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Colour Doppler Demonstrates Venous Flow Abnormalities in Breast Cancer Patients with Chronic Arm Swelling

W.E. Svensson, P.S. Mortimer, E. Tohno and D.O. Cosgrove

Chronic arm oedema following breast cancer treatment is traditionally attributed to lymphatic obstruction, with venous obstruction as an infrequent complicating factor. The axillo-subclavian venous systems of 81 patients with arm swelling following breast cancer treatment were examined with colour Doppler, duplex Doppler and grey scale ultrasound. Over half (57%) had evidence of venous outflow obstruction and a further 14% had signs of venous "congestion". Only 30% of the swollen arms had normal venous outflow. The venous systems of the contralateral non-swollen arms were all normal as were both arms in 28 control patients who had similar treatment but had not developed arm swelling. These findings suggest that venous outflow obstruction is an important contributory factor in the pathophysiology of arm swelling following breast cancer treatment.
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INTRODUCTION

CHRONIC ARM swelling is one of the commonest complications of breast cancer treatment occurring in 25% of 200 consecutive patients in one series [1]. The reported incidence ranges from 7 to 63% [2]. The cause is attributed to lymphatic obstruction, but this may be an oversimplification of the pathophysiology, which is poorly understood.

The contribution of venous obstruction has long been controversial. Veal in 1938 demonstrated abnormal venous anatomy by venography in 46 cases of arm oedema, but not in 28 control patients [3]. Other studies [4, 5] have also supported the view that venous obstruction is a major cause of the swelling. Conversely, MacDonald [6] and Lobb and Harkins [7] demonstrated that axillary vein resection did not increase the incidence or extent of arm swelling.

Clinical observation of compromised venous drainage (dilated skin venules, dilated collaterals around the shoulder or a palpable brachial vein with the arm elevated) prompted a re-evaluation of venous outflow in breast cancer patients with arm swelling.

The recent ultrasound development of colour Doppler imag-

Correspondence to W.E. Svensson at the X-Ray Department, Ealing Hospital, Uxbridge Road, Southall, Middlesex UB1 3HW, U.K.
W.E. Svensson, E. Tohno and D.O. Cosgrove are at the Department of Nucelar Medicine and Ultrasound, the Royal Marsden Hospital, London and Sutton, Surrey; and P.S. Mortimer is at the Lymphoedema Clinic, the Royal Marsden Hospital, Fulham Road, London and Department of Medicine (Dermatology) St George's Hospital Medical School, London, U.K.
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ing (CDI) allows non-invasive mapping of limb and superficial blood vessels. It provides dynamic as well as anatomical information such as the distribution and direction of venous blood flow.

The axillo-subclavian venous system in patients with breast cancer-related arm swelling, attending the lymphoedema clinic at the Royal Marsden Hospital, was examined with CDI for signs of venous outflow obstruction and compared with a control group of similar patients without arm swelling.

PATIENTS AND METHODS

81 consecutive patients with chronic arm swelling (oedema group) related to their breast cancer treatment were examined with CDI. All patients exhibited at least a 200 ml volume difference between the swollen and contralateral normal arm; volumes were calculated according to multiple circumference measurements as described previously [8].

A group of 28 breast cancer patients, with no arm swelling (control group), were randomly recruited from the follow-up clinic of the Breast Unit of the Department of Medicine, the Royal Marsden Hospital, and studied for comparison. Selection criteria were similar treatment, age and time from treatment as the oedema group, as well as willingness to attend for the ultrasound examination (see Tables 1 and 2 for sociodemographic and treatment details).

Methods

Ultrasound and colour Doppler examinations were performed using a 7 MHz linear array transducer on an Acuson 128 ultrasound scanner. Both axillary and subclavian regions were examined with both arms similarly positioned at the patients side, with the patient lying supine. If venous flow and anatomy were normal, further examination was performed with the arms abducted to 90° and 180° and both internally and externally rotated. The position of veins and the direction of flow were examined using CDI. Conventional pulsed Doppler (at 5 MHz) was used to record the spectral wave form of blood flow in the veins. Cardiac and respiratory phasic variations of both flow and vessel wall position were noted. Full details of the methods and examples of results have been described previously [9].

