



Do medical procedures in the arm increase the risk of lymphoedema after axillary surgery? A review

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Abstract

Lymphoedema of the arm is a potentially serious consequence of any axillary procedure performed during the management of breast cancer. In an attempt to reduce its incidence and severity, patients are instructed to avoid venepunctures and blood pressure measurements on the treated arm. These precautions are not possible in some patients and attempts to adhere to them can cause discomfort, anxiety and stress for both patients and their health-care workers. The strength with which these recommendations are made is in contrast to the level of evidence underpinning them. This paper reviews this evidence regarding the safety, or lack thereof, of blood pressure monitoring and intravenous puncture in women who have had axillary surgery. With this evidence generally being anecdotal in nature, there appears to be no rigorous evidence-based support for the risk-reduction behaviours of avoiding blood pressure monitoring and venepuncture in the affected arm in the prevention of lymphoedema after axillary procedure. A clinical trial was proposed to investigate whether such avoidance measures were valuable, but failed during its inception. There remains a need for research from prospective trials on this controversial topic to determine the most appropriate patient recommendations that should be provided after axillary procedure regarding the risks for development of lymphoedema.

Introduction

Breast cancer-related lymphoedema is a chronic condition characterized by swelling of the upper limb or trunk region after treatment for breast cancer. It can result in significant psychological¹⁻⁴ and physical distress⁵ as well as economic consequences, impacting on quality of life.^{6,7}

The reported incidence of breast cancer-related lymphoedema ranges from 6% to 65%, depending on the population studied, method of diagnosis and duration of follow-up.^{8,9} A recent meta-analysis indicates that approximately 21% of all women who undergo surgery for breast cancer develop lymphoedema.¹⁰ Approximately 75% of cases develop within 2 years of surgery and 90% within 3 years,¹¹ with an incidence of 1% per annum thereafter.¹² Patients who undergo axillary procedures (including axillary dissection, sentinel node excision and radiotherapy) are recognized to be at an increased risk of lymphoedema.

Method

MEDLINE searches were conducted using the search terms (lymphoedema or lymphedema) combined with (venipuncture or venepuncture), blood pressure, (breast or axilla or axillary) and (needle or venipuncture or venepuncture), as well as (lymphoedema or lymphedema) and (breast or axilla or axillary) and prevention. One hundred and ninety-five publications were identified, as were 1002 review articles on the subject of (lymphoedema or lymphedema).

Each article and its citations were scrutinized to identify original reports of lymphoedema occurring after non-accidental skin puncture or blood pressure measurement.

Controversy over the development of lymphoedema

Current guidelines for the prevention of lymphoedema published by professional bodies, such as the National Cancer Institute,¹³ National

Table 1 The published associations between risk of lymphoedema and needle puncture

Author	Study type	Risk factor	Method	OR (95% CI)	P
Hayes <i>et al.</i> (2005) ¹⁶	Cohort	Injection	Bioimpedance	0.7 (0.1–5.7)	—
			Arm circumference	0.0 (0.0–0.0)	
			Self-report	0.2 (0.0–2.0)	
		Blood pressure	Bioimpedance	1.1 (0.2–5.4)	
			Arm circumference	3.4 (1.0–11.1)	
			Self-report	1.5 (0.5–4.4)	
Mak <i>et al.</i> (2009) ²¹	Case-control	Medical procedure†	Arm circumference	0.59 (0.31–1.12)	0.11
			• Any lymphoedema	0.49 (0.24–0.99)	0.046
			• Mod-Severe LE		
		Injury	Arm circumference	0.52 (0.22–1.24)	0.14
			• Any lymphoedema	0.39 (0.14–1.09)	0.07
			• Mod-Severe LE		
Clark <i>et al.</i> (2005) ²⁰	Prospective	Needle puncture‡	Arm circumference/clinical	2.44 (1.33–4.47)	—

†Blood drawn or blood pressure recorded on hand/arm on side of cancer. ‡Venepuncture or infusion on side of surgery in immediate post-operative period only. CI, confidence interval; LE, lymphoedema; OR, odds ratio.

