Effect of Obesity on Lymphatic Fluid Filtration in Inguinal Lymph Nodes

Sule Ceylan1*

1 University of Health Sciences, Gaziosmanpasa Training and Research Hospital, Department of Nuclear Medicine, Istanbul, TR

* Corresponding Author: Sule Ceylan1 E-mail: ceylansule2003@gmail.com

ABSTRACT

Objective: The objective of this study was to investigate the potential impact of radionuclide imaging on filtration in the inguinal lymph nodes of obese patients. We aimed to compare the lymphatic transport after the inguinal lymph nodes between obese patients and normal-weight individuals, while ensuring intact lower extremity lymphatic flow.

Methods: A retrospective study design was employed, involving the re-evaluation of patient images. Among the total of 119 patients, 62 were classified as obese, while the remaining patients had body mass indexes within normal limits. All patients included in the study were female, with a mean age of 39 years (ranging from 28 to 47 years). Lymphatic imaging was performed using Tc-99m-labeled nanocolloid particles with a size of 50-70 nm. The nanocolloid was applied to the 1st and 2nd interdigital web areas on the dorsum of both feet. Late images were captured at 45-50 minutes and 2 hours after application.

Results: Out of the 119 patients, 62 (52%) were classified as obese. There was no significant difference in terms of age between the two groups. The pre-inguinal average count values, calculated from the counts before the inguinal node, did not show a significant difference between the two groups. However, the post-inguinal average count values obtained after the inguinal nodes were significantly lower in obese patients compared to normal-weight patients (p<0.0005).

Conclusion: Our findings suggest that even in the early stages, when functional imaging allows observation of the main lymphatic duct, there are differences in the progression of lymphatic flow between obese patients and normal-weight individuals. Detecting these differences may enable early diagnosis of lymphedema disease, which is a reversible disorder if identified promptly.

Keywords: radionuclide imaging, inguinal lymph nodes, lymphatic system, obesity

INTRODUCTION

The lymphatic system plays a crucial role in various physiological processes such as fluid collection, protein balance, lipid transport, and immune function. It adapts to changing conditions to ensure optimal functionality. In an upright position, lymphatic fluid progresses against the hydrostatic gradient (1). Smooth muscles in the collecting lymphatics propel the lymph forward, acting like a pump (2). However, when secondary valves are defective, the pumping efficiency of the lymphatic system is compromised (1,2).

The collecting lymphatics deliver lymph to the lymph nodes, where lymphatic fluid encounters lymphocytes and antigen-carrying cells (3). Consequently, the cellular composition of the lymph undergoes significant changes within the lymph node. For instance, monocytes, macrophages, and dendritic cells, which are abundant in the afferent lymph, are not found in the efferent lymph (3). The number of lymphocytes is higher in postnatal lymphatic fluid (3).

Fluid accumulation in the interstitial space triggers lymph formation. As evident, pressure differentials play a crucial role in the generation and transport of lymphatic fluid (4). It is known that pressures can be altered in both the extremities and the abdomen of obese individuals. Lymphoscintigraphy, a functional radionuclide imaging technique, is utilized for mapping the lymphatic system (5,6). It is widely recognized that fluid in the interstitial space always moves towards areas of lower pressure (7).
In this study, we aimed to investigate the potential impact of radionuclide imaging on filtration within the inguinal lymph nodes of obese patients. Despite intact lower extremity lymphatic flow, we examined whether there are differences in transport after the inguinal lymph nodes between obese patients and normal-weight individuals.

**MATERIAL and METHODS**

Our retrospective study involved 119 patients who underwent bilateral lower extremity lymphoscintigraphy examinations. The bilateral lymphatic flow in all patients was found to be within normal limits. Patients included in the study met the criteria of having a traceable main lymphatic channel bilaterally and sufficient accumulation of activity in the inguinal lymph nodes (Figure 1-2). The presenting complaint in all patients was lower extremity swelling, leading to a preliminary diagnosis of lymphedema. The patient images were re-evaluated as part of our retrospective study.

For lymphatic imaging, nanocolloids with particle sizes ranging from 50 to 70 nm were labeled with Tc-99m pertechnetate. The 50-70 nm nanocolloid particles are filtered through the interstitium into the terminal lymphatics. Due to their size, they cannot pass through capillaries, allowing us to evaluate lymphatic filtration using this method. Tc-99m nanocolloid was intradermally administered in the 1st and 2nd interdigital web areas of both feet using a 26-gauge syringe. The administered dose volume for each injection was approximately 0.2-0.3 ml, with each injector containing 22-25 MBq of activity. The standard protocol, excluding any variations, was followed (8). Prior to injection, the injection site was cleansed using iodine solution and alcohol, and local anesthesia was not administered.

