Characteristics Associated with Upgrading to Invasiveness After Surgery of a DCIS Diagnosed Using Percutaneous Biopsy

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Abstract. *Background/Aim: Ductal carcinoma in situ (DCIS) is a non-invasive malignant breast lesion. Patients diagnosed with a DCIS on percutaneous biopsy usually undergo resection, and the final pathology may reveal that the lesion was in fact invasive (upgrading at surgery), this leading to treatment strategy change during its course. The aim of the present study was to identify factors associated with DCIS-upgrading to invasive carcinoma at surgery, and to identify a subgroup of patients more likely to have an invasive cancer. Patients and Methods: A retrospective study was performed in patients diagnosed with DCIS on percutaneous biopsy between April 1997 and December 2010. Based on available data and on previous studies, 21 clinical, radiological and pathological variables were evaluated using univariate analyses. Variables identified in univariate analyses, when p≤0.10, were included in a multivariate model. Results: Among 608 DCIS lesions, 177 (29.1%) were invasive carcinomas after surgery. Using univariate analyses, core needle biopsy (odds ratio (OR)=1.8), physical symptoms (OR=2.9), palpable masses (OR=4.1), number of specimen obtained (1-9 cores, OR=2.2) and a measurable mammographic lesion (OR=1.7) were significantly associated with upgrading at surgery. However, using multivariate analysis, no factor was significantly associated. Conclusion: No characteristic was identified to be independently associated with DCIS upgrading at surgery, and no sub-group of patients could be identified in whom the appropriate surgery could have been performed first.*

Ductal carcinoma *in situ* (DCIS) of the breast is a malignant breast lesion that is confined within the breast's ductal network, without any stromal invasion (1). The widespread use of screening mammography has led to a subsequent increased detection of asymptomatic micro-calcifications needing investigation (2). Percutaneous needle biopsy is the best modality allowing for a minimally-invasive approach to diagnose these mammographic abnormalities (3-8). However, DCIS diagnosis using percutaneous needle biopsy is challenging, since the needle samples only a part of the lesion, and may miss small foci of invasion (3-8). Therefore, an invasive carcinoma might be diagnosed at surgery, even if the initial needle biopsy showed DCIS as the most offensive lesion: this unfortunate event is known as "upgrading at surgery". Indeed, in a number of published series of DCIS lesions diagnosed using needle biopsy, upgrading occurs in 2-49% of cases (Table I).

The main consequence of upgrading from DCIS to an invasive breast carcinoma is a change in the treatment strategy during its course. Indeed, DCIS is usually treated using breast surgery with or without radiation therapy, while invasive carcinoma is usually treated using breast surgery, lymph node sampling (sentinel node biopsy with or without axillary dissection), radiation therapy, chemotherapy, and adjuvant hormonal therapy (9). However, in cases of upgrading, a second surgery must be undertaken to complete the treatment with lymph node sampling (9), exposing patients to surgery for a second time and anesthesia-related risks (10), as well as in flicting a greater psychological impact on patients to whom the physician first said that they had an easily treatable cancer.

A number of studies have focused on the identification of factors associated with DCIS upgrading at surgery (Table I). These studies were nearly all carried-out in limited patient

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Key Words: Ductal carcinoma *in situ*, breast cancer, upgrade, percutaneous biopsy.

samples and, most importantly, the results are inconsistent between studies. The Deschênes-Fabia Centre for Breast Diseases (Quebec City, Canada) maintains a prospective database of all needle biopsies performed since April 1997, including patients' clinical, radiological and pathological characteristics. The objective of the present study was to determine our upgrading rate of DCIS at surgery, and to identify factors associated with this upgrading. The identification of these factors might help prevent a second surgery in some women through identification of these with a high likelihood of harboring an invasive carcinoma and providing the adequate surgical treatment from the beginning.

Materials and Methods

Study population. At the Deschênes-Fabia Centre for Breast Diseases, pathology results are prospectively compiled in a database, under pathologist supervision, since the beginning of percutaneous image-guided breast biopsies in 1997. A retrospective study of patients who attended the Centre from April 1997 to December 2010 was performed. During this period, radiologists performed 21,340 consecutive percutaneous breast biopsies.

