Does measuring blood pressure post-breast cancer surgical intervention increase the risk of developing ipsilateral arm lymphoedema?

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Key words

Blood pressure, breast cancer, lymphoedema, mastectomy

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Abstract

Despite advances in our medical and surgical treatment modalities, and earlier detection, breast cancer surgery and/or radiotherapy remain the most common causes of secondary lymphoedema. Lymphoedema in the same arm that was exposed to the surgery/radiotherapy is referred to as breast cancer-related lymphoedema (BCRL). To date, the link between transiently compressing the at-risk arm and the subsequent development of BCRL has not been properly assessed. Breast cancer patients are currently given lists of behaviours and interventions to avoid, among which are potentially beneficial operative treatments, such as carpal tunnel, release and other procedures such as venepuncture and blood pressure measurement. With respect to the latter, the best available evidence fails to show any association between blood pressure measurement on the at-risk arm and the development of BCRL. The current practice of 'better safe than sorry' is not supported. Further research is required to confirm the lack of association between transient arm compression in the arm-at-risk and BCRL in breast cancer patients.

Lymphoedema refers to the accumulation of lymphatic fluid, and its contents, usually in the limbs (Harris et al, 2001). This may be due to lymphatic hypoplasia (primary lymphoedema), or to disruption, damage or obstruction of the lymphatic drainage system (secondary lymphoedema). Despite advances in medical and surgical treatment, breast cancer surgery and/or radiotherapy remain the overall most common causes of arm lymphoedema (Douketis, 2015). This is often referred to as breast cancer-related lymphoedema (BCRL).

The incidence of BCRL largely depends on the type of surgery, the extent of axillary node dissection, the use of axillary radiation therapy, patient characteristics and genetic make-up (Cole, 2006). The estimated incidence rate ranges from 3% to 6% for sentinel node removal to as high as 19% for axillary node clearance (Meeske et al, 2009).

The exact pathophysiology of BCRL remains unknown; however, the primary aetiological factor underlying BCRL appears to be the iatrogenic disruption of axillary lymph node drainage. The picture may be further complicated in some patients in whom obstructed venous outflow also contributes to the at-risk arm swelling. The role of haemodynamic changes in the at-risk arm, although once thought to contribute to BCRL, has been refuted by human venous occlusion plethysmography studies (Stanton et al, 1998).

Patients at risk of and with BCRL tend to present with an aching pain in one arm, and describe it feeling as though their arm is heavy and swollen. Although initially reversible, as time progresses the lymphoedema becomes irreversible, with chronic soft-tissue inflammation, fatty epifascial tissue formation and early fibrosis (Douketis, 2015). Although non-BCRL can advance to this irreversible stage, BCRL rarely does so (Harris et al, 2001).

The diagnosis of BCRL is often made clinically based on the history and physical examination findings. Rarely are imaging investigations, for example lymphangiography, required (Douketis, 2015). Most cases of BCRL will appear within 5 years following the surgery (Golematis et al, 1975; Markowski et al, 1981), although BCRL has been reported to develop as late as 30 years after surgery (Golematis et al, 1975).

To date, there is no accepted medical or surgical cure for lymphoedema (Douketis, 2015). Secondary lymphoedema — including BCRL — is largely treated by trying to manage the cause if one is identified, for example an infection, and in providing symptomatic relief as necessary. For this reason, the mainstay of secondary lymphoedema management is mostly focussed on prevention (Douketis, 2015).

Breast cancer patients are often given lists of precautions and prohibitions with regards to the care and use of their at-risk arm. The list includes avoidance of heat, vigorous exercise, constrictive garments, blood pressure measurement, vaccination and phlebotomy in and around the at-risk limb (Dawson et al,

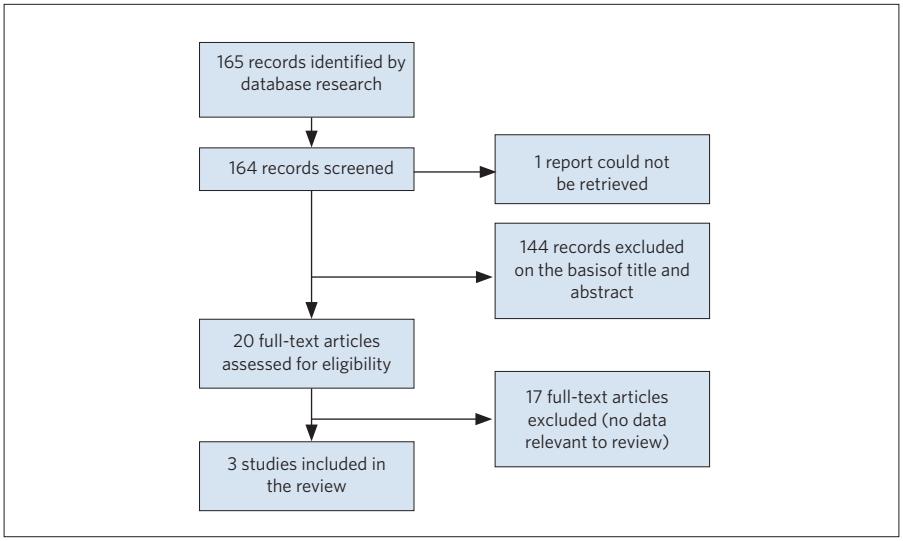

Figure 1. Flow diagram demonstrating the process used to select relevant studies from the systematic review of the published literature.

