Surgical Oncology 28 (2019) 190–194

Contents lists available at ScienceDirect

Surgical Oncology

journal homepage: www.elsevier.com/locate/suronc

Breast-conserving surgery for pure non-classic lobular carcinoma in situ: A single institution's experience

Daniel I. Hoffman[a], Paul J. Zhang[b], Julia Tchou[a,c,*]

[a] Department of Surgery, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, USA
[b] Department of Pathology and Laboratory Medicine, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, USA
[c] Rena Rowan Breast Center, Abramson Cancer Center, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, USA

ARTICLE INFO

Keywords:
Lobular carcinoma in situ
Pleomorphic LCIS
Breast-conserving surgery

ABSTRACT

Background: Non-classic lobular carcinoma in situ (NC-LCIS) is a rare pre-cancer breast lesion that warrants excision to exclude invasive disease. In patients pursuing breast-conserving surgery (BCS) for NC-LCIS, the need for wide surgical margins is controversial. We characterized the outcomes of women diagnosed with NC-LCIS at a large, academic medical center.

Methods: Female patients seen at our institution from 2008 to 2018 with pure NC-LCIS were retrospectively identified. Patients were excluded if NC-LCIS was diagnosed in the background of invasive cancer or ductal carcinoma in situ. Clinicopathologic and follow-up data were collected. Rates of upstage, re-excision, and recurrence were calculated.

Results: We identified 26 patients with pure NC-LCIS diagnosed on biopsy. 80.8% of patients initially pursued breast conservation, while 19.2% underwent mastectomy. At definitive surgery, 11.5% were upstaged. Among 19 non-upstaged patients that underwent BCS, 47.4% had at least one re-excision and 26.3% converted to mastectomy. In patients receiving BCS without completion mastectomy, 64.3% had final surgical margins that were negative for NC-LCIS, while 35.7% had positive or close margins. No recurrences in patients with negative margins were observed. One patient with positive margins developed a recurrence 8.3 years post-surgery, and one patient with close margins did 2.2 years post-surgery. All non-upstaged patients were alive at time of analysis with no evidence of invasive disease.

Conclusion: We presented the outcomes of one of the largest series of pure NC-LCIS. In patients with NC-LCIS pursuing breast conservation, re-excisions and completion mastectomies were common. However, when negative margins were achieved, prognosis was excellent.

1. Introduction

Pleomorphic lobular carcinoma in situ (P-LCIS) is a rare, high-grade, non-invasive breast neoplasm first described by Frost et al., in 1996 [1]. Its histologic appearance is characterized by dyscohesive cells that have a medium to large size, enlarged nuclei, and moderate to marked nuclear pleomorphism, often with prominent nucleoli and vacuolated cytoplasm [2]. Although P-LCIS was first only seen in the background of concomitant invasive lobular carcinoma (ILC), it was subsequently reported in isolation, suggesting P-LCIS as a precursor lesion that warrants excision to prevent local progression to ILC [3]. These finding are in contrast to classic lobular carcinoma in situ (C-LCIS), which is a well-established non-precursor diagnosis that renders increased overall risk of subsequent invasive breast cancers but does not generally warrant surgical excision [4,5].

Other non-classic LCIS variants – which have shared features with P-LCIS and are often referred to as P-LCIS – have been described with variable consistency in terminology, including florid LCIS (also known as LCIS with necrosis), pleomorphic apocrine LCIS, large cell LCIS, and LCIS with pleomorphic features [6]. Collectively referred to as non-classic LCIS (NC-LCIS), these variant lesions share several radiologic and histologic features with ductal carcinoma in situ (DCIS), including high-grade cytology, central necrosis, mammographic calcifications, and solid growth patterns. While such similarities have led to substantial rates of misdiagnoses between NC-LCIS and DCIS [7], the lack of membranous E-cadherin staining in NC-LCIS distinguishes the two lesions by immunohistochemistry [2]. Nonetheless, the similarities between the two have led to the suggestion that NC-LCIS should warrant the same treatment strategy as DCIS: surgical excision to wide margins with or without adjuvant radiation and endocrine

* Corresponding author. 3400 Civic Center Blvd, 10th Floor South Tower, Philadelphia, 19104, PA, USA.
E-mail address: julia.tchou@uphs.upenn.edu (J. Tchou).

https://doi.org/10.1016/j.suronc.2019.01.009
Received 30 October 2018; Received in revised form 31 December 2018; Accepted 27 January 2019

chemoprevention [8].