Imaging was performed using a Siemens E-Cam double-headed SPECT gamma camera equipped with a high-resolution parallel hole collimator. Scanning was conducted at a speed of 10 cm/min, utilizing a 1024 matrix. Dynamic work was obtained with a frame rate of 15s/frame in a 64 x 64 matrix. Early imaging was captured 15 minutes after a 5-minute walking exercise, following the dynamic acquisition. Late images were obtained at 45-50 minutes and 2 hours. In our retrospective study, quantitative values obtained from the 2-hour (late) images were utilized (Figure 1-2).

Out of the total patient cohort, 62 individuals were classified as obese, while the body mass indexes (BMI) of the remaining patients fell within the normal range. All patients included in the study were female, with a mean age of 39 years (ranging from 28 to 47 years). Male patients were excluded from the study due to their prior diagnosis of lymphedema. Additionally, patients with pre-existing lymphedema, chronic drug use, chronic kidney failure, chronic heart disease, chronic liver failure, endocrine system diseases, hypoalbuminemia, inguinal lymphadenopathy detected in abdominal ultrasound, patients diagnosed with lipedema, and those with a history of intra-abdominal surgery were not included.

Localization of the inguinal lymph nodes was achieved, and regions of interest were defined for the pre-inguinal average count (pre-iac) obtained before the nodes, as well as the post-inguinal average count (post-iac) obtained after the inguinal lymph nodes. Average counts were calculated from these regions. Our retrospective study received ethical approval from the Gaziosmanpaşa Training and Research Hospital Ethics Committee under number 18 on March 15, 2023.
**Statistical analysis:** Statistical analysis was performed on variables that were not normally distributed. These variables were presented as median values with the range (minimum-maximum). The Mann-Whitney U test was employed to compare these non-normally distributed variables between groups.

**RESULTS**

Out of the total 119 patients included in the study, 62 (52%) were classified as obese. The mean age of the normal-weight patients was 39 years (ranging from 28 to 47 years), while the mean age of the obese patients was 38 years (ranging from 27 to 48 years). There was no statistically significant difference in age between the two groups. Additionally, there was no significant difference between the two groups in terms of pre-iac values, which were calculated based on the counts before the inguinal node. However, the post-iac values obtained after the inguinal nodes were significantly lower in obese patients compared to normal-weight patients (p<0.0005).

The summarized results are presented in Table 1, and the graphical representation can be seen in Figure 3.

**DISCUSSION**

Understanding the impact of mechanical forces on lymphatic flow is crucial for planning the treatment of lymphedema. Various pressure mechanisms contribute to the transportation of lymph from the lower extremities to the left subclavian vein. One example is the oscillating pressure gradient, which aids in the movement of lymph fluid from the interstitial space to the anterior collecting lymphatics. The lymphatic fluid is then returned to the central circulation through both lymph nodes and larger lymphatic trunks. Maintaining a proper pressure balance is essential for the healthy functioning of this cycle. Optimal inlet and outlet pressures are necessary, as it becomes increasingly difficult to transport the fluid against high pressure beyond a certain threshold. In addition to pressure considerations, the pump mechanism, endothelial permeability, and smooth muscle cells actively contribute to the journey of lymphatic fluid (9). Smooth muscles within the collecting lymphatics guide the flow of lymph, with each segment referred to as a lymphangion. Secondary valves within the lymphangions prevent the reflux of lymph fluid (10).

