The Relationship Between the Presence of Distal Collateral Lymphatic Flow and Obesity in Patients with Bilateral Lower Extremity Edema

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ABSTRACT

Objective: This study aimed to comprehensively assess radionuclide imaging findings to aid in the clinical diagnosis of early-stage lower extremity lymphedema.

Methods: Our retrospective study included 135 patients who underwent lymphoscintigraphy for bilateral lower extremity edema (BLEE) between 2017 and 2022. Of these patients, 117 (86.7%) were female. Lymphoscintigraphic images were acquired at the 10th, 40th, and 2nd hours post-injection of radiopharmaceuticals. Bilateral lower extremity lymphatic congestion (MLC) was observed in the 2nd-hour images of radionuclide imaging (RI), with an associated accumulation of activity in the inguinal lymph nodes. All patients presented with lower extremity edema.

Results: Among our patients, 55 (40.7%) were classified as obese. Bilateral distal collateral flows (BDCF) were identified in 60 (44.4%) of our patients, all of whom were female. Within this group, 13 (21.7%) were obese, and 11 (18.3%) exhibited distal and direct muscle lymphatic congestion (DDMLC). DDMLC was present in 63 (46.7%) patients. Unilateral distal collateral flow (UDCF) was detected in 75 (55.6%) of the patients with BLEE, with 67 (89.3%) of them being obese. Obese patients exhibited a significantly higher prevalence of both UDCF and DDMLC (p: 0.0005). Detailed results can be found in Table 1-4 and Figures 3 and 4.

Conclusion: Functional bilateral radionuclide imaging methods provide valuable data for physicians, enabling bilateral and comparative assessments. However, particular attention should be paid to the interpretation of asymmetric images, especially in specific patient groups.

Keywords: radionuclide imaging, distal collateral lymphatic flows, lymphoscintigraphy, obesity

INTRODUCTION

It is well-established that pressures play a crucial role in the formation and transportation of lymph fluid (1-2). In the context of functional radionuclide imaging (RI) of lower extremity lymphatic flow, the demonstration of lymphatic progression in the main lymphatic channel (MLC) is of paramount importance.

Lower extremity radionuclide imaging using nanocolloid-labeled Tc-99m pertechnetate offers valuable insights into lymphatic function (3-6). In cases of bilateral lower extremity edema (BLEE), lymphoscintigraphy findings may not always lead to a definitive diagnosis of lymphedema. Nevertheless, the presence of asymmetric findings in such patients holds significance.

The observation of asymmetric accumulations in individuals with symmetrical complaints provides valuable insights into the underlying pathophysiology. In this study, our objective was to assess the correlation between unilateral distal collateral flows (UDCF) and the density difference between the main lymphatic channels (DDMLC), and their association with body mass index (BMI).

We aim to contribute valuable insights to the existing literature concerning the early diagnosis of lymphedema.
MATERIAL and METHODS

In our retrospective study, we included a cohort of 135 patients who underwent lymphoscintigraphy due to bilateral lower extremity edema (BLEE) between 2017 and 2022. The mean age of the participants was 45 years, with an age range between 33 and 59 years. Among these patients, 117 (86.7%) were female.

Exclusion criteria for our study encompassed individuals with a diagnosis of lipoedema, significant lymphedema, a history of intra-abdominal surgery, chronic illnesses, chronic medication use, smoking habits, prior lower extremity surgeries, inguinal lymphadenopathy identified via abdominal ultrasonography (USG), those lacking 2nd hour imaging in radionuclide imaging, and those exhibiting asymmetric radioactive counts in the injection area.

In our patient cohort, bilateral main lymphatic channel (MLC) visualizations were observed in the 2nd-hour images of radionuclide imaging (RI). Additionally, an accumulation of activity within the inguinal lymph nodes was detected in the radionuclide images (Figure 1, 2). Notably, all patients presented with lower extremity edema.

For radionuclide imaging (RI), nanocolloids with a size range of 50-70 nm were employed and labeled with technetium (TC)-pertechnetate. Subcutaneous administration of these nanocolloids was carried out bilaterally in the 1st and 2nd interdigital web areas of both feet using a 26-gauge injector (7). Each injector contained 22-25 MBq of activity, and the injection volume ranged from 0.2 to 0.3 ml.

