Histogram Analysis of Magnetization Transfer Measurements Reveals Calf-Muscle Abnormalities in Venous Leg Ulcer Patients

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Introduction

The condition of venous leg ulceration affects between 1% and 2% of the adult population, with increasing prevalence in the elderly population. Venous ulcers usually occur on the side of the leg near to the ankle, are irregular in shape and are surrounded by regions of lipodermatosclerosis. Healing is often impaired and recurrence of the condition after successful treatment reaches levels of up to 70%. Failure of the calf pump, which involves the venous system and the calf muscle, leads to venous hypertension and consequent breakdown of the microcirculation resulting in increased susceptibility to venous ulceration. Attention has thus far been focussed on the venous system, while the purpose of this preliminary study was to investigate the possible role of the calf muscle in the underlying causes of the condition. Magnetization transfer (MT) imaging is a potentially powerful technique for detecting disease-related changes in muscle tissue. A previous study showed a reduction in mean MT ratio (MTR) in the calf muscle of venous ulcer patients compared to normal controls. This could be at least partly be explained by partial filtration of non-MT active material such as fat and oedema in the muscle compartment, but it was unclear whether the muscle tissue itself was also affected. In the study we have used a refined MT sequence with less direct saturation and a histogram analysis of the data. Analysis of the MTR histogram distributions allows more information to be gleaned about the type of changes occurring in the tissue than a simple region of interest measurement.

Methods

Nine patients with a history of unilateral or bilateral venous leg ulceration were recruited for this study, including eight males and one female, ranging in age from 45 to 76 years. The asymptomatic control group contained nine men and two females covering a wide range of ages from 23 to 81 years. This allowed the change in MT parameters with age to be measured and taken into account when comparing the groups. MT measurements were obtained using an interleaved gradient-echo imaging sequence generating a baseline image and a MT-weighted image. MT weighting was achieved using a train of binomial pulses. For each MT image the amplitude of the binomial pulses was first calibrated to eliminate coil loading effects. Where possible MT images were obtained for both legs and one of each subject. MT ratio (MTR) images were computed and analysed to produce histograms of the data for manually selected regions of interest covering the muscle region. The MTR histograms were then normalised to the muscle area and the peak position and height were measured for each individual using a gaussian fit to the data. The skewness of the distributions was assessed using the Pearson’s mode skewness coefficient, given by:

\[(\text{mode} - \text{mean})/\text{standard deviation}\]

Results

An overview of the results is displayed in figures 1 and 2, showing the average of the normalised MTR histograms of the calf muscle and arm muscle for each group. There is a marked difference in the MTR distribution between the ulcer and control groups in the calf muscle, while the arm muscle histograms show similar characteristics for each group. In the calf muscle, both the peak position and height is reduced for the ulcer group compared to the controls. The distribution also appears more skewed towards lower MTR values in the ulcer group. To test the significance of these changes the effect of age on these parameters in the control group was also assessed. In the arm muscle the peak position (mode MTR value) decreased with age \((R^2 = 0.4, P < 0.02)\), but there was no significant change in peak height or skewness. In the calf muscle there was only a weakly significant decrease in mode MTR with age \((R^2 = 0.2, P < 0.05)\), but a more significant decrease in peak height \((R^2 = 0.4, P < 0.02)\) and increase in skewness \((R^2 = 0.3, P < 0.05)\). When compared to the age-matched control group the calf muscle peak MTR \((P < 0.05)\) was significantly lower in the calf muscle of the ulcer group. Furthermore, the downward shift in peak position with age in the arm muscle is probably indicative of a change in the underlying muscle tissue caused by atrophy. These results suggest that the ageing process in the arm muscle is different to that in the calf muscle. The comparison of the results for the venous leg ulcer group with the age-matched control data indicates that there is increased infiltration of fat and/or oedema in the muscle compartment. The downward shift in peak position with age in the arm muscle is probably indicative of a change in the underlying muscle tissue caused by atrophy. These results suggest that the ageing process in the arm muscle is different to that in the calf muscle. The comparison of the results for the venous leg ulcer group with the age-matched control data indicates that there is increased infiltration of fat and/or oedema in the muscle compartment. The downward shift in peak position with age in the arm muscle is probably indicative of a change in the underlying muscle tissue caused by atrophy. These results suggest that there may also be a degenerative change in the calf muscle tissue itself that does not occur with normal ageing. The fact that these changes are not present in the arm muscle indicates a localised effect, although it does not appear to be secondary to ulcer formation since there was no difference between legs in unilateral disease. The variable nature of the venous leg ulcer group and relatively small number of patients studied does not allow specific conclusions about the impact of these muscle abnormalities on the aetiology of venous leg ulcers. However, this study has shown that deficiencies of the calf muscle may be a causative factor in some cases and that histogram analysis of MT data is a useful tool for investigating different disease processes in anatomically complex regions of the body.

Discussion

The reduction in normalised peak height and increase in skewness towards lower values with age in the calf muscle indicates infiltration of fat and/or oedema in the muscle compartment. The downward shift in peak position with age in the arm muscle is probably indicative of a change in the underlying muscle tissue caused by atrophy. These results suggest that there may also be a degenerative change in the calf muscle tissue itself that does not occur with normal ageing. The fact that these changes are not present in the arm muscle indicates a localised effect, although it does not appear to be secondary to ulcer formation since there was no difference between legs in unilateral disease. The variable nature of the venous leg ulcer group and relatively small number of patients studied does not allow specific conclusions about the impact of these muscle abnormalities on the aetiology of venous leg ulcers. However, this study has shown that deficiencies of the calf muscle may be a causative factor in some cases and that histogram analysis of MT data is a useful tool for investigating different disease processes in anatomically complex regions of the body.

References