Percutaneous biopsy methods and analyses. The technique used for needle biopsy depends on the lesion's nature. Needle biopsy is preferably performed under ultrasound guidance using 14G core needle biopsy (CNB) or under stereotactic guidance if non-visible by ultrasound. Prior to 2000, stereotactic-guided biopsies were done using 14G core needles (InterV MD Tech, Gainesville, FL, USA). Vacuum-assisted biopsy (VAB) (Mammotome® Breast biopsy system, Ethicon Endo-Surgery, Cincinnati, OH, USA, using 11G needles between 2000 and 2007 and 8G needles from 2007, and SenoRx, Bard Biopsy Systems, Tempe, AR, USA, using 7G needles from 2006) almost became the exclusive needle biopsy technique by 2002.

Needle biopsy specimen obtained for mammographic calcifications are systematically radiographed to confirm the presence of the targeted microcalcifications. The slides containing needle biopsy tissues are stained using standard hematoxylin & eosin (H&E) staining. A minimum of three H&E levels are made from each of these blocks with micro calcifications. The final diagnosis of DCIS is performed using criteria described by the World Health Organization (11, 12). It is important to note that small high-grade lesions are diagnosed as DCIS, even if they encompass only one duct or are less than 2mm.

Selection of biopsies. All patients diagnosed with DCIS as the most advanced lesion on percutaneous biopsy were identified using the Center's biopsy database. Reports were retrieved and reviewed. Patients were excluded if the biopsy showed signs of invasion or micro-invasion. From April 1997 to December 2010, DCIS without any associated invasion was diagnosed in 1,212 out of 21,340 breast biopsies (5.7%). A total of 608 biopsies (out of 1,212) from 604 patients were included in the final analysis. We excluded 604 biopsies for the following reasons: non-conventional breast biopsy (1 or 2 cm diameter biopsy device used in 20 patients); history of DCIS, invasive breast cancer or primary cancer from any other site (230 patients); biopsy or surgery performed in another hospital (254 patients); men (2 patients); and suspicion of invasiveness or micro-invasion on biopsy (98 patients).

Data collection. After Ethical Review Board approval, data from the pathology database, from the Center for Breast Diseases database and from hospital records were reviewed. Several potential variables were collected, including age at-diagnosis, first-degree familial history of breast cancer, indication for mammography, breast symptoms (nipple discharge, pain, itching), mammographic characteristics (microcalcifications, nodule, density, distortion), instrument used for biopsy (CNB *vs*. VAB), associated diagnosis of papilloma, and the pathological characteristics of the DCIS to name some few. The choice of all variables was made according to factors suggested to influence upgrading at surgery in the published literature (Table I) and according to available data from our databases. Previous hormonal exposition was not analyzed in the present study because of inconsistent and insufficient reporting of these variables.

Statistical analysis. Descriptive statistics were used to present characteristics of the population. A generalized estimating equations (GEE) approach was used in the logistic models to take into account correlations between repeated measures on the same individual (concerning four patients who were biopsied twice) and to evaluate odds ratio (OR) of DCIS upgrading at surgery in relation to selected factors. Variables identified at univariate analyses to be associated with DCIS upgrading at surgery with a $p \leq 0.10$ were included in multivariable analyses to account for potential confounders. All analyses were performed using the SAS 9.3 software (SAS Institute, Inc., Cary, NC, USA), where two-sided, and a nominal p-value of 0.05 was considered statistically significant.

Results

Literature review. Table I presents the published series on upgrading following a DCIS diagnosis by percutaneous biopsy. To be included in this Table, studies had to have >50 cases, had to have been published after January 1st, 2000, and had to assess factors associated with upgrading.

Clinical and radiological characteristics. Table II presents the clinical and radiological characteristics of the 608 breast biopsies performed in 604 women. Most women diagnosed with DCIS on percutaneous biopsies were 50-59 (43.9%) or 60-69 years old (29.0%), and had no 1st degree family history of breast cancer (53.5%). More than half were diagnosed in a screening context (61.7%). Most lesions were microcalcifications-alone (88.5%), and only 22.7% of lesions had a measurable size on mammography. Lesions were biopsied using CNB in 25.3% of cases, and using VAB in 74.7%. The number of cores obtained was highly variable. Most women had no physical symptoms (82.5%). Among those who had physical signs (n=106), a palpable mass was the most common (64/106, 60.4%).