**Table 1:** Data from normal-weight and obese patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal Weight Patients</th>
<th>Obese Patients</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>39 (28-47)</td>
<td>38 (27-48)</td>
<td>0.693</td>
</tr>
<tr>
<td>BMI</td>
<td>23 (20-25)</td>
<td>34 (32-35)</td>
<td>0.0005</td>
</tr>
<tr>
<td>Pre-inguinal average count</td>
<td>3.76 (2.27-4.71)</td>
<td>3.74 (2.26-4.74)</td>
<td>0.915</td>
</tr>
<tr>
<td>Post-inguinal average count</td>
<td>0.88 (0.71-0.93)</td>
<td>0.38 (0.23-0.49)</td>
<td>0.0005</td>
</tr>
</tbody>
</table>

**Figure 3:** Data on post-inguinal counts in normal weight and obese patients.
In our study, despite the presence of lower extremity swelling in obese patients, radionuclide imaging showed normal lymphatic flow in the lower extremities. Treating advanced cases of lymphedema resulting from lymphatic insufficiency can be challenging. Therefore, studies conducted in high-risk groups during the early stages of the disease are crucial for identifying early indicators. Obesity can lead to deterioration in the structure of the pump and valves within the lymphangion. Functional imaging may reveal a decrease in transport after the inguinal lymph nodes in the early stages of the disease. In our study, we observed lower post-iac values in obese patients compared to normal-weight patients, which may hold significance in evaluating lymphatic flow.

Apart from various mechanisms associated with obesity, increased intra-abdominal pressure can hinder lymphatic progression. Although lymphatic flow was not impaired in our patients, the addition of other factors over time could lead to the development of lymphedema. Patients may be advised to follow a low-calorie diet to manage their weight. Lymphocytes exit the lymph nodes via postnodal lymphatics (3), and there is a higher concentration of lymphocytes in post-nodal lymph compared to pre-nodal lymph. In obese patients, increased intra-abdominal pressure and potential decreases in post-nodal lymphatic content due to various reasons may contribute to immune system impairment. Additionally, there is a transfer of low-protein fluid to the central circulation in the lymph node. Consequently, post-nodal lymph exhibits a higher protein content, specifically colloid osmotic pressure (4,11).

The retrograde pressure caused by back reflection can create a vicious cycle and contribute to increased lymph fluid accumulation over time. Simultaneous measurement of interstitial and intralymphatic pressure reveals a notable pressure gradient (12). Lymphatic flow is influenced by various factors such as walking, passive limb movements, skin massage, and respiratory actions during spontaneous expiration and inspiration. Secondary valves play a role in countering the effects of gravity in an upright position (13). In conditions like obesity, where body tone and internal pressure are altered, lymphatic flow can be maintained to a certain extent. Therefore, close monitoring and imaging examinations in the early stages are crucial for patients in this group.

In a study evaluating the pressure-volume relationship in the lymphatic system, it was observed that lumen pressure increased with increasing outlet pressure (10). Another study reported an increase in pump function with an increase in outlet pressure (14). However, beyond a critical threshold, these mechanisms may become insufficient, leading to pump dysfunction. If the preload is too low, the force of contraction is increased to overcome the afterload (14). Extrinsic and intrinsic forces have an impact on lymph flow in the collecting lymphatics (15). Under normal physiological conditions, approximately 8-10 liters of interstitial fluid are formed in humans per day (16). Most of this fluid must be reabsorbed into the circulation to prevent tissue edema (17). Lymphoscintigraphy has been reported to have a success rate of 100% in evaluating lymphatic flow (18). A study examining the effects of morbid obesity on lymphatic function indicated a decrease in lymphatic pump function (19). Additionally, another study highlighted disruptions in the lymphatic capillary structure in obesity (20). The increased chronic inflammation associated with obesity may lead to fibrosis, which can adversely affect lymphatic function.

**Study Limitations:**
The weakness of our study is that it is retrospective.

**CONCLUSION**

In conclusion, our study highlights the impact of obesity on lymphatic flow in the lower extremities. The findings demonstrate that even in the early stages of the disease, when functional imaging reveals the presence of the main lymphatic duct, there are notable differences in the progression of lymphatic flow between obese and normal-weight individuals. These differences hold significance in the early diagnosis of lymphedema, a reversible disorder resulting from lymphatic insufficiency. Our study underscores the importance of close monitoring and imaging examinations in patients with obesity to identify and manage lymphatic abnormalities at an early stage. Further prospective studies are warranted to deepen our understanding of this subject and explore potential interventions to improve lymphatic function in obese individuals.

**Acknowledgements:** none

**Abbreviations:**

post-iac: post-inguinal average count

pre-iac: pre-inguinal average count

**Conflict of interest:** The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**Author Contributions:** SC: DataCollection, design of the study, SC: manuscript preparation, revisions. All the authors have read, and confirm that they meet, ICMJE criteria for authorship.

**Ethical approval:** All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and/or with the Helsinki Declaration of 1964 and later versions.

**REFERENCES**


