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ORIGINAL ARTICLE

Assessment of primary lymphedema and post thrombotic lower limb edema patient's pathway

Short title: Assessment of primary lymphedema and post thrombotic syndrom patients' pathway

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Abbreviation

CE : chronic edema
PL : primary lymphedema
PTS : post thrombotic syndrome
DVT : deep vein thrombosis
GP : general practitioner
VMP : vascular medicine physician
HAS : Haute autorité de santé (French heath authorities)

Summary

Objectives: To assess: 1) lower limb primary lymphedema or post-thrombotic syndrome patient's pathway in terms of health care professional use; 2) if aetiology of edema has an impact on this pathway.

Methods: Ancillary survey of the transversal prospective CHROEDEM pilot study. 40 patients with either lower limb primary lymphedema or post-thrombotic syndrome were invited to participate.

Results: 75% of primary lymphedema patients and 50% of post-thrombotic patients benefited from a multidisciplinary management (p=0.10) including the general practitioner, the vascular medicine physician and either a physiotherapist (particularly in case of primary lymphedema), a registered nurse (particularly in case of post-thrombotic syndrome). Main ambulatory health care professionals' correspondent of hospital-based vascular medicine physicians were general practitioners (80%) in post-thrombotic patients, and general practitioners (60%) and physiotherapists (45%) in primary lymphedema patients. Pharmacists were also involved in patient education. Conclusion: Management of primary lymphedema and post-thrombotic related chronic edema is usually multidisciplinary. General practitioners and vascular medicine physicians are the cornerstones of this management, that also involves the physiotherapist in case of primary lymphedema and in a lesser extent the registered nurse and the pharmacist. This suggests that these five healthcare professional should play a key role in case of development of standardized patient pathways for primary lymphedema and post thrombotic syndrome.

Keywords: chronic edema, primary lymphedema, post-thrombotic syndrome.

Introduction

Chronic edema (CE) of the lower limbs (>3 months of evolution) is a frequent symptom, the prevalence of which in the primary care setting is estimated to be 1.3 %₀ patients.(1) There are multiple possible etiologies to CE and its diagnosis can be challenging. This is particularly true in the case of rare etiology such as primary lymphedema (PL).(1) On the contrary, post thrombotic syndrome (PTS) is much more frequent than PL and its diagnosis is usually easy to make in case of leg swelling in a patient with a history of deep vein thrombosis (DVT).(2) If those 2 diseases are usually managed in the ambulatory care setting, they may require a very specialized diagnostic and therapeutic management only available in a hospital setting.(3)

In 2016, in order to improve the management of chronic diseases, the French government has decided that a specific formal patient's pathway under the supervision of the general practitioner (GP) should be established for the – therapeutic – management chronic disease.(4) Thus, according to this law, in France, patients suffering from PTS and PL should be managed in agreement with a standardized patient's pathway fulfilling general requirements.(5)

From a quality improvement and standardization of care perspective, we have conducted a survey among patients managed for a PL or a PTS at Montpellier University Hospital (Montpellier, France). The primary objective of this survey was to determine the current patient's pathway for PTS and PL management and to ascertain, in routine clinical practice, whether or not each patient's pathway fulfilled legal general requirements. Secondary objectives were to determine the impact of PL and PTS on patient's pathway and to assess PTS and PL patient's diagnostic pathway.

Methods

This is an ancillary study from the Chronic Edema (CHROEDEM) study conducted since 2016. CHROEDEM study is an ongoing, prospective, observational and pilot study conducted in Montpellier and Nimes University hospitals (France). Its primary objective is to assess and compare the different tissue components (edema, fat, muscle, inflammation/fibrosis) of the lower limb CE of venous vs. lymphatic origins through magnetic resonance imaging (MRI). Its main secondary objective is to assess genetic factors associated with tissue heterogeneity of each of PTS and PL CE.

CHROEDEM study participants are patients followed in Nimes and Montpellier University hospital for a PL or a PTS. PTS and PL patients with lower limb CE are matched on age (+/-10 years), sex, CE evolution (0-5 years, 5-10 years, >10 years). Main exclusion criteria are

the bilateral or multifactor characters of the lower limb CE, Grade II or greater obesity, any contraindication to MRI, unable or unwilling to provide consent.

Until July 2017, all patients enrolled in CHROEDEM study were invited to participate in the survey on patient's pathway at time of enrolment (baseline) visit. Those patients who agreed to participate were asked questions about the management of their disease and on the role of the different healthcare providers in the management of their disease. Those data were collected in an anonymized standardized questionnaire at the time of enrolment visit. For those patients that could not fill in the questionnaire at the time of enrolment visit, a phone interview was scheduled. A questionnaire had been tested beforehand among a sample of 10 patients with PL or SPT to ensure that the questions were clear and unambiguous.

The main following data were collected : demographics (age, sex, weight, height), diagnostic pathway (in case of PL and in case of PTS they were asked where the index DVT had been managed), current therapeutic management pathway (healthcare providers involved, frequency of visit to each and the role of each), treatments and patient's information provided/received. This survey was conducted in agreement with the French legislation on health research. The CHROEDEM study was approved by the ethics committee (Comité Consultatif de Protections des Personnes Sud Méditerranée III) and is referenced on ClinicalTrials.gov (NCT02914808).

