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Systematic review of breast cancer related lymphoedema: making a balanced decision to perform an axillary clearance

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Abstract

Aim: **Breast cancer-related lymphoedema (BCRL) is a disabling complication developing after breast cancer treatment in a proportion of patients. Its impact on quality of life becomes more substantial as survival after breast cancer diagnosis increases. The incidence of BCRL following breast cancer treatment varies due to a lack of uniform definition and measurement criteria. This review aims to determine the prevalence of BCRL following axillary lymph node dissection (ALND) as a benchmark to be used in a risk-benefit medical decision whether to proceed with ALND or not. The risk of leaving unresected non-sentinel metastatic lymph nodes with a presumed inherent risk of local recurrence will be balanced against the risk of BCRL following a potentially unnecessary ALND.**

Methods: **Pubmed and Embase databases were searched for all publications on BCRL in order to estimate its incidence and to decide on the most appropriate measurement method to use in clinical practice.**

Results: **51 articles were identified on BCRL incidence and measurement technique. Most studies measured BCRL based on differences in arm circumference (n = 18) or by self-reported symptoms (n = 18). The weighted average of BCRL incidence following ALND measured by self-report and circumference method was 28% and 16%, respectively.**

Conclusion: **The importance of ALND and irradiation as part of the treatment of operable breast carcinoma is well established, but its morbidity is less well documented. We argue self-report as the most appropriate method to establish a diagnosis of BCRL. Therefore a 28% risk of finding non-sentinel lymph node metastases in a completion ALND will be regarded as the cut-off in a medical decision to proceed with ALND.**

Key words: **Breast cancer, lymphoedema, axillary lymph node dissection, definition, incidence, prevalence.**

Introduction

In women, breast cancer causes up to 458 000 deaths each year, worldwide (http://www.who.int/cancer/detection/breastcancer). Notwithstanding, since the mid-1970s, survival from breast cancer increases in particular in women with early stage breast cancer. This improvement is attributed to screening and improved treatment of breast cancer (Peto et al., 2012). Some of these women will potentially face treatment related side-effects (Geller et al., 2003; Ridner et al., 2007). The most disabling side-effect with long term impact on quality on life is the development of lymphedema (Petrek et al., 1998; Cheifetz et al., 2010; Cidon et al., 2011; Fu MR et al., 2012). Several studies have examined the incidence of breast cancer-related lymphedema (BCRL) in women treated for breast cancer (Clark et al., 2005; Paskett et al.,2007; Hayes et al., 2008; MacLean et al., 2008; Park et al., 2008). The reported incidence of BCRL varies between 0% and 73% mainly due to differences in measurement techniques and lack of a uniform diagnostic criterion (Erickson et al., 2001). In clinical practice BCRL is diagnosed by objective measurements or by a validated self-administered questionnaire (Cidon et al., 2011). Volume displacement measurement technique is considered as the gold standard in assessing BCRL. However this technique can be cumbersome in a busy clinical setting. Most series on BCRL therefore have used circumferential measurements of the upper arm and forearm to diagnose oedema. Compared to the water displacement method, arm circumference measurements indicate where the swelling is most pronounced (Tengrup et al., 2000).

Risk factors contributing to the development of BCRL include axillary lymph node dissection (ALND), radiation therapy, high body mass index, cellulites and advanced age (Park et al., 2008; Clark et al., 2005; Hayes et al., 2008; Soran et al., 2006). The most important risk factors for BCRL are ALND and radiation therapy of axilla (Petrek et al., 2001; Erickson et al., 2001; Armer et al., 2003; Mortimer et al., 1996). Whilst 23-58% of women with breast cancer and radiotherapy of the axilla developed BCRL, only 5-21% of the patients without postoperative irradiation developed lymphedema (Erickson et al., 2001).