When NC-LCIS is diagnosed in isolation on core-needle biopsy, upstage rates to invasive carcinoma on definitive surgery have been reported as high as 65% [9], affirming the current recommendation by National Comprehensive Cancer Network that surgical excision is warranted after a biopsy diagnosis of NC-LCIS to rule out invasive disease [10]. However, NC-LCIS as a pure diagnosis is a rare event; the largest series reported 31 cases without subsequent upstaging to invasive cancer [11]. Accordingly, there is no expert consensus amongst breast surgeons on the surgical or medical management for patients with NC-LCIS without an invasive component [12]. In particular, the role of breast-conserving surgery (BCS) for NC-LCIS remains controversial: there is a lack of evidence guiding the need for re-excision when surgical margins are positive or close (< 1 mm) for NC-LCIS. Rate of recurrence based on retrospective data in patients with positive or close margins for NC-LCIS has ranged from 0 to 100% [13–15].

To better understand the impact of margin status in BCS for recurrence risk in non-classic LCIS variants and the viability of breast-conservation when negative margins are pursued, we aimed to retrospectively examine our institutional experience treating patients diagnosed with NC-LCIS on biopsy over a 10-year period. Specifically, we sought to (1) report the clinical, radiologic, and pathological features of patients diagnosed with NC-LCIS on biopsy, (2) characterize the surgical and medical management in patients with NC-LCIS, and (3) evaluate disease outcomes in patients undergoing BCS for NC-LCIS.

2. Materials and methods

Following approval from our Institutional Review Board, an electronic database query was conducted to identify patients treated at the University of Pennsylvania Health System (UPHS) between January 1, 2008 and March 1, 2018 with any mention of pleomorphism, necrosis, or variant morphology within a diagnosis of lobular carcinoma in situ in surgical pathology reports or clinical encounter notes. This search query yielded 165 unique patient records. Patients were included if they had a documented diagnosis of NC-LCIS by a breast pathologist on core-needle or excisional biopsy, including pleomorphic LCIS, LCIS with pleomorphic features (LCIS-PF), and florid LCIS (F-LCIS). Diagnoses of NC-LCIS were confirmed by documented presence of non-classic or variant LCIS histology in addition to negative membrane reactivity for E-cadherin stain by immunohistochemistry (IHC) to verify lobular differentiation. Patients were excluded if they had a personal history of ipsilateral invasive breast carcinoma (IBC), if NC-LCIS was diagnosed in the background of concomitant IBC or ductal carcinoma in situ (DCIS), or if no pathologic data was available in the EMR.

A comprehensive chart review was then conducted for 26 patients who met all selection criteria. Relevant clinical, radiologic, and pathologic data were collected. A complete surgical history was obtained, including upstage events to DCIS or IBC and all surgical margins with respect to NC-LCIS (close margins defined as less than 1 mm). Use and duration of adjuvant therapies (endocrine therapy and/or radiation), recurrence or progression events, most recent disease status by clinical or imaging follow-up, and follow-up times were collected. Rate of upstage was calculated. In patients with a final diagnosis of NC-LCIS (i.e. patients without a subsequent upstage), the following descriptive statistics were calculated: recurrence rate based on final margin status, rate of breast-conserving surgery (BCS), rate of re-excision for BCS, rate of completion mastectomy, and mean clinical follow-up time. Patients were considered to have undergone BCS if they opted for lumpectomy or if no further surgeries were performed after an excisional biopsy.

3. Results

3.1. Patient characteristics and clinicopathologic features

Twenty-six patients diagnosed with NC-LCIS without invasive carcinoma on biopsy were encountered at UPHS from January 1, 2008 to March 1, 2018. Relevant clinical, pathologic, and radiologic characteristics of the patient cohort are reported in Table 1. The cohort was mostly white with a median age of 54 years (range 40–70). Half were postmenopausal at time of diagnosis. No patients had a personal history of breast cancer, 41.7% (10/24) had a first-degree family history of breast cancer, and none were known BRCA1/2 carriers.