Lymphoedema Network (NLN)¹⁴ and National Breast and Ovarian Cancer Centre,¹⁵ recommend the avoidance of venepuncture and blood pressure measurement on the affected side, although each comments on the anecdotal nature of the evidence base. The NLN writes ‘given that there is little evidence-based literature regarding many of these practices, the majority of these recommendations must at this time be based on the knowledge of pathophysiology and decades of clinical experience by experts in the field’.¹⁴

Our understanding of the aetiology of lymphoedema is incomplete.¹⁶ Traditionally, the development of lymphoedema has been ascribed to the damage to lymphatic outflow caused by surgery and radiotherapy. This model does not explain why the onset of limb swelling is not immediate after surgery, or why it can occur 30 years later.^{12,17} Women with constitutively rapid lymphatic drainage from the limb are more susceptible to developing lymphoedema after axillary surgery,¹⁸ as are obese women.^{19–31} Evidence from various sources suggests that neither blood pressure measurement nor skin puncture in the ipsilateral limb causes lymphoedema. Evidence from various sources suggests that neither blood pressure measurement nor skin puncture in the ipsilateral limb causes lymphoedema (Table 1).

A case-control study of 202 women who had undergone unilateral breast surgery, which included axillary dissection, reports that blood pressure monitoring or skin puncture does not increase the risk of lymphoedema (odds ratio (OR): 0.59, 95% confidence interval (CI): 0.31–1.12; $P = 0.11$).²¹

Similarly, a cohort study of 176 women from Queensland states that neither injections (OR: 0.7 (95% CI: 0.1–5.7)) nor blood pressure recording (OR: 1.1 (95% CI: 0.2–5.4)) increases the risk of arm swelling.¹⁶

Winge *et al.* surveyed 311 women who had undergone breast surgery that included level 2 axillary dissection.³² Eighty-seven respondents admitted allowing intravenous procedures in the ipsilateral arm, often repeatedly. Despite this, only five women reported limb swelling after venepuncture, whereas reports of limb swelling were also frequent in women who had protected their arm from such use.

Historical data from studies conducted when the use of implanted central venous catheters was not widespread, that is, intravenous

treatments¹⁴ were administered via peripheral veins, do not show an increased prevalence of lymphoedema in women with bilateral breast cancer,^{9,33} arguing against an important effect of blood pressure monitoring or intravenous puncture on lymphoedema rates.

Stanton *et al.* reported on 36 women who had undergone lymphoscintigraphy, a procedure that involves injection of contrast material into the at-risk limb, up to four times.¹⁸ At 30 months, increased limb volume was found in 19% of women who did not have limb swelling prior to these injections. Three case series examined the effect of hand surgery following an ipsilateral axillary dissection in women treated for breast cancer.^{34–36} Collectively, these report that 3/14 and 3/90 women with and without pre-existing lymphoedema experienced temporary limb swelling that lasted 3 months or less, despite the use of pneumatic tourniquets during the procedure. Correspondingly, more than 95% of specialist hand surgeons are willing to perform hand surgery after lymphadenectomy or axillary irradiation.³⁷ This proportion decreased to 85% if the patient has pre-existing chronic lymphoedema. The surgeons express the view that breast cancer patients and their physicians are overly sensitized to precautions after axillary surgery and that their fears of complications are unfounded. Olsha *et al.* reinforced this opinion, citing three patients who had fistulae formed for haemodialysis in the ipsilateral arm after axillary dissections that removed more than 20 axillary nodes in each case.³⁸ None of the three developed significant lymphoedema at 2, 20 or 76 months of haemodialysis that involved thrice-weekly cannulation.