Histological characteristics. Table III shows the histological characteristics of 608 breast biopsies performed in 604 women. Most micro-calcifications were observed in the biopsy sample (91.1%). Most lesions

Table I. *Published series on upgrading following a DCIS diagnosis by percutaneous biopsy.*

Source	Year	Biopsy type	DCIS frequency	n	Upgrading	Factors associated with upgrading
Present study	2013	14G CNB, 7/8/11G VAB	5.7%	608	177 (28.9)	None in the multivariate analysis
Kim *et al*. (16)	2012	14G CNB, 8/11G VAB	NR	506	216 (42.7%)	Palpable mass, lesion >20 mm, high grade, 14G CNB
Schulz *et al*. (29)	2012	14G CNB	NR	205	37 (18.0%)	Palpable mass, >3/5 risk factors
Trentin *et al*. (17)	2012	11/8G VAB	10.9%	733	148 (20.2%)	Residual disease after VAB
Han *et al*. (18)	2011	CNB	NR	255	52 (20.4%)	Multivariate analysis not performed. Microcalcifications, mammographic/ palpable mass, solid type
Houssami *et al*. (32)	2011	11G VAB	NR	442	77 (17.4%)	Imaging lesion >50 mm, high grade
Wiratkapun *et al*. (24)	2011	14/11G CNB	4.6%	128	31 (24.2%)	High grade, 14G, comedonecrosis
Miyake *et al*. (30)	2011	11G VAB	NR	103	37 (35.9%)	Palpable mass, lesions >20 mm on MRI
Ventrella *et al*. (39)	2011	11G VAB	8.2%	114	6 (5.3%)	BI-RADS 5, irregular nodule
Go *et al*. (40)	2010	CNB	NR	157	48 (30.6%)	Multivariate analysis not performed. Higher number of positive cores, low lobulular cancerization, papillary pattern, large size
Chan *et al*. (28)	2010	14G CNB, 11G VAB	NR	100	23 (23.0%)	Lesion >20 mm, <10 cores sampled
Kurniawan *et al*. (19)	2010	14G CNB	NR	375	65 (17.3%)	Mammographic lesion other than microcalcifications, lesion >20 mm, screening intervals >3 years
Sakr *et al*. (41)	2008	VAB	NR	110	31 (28.2%)	Multivariate analysis not performed. Micro-invasion, lesion >30 mm
Meijnen *et al*. (20)	2007	14G CNB	NR	172	45 (26.2%)	Palpable mass, mammographic mass, intermediate or high grade
Rutstein *et al*. (36)	2007	14G CNB, 11G VAB	NR	254	21 (8.3%)	Multivariate analysis not performed. Comedonecrosis
Leikola *et al*. (42)	2007	14G CNB, 11G VAB	NR	67	20 (29.9%)	Visible on ultrasound, comedo histological architecture
Houssami *et al*. (25)	2007	14G CNB, 11G VAB	11.9%	479	109 (22.8%)	Multivariate analysis not performed. 14G CNB
Tan *et al*. (37)	2007	NR	NR	90	30 (33.3%)	Comedonecrosis, CNB
Huo *et al*. (21)	2006	14/18G CNB, 9/11G VAB	7.7%	200	41 (20.5%)	Mammographic mass, lesion >15mm, lobular cancerization
Dillon *et al*. (43)	2006	14G CNB	10.4%	93	44 (47.3%)	Multivariate analysis not performed. Mammographic lesion other than microcalcifications, lesion >50mm
Goyal *et al*. (22)	2006	11/14G CNB	NR	587	220 (37.5%)	Palpable mass, mammographic mass
Mittendorf *et al*. (44)	2005	NR	NR	55	1 (1.8%)	Multivariate analysis not performed. CNB
Wilkie *et al*. (33)	2005	NR	NR	675	66 (9.8%)	High grade, mammaographic mass, microinvasion
Yen *et al*. (34)	2005	14/11G VAB	NR	260	66 (25.4%)	<55 years old, CNB, mammographic lesion >40 mm, high grade
Hoorntje *et al*. (35)	2003	14G CNB	NR	255	41 (16.1%)	Multivariate analysis not performed. High grade, periductal inflammation
Pandelidis *et al*. (13)	2003	11G VAB	6.8%	91	12 (13.2%)	Multivariate analysis not performed. None.
Renshaw *et al*. (38)	2002	14G CNB, 11G VAB	3.0%	91	17 (18.7%)	Multivariate analysis not performed. Comedo, lesion >4 mm associated with lobular extension
Wahedna *et al*. (14)	2001	14G CNB	NR	140	61 (43.6%)	Multivariate analysis not performed. None.
Brem *et al*. (26)	2001	8/11G VAB	7.7%	61	5 (8.2%)	Multivariate analysis not performed. Lesion >30 mm, 11G VAB
Cox *et al*. (15)	2001	NR	NR	224	23 (10.3%)	Multivariate analysis not performed. None.
Jackman *et al*. (27)	2001	14G CNB, 11G VAB	2.7%	373	183 (49.1%)	Multivariate analysis not performed. CNB, mass on imaging, large lesion, <10 cores sampled
King *et al*. (23)	2001	NR	NR	140	36 (25.7%)	Mammographic mass
Lee *et al*. (12)	2000	14G CNB, 11G VAB	5.3%	72	17 (23.6%)	Multivariate analysis not performed. None.