Over the past years, breast cancer surgery has become less radical. The widely accepted use of the sentinel lymph node biopsy (SLNB) (Mansel et al., 2006; McLaughlin et al., 2008; Mathew et al., 2006) was a major step forward in the prevention of BCRL. Studies reporting on the performance of SLNB revealed that still in 50% of the women undergoing an ALND after a positive SLNB, the sentinel lymph node (SLN) was the only affected lymph node (Kim et al., 2006). Moreover two randomized trials showed no improvement in disease-free and overall survival related to performing additional ALND versus no ALND in women with SLN positive early stage breast cancer (Giuliano et al., 2011; Galimberti et al., 2011). Whereas the wide acceptance and implementation of the SLNB in clinical practice took only a few years, it is not clear to what extent the results of the Giuliano trial will cause a paradigm shift in the surgical management of the axilla. The answer to this will depend on the impact that unresected axillary lymph nodes will have on local recurrence rates. Nomograms have been developed calculating the risk of metastatic non-SLN to assist decision making with regard to perform an ALND. The interpretation of this risk however is subdue to a sense of numeracy (quantitative literacy) (de Jonge et al., 2009). Moreover this risk figure stands on its own and refers anywhere to a risk-benefit balancing. Clearly a safe strategy for the management of the axilla following a positive SLNB is missing. Until a save strategy following a positive SLND has been found it is a valid approach to balance the risk of unresected metastatic non-SLN and so the risk of local recurrence against the risk of developing BCRL.

Therefore the aim of this systematic review is to determine the incidence of BCRL following ALND using the measurement method most appropriate in clinical practice. This incidence will be used as a benchmark in a risk-benefit medical decision whether or not to proceed with ALND. In the risk-benefit analysis, the risk of leaving unresected metastatic non-SLNs with a presumed inherent risk of local recurrence will be balanced against this risk of BCRL following a potentially unnecessary ALND.

Methods

Types of studies

All studies reporting incidence of BCRL with a follow-up of at least 12 months were included. A broad search strategy without restriction of search criteria was used. Prospective and retrospective studies were included. In retrospective studies the development of BCRL was traced by chart review and/or a questionnaire. Studies examining the preventive effect of an intervention on the development of BCRL were excluded. In case of a randomized controlled trial, only data from the control arm was retained.

Subjects

Patients undergoing ALND for breast cancer were included. No restrictions were retained regarding age, menopausal status, type of breast surgery.

Types of outcome measures

Studies reporting incidence and prevalence of BCRL assessed objectively with water displacement method, circumference measurements, bioelectrical impedance analyses and opto-electronic volumeter (perometer) and subjectively with self-reports were included.

Search strategies for articles on BCRL

Articles were traced using a comprehensive search of several electronic databases, including Pubmed and Embase and published from January 1990 until 2013. The MeSH headings and key words used in this search included: ‘breast neoplasm’, ‘breast tumour’, ‘breast cancer, ‘sentinel lymph node’, ‘axillary lymph node dissection’, ‘lymphedema’ and ‘surgery’. The terms ‘prevalence’, ‘incidence’ and ‘epidemiology’ were also included. Only trials that included incidence of BCRL were selected and analyzed further. Studies that did not mention how lymphedema was defined were excluded. Only full text articles written in English were selected. Two reviewers (MG and EDJ) independently performed the selection of articles based on the content of the abstract. See appendix for the extensive search strategy.

Data extraction and analysis

Studies were divided according to the measurement method into the following categories, 1) arm circumference, 2) water displacement method, 3) self-reported arm symptoms, 4) bioelectrical impedance analysis, 5) optoelectronic volumetry. The incidence of BCRL specific to each method was presented as the weighted mean of all incidence rates reported by the different studies. A policy concerning completion ALND after a positive SLNB will be formulated based on the incidence of BCRL for the measurement method that is most useful in clinical practice.

Results

The literature search as described yielded a total of 466 reports (179 Pubmed - 287 Embase). Further selection by title identified 223 articles. Reports were screened on the relevance of abstract content by two reviewers. This resulted in 100 full text articles. From the reference list, new articles were selected and included if they met the inclusion criteria. Finally, we selected a total of 51articles that described both the method of measurement of BCRL and the corresponding incidence (Fig. 1).

Most studies measured BCRL based on differences in arm circumference and self-report of various arm symptoms. A minority of reports used water displacement method, optoelectronic volumetry and bioelectrical impedance analysis as measurement method for lymphoedema (Table I). Hence, the further discussion is based on the analyses of the incidence of BCRL measured by arm circumference and self-reports. A second reason is that these two methods are used in clinical practice.

There is a wide range of incidences of BCRL (5 – 39%) between the different studies (Table I). The incidence of BCRL varied not only according to the measurement method for lymphedema, but varied also according to patient characteristics such as type of surgery and adjuvant treatment, the length of follow-up period, and the interval between ALND and the measurement of BCRL. All studies included had a follow-up of at least 12 months. Only four studies had a follow-up of less than 24 months.

