either CT or MRI (or PET-CT) may be the preferred procedures.

Conclusion

Regardless of the recommendations against image staging in cases of EBC, 91% of our patients underwent radiologic staging. Despite having found a slightly higher prevalence than previously reported, our results confirm that stage I–II BC has a low rate of metastatic disease at presentation (4.7% of staged patients). The most frequent metastatic site was the bones (3.9%), followed by the liver (1.8%) and the lungs (1.6%). Although frequently used in the clinical practice, CXR and AUS were futile methods in our hands – almost all metastatic lesions were diagnosed by BS and/or CT scan. Stage II and pN+ were identified as risk factors in the univariate analyses, while Her2 positive and the TN subtype showed only a non-significant trend. When focusing only on patients staged with highly effective methods, stage I–II patients with unfavorable biology (TN or Her2 positive) had a DM prevalence of 14.4%, one of the highest reported in these stages of the disease. Overall, our results confirm that systemic staging of asymptomatic, unselected patients with stage I–II BC is not warranted as a routine practice. However, we have identified subgroups of patients to whom a full staging could be indicated.

Contributors

Soares G. P., Pereira A. A. L., Boas M. S. V., Vaisberg V. V., Magalhães M. C. F., Linck R. D. M. and Mano M. S. contributed with the project and interpretation of data, writing of the article, critical review of the intellectual content and final approval of the version to be published.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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