Department for Obstetrics and Gynecology
Hanover Medical School
Carl-Neuberg-Str. 1
30625 Hanover, Germany

Medizinische Hochschule Hannover

Unexpected invasive breast cancer after mastectomy for in situ carcinoma and implication on axillary management – data from a real-world collective

Kuehnle E[1], Steinkasserer L[1], Mueller C[2], Kuehnle H[3], Luebbe K[4], Noeding KH[5], Noeding S[6], Arfsten M[7], Hillemanns P[1], Park-Simon TW[1]

[1]Department of Obstetrics and Gynecology, Breast Center, Hannover Medical School, Carl-Neuberg-Straße 1, 30625 Hanover, Germany
[2]University of Applied Sciences and Arts, Hochschule Hannover, Expo Plaza 3, 30539 Hannover, Germany
[3]Department of Human Centered Design and Engineering, University of Washington, Seattle, WA 98195, USA
[4] DIAKOVERE Henriettenstift, Breast Center, Schwemannstraßee 17, 30559 Hanover, Germany
[5]HELIOS Klinikum Hildesheim, Breast Center, Senator-Braun-Allee 33, 31135 Hildesheim, Germany
[6]Gynäkoonkologische Praxis am Pelikan Platz Hannover, Germany
[7]Kreiskrankenhaus Stadthagen, Breast Center Schaumburg, Am Krankenhaus 1, 31655 Stadthagen, Germany

Introduction

Mastectomy for large in situ carcinoma is a commonly used therapy. Currently most national and international guidelines recommend sentinel lymph node biopsy because unexpected invasive breast cancer after mastectomy is an indication for sentinel lymph node staging. This cannot be performed after mastectomy and complete axillary dissection would be necessary in these cases. SLN as well as axillary dissection both can cause lifelong complications, especially arm movement impairment. Therefore, the necessity for this additional procedure needs to be addressed. We sought to gain insight into the frequency of unexpected upstaging to invasive breast cancer in case of mastectomy for in situ carcinoma and invasive nodal involvement in a real-world collective.

Material and methods

Data collection was conducted from 2012-2024 in six certified breast cancer centers using a personal interview and data from the patients' medical records. All patients had histologically confirmed pure DCIS or LCIS prior to mastectomy. All preoperatively diagnosed invasive breast cancer cases were excluded from final analysis. Descriptive statistics and multivariate analyzes were utilized to identify risk factors for upstaging from in situ carcinoma to invasive breast cancer.

Results

The study collective included 4307 patients with primary breast cancer or in situ carcinoma (Tab. 1). 238 preoperatively diagnosed in situ carcinomas were analyzed. 41/238 (18%) cases were upstaged to invasive breast cancer (Fig. 1) and positive lymph nodes were found in 8/238 (3%) cases. 71 cases of primary and secondary mastectomy were performed with an upstaging to invasive breast cancer occurring in 19 cases (31%). SLN biopsy in combination with mastectomy was performed in 60 patients and 3 patients with positive lymph nodes were detected. Looking into risk factors (Tab. 2) for unexpected upstaging on multivariate analyzes only a Ki67 higher then 20% (Fig. 4) and HER2 positive status was significantly correlated with an upstaging to invasive carcinoma ($p = 0.037$ and $p = 0.014$).

Tab. 1

Patient characteristics	N	% total	% in situ carcinomas	% mastectomies
Study collective	**4307**	**100.0**		
In situ carcinomas	**238**	5.5	**100.0**	
Ductal in situ carcinomas/M. Paget	231		97.1	
Lobular in situ carcinomas	7		2.9	
Operation				
Mastectomy	71		29.8	**100.0**
Sentinel lymphnode biopsy	60		25.2	84.5
Upstaging to invasive breast cancer	19		8.0	26.8
Primary mastectomy	50		21.0	4.2
Axillary Lymphnode invasion on primary mastectomy	3		1.3	29.6
Secondary mastectomy	21		8.8	7.0
Axillary Lymphnode invasion on secondary mastectomy	5		2.1	
Breast conserving surgery only	163		68.5	
Outcome				
Upstaging to invasive breast cancer	41		17.2	
Axillary Lymphnode invasion	8		3.4	

Fig. 1
Ratio of in situ carcinoma with and without upstaging

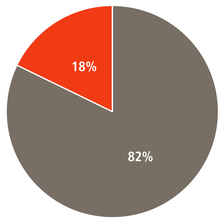


Fig. 2
Age distribution of study collective with in situ carcinoma with and without upstaging

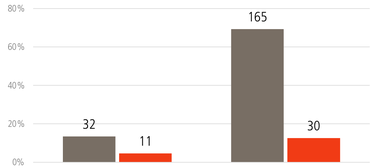
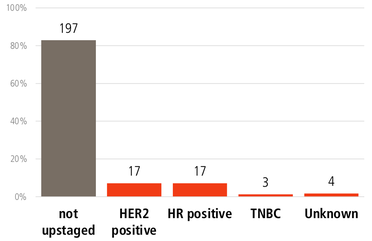


Fig. 3
Distribution of subtypes of in situ carcinoma with and without upstaging

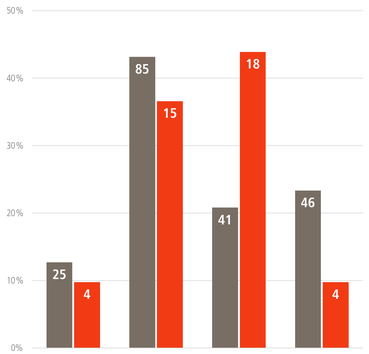


Conclusion

The frequency of unexpected detection of invasive breast cancer in mastectomy for in situ carcinoma, is relatively low, despite comprehensive clinical work up including core needle biopsy. The likelihood of positive nodal involvement is also rather low but remains apparent and has clinical implications for adjuvant therapies. Still, postoperative and long-term complications of SLN biopsy remain an issue.

Therefore, omission of SLN biopsy during mastectomy for in situ carcinoma should be discussed individually. Risk factors for upstaging need to be identified and long-term follow up is needed. Novel approaches to a two stage SLN biopsy offer surgical strategies to avoid unnecessary axillary interventions.

Fig. 4
Comparison of Ki67 values of in situ carcinoma with and without upstaging



Tab. 2

Risk factors	N (238)	%	P
In situ carcinoma size (pathological)			
<20mm	127	53.4	na
20-50mm	72	30.3	na
>50mm	39	16.4	na
Unifokal	64	26.9	na
multifokal	8	3.4	na
Unknown	162	68.1	na
Grading			
G1	33	13.9	na
G2	100	42.0	0.06
G3	96	40.3	0.059
Unknown	9	3.8	na
Age (years)			
<50	43	18.1	
>50	195	81.9	0.041
Hormon replacement therapy	45	18.9	na
Ki67			
Ki67 <20%	127	53.4	ns
Ki67 >20%	58	24.4	0.037
HER2 status			
Negative (0/1/2)	62	26.1	0.093
Positive (3+)	40	16.8	0.014
Unknown	116	48.7	na

na: not applicable due to small sample size
ns: not significant