The overall weighted average incidence of BCRL was 16% (5% up to 33%) for the arm circumference method and 28% (11% up to 39%) for the self-report method (Table I, Fig. 2). Tables II and III summarize a total of 36 reports on BCRL incidence based on arm circumference and self-report respectively, following treatment for breast cancer including ALND. The studies are a mixture of retro- and prospective studies. Most studies were published after the year 2000 and included almost nineteen thousand patients.

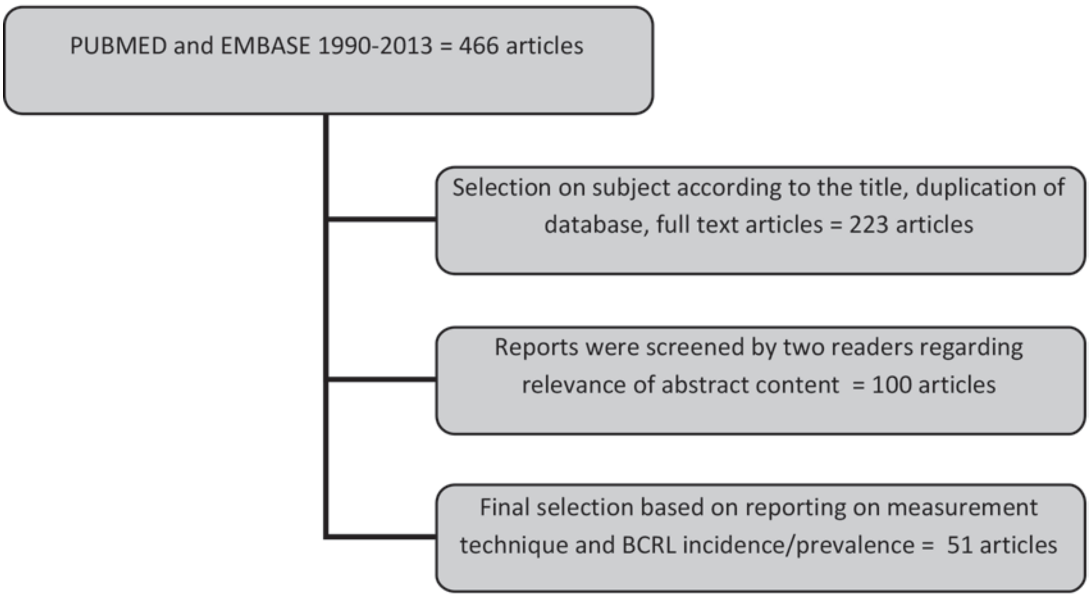

Fig. 1. — Overview of the systematic literature search concerning incidence and prevalence of BCRL

Measurement method	Number of articles	Incidence weighted average (range)
Circumference	18	16% (5-33%)
Self-report	18	28% (11-39%)
Water displacement	10	17% (10-54%)
Perometry	3	18% (10-45%)
Bio-impedance	2	22% (11-33%)

Table I. — The number of articles about incidence of BCRL for each measurement method.