Table 1
Clinical, radiologic, and pathologic characteristics of 26 patients with non-classic lobular carcinoma in situ alone on biopsy.

Characteristic [no. evaluable cases]	*n*	%
Demographic and clinical information		
Caucasian race [26]	24	92.3
Mean age (range) [26]	54.2 (40–70)	
Postmenopausal [26]	13	50.0
History of hormone replacement therapy [26]	5	19.2
First-degree family history of breast carcinoma [24]	10	41.7
History of invasive breast carcinoma [26]	0	0.0
History of ipsilateral benign breast findings [6]	12	46.2
BRCA1 or BRCA2 mutation [9]	0	0.0
Radiologic findings		
Mammographic breast density [26]		
Extremely dense	4	15.4
Heterogeneously dense	12	46.2
Scattered fibroglandular densities	10	38.5
Almost entirely fat	0	0.0
Mode of first detection [26]		
Screening mammogram	24	92.3
Screening MRI	1	3.8
Palpation	1	3.8
Calcifications on mammogram [26]	22	84.6
MRI lesion characteristics [13]		
Non-mass enhancement	9	69.2
Irregular mass	3	23.1
No abnormal findings	1	7.7
Mean lesion size (range) on imaging in mm [11]	22.1 (7–53)	
Pathologic findings		
Histologic diagnosis [26]		
Pleomorphic LCIS	13	50.0
LCIS with pleomorphic features	10	38.5
Florid LCIS	3	11.5
Hormone receptor status [21]		
ER+/PR+	19	90.5
ER+/PR–	1	4.8
ER–/PR–	1	4.8

BMI body mass index, *LCIS* lobular carcinoma in situ, *ER* estrogen receptor, *PR* progesterone receptor.

Almost all patients (24/26) first presented with an abnormal screening mammogram, 22 of which had suspicious calcifications. One patient presented with a palpable mass in axillary breast tissue, and one patient presented with non-mass like enhancement on screening MRI.

Amongst the 26 patients with NC-LCIS, 13 patients were diagnosed with P-LCIS, 10 patients were diagnosed as LCIS with pleomorphic features, and 3 patients were diagnosed with florid LCIS.

3.2. Surgical management of NC-LCIS

Surgical decision-making following an initial diagnosis of NC-LCIS, summarized in Fig. 1, was heterogeneous. Subsequent to the first biopsy diagnosis of NC-LCIS (core-needle or excisional), 53.8% (14/26) of patients underwent lumpectomy, 34.6% (9/26) of patients underwent mastectomy (seven bilateral, two unilateral), and 3 patients who had undergone an excisional deferred further surgery. One patient receiving bilateral mastectomy revealed a final pathology of multifocal, bilateral P-LCIS with close (< 1 mm) margins.

There were three upstage events in the cohort, yielding a cumulative upstage rate of 11.5%. Amongst patients originally diagnosed with NC-LCIS on excisional biopsy ($n = 11$) the upstage rate was 9.1%; one patient upstaged to DCIS upon subsequent lumpectomy. In patients