1995). The majority of the published literature supporting the notion of a 'precautionary' list, however, has merely repeated suggestions published in a single article in 1966 (Nelson, 1966). The rest of the studies have failed to provide methodologically-sound supportive data (Clark et al, 2005).

Published clinical guidelines on blood pressure monitoring, for example the National Institute for Health and Care Excellence (2011) clinical guideline 127, recommend obtaining blood pressure readings from both arms and recording the higher reading as the patient's blood pressure. More importantly, perhaps, are the recent findings of clinically-significant associations between inter-arm blood pressure differences (of ≥15 mmHg) and future risk of cardiovascular mortality and all-cause mortality, in the primary care setting (Centre for Reviews and Dissemination, 2009; Clark et al, 2012a, 2012b). It is likely, therefore, that more breast cancer survivors will be persuaded to have their blood pressure checked on both arms by their GPs.

This report aimed to review all the relevant published literature to date in order to establish whether measuring a breast cancer patient's blood pressure using constrictive apparatus, for example, a sphygmomanometer, increased their risk of developing BCRL.

Methods

Search strategy

A systematic review of the literature was undertaken in accordance with recognised methods (Centre for Reviews and Dissemination, 2009). The author searched the Medline, Embase, Cochrane Library (including the Cochrane Database of Systematic Reviews), DARE, Trip and Clinical Evidence databases for published reports. This was carried out by combining the keywords lymphoedema/lymphedema, lumpectomy, breast-conserving therapy or mastectomy, with one of the following terms: blood pressure, sphygmomanometer or risk factors. Furthermore, international expert opinion was sought from the official breast cancer foundations, as well as lymphoedema networks in USA, Canada, UK, Australia and New Zealand.

Inclusion criteria

To be included, studies needed to:

I. Include participants who were adult female patients with a diagnosis of breast cancer who had undergone breast-conserving therapy with sentinel node biopsy or mastectomy and surgical dissection/radiation of one or more axillary lymph nodes
II. Have development of BCRL in the at-risk arm in the context of ipsilateral sphygmomanometer use as the outcome of interest.

Results

One-hundred-and-sixty-five unique reports were identified by searching the databases. *Figure 1* provides a detailed scheme of the study selection process.

Only three studies met the inclusion criteria and were used in an attempt to answer the clinical question in hand. In one case-control study (Markowski et al, 1981), the authors described 15 breast cancer patients who underwent a surgical carpal tunnel release (CTR) in the at-risk arm. Six of these patients had some degree of BCRL prior to the surgery. Breast cancer patients were compared to 302 non-breast cancer patients of similar age and characteristics undergoing the same surgery by the same surgeon. The surgery involved inflating a pneumatic tourniquet high on the ipsilateral arm to 300 mmHg, for a mean duration of 41 minutes. None of the breast cancer patients exhibited any signs of lymphoedema or worsening of pre-existing BCRL postoperatively. This was sustained even after a mean follow-up period of 14–16 months.

The other two studies were case reports. One case report (Donachy and Christian, 2002) described a 53-year-old patient, who had undergone a modified radical mastectomy 9 years earlier, successfully undergoing a CTR with no significant changes to her arm at follow-up 6 months post-operatively. The other case report (Smith and Giddins, 1999), however, reported that an 81-year-old patient developed gross lymphoedema 10 weeks after her CTR. She had undergone a radical mastectomy 13 years earlier, and her CTR was complicated by a wound infection, for which antibiotics had not been started until 2 weeks later.

Upon searching five official international breast cancer websites, only the Canadian Breast Cancer Foundation (2010) and Breast Cancer Network Australia (2010) offered explicit information on BCRL and its risk factors. The New Zealand Breast Cancer Foundation's (2012) recommendations were confined to mentioning its support of 'The New Zealand Lymphoedema Therapists'' recommendations (Lymphoedema NZ, 2010). All three expert recommendations echoed each other, having issued a precautionary list for breast cancer patients. Patients are currently recommended to avoid wearing tight-fitting clothes or jewellery, carrying a heavy bag, having injections and blood pressure measurements on the at-risk arm. The Australian recommendations

follow this avoidance list, however, by stating that "while there is not yet enough evidence to determine whether these procedures can trigger lymphoedema, these precautions are recommended" (Breast Cancer Network Australia, 2010).

