



Resource overutilization in the diagnosis of lymphedema praecox[☆]

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ABSTRACT

Purpose: Primary lymphedema presenting in adolescence is known as lymphedema praecox. Older children presenting with leg swelling are often subjected to a myriad of diagnostic tests. The purpose of this study is to review a large-cohort of patients with lymphedema praecox to determine the fiscal impact of diagnostic testing on these patients.

Methods: A 13-year review was performed of patients with lymphedema praecox. Information was obtained on demographic parameters, diagnostic studies performed, and clinical outcomes.

Results: Forty-nine patients were identified. The median age was 14 (range: 7–21) years. Participants were predominantly female ($n = 40, 81.6\%$). 19 patients had bilateral disease and 30 had unilateral disease. The diagnosis was made on clinical exam only in 14 patients. 35 patients had imaging which consisted of plain X rays, Doppler ultrasound (DUS), lymphoscintigraphy (LSG) or MRI as the sole imaging study ($n = 28$) or in combination with others ($n = 7$). The charges for plain X-rays, DUS, LSG, and MRI with contrast were \$335, \$1715, \$1269, and \$6006 respectively.

Conclusion: We believe that in the adolescent female with physical findings consistent with lymphedema praecox, diagnostic imaging should be limited to a Doppler ultrasound to rule out a secondary cause of the swelling.

Level of Evidence: IV

Type of Evidence: Case series with no comparison group.

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1. Introduction

Lymphedema is the accumulation of lymphatic fluid within tissues. This can be divided into primary and secondary causes. While a number of secondary causes are well known and described, primary lymphedema in the pediatric population is a far rarer entity. Reports in literature describe an incidence of 1.15/100,000 in individuals less than 20 years of age [1]. Primary lymphedema in the newborn is called congenital lymphedema whereas lymphedema in the older child especially between puberty and the age of 25 is categorized as lymphedema praecox [2]. Lymphedema praecox almost always presents as painless swelling of the lower extremity from the knee to the toes which has gradually worsened over a period of months with no history of injury to the extremity.

Abbreviations: DUS, Doppler ultrasound; LSG, Lymphoscintigraphy.

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The ensuing limb swelling noted in these patients can be debilitating and the source of significant psychosocial stress. These patients are often subjected to a number of costly and time consuming diagnostic studies which have little impact on their management.

Estimates have suggested that roughly 30% of healthcare expenditure is unnecessary [3]; therefore, physicians play a vital role in determining what imaging is necessary to make the diagnosis in the most accurate and cost effective manner. The purpose of this study is to review a group of lymphedema praecox patients to determine what are appropriate diagnostic studies, as well as the fiscal impact of testing patients.

2. Methods

Children's National Health System is the largest tertiary care pediatric referral center in the Washington, DC area that includes the neighboring states of Maryland and Virginia. A 13-year (2005 to 2017) retrospective review of institutional medical records was performed for patients between the ages of 7 and 21 with a diagnosis of lymphedema praecox seen in the general surgery, orthopedics, rheumatology or multidisciplinary vascular anomaly clinic. Information was obtained

on demographic parameters, diagnostic studies performed, premorbid conditions, complications, follow up, and charges of diagnostic workup. All charges were reported in 2018 United States Dollars (USD). Descriptive analyses were performed. Approval was obtained to conduct the study from the institutional review board (IRB) prior to data collection.

3. Results

After excluding all patients with lower extremity lymphedema with a known cause, we analyzed 49 patient records. The median age was 14 (range: 7–21) years. Participants were predominantly female ($n = 40$, 81.6%). Thirty-one patients (64%) were African-Americans, although more than 50% of our outpatients are African-American. 19 patients (38%) had bilateral disease. In patients with unilateral disease, 16 were on the right and 14 were on the left. 52% ($n = 27$) did not have any associated comorbidities. Of those with comorbidities 4 patients were suffering from obesity, 3 had neurodevelopmental abnormalities, and 3 patients had asthma. Table 1 provides a complete list of comorbidities.

The diagnosis was made on clinical exam only in 14 patients. 35 patients had imaging. Twenty-eight patients had only one imaging study: 3 plain X rays; 2 lymphoscintigraphy (LSG), 12 Doppler ultrasounds (DUS) and 11 MRI. Seven patients underwent more than 1 imaging study: 3 DUS and MRI; 3 DUS, MRI and LSG, and 1 DUS and LSG. The charges for lower extremity lower extremity X-ray, DUS, LSG, and MRI with contrast were \$335, \$1715, \$1269, and \$6006 respectively. There was a wide range in the number of diagnostic tests done depending upon which provider/specialist the patient first saw for leg swelling. Rheumatology, Vascular Anomalies Clinic, and a nonspecialist ordered imaging in 100%, 55% and 33% of the patients respectively. The average total charge of clinical evaluation and follow up for those who did not undergo diagnostic imaging was \$4659 compared to a maximum of \$13,649 for patients who had DUS, LSG and MRI. There was no difference in diagnostic tests ordered between patients that unilateral disease compared to those with bilateral disease ($p = 0.26$). Table 2 describes the total charges and average charges for patients with the use of singular or multimodal diagnostic testing. In no patient who had DUS as his/her only imaging study did plain X ray, LSG, or MRI add to the accuracy of the diagnosis. Two patients were treated for cellulitis during the follow up period (both of whom were diagnosed with lymphedema praecox after presentation for their initial episode of cellulitis). All patients were treated with compression stockings and follow up. Median follow up was 18 months.