In contrast, there are only a handful of original reports that document lymphoedema occurring after needle puncture. The first case report of lymphoedema occurring in association with needle-stick injury was presented in 1992.¹⁷ It described a woman who noticed the onset of lymphoedema 30 years after her breast surgery, 10 days after she commenced finger prick testing to monitor her diabetes. The authors considered that the inflammation caused by the finger prick testing overwhelmed an already compromised lymphatic drainage and resulted in lymphoedema. Whether investigations to detect local recurrence were performed was not discussed. Neither was obesity, a common risk factor for both diabetes and lymphoedema.^{19–31}

Other examples of single cases arising from needle-stick trauma have also been reported.² Notably these have occurred as a

consequence of vaccinations³⁹ or venepuncture.⁴⁰ For example, a woman developed lymphoedema after a finger injury caused by a sewing machine needle.²

Limb swelling lasting some months resulted after vaccination in the same arm as an axillary dissection 26 years earlier, as was a second case resulting from vaccination in the contralateral limb.³⁹ Arm swelling after the same vaccination has also been recorded in the absence of axillary surgery.³⁹ Cole described how one of seven respondents to a survey of women in a lymphoedema network attributed the onset of her lymphoedema to venepuncture.⁴⁰ Smith reported on 10 women who were referred to a lymphoedema service over a 2-year period who 'cited venepuncture as a significant event in the history of their swelling' and had undergone venepuncture in that limb.⁴¹ This equates to 1.5% of the 691 women referred to that unit over the same time period.

Clark *et al.* prospectively identified 295 women with breast cancer and examined them for lymphoedema at baseline, 6 months and 3 years after axillary surgery.²⁰ One hundred and sixty-eight women were evaluated with limb circumference recordings at the 3-year time point. Of these, 19 met the criteria for lymphoedema based on arm volume calculations. A further 20 women had a clinical diagnosis of lymphoedema prior to the 3-year time point, but it is unclear why arm volume measurements were not performed to corroborate the diagnosis in these women. There is little concordance on the diagnosis of mild lymphoedema even between expert clinicians,⁴² which questions the utility of clinical diagnosis as an endpoint in studies of lymphoedema. To compound this problem, the thresholds for arm circumference and volume are arbitrarily selected and not centred around evidence-based criteria.⁴³

Another weakness of this study is that it recorded venepuncture performed only in the days prior to discharge after surgery, not in the subsequent years of follow-up, so it may not represent the total exposure of the participants to needle puncture. Further, possible confounders, such as extent of surgery and tumour staging, were not taken into account. Nonetheless, this study reports that skin puncture (while in hospital) increases the hazard of lymphoedema by a factor of 2.44 (95% CI: 1.33–4.47).

Dissecting current beliefs

Halsted concluded that inflammation resulting from infection or local recurrence after breast cancer surgery was responsible for the onset of elephantiasis of the limb.⁴⁴ This theme was picked up by Brennan, who related how inflammation caused by apparently uncomplicated finger prick testing caused limb swelling in this circumstance.¹⁷

If this model is correct, then there should be a close temporal relationship between the injury and the onset of lymphoedema. This is only reported in one other case; in a woman whose intravenous puncture was complicated by infection that required antibiotic treatment,³² but in whom the duration of swelling could not be determined because of the study design. No temporal relationship between the time of injury and the onset of lymphoedema is presented in any other case presentation or case series.

The case for non-avoidance of the limb

Situations exist wherein the use of the ipsilateral arm for intravenous procedures is desirable or necessary. These include venepuncture when venous access has become difficult in the contralateral arm, because of the repeated insults already sustained to this arm, and in emergency situations where immediate intravenous access is of paramount importance. These problems are compounded after bilateral axillary surgery.

Avoidance of the affected arm for routine procedures limits the number of veins available for intravenous infusions or blood samples⁴⁵ might potentially lead to increased discomfort and create barriers to providing optimal medical care. Repeated insults to the same veins may cause scarring and fibrosis of the available veins, fixed flexion deformities of the elbow and thrombosis of the deep veins of the upper limb (D. Porter, unpublished), as well as potentially increase the risk of extravasation injury when venous access becomes less secure. Furthermore, in women with bilateral breast cancer, veins in the foot may be required, which may cause more discomfort and pain.⁴⁵

Increasingly, central venous catheters are used to allow chemotherapy to be given without using the ipsilateral arm. Thrombosis affecting the central veins occurs in up to 16% of recipients of these devices⁴⁶ and catheter-related infection in up to 36%.⁴⁷ The resultant treatment delays potentially compromise the dose intensity of chemotherapy and could impair survival.⁴⁸ Pulmonary embolism is not uncommon following catheter-related thrombosis^{49,50} and post-thrombotic syndrome, a chronic illness characterized by heaviness, pain, paraesthesiae, functional limitation and pruritus of the upper limb was identified in 27% of patients followed prospectively after a diagnosis of deep vein thrombosis in the upper limb.⁵¹ These complications are well documented and are potentially more serious than those problems the insertion of these devices is intended to avoid.