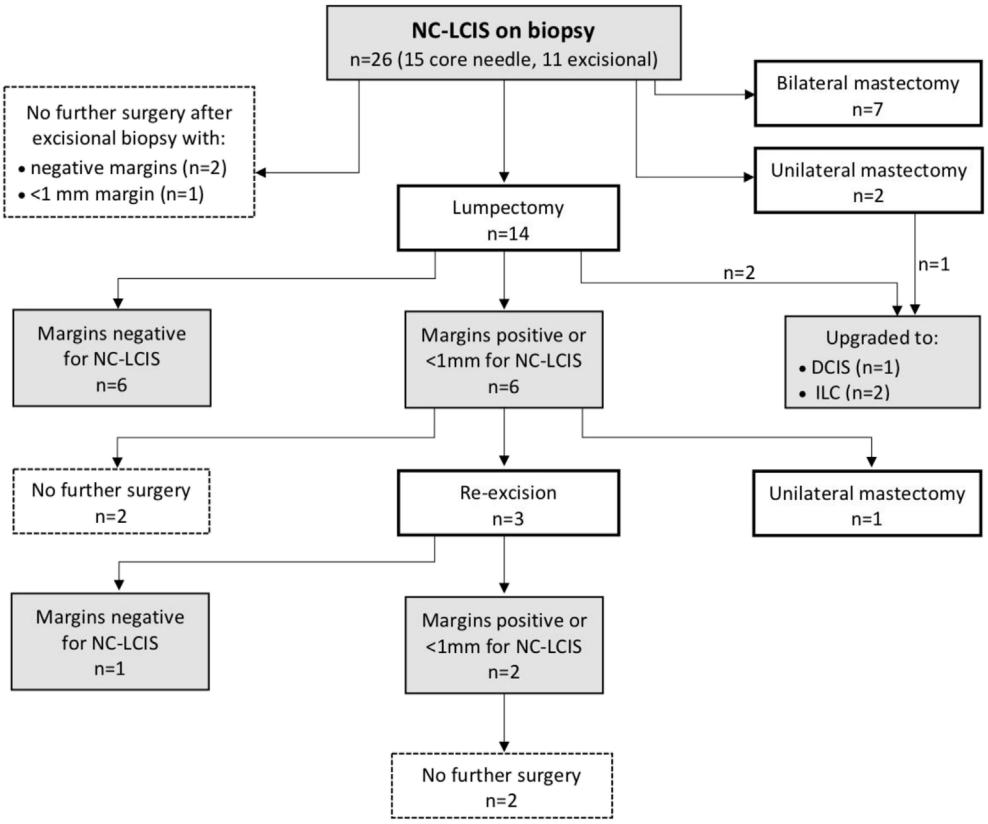

Fig. 1. Surgical management of 26 patients with non-classic lobular carcinoma in situ on excisional or core needle biopsy. Grey boxes represent pathology findings, bold-lined boxes represent surgical procedures, and dashed-lined boxes represent deferral of further surgery. *NC-LCIS* non-classic lobular carcinoma in situ, *DCIS* ductal carcinoma in situ, *ILC* invasive lobular carcinoma.

originally diagnosed with NC-LCIS on core needle biopsy (n = 15), the upstage rate was 13.3%; one patient upstaged to ILC upon subsequent lumpectomy, and one patient upstaged to ILC upon subsequent unilateral mastectomy.

Surgical decisions and final margin status in patients opting for BCS after biopsy are summarized in Table 2. Amongst 19 patients with a final pathology of NC-LCIS initially preferring BCS, 47.4% (9/19) had at least one re-excision and five converted to a completion mastectomy after an initial lumpectomy with margins positive or close for NC-LCIS. In the 14 patients who received BCS without conversion to completion mastectomy, 64.3% (9/14) had final surgical margins that were negative for NC-LCIS, while 35.7% (5/14) had close or positive margins.

Table 2
Surgical decisions and final margin status in patients with NC-LCIS undergoing breast-conserving surgery.

Measure (no. relevant cases)	*n*	%
Primary surgery[a] for NC-LCIS (n = 26)		
Lumpectomy	21	80.8
Unilateral mastectomy	2	7.7
Bilateral mastectomy	3	11.5
Completion mastectomies in patients with pure NC-LCIS undergoing BCS (n = 19)		
None	14	73.7
Unilateral mastectomy	1	5.3
Bilateral mastectomy	4	21.1
Number of re-excisions[a] in patients undergoing BCS (n = 19)		
0	10	52.6
1	8	42.1
2	1	5.3
Final margins in patients undergoing BCS without completion mastectomy (n = 14)		
Negative	9	64.3
Positive	1	7.1
Close (< 1 mm)	4	28.6

NC-LCIS non-classic lobular carcinoma in situ, *BCS* breast-conserving surgery.
[a] For patients in which biopsies were excisional, lumpectomy was considered the primary surgery.

3.3. Adjuvant therapy

In patients with a final pathology of NC-LCIS, 30.4% (7/23) completed Tamoxifen therapy, 8.7% (2/23) completed an aromatase inhibitor therapy, 43.5% (10/23) did not receive endocrine therapy, and one patient was recommended Tamoxifen but receipt was not known. 92.3% (13/14) of patients who received BCS without conversion to mastectomy were offered endocrine therapy, and 50.0% (7/14) chose to receive endocrine therapy. Two patients undergoing unilateral mastectomy received endocrine therapy for risk reduction.