To be included in this Table, studies had to have >50 cases, had to have been published after January 1st, 2000, and had to assess factors associated with upgrading. NR: Not reported; CNB: core needle biopsy; VAB: vacuum-assisted biopsy; G: gauge; BI-RADS: Breast Imaging-Reporting and Data System.

Table II. *Clinical and radiological characteristics of 608 DCIS breast biopsies.*

Characteristic	Number of biopsies[a]	% of total
Age (years)		
<50	97	16.0
50-59	267	43.9
60-69	176	29.0
≥70	68	11.1
1st degree family history of breast disease		
No	315	53.5
Yes	274	46.5
Mammography indication		
Screening program	358	61.7
Investigation	222	38.3
Mammographic lesion		
Microcalcifications-alone	530	88.5
Other than microcalcifications-alone	69	11.5
Radiographic lesion's size		
Measurable lesion	134	22.7
Microcalcifications-only	457	77.3
Biopsy instrument		
CNB	153	25.3
VAB	452	74.7
Number of cores sampled		
1-9	224	36.8
10-15	171	28.1
≥16	117	19.2
Unknown	96	15.8
Physical symptoms		
No	499	82.5
Yes	106	17.5
Physical signs		
No	575	95.7
Yes	26	4.3
Palpable mass		
No	497	81.7
Yes	64	10.5
Unknown	47	7.7
Body mass index (kg/m^2)		
<25	329	55.5
25.0-29.9	186	31.4
≥30	78	13.1

[a]Total number of biopsies is not always 608 because of missing values.

Table III. *Histological characteristics of biopsies showing DCIS and upgrading at surgery in 608 breast biopsies showing DCIS.*

Characteristic	Number of biopsies[a]	% of total
Presence of microcalcifications in biopsy		
No	50	8.9
Yes	511	91.1
Nuclear grade		
I	53	10.2
II	286	54.8
III	183	35.0
Necrosis		
No	160	26.3
Yes	448	73.7
Micropapillary		
No	467	76.8
Yes	141	23.2
Cribriform		
No	281	46.3
Yes	326	23.7
Papillary		
No	590	97.2
Yes	17	2.8
Comedocarcinoma		
No	517	85.0
Yes	91	15.0
Solid		
No	245	40.3
Yes	363	59.7
Estrogen receptors		
Negative	132	23.0
Positive	443	77.0
Progesterone receptor		
Negative	270	47.0
Positive	305	53.0
Surgical histological results		
Upgrading to invasive carcinoma	177	29.1
Final diagnosis of DCIS	431	70.9

[a]Total number of biopsies is not always 608 because of missing values.

displayed a nuclear grade of II (54.8%) or III (35.0%). Necrosis was present in 73.7%. Concerning architecture, 23.2% of lesions displayed a micropapillary, 23.7% a cribriform, 2.8% a papillary, 15.0% a comedocarcinoma and 59.7% a solid architecture. Some lesions presented more than one architecture. Seventy-seven percent of lesions were positive for estrogen receptors and 53% for progesterone receptor.