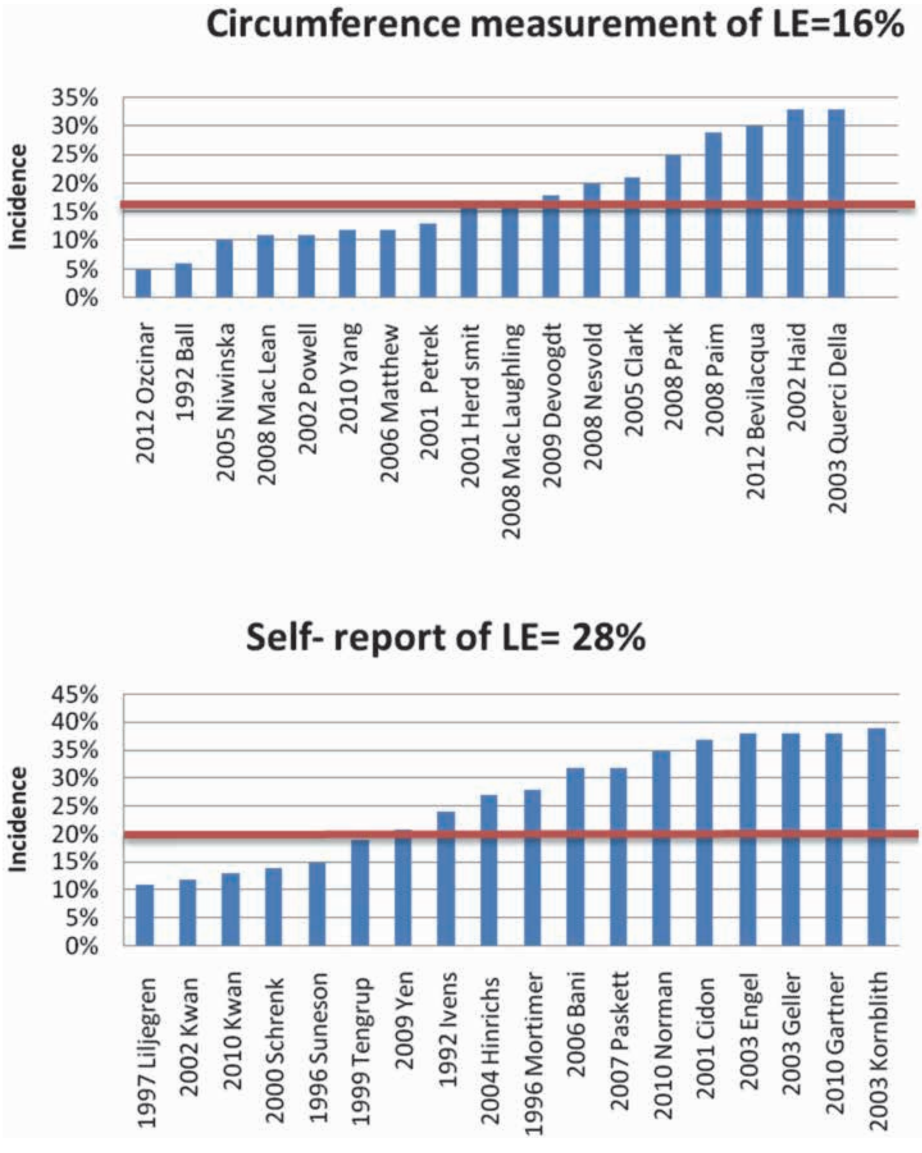

Fig. 2. — Incidence of BCRL assessed by arm circumference measurements and by self-report for the different studies with more than 12 months of follow-up and the weighted mean incidence.

Discussion

Arm and/or hand lymphoedema is a debilitating side-effect from breast cancer treatment with long-term and chronic negative impact on quality of life. The studies of BCRL are relatively recent as initial reports only date from the early 2000's. The literature on incidence of BCRL remains controversial. A significant number of studies are retrospective chart reviews, have small sample sizes, are single institutional, and the definition of BCRL and/or its measurement varies from study to study (Soran et al., 2006). Tsai et al. (2009) conducted a meta-analysis to examine the association between treatment factors and lymphoedema secondary to breast cancer. The risk ratio of arm lymphoedema was increased after mastectomy when compared with lumpectomy, axillary dissection compared with no axillary dissection, axillary dissection compared with sentinel node biopsy, radiation therapy, and positive axillary nodes.

The literature on BCRL shows a number of measurement techniques each with its advantages and disadvantages as well as its own incidence of BCRL (Table I). Frequently used techniques include circumferential measures at various points along the arm, volumetric measurements using immersion of the limb in water, skin tonometry, or self-report of BCRL. The most common reported methods to measure BCRL were arm circumference measurements and self-report (both 18 studies). Eight of 18 studies defined BCRL as a difference of ≥ 2 cm in arm circumference at a corresponding point between the affected and non-affected limb. Although circumferences appear to be a simple method it is difficult to obtain reproducible measurements (Armer et al., 2009). Self-report of BCRL may be obtained by using a screening questionnaire for lymphoedema-related symptoms, such as heaviness, swelling or numbness. Such a questionnaire needs to be well-structured and tested on validity and has to be presented by a trained interviewer (Norman et al., 2010). In some of these self-report trials patients also underwent an objective arm measurement showing a good correlation between measured lymphoedema and subjective complaints on the questionnaire (Tengrup et al., 2000; Schrenk et al., 2000; Kwan et al., 2002). Penha et al. (2011) studied the incidence of BCRL in breast cancer survivors by subjective and objective methods and concluded that self-report was significantly more accurate in diagnosing clinically relevant BCRL (sensitivity 91%, specificity 89%) than the water displacement method (sensitivity 82%, specificity 73%).