91.3% (21/23) of patients with a final pathology of NC-LCIS did not undergo adjuvant radiation therapy. One patient received radiation, and one patient was recommended radiation but receipt was not known.

3.4. Disease outcomes

In patients with a final pathology of NC-LCIS, 91.3% (21/23) had no evidence of local disease recurrence as assessed by most recent mammogram/MRI or clinical monitoring by a surgical or medical oncologist, mean follow-up time 4.5 years (range 20 days–10.5 years). Aggregating both mastectomy and lumpectomy outcomes, local recurrence rates were 0.0% (0/17) in patients with negative margins, 100.0% (1/1) in patients with positive margins, and 20.0% (1/5) in patients with close margins (Table 3).

Disease outcomes specific to the 14 patients undergoing BCS for pure NC-LCIS without completion mastectomy are summarized in Table 4. Two patients had local recurrences of NC-LCIS adjacent to the original surgical cavity (Study IDs #008 and #015). Patient #008 had final margins that were < 1 mm with respect to NC-LCIS, did not receive any adjuvant therapy, and presented with a recurrence of NC-LCIS 22.2 months after surgery. The recurrence was detected on screening MRI and was excised with lumpectomy, which again resulted in close margins with respect to NC-LCIS. As of 25 months after surgery for the

Table 3
Disease outcomes in 23 patients with final pathology of NC-LCIS based on surgical margin status.

Outcome	Final margin status with respect to NC-LCIS					
	Negative (n = 17)		Positive (n = 1)		< 1 mm (n = 5)	
	n	%	n	%	n	%
No evidence of disease[a]	17	100.0	0	0.0	4	80.0
Local recurrence	0	0.0	1	100.0	1	20.0
Progression to IBC	0	0.0	0	0.0	0	0.0

NC-LCIS non-classic lobular carcinoma in situ, *IBC* invasive breast carcinoma.
[a] No evidence of disease by either imaging or clinical modalities, mean follow-up time 4.5 years.

recurrence, Patient #008 has no evidence of disease by imaging or clinical modalities.

Patient #015 had final margins that were positive for NC-LCIS and completed 5 years of adjuvant Tamoxifen therapy. A local recurrence of NC-LCIS was detected 8.3 years after the final surgery on a screening mammogram, which was treated with lumpectomy and adjuvant radiation. As of 23 months after surgery for the local recurrence, Patient #015 has no evidence of disease by imaging or clinical modalities.

All 23 patients with a final pathology of NC-LCIS were alive with no evidence of invasive breast carcinoma by imaging or clinical modalities at time of analysis, mean follow-up time 4.5 years (range 20 days–10.5 years).

4. Discussion

In this institutional report, we presented one of the largest series on the natural history of NC-LCIS variants not associated with an invasive component. Identifying only 26 cases of NC-LCIS without concomitant DCIS or invasive cancer on biopsy over a 10-year period, this study indeed confirmed the rarity of the diagnosis. The rarity of a pure NC-LCIS lesion, as well as inconsistent diagnostic criteria, has precluded evidence-based recommendations on the surgical and medical management of both pleomorphic and florid variants. However, the incidence of pure NC-LCIS is likely higher than previously believed, as its morphologic and radiologic similarities to DCIS has led to under-diagnosis; Sullivan and colleagues have suggested that as much as 10% of DCIS biopsies could represent misdiagnosed NC-LCIS variants [7]. While triggering DCIS management for ambiguous cases that have both ductal and lobular features may not radically alter surgical strategies for NC-LCIS, the benefit of radiation therapy and medical adjuvants for NC-LCIS is not known; thus, misdiagnosis of NC-LCIS variants as DCIS may be leading to substantial amounts of inappropriate treatment. Thus, disambiguation between DCIS and NC-LCIS is needed in order to better understand the natural history of variant NC-LCIS to formulate evidence-based recommendations from larger, multi-institutional cohorts. Increasing awareness of the NC-LCIS diagnostic designation, as well as consistent use of E-Cadherin immunohistochemical stains will likely ameliorate this discrepancy.