Among the 608 lesions, 177 were upgraded to invasive carcinoma at surgery, for an upgrading rate of 29.1% (Table III).

Univariate analysis. Table IV shows the univariate associations between upgrading at surgery and clinical and radiological characteristics in 608 breast biopsies in 604 women. A measurable lesion on mammography was associated with an increased risk of upgrading (OR=1.67, 95%CI: 1.11-2.51, p=0.01), the use of CNB (OR=1.80, 95%CI: 1.22-2.65, p=0.003), sampling of 1-9 cores (OR=2.15, 95%CI: 1.27-3.64, p=0.009), the presence of a physical symptom (OR=2.91, 95%CI: 1.89-4.48, p<0.0001), the presence of a physical sign (OR=2.17, 95%CI: 0.98-4.79, p=0.05), and the presence of a palpable mass (OR=4.08, 95%CI: 2.39-6.97, p<0.0001). All remaining characteristics were not significantly associated with upgrading.

Table V shows the univariate associations between upgrade at surgery and histological characteristics in 608 breast

Table IV. *Univariate models for upgrade risk of patients' clinical and radiological characteristics in 608 breast biopsies showing DCIS.*

Variable	No upgrade		Upgrade		OR	95%CI	*p*-Value
	n	%	n	%			
Age (years)							0.49
<50	64	66.0	33	34.0	1.45	0.88-2.39	
50-59	197	73.8	70	26.2	1.00		
60-69	123	69.9	53	30.1	1.21	0.80-1.85	
≥70	47	69.1	21	30.9	1.26	0.70-2.25	
1st degree family history of breast disease							0.24
No	229	72.7	86	27.3	1.00		
Yes	187	68.3	87	31.7	1.24	0.87-1.77	
Mammography indication							0.35
Screening program	258	68.5	70	31.5	1.00		
Investigation mammography	152	72.1	100	27.9	0.84	0.58-1.21	
Mammographic lesion							0.35
Microcalcifications-alone	382	72.1	148	27.9	1.00		
Other than microcalcifications alone	46	66.7	23	33.3	1.29	0.76-2.20	
Radiographic lesion's size							0.01
Measurable lesion	84	62.7	50	37.3	1.67	1.11-2.51	
Microcalcifications-only	337	73.7	120	26.3	1.00		
Biopsy instrument							0.003
CNB	94	61.4	59	38.6	1.80	1.22-2.65	
VAB	335	74.1	117	25.9	1.00		
Number of cores sampled							0.009
1-9	144	64.3	80	35.7	2.15	1.27-3.64	
10-15	119	69.6	52	30.4	1.69	0.97-2.95	
≥16	93	79.5	24	20.5	1.00		
Unknown	75	78.1	21	21.9	1.09	0.56-2.10	
Physical symptoms							<0.0001
No	375	75.2	124	24.9	1.00		
Yes	54	50.9	52	46.1	2.91	1.89-4.48	
Physical signs							0.05
No	412	71.7	163	28.3	1.00		
Yes	14	53.9	12	46.1	2.17	0.98-4.79	
Palpable mass							<0.0001
No	372	42.2	125	57.8	1.00		
Yes	27	74.9	37	25.1	4.08	2.39-6.97	
Unknown	32	68.1	15	31.9	1.40	0.73-2.66	
Body mass index (kg/m^2)							0.35
<25	226	68.7	103	31.3	1.00		
25.0-29.9	139	74.7	47	25.3	0.74	0.50-1.11	
≥30	55	70.5	23	29.5	0.92	0.54-1.57	

OR, Odds ratio.

biopsies in 604 women. The presence of necrosis in the biopsy was associated with a lower upgrade rate (OR=0.64, 95%CI: 0.43-0.93, p=0.02), while the presence of a cribriform architecture had a tendency towards a lower upgrade rate (OR=0.75, 95%CI: 0.53-1.06, p=0.10). All remaining characteristics were not significantly associated with upgrade.

Multivariate analysis. All characteristics displaying an univariate association with upgrade with a p-value ≤0.10 were included in a multivariate model. Thus, in the model we included: type of biopsy, number of sampled cores, physical symptoms, physical signs, palpable mass, lesion size on mammography, necrosis and cribriform architecture (Table VI). Among all these characteristics, only the presence of a palpable mass (OR=2.11, 95%CI: 0.99-4.47, p=0.05) and the presence of a cribriform architecture (OR=0.72, 95%CI: 0.49-1.06, p=0.09) had a tendency to associate with upgrade at surgery. All remaining characteristics were not significantly associated with upgrade on multivariate analyses.