The water displacement method as next most common reported method (10 trials) detected BCRL in 17% of patients (range 10-54%). This method is a cumbersome way of measurement. Moreover it does not provide data on localization of the lymphedema or the shape of the extremity. Perometry was developed to meet the need for a quick, hygienic, and accurate method of limb volume measurement. More and above the fact that it is expensive, the method is not suitable for patients with movement restriction of the arm. Three studies measured BCRL using perometry and reported a BCRL incidence ranging between 10% and 45%. Finally the bio-impedance method uses the impedance of the extracellular fluid for each limb calculated according to the manufacturer's software to diagnose lymphoedema. Participants were diagnosed with BCRL when the impedance ratio was more than three standard deviations more than normative data (Hayes et al., 2008). This method is very accurate and reliable and has been successfully used in the estimation of unilateral lymphedema. The method is expensive and not suitable for patients with a pacemaker. Two trials reported on bio-impedance as a measuring tool for BCRL and found a mean incidence for BCRL of 22% (11% and 33%).

It is obvious from this review that the incidence of BCRL differs depending on the measurement method used. Armer et al. (2009) however demonstrated a BCRL incidence at 30 months follow-up varying between 41% and 91% according to four diagnostic criteria: i) 2 cm circumferential change at any measured location; ii) 200 ml perometry limb volume change; iii) 10% perometry limb volume change; iv) self-report of limb heaviness and swelling in the past year. A 2cm circumferential change was the most liberal diagnostic criterion (incidence 91%) and self report the most conservative (incidence 41%).

Consensus on the preferred method of measuring lymphoedema is missing as reproducibility of the techniques is inconsistent. In defining BCRL, the availability of both baseline measurements and of contralateral arm measurements are necessary. In this way asymmetric measurements found postoperatively may be attributed to baseline arm differences rather than the development of BCRL (Yen et al., 2009; Mc Lauglin et al., 2008). It is recommended that BCRL assessment should begin preoperatively with assessment of both arms and should continue at regular intervals (Park et al., 2008).

Furthermore it is remarkable that the mean incidence rates of the two most commonly used measurement methods differ notable: 16% (range 5-33%) for arm circumference and 28% (range 11-39%) for self-report. Some authors suggested that self-reporting signs and symptoms might not be as good as using an objective definition of BCRL like a 2 cm increase in arm circumference (Engel et al., 2003). Others have demonstrated that self-reported differences in arm size and related symptoms could be an early indication of BCRL preceding objective signs of lymphedema by several weeks or even months (Ridner et al., 2007; Norman et al., 2009). Moreover Armer et al. (2003) demonstrated self-reported arm symptoms such as 'heaviness in past year' and 'swelling now' to be highly predictive of a circumferential limb difference of ≥ 2 cm. Objective measures may not be sensitive enough to pick up subtle changes that cause symptoms or may be measuring effects that cause no symptoms (Edwards et al., 2000; Tengrup et al., 2000; Geller et al., 2003). That subjective symptoms do not always correlate with objective lymphoedema could be explained by existing sensory changes in the treated arm due to neurological damage caused by axillary surgery or radiation treatment in absence of swelling of the arm (Ridner et al., 2007; Penha et al., 2011).

Patient's appreciation of symptoms related to lymphoedema is pivotal in diagnosing BCRL as they themselves can judge the impact of BCRL on quality of life more accurately than anyone else. In our opinion this argument is decisive in taking self-report as the reference method to diagnose BCRL. However it is important to subject patients who report arm symptoms to a clinical examination specifically to exclude a primary shoulder problem (for example, referred pain from impingement of rotator cuff) that could provoke BCRL-like symptoms. The incidence of arm or shoulder dysfunction after ALND ranges between 30% and 40% (Bani et al., 2007; Liljegren et al.,1997; Engel et al., 2003). The treatment of BCRL and arm/ shoulder dysfunctions differs completely. Health professionals do not always routinely assess arm morbidity in the follow-up of breast cancer patients. The difference between qualitative and quantitative changes at the arm/ shoulder level is a plausible explanation of the difference in incidence of BCRL between the 'self-report group' and 'arm circumference group' (Fig. 1).