With an overall upstage rate of 11.5%, our results suggested that excision to rule out invasive carcinoma in patients with pure NC-LCIS variants identified on biopsy is warranted. Once invasive cancer or DCIS was ruled out, however, we demonstrated that NC-LCIS diagnoses result in highly variable surgical pathways, in part due to individual patient preference regarding breast conservation. Perhaps because of the uncertainty surrounding the lack of evidence-based recommendations for NC-LCIS, five patients in our study immediately opted for mastectomy following a core-needle biopsy diagnosis. Given the substantial rate of re-excision in patients undergoing BCS in our study, as well cases of progression to invasive carcinoma years after lumpectomy reported in other studies [15,16], the definitive nature of mastectomy may appeal to many patients with NC- LCIS so long as treatment guidelines remain nebulous. However, the option for contralateral prophylactic mastectomy adds complexity to the decision, relying on consideration of other predisposing risk factors and individual preferences. Three patients in our study underwent bilateral mastectomy immediately after core-needle biopsy, two of which had a first-degree family history of breast cancer. Therefore, in patients with additional breast cancer risk factors, such as family history, personal history of classic LCIS, or BRCA mutations, bilateral mastectomy may be an appropriate strategy for simultaneous treatment and risk reduction. A patient in our study whose bilateral mastectomy specimens yielded multifocal, bilateral NC-LCIS highlights the potential benefit of this surgical strategy.

For patients pursuing BCS for pure NC-LCIS at our institution, the surgical courses were heterogenous. Of the 19 patients with a final pathology of pure NC-LCIS that pursued BCS, only 8 achieved negative margins with a single lumpectomy, emphasizing that BCS for NC-LCIS is not without challenge. Over half had at least one re-excision, and roughly 25% eventually converted to completion mastectomy. It is therefore crucial for patients preferring BCS to understand the substantial likelihood for re-excision and the modest likelihood for completion mastectomy before undergoing lumpectomy, assuming negative margins are to be pursued.

Our study did suggest a potential benefit of negative margins for NC-LCIS excisions. Although the cohort size was small, the only recurrences seen in our cohort were in margin-positive or close-margin

Table 4
Characteristics and disease outcomes of 14 patients completing breast-conserving surgery for pure non-classic lobular carcinoma in situ.

ID	NC-LCIS Variant	ER/PR status	Surgeries	Adjuvant Therapy	Final margins	Local recurrence?	Time to recurrence or follow-up (months)
001	LCIS-PF	ER + /PR +	Lumpectomy	–	Negative	No	1.1
002	P-LCIS	ER + /PR +	Lumpectomy	–	Negative	No	62.8
006	P-LCIS	ER + /PR +	Lumpectomy + re-excision	–	Negative	No	29.4
008	P-LCIS	ER + /PR-	Lumpectomy + re-excision	–	Close	Yes	22.2
009	P-LCIS	ER-/PR-	Lumpectomy	–	Negative	No	11.7
010	P-LCIS	NA	Lumpectomy	CP	Negative	No	82.0
012	F-LCIS	ER + /PR +	Lumpectomy	CP	Negative	No	7.8
015	F-LCIS	ER + /PR +	Lumpectomy + 2 re-excisions	CP	Positive	Yes	99.2
016	F-LCIS	ER + /PR +	Lumpectomy	N/A	Close	No	3.6
018	LCIS-PF	N/A	Lumpectomy + re-excision	–	Negative	No	0.7
021	LCIS-PF	N/A	Lumpectomy	CP	Close	No	124.7
022	P-LCIS	ER + /PR +	Lumpectomy	CP + RT	Negative	No	54.1
023	LCIS-PF	ER + /PR +	Lumpectomy	CP	Close	No	19.9
026	P-LCIS	ER + /PR +	Lumpectomy	CP	Negative	No	51.0

ER estrogen receptor, *PR* progesterone receptor, *CP* chemoprevention, *RT* radiation therapy, *LCIS-PF* lobular carcinoma in situ with pleomorphic features, *P-LCIS* pleomorphic lobular carcinoma in situ, *F-LCIS* florid lobular carcinoma in situ.

Table 5
Post-lumpectomy[a] recurrences rates for pure NC-LCIS by final margin status.