Discussion

Identification of invasion in a malignant breast disease is crucial, since the surgical axillary approach will be different,

Table V. *Univariate models for upgrade risk of histological characteristics of biopsies showing DCIS and upgrading at surgery in 608 breast biopsies showing DCIS.*

Variable	No upgrade		Upgrade		OR	95%CI	*p*-Value
	n	%	n	%			
Presence of microcalcifications in biopsy							0.51
No	33	66.0	17	34.0	1.00		
Yes	371	72.6	140	27.4	0.73	0.40-1.36	
Nuclear grade							0.45
I	40	75.5	13	24.5	1.00		
II	206	72.0	80	28.0	1.20	0.61-2.35	
III	124	67.8	59	32.2	1.46	0.73-2.94	
Necrosis							0.02
No	102	63.8	58	32.2	1.00		
Yes	329	73.4	119	26.6	0.64	0.43-0.93	
Micropapillary architecture							0.84
No	332	71.1	135	28.9	1.00		
Yes	99	70.2	42	29.8	1.04	0.69-1.58	
Cribriform architecture							0.10
No	190	67.6	91	32.4	1.00		
Yes	240	73.6	86	26.4	0.75	0.53-1.06	
Papillary architecture							0.30
No	417	70.7	173	29.3	1.00		
Yes	14	82.4	3	17.6	0.52	0.15-1.82	
Comedocarcinoma architecture							0.17
No	372	72.0	145	28.0	1.00		
Yes	59	64.8	32	35.2	1.39	0.87-2.23	
Solid architecture							0.67
No	176	71.8	69	28.2	1.00		
Yes	255	70.3	108	29.7	1.08	0.76-1.55	
Estrogen receptors							0.54
Negative	89	67.4	43	32.6	1.14	0.75-1.73	
Positive	311	70.2	132	29.8	1.00		
Progesterone receptor							0.29
Negative	182	67.4	88	32.6	1.21	0.85-1.73	
Positive	218	71.5	87	28.5	1.00		

OR, Odds ratio.

and since the axillary status is one of the most important prognosis factors in breast cancer (9). Thus, the aim of the current study was to assess the upgrade rate at surgery in a tertiary breast cancer care Center, and to identify factors associated with the presence of invasion in percutaneous needle biopsies diagnosed with DCIS only. Results from the present study revealed an upgrading rate of 29.1%. Univariate analyses suggest that the use of CNB, a small number of sampled cores, the presence of physical symptoms, the presence of physical signs, a palpable mass, a measurable lesion on mammography, absence of necrosis and absence of a cribriform architecture were associated with a higher risk of upgrade. However, using multivariate analyses, no characteristic was identified to be statistically associated with the presence of invasiveness in women diagnosed with DCIS on percutaneous needle biopsy. The percutaneous image-guided needle biopsy approach is less traumatic for the patient and provides good results, but is associated with some disadvantages. Indeed, the diagnosis of many lesions is based on the size and/or on the invasiveness of the lesion, and these factors might be difficult to estimate using limited sampling (3-8). Furthermore, DCIS and invasive carcinoma are frequently concomitant, and the needle may simply miss the invasive region. Thus, previous studies report an upgrading rate ranging from 2%-49% (Table I). However, these previous studies all reported a variety of different factors associated with upgrade at surgery and, taken together, they mostly failed to identify common characteristics. Furthermore, some studies did not identify any factor associated with upgrading at surgery (12-15). Nevertheless, a few characteristics were more common across studies than others.