From this systematic review we can conclude that the mean risk to develop BCRL after ALND is 28%. This incidence rate is based on self-reporting, since this is the most appropriate measurement method in clinical practice. We propose to use this risk as a risk-benefit tool in the decision-making whether to proceed with ALND after a positive SLNB or not. In theory it would have been preferable to include only trials designed to report on BCRL incidence instead of prevalence because incidence figures will be marginally higher as women who develop BCRL at a certain stage will receive treatment to counter symptomatology. In the studies, it is not always evident to differentiate whether data on BCRL are presented as an incidence or a prevalence figure. Almost 70% of the reports included in this review reported on what we interpreted as 'incidence' of BCRL (Table II, Table III).

Table II. — Summary of all the reports published since 1990 about the incidence of BCRL assessed by arm circumference measurements and a follow-up of more than 12 months (n = 18).

Year	Author	Definition	Study design	N (period)	FU	Incidence	(proportion ALND)
1992	Ball	≥ 3 cm	R	50 (1982-'90)	12 mo	6%#	(100%)
2001	Herd-Smith	> 5%	R	1278 (1989-'97)	56 mo	16%#	(100%)
2001	Petrek	Severe, Moderate, Mild	R	263 (1976-'78)	20 yrs	13%∞	(100%)
2002	Haid	> 10%		151 (1997-'01)	4 yrs	33%∞	(56%)
2002	Powell	> 2 cm	R	714 (1982-'95)	72 mo	11%#	(86%)
2003	Querci	> 5% PVD > 20%, PVD change	R	199	35 mo	33%#	(100%)
2005	Clark	> 5%	P	188 (1999-'00)	3 yrs	21%#	(100%)
2005	Niwinska	4-6 cm or > 6 cm difference	P	174 (1995-'99)	78 mo	10%#	(100%)
2006	Mathew	> 2 cm	R	506 (2000-'02)	2 yrs	12%#	(40%)
2008	Nesvold	> 10% or ≥ 2 cm	CS	263 (1998-'02)	47 mo	RM : 20%∞ / BCS : 8%	(100%)
2008	Paim	> 2 cm	CS	96 (2006)	5 yrs	SLNB 4% / ALND 29%#	(50%)
2008	Mc Lauglin	> 2 cm	P	936 (1999-'03)	5 yrs	SLNB 5% / ALND 16%∞	(36%)
2008	Park	> 2 cm	R	450 (2003-'04)	24 mo	25%# (90%)	(90%)
2008	Mac-Lean	> 2 cm	P	337	12 mo	12%∞ (77%)	(77%)
2009	Devoogdt	> 10% difference	P	49 (2004)	3,4 yrs	18%#	(100%)
2010	Yang	> 1 cm	P	191 (2006-'07)	12 mo	12%∞	(33%)
2012	Ozcinar	> 2 cm	P	218 (2004-'08)	64 mo	SLNB 2% / ALND 5%#	(63%)
2012	Bevilacqua	> 200 ml	P	1054 (2001-'02)	5 yrs	30%#	(100%)

R : retrospective ; P : prospective ; CS :cross-sectional ; PVD : percentage volume difference ; RM : radical mastectomy ; BCT : breast conservative surgery ; SLND : sentinel lymph node dissection ; ALND : axillary lymph node dissection ; # : Incidence ; ∞ : Prevalence.

Table III. — Summary of all the reports published since 1990 on the incidence of BCRL by self-report with a follow-up of more than 12 months (n = 18).