Table 1. Characteristics of the patients examined

	Oedema group (swollen arms)	Control group (no arm swelling)
Number of patients	81	28
Age (years)		
Average	61.9	60.8
Range	33–85	44–82
Sex		
Female	80	28
Male	1	0
Bilateral breast disease	9 (11%)	1 (4%)
Side		
Right	34 (42%)	8 (29%)
Left	47 (58%)	20 (71%)
Patients with metastatic disease distant to the region of swelling/treatment	23 (28%)	7 (25%)
Average time (years) since disease was first treated	8.3	6.52
Range	1m–39 years	3m–28 years

m, months.

Table 2. Treatment received by each group of patients

	Oedema group (swollen arm)		Control group (no arm swelling)	
	n=81	n=28		
Surgery	No RT	RT	No RT	RT
None	0	3 (4%)	0	1 (4%)
Wide local excision	1 (1%)	38 (47%)	2 (7%)	11 (39%)
Simple mastectomy	4 (5%)	18 (22%)	3 (11%)	8 (29%)
Radical or modified radical mastectomy	6 (7%)	11 (14%)	1 (4%)	2 (7%)

RT, Radiotherapy.

Analysis

The criteria used for judging venous outflow obstruction were (a) direct signs (anatomic and functional): echogenic thrombus in the axillary and/or subclavian vein with absence of Doppler flow signal from the affected segment of vein, absent axillary and/or subclavian vein, narrowed axillary and/or subclavian vein with immobility of vein walls during respiration, venous flow stopped by elevation and or external rotation of swollen arm with no reduction of flow in the contralateral normal arm; (b) indirect signs (functional alone): multiple draining veins around the shoulder demonstrated by CDI as well as, or instead of, the normal axillary and subclavian veins, loss of the normal phasic flow pattern in the axillo/subclavian vein with a continuous Doppler spectral trace and associated loss of the normal phasic movement of the vein walls.

Comparison was made with the contralateral side to confirm that any abnormality was present on the one side only.

Statistics

The χ^2 test with Yates correction was used to compare frequencies.

Ethics

Ethical approval was received from the Royal Marsden Hospital ethics committee.

RESULTS

All the 137 non-swollen arms had normal venous anatomy, wall movement and Doppler flow spectra (28 treated arms in the control group and 81 + 28 contralateral arms in the oedema and control groups).

57 (70%) of the oedema group exhibited venous abnormalities of the axillo-subclavian region in the swollen arms. 46 (57%) had direct evidence of venous outflow obstruction and a further 11 (14%) had indirect signs of venous outflow obstruction alone (loss of phasic variation and/or presence of collaterals). Only 24 swollen arms (30%) had both normal venous anatomy and flow pattern (Table 3).

13 patients (16%) had echogenic thrombus in the axillary or subclavian vein with no flow apparent on CDI. The axillary or subclavian vein could not be identified on the side of swelling in 16 patients (20%) despite clear identification of the artery.

Table 3. Incidence of venous abnormalities in patients with swollen arms

Venous abnormalities in swollen arm	No. of patients $n=81$	Right arm $n=34$	Left arm $n=47$	Patients with clinical evidence of venous abnormalities $n=38$
None, normal venous drainage	24 (30%)	10 (29%)	14 (30%)	9 (24%)
Thrombosis or absent axillary/subclavian vein or loss of low with position	35 (43%)	16 (47%)	19 (40%)	16 (42%)
Axillo/subclavian narrowing with fixed vein walls	11 (14%)	4 (12%)	7 (15%)	6 (16%)
Collaterals and/or loss of phasic variation of the Doppler trace in the axillo/subclavian venous anatomy	11 (14%)	4 (12%)	7 (15%)	7 (18%)

Venous collaterals were easily identified in all these cases, confirming absence of a patent axillary or subclavian vein. A further 6 patients (7%) had veins in which flow stopped when the arm was internally or externally rotated in a position of 90° abduction. Flow continued in the contralateral normal arm in the same position. 11 patients (14%) had a narrowed axillary or subclavian vein with immobility of the vein walls and loss of the normal phasic flow variation on spectral Doppler.

Many patients had more than one sign of venous outflow disturbance. 11 (14%) had changes in the flow pattern or collaterals alone without evidence of axillary or subclavian vein obstruction. Neither abnormal flow patterns nor collaterals were seen in any of the non-swollen arms.