4. Discussion

Lymphedema praecox represents the most common form of primary lymphedema. It is believed to be the delayed presentation of an underlying genetic defect [4]. A number of genetic defects have been postulated to be responsible for this condition including: FOXC2 [5], fatty acid binding protein 4 (FABP4), vascular endothelial growth factor receptor-2 (NRP2), sry-related HMG-box gene 17 (SOX17), and vascular cell adhesion molecule 1 (VCAM1). However, these remain largely controversial and to date, no definitive causal relationship has been established.

Previous work has suggested that classically lymphedema praecox presents in adolescent females as a painless swelling of a lower extremity [6]. Our results agree with this, with a large majority of our patients being predominantly female (81%) which has led to the theory of a possible hormonal link which is supported by the onset of most disease at puberty or pregnancy [6]. In our series, a significant number of patients (38%) presented with bilateral disease which is consistent with previously reported rates of approximately 30% [7].

Given the rarity of this disease, currently there is a paucity of data to guide clinicians in its diagnostic workup, but we believe that it is prudent that some imaging be done to rule out other potential causes of

Table 1
Comorbidities affecting the patient population.

Comorbidities	Frequency (n)
• Anemia	1
• Asthma	3
• Autism	1
• Ehler Danlos Syndrome	1
• Factor 2 Mutation	1
• Fracture Of The Lower Extremity	2
• Lymphatic Malformation	1
• Neurodevelopmental Delay	3
• None	27
• Obesity	4
• Osteochondromatosis	1
• Patellar Dislocation	1
• Pregnancy	1
• Raynaud's Syndrome	1
• Scald Burn To Lower Extremity	1
Total	49

leg swelling such as deep venous thrombosis, a vascular anomaly or a mass obstructing the lymphatics. It has been reported that approximately one quarter of children referred with a diagnosis of lymphedema to a children's hospital had another diagnosis when fully evaluated [8]. Patients with lymphedema praecox universally present with swelling occurring gradually over months that is painless except for a feeling of heaviness at the end of the day. If the swelling had an acute onset or was associated with significant pain one should be suspicious of the swelling being caused by something other than lymphedema praecox. Decades ago contrast lymphangiography was the diagnostic test of choice but it has now largely been abandoned owing to its associated complications and technical difficulties. Currently lymphoscintigraphy, ultrasound and MRI [9] can be used to make the diagnosis but what is really necessary remains uncertain. In our series, no patient with lymphedema praecox and a normal extremity DUS of the effected extremity was later diagnosed with a secondary cause of the lymphedema or another diagnosis. We believe that in the typical adolescent female presenting with painless lower extremity swelling and a normal DUS no additional imaging is needed to confirm the diagnosis of lymphedema praecox.

While no official guidelines exist for management of lymphedema praecox, treatment is often successful with conservative and supportive measures. These are focused on improving drainage and involve a number of measures including: frequent exercise, lymphedema massage, and elevation of the affected extremities, use of compression garments, and use of sequential compression devices. These measures have been shown to be effective in approximately 75% of cases [9]. For patients who fail nonoperative management, surgery is an option, but resection of the lymphedema tissue may be complicated by an unacceptable cosmetic result [8]. Attempts to treat the lymphedema with staged subcutaneous excision for lymphedema of the lower extremity were first reported in children by Feins et al in 1977 [10] but the operation was found to be tedious and did not result in durable relief from symptoms and thus has largely been abandoned. About 20% of patients develop cellulitis and patients should maintain appropriate local skin care to prevent cellulitis.

5. Conclusions

Painless lower extremity swelling in the older child can be accurately diagnosed to be because of lymphedema praecox by careful history, physical exam and DUS of the effected extremity (ies) and unwarranted, time consuming, and invasive testing may be the source of significant cost, stress and anxiety for patients and parents. Based

Table 2

Total charges of comprehensive clinical and diagnostic evaluation with total and average charges per patient.

	Type of Diagnostic Evaluation	(n)	Total Charges (USD) ^b	Average Charge Per Patient (USD)
Single Diagnostic Modality	Clinical Exam alone	14	\$65,226	\$4659
	Doppler Ultrasound ^a	12	\$76,488	\$6374
	Magnetic Resonance Imaging ^a	11	\$117,315	\$10,665
	Lymphoscintigraphy ^a	2	\$11,856	\$5928
Multiple Modalities	X-Rays ^a	3	\$14,982	\$4994
	US + MRI	3	\$37,140	\$12,380
	US + LSG	1	\$7643	\$7643
	US + MRI + LSG	3	\$40,947	\$13,649

^a The charges for lower extremity lower extremity X-ray, Doppler ultrasound, lymphoscintigraphy, and MRI with contrast were \$335, \$1715, \$1269, and \$6006 respectively. The average total charge of clinical evaluation and follow up for those who did not undergo diagnostic imaging was \$4659

^b Total charges of imaging related diagnostic evaluation includes average charge of clinical evaluation and follow-up.

on our experience with 49 patients with lymphedema praecox, we believe that this approach is accurate and cost effective.

Potential conflicts of interest

The authors have no conflicts of interest relevant to this article to disclose.

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