Year	Author	Study design	N (period)	FU	Incidence (proportion ALND)	
1992	Ivens	R	126 (1990-’91)	4 yrs	24%$^{\%\#}$	(100%)
1996	Suneson	R	362 (1983-’88)	3 yrs	15%$^{\%\infty}$	(> 90%)
1996	Mortimer	R	1077 (1991)	9.5 yrs	28%$^{\#}$	
1997	Liljegren	P	381 (1981-’88)	36 mo	11%$^{\%\#}$	(100%)
1999	Tengrup	P	110 (1992)	5 yrs	19%$^{\%\#}$	(100%)
2000	Schrenk	P	70 (1996-’98)	28 mo	14%$^{\%\infty}$	(50%)
2002	Kwan	R	467 (1993-’97)	2 yrs	12%$^{\%\infty}$	(80%)
2003	Engel	P	990 (1996-’98)	5 yrs	38%$^{\%\infty}$	(100%)
2003	Geller	R	145 (1996-’97)	35 mo	38%$^{\#}$	
2003	Kornblith	R	153 (1975-’80)	20 yrs	39%$^{\%\infty}$	(100%)
2004	Hinrichs	R	105 (1995-’01)	2 yrs	27%$^{\%\#}$	(100%)
2007	Bani	R	742 (2004-’05)	4.3 yrs	32%$^{\#}$	
2007	Paskett	P	622 (1998-’05)	3 yrs	32%$^{\%\#}$	(93%)
2009	Yen	R	1338 (2005-’07)	4 years	ALND 21%$^{\#}$-SLNB 7%	(57%)
2010	Gärtner	CS	3253 (2005-’06)	1-3 years	38%$^{\%\infty}$	(93%)
2010	Kwan	P	997 (2006-’07)	20.9 mo	13%$^{\%\infty}$	(74%)
2010	Norman	P	631 (1999-’01)	5 yrs	35%$^{\%\#}$	(81%)
2011	Cidon	P	127 (2004-’05)	5 yrs	37%$^{\%\#}$	(100%)

R: retrospective; P: prospective ; CS: cross-sectional; ; #: Incidence; ∞: Prevalence only moderate LE with constant physical discomfort without decrease in functional activity was retained.

Morbidity of ALND and SLNB has been compared in two large randomized trials: the ALMANAC trial (Mansel et al., 2006) and the ACOSOG Z11 trial (Mc Laughlin et al., 2008). The incidence of any side-effect of SLNB followed by ALND was 70% compared to 25% in the SLNB-only arm ($p < 0.001$). The incidence of BCRL has dropped since the introduction of SLNB. Contra-indications for SLNB are scarce and include clinically node-positive breast cancer, neo-adjuvant treatment of breast cancer, pregnancy and lactation and inflammatory and other T4 breast cancers (Pesce et al., 2013). A major concern with SLNB during the years of introduction in clinical practice was the false negative rate associated with the failure to identify the ‘affected’ node (Pesce et al., 2013). In the NSABP B32 study, patients with a negative SLNB were randomized to ALND or no further surgery and the false negative rate in the ALND was 9.8% (Krag et al., 2007). Differences in tumor location, type of biopsy, and number of removed SLNs affected significantly the false-negative rate. Clinical rates of axillary recurrence in patients with negative SLN after a mean follow-up period of 10 years are less than 1%. That is considerably lower than the false negative rates seen in the validation studies of completion ALND (Veronesi et al., 2010). Others have showed that survival is excellent (98%) and local axillary control is adequate (99%) after omitting ALND in a group of 104 SN negative breast cancer patients (Torrenga et al., 2004). Omitting an ALND in women with a positive SLNB as suggested by the results of the randomized studies ACOSOG Z0011 and IBCSG 23-01 inevitably raises this fear for axillary recurrences due to unresected metastatic non-SLN. Delpech et al. (2013) already warned against the broadening of the ACOSOG Z0011 selection criteria to omit a ALND as this resulted in a worse outcome in a historic group with positive SLN. Moreover the MIRROR study has demonstrated an increased 5-year regional recurrence rate in women with micrometastases in the SLN and no completion of ALND (Pepels et al., 2012). Nevertheless a randomised clinical trial in older patients (65-80 years) with early breast cancer (T1N0) and a clinically clear axilla showed no benefit from axillary dissection: at 15 years of follow-up both groups showed a comparable distant metastasis rate, overall survival, and breast cancer mortality whilst the cumulative incidence of axillary disease in the no axillary dissection arm was only 6% (Martelli et al., 2012).