A measurable (mass image) lesion on mammography, compared with microcalcifications alone, has been associated with an increased risk of upgrading in a number of studies

Table VI. *Multivariate model of selected characteristics with DCIS upgrading rate at surgery.*

Variable	No upgrade		Upgrade		OR	95%CI	*p*-Value
	n	%	n	%			
Biopsy instrument							
CNB	91	62.8	54	37.2	0.86	0.46-4.61	0.64
VAB	319	74.0	112	26.0	1.00		
Number of cores sampled							
1-9	139	65.3	74	34.7	1.85	0.93-3.68	0.08
10-15	114	69.5	50	30.5	1.77	0.98-3.21	0.06
≥16	87	80.6	21	19.4	1.00		
Unknown	70	76.9	21	23.1	1.19	0.59-2.38	0.63
Physical symptoms							
No	359	74.8	121	26.2	1.00		
Yes	51	53.1	45	46.9	1.46	0.78-2.72	0.24
Physical signs							
No	397	71.8	156	28.2	1.00		
Yes	13	56.5	10	43.5	1.38	0.56-3.40	0.49
Palpable mass							
No	355	74.7	120	25.3	1.00		
Yes	26	45.6	31	54.4	2.11	0.99-4.47	0.05
Unknown	29	65.9	15	34.1	1.44	0.72-2.88	0.30
Radiographic lesion's size							
Measurable lesion	81	62.3	49	37.7	1.00		
Microcalcifications only	329	73.8	117	26.3	1.26	0.80-1.97	0.32
Necrosis							
No	98	66.2	50	33.8	1.00		
Yes	312	72.9	116	27.1	0.91	0.79-1.22	0.29
Cribriform architecture							
No	177	66.8	88	33.2	1.00		
Yes	233	74.9	78	25.1	0.72	0.49-1.06	0.09

and is suggestive of a more advanced lesion (16-23). The use of CNB has been demonstrated to sample a lesser amount of lesion than vacuum-assisted techniques. Since fewer tissues are sampled, the risk of missing an invasive focus is increased (16, 24-26). In the same way, sampling a smaller number of cores also increased the risk of upgrading at surgery (27, 28).

Since DCIS is, by definition, confined within the mammary ducts without invasion of the stroma, it usually does not form a palpable mass in the same way as an invasive tumor does (1). Thus, the presence of a palpable mass diagnosed as DCIS on percutaneous biopsy might be indicative of a more advanced disease. Indeed, a number of studies reported that a palpable mass concomitant with a DCIS diagnosis on percutaneous needle biopsy was associated with upgrading at surgery (16, 18, 20, 22, 29, 30). In the present study, even if not significant, the presence of a palpable mass had a tendency to be associated with DCIS upgrading at surgery.

DCIS is a member of a continuum starting with atypical ductal hyperplasia, going through DCIS, to end with invasive ductal carcinoma (31). Thus, a number of histopatological factors observed on DCIS might be associated with a higher risk of upgrading. Indeed, some studies identified a high DCIS grade as a risk factor for upgrading (16, 20, 24, 32-35). However, there is a controversy regarding the DCIS architecture associated with a higher risk of upgrading. Indeed, comedonecrosis has been associated with upgrading (24, 36-38), as well as the solid type (18). Beside these, a number of other pathological risk factors were observed in one or a few studies, preventing any conclusion on the matter (Table I). In the present study, presence of necrosis was significantly associated with lower upgrade rate, which is in contradiction with previous studies. Indeed, necrosis is usually indicative of hypoxia within a larger tumor, and is usually associated with a more advanced disease. For this reason, this statistical result must be validated with caution.

However, when all factors identified by univariate analyses were analyzed together in a multivariate model, no factor remained statistically associated with upgrading at surgery. The same conclusion was reached by four studies (12-15) in smaller numbers of patients. Furthermore, when considering all studies that identified at least one factor associated with upgrading (Table I), no factor is common to all studies.

The present study may suffer some limitations. Ours was a retrospective study in a clinical setting, and we had to work with the data available. A prospective study would allow us to assess characteristics that are not routinely assessed in clinical practice. On the other hand, we assessed characteristics that are more likely to be evaluated in any breast cancer care Center.

In conclusion, the present study was unable to identify a sub-group of patients diagnosed with a DCIS on percutaneous image-guided breast biopsy in whom an invasive cancer is more likely to be present. Thus, patients with DCIS-upgrading after surgery will still have to undergo a second surgery.

Conflicts of Interest

The Authors declare that there are no competing financial interests.

Acknowledgements

This work was funded by the Enfant-Jésus-St-Sacrement Hospitals Foundation. CD is a Junior Investigator of the Canadian Cancer Society (2011-700657).

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Received December 16, 2013
Revised January 13, 2014
Accepted January 14, 2014