Furthermore, the psychological burden of constantly having to be protective of the affected arm may cause unnecessary anxiety. Winge *et al.* noted open comments from women participating in their study: there was considerable anxiety about the development of lymphoedema, especially regarding the contradictory information about the importance of avoiding intravenous procedures.³² As lymphoedema can develop several decades after axillary treatment, these demanding risk-reduction precautions must be followed for the remainder of the patients' lives. This can be a disturbing experience that reduces patient confidence in the health-care professionals in the long term.¹⁷

The need for a randomized trial

We proposed a pilot study whereby women with early stage breast cancer would have blood pressure measurements and venepuncture performed only on their non-dominant arm, irrespective of the side of surgery. This would allow comparison between patients having the procedures on the operated and non-operated arms. Baseline measurement of arm circumferences would be performed in both arms before and 6 months after surgery. Participants would record the dates of needle punctures and blood pressure measurements in a diary.

This trial failed to progress beyond the concept phase for two reasons. Firstly, some potential investigators voiced the view that maintaining skin integrity on the ipsilateral arm was a vital contributor to the avoidance of infection and hence prevention of lymphoedema. Putting this at risk by repeated venesection in an immunocompromised patient's treated arm would be detrimental. Secondly, patients are taught to protect their arm before they have any contact with the medical oncology department where this trial would be conducted.

These factors formed an insurmountable obstacle to conducting the proposed trial.

Conclusion

The recommendation that skin puncture must be avoided at all cost appears to be derived from conjecture in the pre-antibiotic era that infection was the predominant cause of breast cancer-related lymphoedema.⁴⁴ Today, the evidence of harm from medically indicated skin puncture remains limited to case reports, small case series and one prospective study with methodological issues. We were unable to retrieve any evidence of harm resulting from blood pressure recording using the ipsilateral arm.

In contrast, one case-control study and a prospective cohort study, both of moderate size, indicate that blood pressure monitoring and blood drawing are safe procedures after breast cancer. The data on hand surgery and haemodialysis indicate that these activities also have minimal risk, particularly in women without pre-existing lymphoedema. By inference, the lesser procedure of needle puncture and the transient obstruction to lymphatic outflow resulting from blood pressure recording must pose a substantially smaller risk.

Fear of lymphoedema is not innate; patients are taught to be afraid of this complication.⁵² Rigid practice parameters and excessive warnings, such as the use of pink lymphoedema bracelets, may unnecessarily increase patient fears over minor events as the measurement of blood pressure, blood drawing and intravenous treatments and can interfere with important medical/surgical interventions such as when immediate venous access is required during emergencies.^{32,53}

Once detected, determining whether lymphoedema is caused by needle-stick injury or the two are coincidental is problematic. It can be argued that the longer the interval is between the two events, the more likely it is that the association is coincidental. Conversely, clinically evident lymphoedema may take some time to develop, making a relationship difficult to define. The advent of bio-impedance, which has the ability to detect subclinical lymphoedema, may help answer this question.

It may be that the risk of chronic lymphoedema is dependent on several factors including the patient's innate predisposition and whether skin puncture is performed for blood sampling or the administration substances that are pro-inflammatory or immunogenic. However, the use of chemotherapy, arguably the greatest irritant instilled into veins, is not an independent risk factor for developing lymphoedema.⁵⁴

With the widespread use of sentinel lymph node biopsy, it is timely to question whether long-established practices pertaining to lymphoedema risk management are still applicable. A need for rig-

orous evidence-based medicine based on well-conducted prospective research is apparent. Without it, there can be little progress in this controversial subject. A precedent has been set by the research that has established the safety of exercise after breast cancer, which is associated with both improved survival, as well as a reduced incidence of lymphoedema.^{55,56}

We continue to advocate for aggressive management of infection in the at-risk limb, as it heightens the risk of subsequent lymphoedema.^{12,21}

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