Study	Final margin status with respect to NC-LCIS			Overall
	Negative	< 1 mm	Positive	
Sneige et al. [3]	0/4	1/1	0/0	1/5
Downs-Kelly et al. [14]	0/13	0/7	1/6	1/26
Khoury et al. [11]	2/20	–	4/9	6/29
Flanagan al [13].	0/7	0/4	0/0	0/11
Fasola et al. [17]	0/9	–	0/2	0/11
De Brot et al. [15]	0/2	3/3	1/2	4/7
Desai et al. [16]	1/10	0/0	1/1	2/11
Savage et al. [18]	0/11	–	0/1	0/12
Current study	0/9	1/4	1/1	2/14
Pooled	**3/85 (3.5%)**	**5/19 (26.3%)**	**8/22 (36.4%)**	**16/126 (12.7%)**

Dashs represent studies that did not include a close margin category.
NC-LCIS non-classic lobular carcinoma in situ.
[a] Patients who underwent completion mastectomies were excluded from analysis.

(defined as < 1 mm) surgeries. Our results are similar to other series reporting post-lumpectomy outcomes for pure NC-LCIS cases based on surgical margin status, summarized in Table 5. Pooling all available series including our own, outcomes for margin-negative lumpectomies were quite good, with a recurrence rate of 3.5% (3/85). While Flanagan and colleagues cautioned against aggressive pursuit of negative surgical margins in their 2015 report, our data in conjunction with the most recent series suggest a role for consideration of negative margins. However, further multi-institutional, prospective data will be needed to examine if there is a statistically significant association between recurrence risk and definitive margin status.

The question of appropriate adjuvant therapies for patients with pure NC-LCIS remains a challenge. As future recurrence or progression is a concern for patients undergoing lumpectomy for NC- LCIS, this subgroup may benefit from adjuvant radiation and/or endocrine therapy. In our experience, these patients received inconsistent medical management. Of the 14 patients with pure NC-LCIS treated with lumpectomy alone, six received no adjuvants, six received endocrine therapy, one received both endocrine therapy and radiation, and one patient's receipt was not known. Such limited outcome data due to the rarity of the diagnosis precludes any interpretation as to the efficacy of endocrine or radiation therapy, but highlights the need for prospective registry studies to address the potential under- or over-treatment received by these patients.

In summary, our series supports therapeutic excision of pure NC-LCIS to clear margins as an important strategy to exclude a cancer diagnosis and prevent local recurrence. Breast-conserving surgery is a safe and reasonable treatment strategy for NC-LCIS; however, appropriate counseling is critical, as re-excisions and completion mastectomies are commonly performed when negative margins are achieved.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Disclosures

The authors do not have any relevant financial relationships with any commercial interest that pertains to the content of this manuscript.

Acknowledgements

D.I.H. was supported by the Agnew Surgical Society's first year fellowship from the Department of Surgery at the University of Pennsylvania.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.suronc.2019.01.009.