Lymphoscintigraphic images of the patients were captured at the 10th, 40th, and 60th hour images. Patients exhibiting significant asymmetric activity in these regions were excluded from the study.

Scintigraphic imaging procedures were conducted utilizing a Mediso-AnyscanS double-headed gamma camera, equipped with a high-resolution parallel hole collimator.

It is important to note that our retrospective study received approval from the Gaziosmanpaşa Training and Research Hospital Ethics Committee, with the assigned reference number 18, on March 15, 2023.

Statistics: Continuous variables not normally distributed were expressed as median (min-max), categorical variables as number of cases, and percentage. Mann-Whitney U test was used for non-normally distributed continuous variables, and the chi-square test was used for categorical variables. Logistic regression analysis was used for multidimensional analysis. p<0.05 was accepted as statistically significant.

RESULTS

Among our patient cohort, 55 individuals (40.7%) were classified as obese. Bilateral distal collateral flows (BDCF) were identified in 60 patients (44.4%). Notably, all patients with BDCF were females. Within this subgroup of 60 patients with BDCF, 13 (21.7%) were obese. Furthermore, 11 of these 60 patients (18.3%) exhibited a density difference between main lymphatic channels (DDMLC). DDMLC was observed in a total of 63 patients (46.7%).

Unilateral distal collateral flow (UDCF) was detected in 75 patients (55.6%) who presented with bilateral lower extremity edema (BLEE). Remarkably, among these 75 patients, 67 (89.3%) were classified as obese. It is noteworthy that both UDCF and DDMLC were found to be significantly more prevalent in obese patients, as demonstrated by a p-value of 0.0005.

A summary of these findings is provided in Tables 1 to 4 and Figures 3 and 4.

Table 1: Data of radionuclide imaging in two groups categorized according to body mass index

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (normal weight patients)</th>
<th>Group 2 (obese patients)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>45 (33-59)</td>
<td>46 (35-55)</td>
<td>0.939</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>0(0%)/55(100%)</td>
<td>18 (22.5%)/62(77.5%)</td>
<td>0.0005</td>
</tr>
<tr>
<td>Unilateral distal collateral flows</td>
<td>8 (14.5%)</td>
<td>67 (83.8%)</td>
<td>0.0005</td>
</tr>
<tr>
<td>The density difference between main lymphatic channels</td>
<td>12 (21.8%)</td>
<td>51 (63.7%)</td>
<td>0.0005</td>
</tr>
</tbody>
</table>

Table 2: Logistic regression analysis showing the difference between the two groups

<table>
<thead>
<tr>
<th></th>
<th>Odds</th>
<th>Confidence Interval</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Unilateral distal collateral flows</td>
<td>19.056</td>
<td>6.857-52.958</td>
<td>0.0005</td>
</tr>
</tbody>
</table>

Table 3: Data from patients with bilateral and unilateral distal collateral lymphatic flows.

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=60)</th>
<th>Group 2 (n=75)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>45 (33-57)</td>
<td>45 (33-55)</td>
<td>0.766</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>0(0%)/60(100%)</td>
<td>18(24%)/57(76%)</td>
<td>0.0005</td>
</tr>
<tr>
<td>Obesity</td>
<td>13 (21.7%)</td>
<td>67 (89.3%)</td>
<td>0.0005</td>
</tr>
<tr>
<td>the density difference between main lymphatic channels</td>
<td>11 (18.3%)</td>
<td>52 (69.3%)</td>
<td>0.0005</td>
</tr>
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</table>

Table 4: Logistic regression analysis for significant variables

<table>
<thead>
<tr>
<th></th>
<th>Odds</th>
<th>Confidence Interval</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>obesity</td>
<td>19.056</td>
<td>6.857-52.958</td>
<td>0.0005</td>
</tr>
<tr>
<td>the density difference between main lymphatic channels</td>
<td>5.088</td>
<td>1.781-14.539</td>
<td>0.0002</td>
</tr>
</tbody>
</table>
Figure 1: Presence of bilateral distal collateral flow in radionuclide imaging

Figure 2: Presence of distal collateral flow in the left lower extremity on radionuclide imaging

Figure 3: Schematic representation of the relationship between obesity and distal collateral lymphatic flows.
DISCUSSION