Searching lymphoedema networks yielded mixed results. The National Lymphoedema Network has published the most advice on blood pressure measurement in patients at risk of BCRL (NLN Medical Advisory Committee, 2012). While acknowledging this issue is controversial, it remains against blood pressure measurement in the at-risk arm for several reasons. These include the fact that sphygmomanometer cuffs often lead to localised high-pressure compression of underlying tissues, and because automated sphygmomanometers compress the arm to a pre-set high systolic level that then oscillates as it decreases, as opposed to a constant and gradual decrease when the pressure is released from a manual sphygmomanometer (NLN Medical Advisory Committee, 2012). The International Lymphoedema Framework does not offer explicit advice, although it appears to encourage using a blood pressure cuff to measure the ankle-brachial pressure index in patients with lower-limb oedema (Glover, 2012).

Discussion

Summary of the current literature

The currently-held belief that transiently compressing the at-risk arm increases the patient's chances of developing BCRL is not supported by the published evidence. This is further supported by the negative findings of a recent review on the risk of lymphoedema when medical procedures are performed on the ipsilateral arm (Cheng, 2014). Dawson and his colleagues reported on 15 breast cancer patients with no postoperative complications 14–16 months after CTR on the at-risk arm (Dawson et al, 1995). The surgery involved an average of 41 minutes of ipsilateral inflation of a pneumatic tourniquet (which is very similar to a sphygmomanometer in principle) to an astounding 300 mmHg pressure. Yet this did not seem to have caused lymphoedema in the at-risk arm; and in the subgroup with pre-operative BCRL, surgery did not seem to have worsened the condition.

The outcome of the two case reports (Smith and Giddins, 1999; Donachy and Christian, 2002), while initially appearing conflicting, are likely to have been influenced by pre- and peri-operative factors. The fact that the patient who developed post-CTR lymphoedema had undergone a prior radical mastectomy (rather than the modified approach), as well as having postoperative infection cannot be disregarded. Despite this, international expert opinion on some official breast cancer websites recommends against constricting the at-risk arm even for such trivial matters as wearing tight-fitting jewellery (Breast Cancer Network Australia, 2010; Canadian Breast Cancer Foundation, 2010; Lymphoedema NZ, 2010; New Zealand Breast Cancer Foundation, 2012).

Critical appraisal of available evidence

When there is an apparent conflict in published literature in the arena of patient care, it is pivotal to consider the quality of the evidence and the rationale behind the opposing views. Observational studies and anecdotal experience/expert opinion are prone to methodological flaws and biases, and are often considered the lowest echelon of clinical evidence (Duke University Medical Center Library, 2010). Notwithstanding this fact, it is generally accepted that case-control studies rank above expert opinion (Duke University Medical Center Library, 2010).

Measurement of blood pressure usually involves lower pressures and is more transient compared to techniques used in CTR surgery. One could thus extrapolate that the temporary use of a sphygmomanometer on the at-risk arm should be safe. That said, however, it is imperative to note that the above-mentioned studies are not without shortcomings. The study populations were small and the follow-up period was short. Besides, had BCRL developed in these patients one cannot be confident whether it was purely due to the pneumatic compression or confounded by the surgery itself, an underlying infection, or both.

Despite the conservative stance taken by several major international breast cancer foundations and lymphoedema networks on BCRL, one should question the ethics of a 'better be safe than sorry' approach. With breast cancer patients living longer than ever before, patient advocate groups should consider the potential long-term repercussions of such recommendations, including denying patients and persuading them to forego operative treatments and other procedures.

Future research

Designing a study that directly investigates causality in this case would be costly, arduous and potentially impractical. Driven by the potential for profit and the urge to be cost-effective, it is often hard to convince funding bodies to financially support a long methodologically-sophisticated clinical trial; however, a less-complicated study within the primary care setting might provide an adequate amount of information, albeit at the expense of the quality of the information generated. GPs are the ideal clinicians to lead such a study because they can afford the logistics involved, for example bilateral arm blood pressure measurement of a large number of breast cancer patients. GPs also usually have much longer-lasting relationships with their patients than secondary care practitioners, which makes it easier for them to follow-up on such a long-term outcome as BCRL.

Conclusion

To date, the link between transiently compressing the at-risk arm and the subsequent development of BCRL has not been properly assessed. Breast cancer patients are currently given lists of behaviours and interventions to avoid, among which are potentially beneficial operative treatments (e.g. CTR) and other procedures (e.g. blood pressure measurement). This is in spite of the fact that the best available evidence has failed to show any association between blood pressure measurement on the at-risk arm and the pathogenesis of BCRL. The current practice of 'better safe than sorry' may not be supported. Further research is required to confirm the lack of association between arm compression and ipsilateral BCRL in breast cancer patients.

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