References

[1] A. Frost, T. Tsangaris, S. Silverberg, Pleomorphic lobular carcinoma in situ, Pathol. Case Rev. 1 (1) (1996) 27–31, https://doi.org/10.1097/00132583-199605000-00009.
[2] Y.-Y. Chen, E.-S.S. Hwang, R. Roy, et al., Genetic and phenotypic characteristics of pleomorphic lobular carcinoma in situ of the breast, Am. J. Surg. Pathol. 33 (11) (2009) 1683–1694, https://doi.org/10.1097/PAS.0b013e3181b18a89.
[3] N. Sneige, J. Wang, B.A. Baker, S. Krishnamurthy, L.P. Middleton, Clinical, histopathologic, and biologic features of pleomorphic lobular (ductal-lobular) carcinoma in situ of the breast: a report of 24 cases, Mod. Pathol. 15 (10) (2002) 1044–1050, https://doi.org/10.1097/01.MP.0000027624.08159.19.
[4] C.I. Li, K.E. Malone, B.S. Saltzman, J.R. Daling, Risk of invasive breast carcinoma among women diagnosed with ductal carcinoma in situ and lobular carcinoma in situ, 1988-2001, Cancer 106 (10) (2006) 2104–2112, https://doi.org/10.1002/cncr.21864.
[5] C.S. Nagi, J.E. O'Donnell, M. Tismenetsky, I.J. Bleiweiss, S.M. Jaffer, Lobular neoplasia on core needle biopsy does not require excision, Cancer 112 (10) (2008) 2152–2158, https://doi.org/10.1002/cncr.23415.
[6] F. Nakhlis, B.T. Harrison, T.A. King. Non-classic LCIS versus Classic LCIS versus Atypical Hyperplasia: Should Management Be the Same? https://doi.org/10.1007/s40137-018-0201-1.
[7] M.E. Sullivan, S.A. Khan, Y. Sullu, C. Schiller, B. Susnik, Lobular carcinoma in situ variants in breast cores: potential for misdiagnosis, upgrade rates at surgical excision, and practical implications, Arch. Pathol. Lab Med. 134 (7) (2010) 1024–1028, https://doi.org/10.1043/2009-0300-OA.1.
[8] A. Pieri, J. Harvey, N. Bundred, Pleomorphic lobular carcinoma in situ of the breast: can the evidence guide practice? World J. Clin. Oncol. 5 (3) (2014) 546–553, https://doi.org/10.5306/wjco.v5.i3.546.
[9] T. Guo, Y. Wang, N. Shapiro, S. Fineberg, Pleomorphic lobular carcinoma in situ diagnosed by breast core biopsy: clinicopathologic features and correlation with subsequent excision, Clin. Breast Canc. (October 2017), https://doi.org/10.1016/j.clbc.2017.10.004.
[10] National Comprehensive Cancer Network, NCCN Clinical Practice Guidelines in Oncology: Breast Cancer, NCCN.org, 2018.
[11] T. Khoury, R.G. Karabakhtsian, D. Mattson, et al., Pleomorphic lobular carcinoma *in situ* of the breast: clinicopathological review of 47 cases, Histopathology 64 (7) (2014) 981–993, https://doi.org/10.1111/his.12353.
[12] S.L. Blair, D.K. Emerson, S. Kulkarni, E.S. Hwang, V. Malcarne, D.W. Ollila, Breast surgeon's survey: no consensus for surgical treatment of pleomorphic lobular carcinoma in situ, Breast J. 19 (1) (2013) 116–118, https://doi.org/10.1111/tbj.12062.
[13] M.R. Flanagan, M.H. Rendi, K.E. Calhoun, B.O. Anderson, S.H. Javid, Pleomorphic lobular carcinoma in situ: radiologic–pathologic features and clinical management, Ann. Surg. Oncol. 22 (13) (2015) 4263–4269, https://doi.org/10.1245/s10434-015-4552-x.
[14] E. Downs-Kelly, D. Bell, G.H. Perkins, N. Sneige, L.P. Middleton, Clinical implications of margin involvement by pleomorphic lobular carcinoma in situ, Arch. Pathol. Lab Med. 135 (6) (2011) 737–743, https://doi.org/10.1043/2010-0204-OA.1.
[15] M. De Brot, S. Koslow Mautner, S. Muhsen, et al., Pleomorphic lobular carcinoma in situ of the breast: a single institution experience with clinical follow-up and centralized pathology review, Breast Canc. Res. Treat. 165 (2) (2017) 411–420, https://doi.org/10.1007/s10549-017-4334-1.
[16] A.A. Desai, R.E. Jimenez, T.L. Hoskin, C.N. Day, J.C. Boughey, T.J. Hieken, Treatment outcomes for pleomorphic lobular carcinoma in situ of the breast, Ann. Surg. Oncol. (June 2018), https://doi.org/10.1245/s10434-018-6591-6.
[17] C.E. Fasola, J.J. Chen, K.C. Jensen, K.H. Allison, K.C. Horst, Characteristics and clinical outcomes of pleomorphic lobular carcinoma in situ of the breast, Breast J. 24 (1) (2018) 66–69, https://doi.org/10.1111/tbj.12843.
[18] J.L. Savage, D.O. Jeffries, M. Noroozian, M.S. Sabel, J.M. Jorns, M.A. Helvie, Pleomorphic lobular carcinoma in situ: imaging features, upgrade rate, and clinical outcomes, Am. J. Roentgenol. 211 (2) (2018) 462–467, https://doi.org/10.2214/AJR.17.19088.