The presence of asymmetric function in RIs interpreted comparatively bilaterally may cause errors in the evaluation of the images. In patients with unilateral complaints, decreased function is expected on the same side as the complaint. The presence of asymmetric accumulation is frequently observed in lymphoscintigraphy imaging in patients with bilateral complaints. In the presence of BLEE, lipedema or hypoalbuminemia can be considered if MLC is observed in RI and there are no findings suggestive of the diagnosis of lymphedema. There was no diagnosis of lipedema in the patients included in our study. There was no Stummer's sign or cuff sign in the patients. In the case of hypoalbuminemia, findings can be expected to be symmetrical. DDMLC and UDCF were significantly less frequent in normal-weight patients than in obese patients. It is stated that diagnosis is more difficult in the presence of obesity (8-10). Obesity negatively affects the clinical course of lipedema and lymphedema (11-13). In our study, while MLC was present in obese patients and the complaint was bilateral, the asymmetry detected on imaging was more common than in normal-weight patients. This may occur due to changes in the content of the circulating lymph, even though the patients still have functional lymphatic flow. There was no finding that could explain UDCF and DDMLC in our patients. The rate of occurrence of symmetrical findings was higher in patients with normal weight in the presence of bilateral complaints. In the presence of obesity, there may be additional pathologies that cause decreased function. Fibrotic tissue formation increases in obese patients (11,13). Activation of adipocytes triggers fibroblast and collagen production (14). The increase in fibrotic tissue may have led to UDCF and DDMLC findings in RI. There are no or very few studies comparing RIs in the same patient group with obesity and after a low-calorie diet. Our study shows that; In obese patients, there is an asymmetrical decrease in function even before lymphedema appears scintigraphically. Evaluation of early findings is meaningful for early diagnosis. Thus, the success of treatment will increase. In our study, the number of female patients was higher. Smoking was an exclusion criterion, and the smoking rate between the ages of 30-50 is quite high in our country. Additionally, the female gender is more common in patients admitted to the hospital due to BLEE (15). Our patients had no skin lesions, pain, itching, or easy bruising complaints. Many studies examine the mechanical forces that affect lymphatic flow (16,17). There are many mechanisms by which lower limb lymph reaches the left subclavian vein. Pressure balance is very important in the proper operation of this mechanism. It will be difficult for the liquid to move against high pressure, and changes in the liquid content may also cause dysfunction. In the presence of obesity, this may affect the lymphatic flow in both situations. Collecting lymphatics contain smooth muscles that ensure lymph transmission (17). Secondary valves prevent the reflux of lymph. Defects in these structures may result in obesity. Early detection of these problems will increase the success of treatment and also protect the patient from cosmetic problems. UDCF and DDMLC may lead to decreased post-nodal lymph quantity. This may cause the body's immune system to malfunction. In fact, this problem may be widespread throughout the body, and in this case, a general immune disorder occurs in obese patients. Even if the pump function is increased up to a certain value against high pressure, failure may begin after the critical value (18). UDCF and DDMLC, which are more common in obese patients, may have early findings of lymphedema. It has been stated that the quality of life decreases in the advanced stages of lymphedema (19-20). Understanding the pathophysiology of lymphedema will be significant for developing treatment options and prevention practices.

Study Limitations:

Our study possesses a limitation attributable to its retrospective nature, which entails an inherent susceptibility to recall bias, potential inconsistencies in data collection, and the inability to establish causal relationships due to the absence of controlled experimental

CONCLUSION

Functional bilateral radionuclide imaging methods are valuable for physicians in terms of providing bilateral and comparative data. However, more care should be taken in interpreting asymmetric images in certain patient groups.

Abbreviations:

UDCF: unilateral distal collateral flows
BDCF: bilateral distal collateral flows
DDMLC: density difference between main lymphatic channels
MLC: main lymphatic channel
RI: radionuclide imaging
USG: ultrasonography
ROI: Regions of interest
BLEE: bilateral lower extremity edema

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Author Contributions: SC; contributed to the conception of the work, execution of the study, revision of the draft, SC; approval of the final manuscript version, and concur with all aspects of the work. All authors have reviewed the manuscript, and affirm that they fulfill the ICMJE criteria for authorship.

Ethical approval: The present study was conducted in strict accordance with the principles outlined in the Declaration of Helsinki. Ethical approval for the study was obtained from the appropriate ethics committee, and all participants provided informed consent before participating in the study.

REFERENCES