For this reason and given the limited and relatively immature data on minimally invasive surgery in a select group of women with sentinel positive early breast cancer, there is no consensus on the safety of abandoning completion of ALND. Further research is needed. A medical decision based on a risk/benefit analysis between risk of recurrence and excess morbidity due to unnecessary ALND seems an appropriate intermediate approach before adopting a generalized strategy of no ALND until proven safe. Many nomograms predicting the risk of non-SLN metastases have been developed from single-institution retrospective series. It is important to perform an internal validation of the nomogram prior to implementation. Prevalence of metastatic non-SLN differs from one institution to another for a number of reasons: tumour diameter inclusion cut-off or whether preoperative ultrasound is used to filter a 'clinically' negative axillary lymph node status (Meretoja et al., 2012). It is also possible to calculate an individual woman's risk to acquire lymphedema after ALND. A nomogram developed to predict the 5-year probability of BCRL showed a 5-year cumulative incidence of BCRL of 30.3%. Independent risk factors for developing lymphoedema were age, body mass index, ipsilateral arm chemotherapy infusions, level of ALND, location of radiotherapy field, development of postoperative seroma, infection, and early oedema (Bevilacqua et al., 2012). Finally it may be clear that there is also a need for internal validation of this benchmark risk of self-reported lymphoedema. A pragmatic approach would be to balance the risk of metastatic non-SLN against the risk of BCRL when an ALND is performed.

In conclusion, we presented a systematic review of the literature regarding the incidence of BCRL after ALND. We motivated that self-report of BCRL is the most clinical relevant method to decide whether a women suffers from lymphoedema. We agree with other authors (Yen et al., 2009) that self-report should become the standard in reporting on BCRL alone or combined with arm measurement like circumference method. The risk of BCRL after ALND can be estimated around 30% both according to this review of the literature and supported by the results of a recently published nomogram (Bevilacqua et al., 2012). This risk of BCRL of 30% is the number that we take into account in our decision-making regarding the clinical benefit of performing a completion of ALND in cases of a positive SLN. This risk/benefit decision-making may become obsolete in the future when abandoning ALND is proven to be safe.

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Appendix: Search strategy of BCRL.

Pubmed: ("Breast Neoplasms"[Mesh] OR Breast Neoplasm* OR Breast Cancer*[tiab] OR Breast Tumor* OR (Mammary AND (Carcinoma* OR Neoplasm*)) OR "Cancer of the Breast" OR "Cancer of Breast" OR Breast malignancy*) AND ("Sentinel Lymph Node Biopsy"[Mesh] OR "Lymph Node Excision"[Mesh: NoExp] OR Lymphadenectomy* OR Sentinel Node* OR ("Axillary Lymph Node" AND (Dissection OR Procedure* OR Surgery)) OR ("Sentinel Lymph Node" AND (Biopsy OR Dissection OR Procedure*)) OR (Lymph Node* AND surgical procedure*)) AND ("Lymphedema"[Mesh:NoExp] OR Lymphedema* OR Lymphoedema*) AND (morbidity OR prevalence OR incidence OR disability*) NOT (animals[mh] NOT humans[mh]) AND ("1990"[PDAT]: "3000"[PDAT])

Embase: 'breast tumor'/exp OR 'breast cancer'/exp OR ('breast neoplasm' OR 'breast neoplasms'/exp AND [embase]/lim) OR (breast NEAR/1 (cancer OR tumor* OR malign*) AND [embase]/lim) OR (mammary AND (carcinoma* OR neoplasm*) AND [embase]/lim) AND ('sentinel lymph node biopsy'/exp OR 'lymph node dissection'/exp OR (lymphadenectomy* AND [embase]/lim) OR ('sentinel node' OR sentinel AND nodes AND [embase]/lim) OR ('axillary lymph node'/exp AND ('dissection'/exp OR procedure* OR surg*) AND [embase]/lim) OR ('sentinel lymph node'/exp AND ('biopsy'/exp OR 'dissection'/exp OR 'excision'/exp OR procedure*) AND [embase]/lim) OR ('lymph node'/exp OR 'lymphe nodes' AND ('surgical procedure'/exp OR 'surgical procedures') AND [embase]/lim)) AND ('lymphedema'/exp OR (lymph?edema* AND [embase]/lim)) AND ('morbidity'/exp OR ('morbidity'/exp AND [embase]/lim) OR 'prevalence'/exp OR ('prevalence'/exp AND [embase]/lim) OR 'incidence'/exp OR (disability* AND [embase]/lim) OR (epidemiology* AND [embase]/lim)) NOT ('animal'/exp NOT 'human'/exp) AND [1990-2013]/py AND [english]/lim