The distribution of normal anatomy and venous abnormalities as demonstrated by CDI was similar in left and right arms ($P = 0.97$). The distribution was also similar in patients with and without clinical evidence of venous outflow obstruction ($P = 0.50$).

3 of the 10 cases with thrombus occluding the vein presented with acute swelling. In only one of these was acute thrombosis suspected clinically prior to ultrasound. A further 3 patients had a past clinical or venographic history of thrombosis.

DISCUSSION

CDI allows the assessment of both venous anatomy and haemodynamics. It is non-invasive and safe. Vessels as small as 1–2 mm diameter can be clearly demonstrted, and the course and direction of flow can be identified. CDI is now well established as a reliable and reproducible method of venous assessment [9–15]. Colour flow images outline the vein lumen allowing ready definition of lumen dimensions and detection of luminal encroachment such as by thrombus.

This is the first study using CDI to examine venous outflow in breast cancer patients with chronic arm swelling. The 57% incidence of venous obstruction is within the 20–80% range of venographic abnormalities reported by other authors [5, 16–18]. The striking difference in venous abnormalities between oedema and control groups (57% versus none) suggests that a compromised venous drainage may be an important factor in the genesis of the arm swelling.

Conventional venography is an invasive technique which may exacerbate swelling. Additional problems such as contrast reaction or ascending phlebitis limit its use. The anatomy demonstrated by venography is non-physiological because flow is approximately doubled by the added 5–10 ml/s of contrast agent whereas the flow dynamics demonstrated by Doppler remain unaffected by the examination. Thus, venography demonstrates anatomical defects which may not be significant. This could account for the discrepancy between our results and those of Schorr and colleagues, who demonstrated abnormalities of calibre in venograms of treated patients both with and without swelling [17].

Halstead, in 1921, suggested that postmastectomy lymphoedema could have a multifactorial aetiology [19]. Veal, in 1936, demonstrated that venous obstruction was associated with arm swelling following breast cancer treatment [3]. He stated that 90% of cases of postmastectomy arm swelling were due to venous obstruction. His observation has been supported by others [4, 5], but the work of Lobb and Harkins [7] and MacDonald [6, 20], showing that resection of the axillary vein did not increase the incidence of arm swelling, has been widely quoted as evidence of the unimportance of venous obstruction. Closer analysis of MacDonald's report reveals that the incidence of arm swelling in their "control" group of 40 patients, who did not receive axillary vein resection, was very high at approximately 95% compared with 75% in the 15 cases with axillary vein resection (3 of whom were followed up for less than 6 months postoperatively) [6]. Lobb and Hawkins refer only to case reports and MacDonald's work in support of their claim. These authors' conclusion that axillary vein resection did not contribute to arm swelling is difficult to substantiate.

The pathophysiology of chronic arm swelling following breast cancer treatment remains unclear. According to the Starling equation, oedema represents an imbalance between net capillary filtration and lymph drainage. It has been assumed in the past that lymph flow in breast cancer patients with arm swelling is reduced considerably. These claims are based entirely on lymphangiographic findings which, not surprisingly, demonstrate anatomical abnormalities of lymph vessels following axillary surgery and radiotherapy [18, 21–23]. Lymph flow, however, has never been measured, and these same lymphangiographic findings are frequently found in patients without arm swelling [24–27].

Any increase in net capillary filtration would encourage swelling, particularly in the presence of a compromised lymph drainage capacity. Recent work has suggested that the capillary filtration rate is increased [28] and one explanation could be venous outflow obstruction.

A parallel study using spectral Doppler, also reported in this issue, estimated arterial inflow in a similar group of breast cancer patients with chronic arm swelling. A mean increase in subclavian artery flow of 68% was measured in the swollen limb compared to the contralateral normal arm. Increased flow did not correlate with increase in arm volume. All these findings suggest that blood vascular abnormalities may be as important as lymphatic abnormalities in the genesis of arm swelling following breast cancer treatment. CDI provides a simple, quick, non-invasive assessment of the venous system of the upper limb. Its value is that it can be repeated as necessary. Work is underway to explore the relationship between the development of venous abnormalities and the onset of swelling. By using CDI prospectively from the time of the cancer treatment, the sequence of events leading to the blood vascular abnormalities should be identified whereupon early treatment, for example an elastic sleeve, can be implemented and perhaps chronic swelling prevented.

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