

*SPECIAL REPORT***ARE HEMODYNAMIC FACTORS IMPORTANT IN ARM LYMPHEDEMA AFTER TREATMENT OF BREAST CANCER?**

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In 1967 Jacobsson observed (1) that arterial inflow was higher in the lymphedematous arm of a patient after treatment of breast cancer but that edema was not likely caused by venous congestion. The recent availability of non-invasive color duplex-Doppler technology stimulated Svensson et al (2-4) to reexamine this issue. In 70% of patients treated for breast cancer they found venous flow abnormalities and in 68% increased arterial inflow and concluded that these hemodynamic factors in addition to lymphatic blockade contributed to arm edema. Whereas these authors recommended harmless therapeutic measures such as "avoiding clothing that would compress the venous drainage over the clavicle and to stop carrying [a] shoulder bag", we decided to reexamine the "hemodynamic" issue lest misguided operations be designed to correct putative venous outflow abnormalities.

A cohort of 48 women (mean age 60 years) treated for breast cancer without relapse of malignancy but with unilateral arm lymphedema were studied. In 40 patients, breast cancer treatment included both surgery and irradiation and in 8 patients only operation. Twelve of the 40 patients also had radiation-induced neuropathy. The volume of the edematous arm was greater than the contralateral arm by 400 ml in 21 patients; between 400-600 ml in 12 patients and >800 ml in 15 patients. The axillary-subclavian

circulation was examined using an ATL-ultramark 9 HDI color duplex ultrasound apparatus with a 5-10 MHz linear transducer (wall filter 50 Hz). To visualize the subclavian artery and vein, each patient was lying supine, the arm fully adducted and positioned at the level of the heart. To display the brachial artery and axillary vein, the arm was abducted to 60°. Blood flow (ml/min) in the subclavian artery was computer calculated based on the mean flow velocity and the cross-sectional area in the β -mode image. The program utilized spectral data obtained before gray-scale conversion. The sample volume covered the artery completely. The diameters of the subclavian vessels were determined from the systolic inner or luminal diameter in the β -mode image. Axillary-subclavian venous occlusion was diagnosed when 1) the veins were not seen, 2) the veins were obstructed by an echogenic filling defects, 3) no venous flow was detected, 4) the profile of venous flow was altered, i.e., flow was discontinuous, 5) venous collaterals were detected, 6) the veins of the upper arm were non-compressible.

Seven patients (14.5%) had evidence of venous occlusion in the swollen arm. Six had radiation changes in the skin and in 2 wound healing after initial operative treatment was complicated by recurring "seromas." In contrast, delayed wound healing occurred in only 2 of 41 patients without ultrasound evidence of

axillary-subclavian venous occlusion.

In a second phase of study, subclavian arterial inflow bilaterally was measured in 20 other patients with unilateral arm lymphedema after breast cancer treatment (mean age 61 years). After arterial inflow was determined, measurements were repeated 4 hours after circumferential bandage-wrapping of the swollen arm. We also for purposes of accuracy compared these findings with arm arterial inflow measurements bilaterally in 10 healthy subjects before and 4 hours after bandage-wrapping of one arm. Statistical analysis was performed using the paired student t and Wilcoxon tests.

In these 20 patients, arterial inflow was greater in the swollen arm (287.6 ± 100.1 ml/min) compared with the non-edematous contralateral arm (198.7 ± 72.8 ml/min) ($p < 0.001$). After circumferential bandage-wrapping of the edematous arm for 4 hours, arterial inflow decreased (317.9 ± 75.3 ml/min to 229.3 ± 70.5 ml/min; $p < 0.001$) whereas arterial inflow remained unchanged in the contralateral arm (189.7 ± 66.3 ml/min and 196.1 ± 79.9 ml/min). In healthy subjects, arterial flow in the left arm was 217.2 ± 38 ml/min and in the right arm was 212 ± 53 ml/min. After bandage-wrapping of the left arm, arterial flow was unchanged (222 ± 50 ml) and also remained unchanged in the right arm (221 ± 68 ml/min) where no bandaging was done.

Understanding the pathophysiology of arm edema after breast cancer treatment is critical for determining therapy. If one regards arm swelling as lymphedema or low output failure of the lymphatic circulation (i.e., the lymphatic transport capacity has been reduced below that needed to optimally transport microvascular filtration), treatment will be directed at improving lymph return. If, on the other hand, one considers "venous flow abnormalities" as playing an important role, one might be misguidedly tempted to perform "venolysis" or other venous reconstruction operations which may further interrupt residual lymphatic collectors.

Contrary to Svensson et al (2,3) who found "venous flow abnormalities" in 70% of their patients treated for breast cancer, we documented axillary-subclavian occlusion in only 14.5%. Moreover, these venous occlusions were linked to scar formation in the axilla after irradiation and/or delayed wound healing. Nonetheless, there is no convincing evidence that these venous abnormalities contributed to arm swelling in these patients; that is, there were no clinical signs of venous congestion. Although neither we nor Svensson et al (2) measured venous pressure, in 15 patients studied by Jacobsson (1), only one had elevated arm venous pressure. In this one patient, however, even if venous and accordingly blood capillary hydrostatic pressure was elevated, an autoregulatory decrease in the capillary filtration coefficient could readily offset a tendency to greater microvascular filtration. To date, microvascular hydraulic conductivity has not been measured in these lymphedematous arms and accordingly it seems inappropriate to deduce that increased microvascular filtration contributes to arm swelling (4). Based on these considerations and the fact that in 85.5% of our patients venous flow was uninterrupted makes it highly unlikely as suggested by Svensson et al that "venous outflow obstruction is an important contributory factor in the pathophysiology of arm swelling following breast cancer treatment." The advice of Svensson et al given to patients in whom they found venous flow abnormalities, namely "avoiding clothing that would compress the venous drainage over the clavicle and to stop carrying a shoulder bag" is probably sound for all patients with lymphedema of the arm after breast cancer treatment whether or not they have venous abnormalities.

Our study also confirms that arm arterial inflow is increased (45%) in lymphedema after breast cancer treatment, findings similar to that of Jacobsson (42%) (1) but somewhat less that of Svensson et al (68%) (4). On the other hand, this hemodynamic perturbation

does not mean as suggested by Svensson et al that "increased blood flow is likely to contribute to arm swelling." This conclusion can rightfully only be drawn after all the microvascular hydrodynamic forces are determined including capillary filtration coefficient and/or capillary hydrostatic pressure. Indeed, as suggested by Solti (5), most hyperdynamic blood flow in lymphedema takes place in dermal microvascular arteriovenous shunts, and as shown in this study is nearly abolished by short-term circumferential arm bandaging. Together, these findings support that hyperdynamic blood flow is more likely a *consequence* and not a proximate *cause* of arm edema.

In summary, arm edema after treatment of breast cancer is primarily a consequence of low-output failure of the lymphatic circulation, i.e., lymphedema. Over time, the intrinsic pulsation of the residual peripheral arm lymphatics weakens, lymphatic collectors become sclerosed (particularly with superimposed lymphangitis), and lymph flow progressively decreases. Hemodynamic alterations are a consequence of either the treatment of breast cancer or a response to skin and subcutaneous edema itself, or possibly in response to a low-grade smoldering inflammation in the lymphedematous arm.

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