From a statistical standpoint, our survey sample size was determined by the number of patients enrolled in the CHROEDEM study at time this ancillary study was conducted.

Categorical variables were expressed as frequencies and percentages and continuous variables as means with standard deviation or median with interquartile range. Chi-square or Fisher t tests were used for categorical variables. Wilcoxon and student t tests were used for continuous variables according to their distribution.

Two-sided p-values of 0.05 or less were considered to be statistically significant. Data were anonymously analysed in the Department of Biostatistics using SAS® Enterprise software (SAS Institute Cary, N.C.).

Results

Forty patients were included between December 2016 and July 2017, 20 in each group. 57 % (n=23) were men and their median age was 55,5 year (38.0; 68.0). Characteristics of enrolled patients according to type of CE (PL or PTS) are provided in Table 1.

Therapeutic management according to CE type

Elastic Compression: All patients with PTS and PL stated that they were wearing compression garments. Type and strengths differed according to the type of CE (Table 2). It had been initiated in 100% of cases by a vascular medicine physician (VMP) in both groups. Compression renewal was made in 60 % (n=12) of the cases by VMP in the PL group and in 60 % (n=12) of the cases by the general practitioner in the PTS group.

Compliance to compression (defined as good if patient answered Yes on 2 of the following 3 statements: I wear my compression at least five days a week, I never forget to wear my compression, my compliance to compression is not modified by season) was considered as good in 40% (n=8) of cases in the case of PTS and in 55 % (n=11) of cases in case of PL (p=0,34). 95% (n=19) of PTS patients and 100% (n=20) of PL patients put their compression themselves. If they required help, this was mainly done by a registered nurse (75 % of the cases, n=3) in case of PTS and by a physiotherapist (100 %, n=4) in case of PL.

Other treatments: Patients with PL were more likely to benefit from additional treatments for their CE than those patients with PTS (75 % vs. 35 % respectively, p=0.01) (**Table 2**). These treatments consisted of manual lymphatic drainage in most cases.

Current patient's management pathway according to the type of CE

The main healthcare contact in the ambulatory care setting for the hospital-based VMP was GP in 60 % (n=12) of the case in PL patients and 80 % (n=16) in case of PTS. A physiotherapist was also considered as a major healthcare contact in the ambulatory care setting for the hospital-based VMP by 45% of PL patients but by none of the PTS patients, p<0.001. Patients with PTS were more frequently benefited from nurse care than patients with PL (30 % (n=6) vs. 0 %, p=0.02); conversely, patients with PL were more frequently managed by a physiotherapist (85 % (n=17) vs. 25 % (n=5), p<0.01). Seventy five percent of the patients with PL (n=15) and 50 % (n=10) of the patients with PTS benefited from a multidisciplinary management p=0.10. The latter was defined as management by at least 3 healthcare professionals (among them include GP, VMP, physiotherapist, nurse and a podiatrist). Healthcare professionals involved in PL and PTS management pathway as well as the frequency of visits to these healthcare professionals have been provided in **figure 1** and **figure 2**.

Role of the different healthcare professionals in patients with PL and PTS

In both groups of patients, it is the VMP who started and modified the type and the strength of the compression garments. Compression renewal, patient's information on disease management and possible complications were provided/done both by GP and VMP.

VMP and GP prescribed significantly more often lymphatic drainages to patients with PL than to PTS patients: 85% vs. 35%, p<0,01 and 60% vs. 5%, p<0,001 respectively. VMP and GP instructed more often their PTS than their PL patients on prevention of venous thromboembolism : 100% vs. 40%, p<0,0001 and 50% vs. 0%, p<0,001 respectively. There was no statistical difference in terms of role of physiotherapists, nurses, pharmacists and podiatrists in the management of PL and PTS when considering help to put on compression, patient's information, surveillance of PL/PTS complications and podiatrist care.

Patient's diagnostic pathway

There was no statistical difference between groups in terms of identification of the healthcare professional who had first been diagnosed PL or PTS : VMP set up the diagnosis in 60% of PL patients and in 72% of PTS patients, whereas GP set up the diagnosis in 30% of PL patients and 22% of PTS patients, p=0,8. Time between development of CE and disease diagnosis was shorter in the PTS than PL patients: in 83 % vs. 35 % of cases respectively disease diagnosis was established within 6 months, p<0,001.

Discussion

Our results suggest that the management of patients followed by a hospital-based VMP at Montpellier or Nimes University hospitals for a PL or a PTS is usually multidisciplinary and that GP and VMP play a key role in this management. Physiotherapists are also critical in the management of PL.

Our study's main objective was to determine the current therapeutic management pathway of patients with PL and PTS. In agreement with the 2016 French law, our patients had benefited from a multidisciplinary management where GP played a central role.(4) In the case of PL, our survey identifies physicians, physiotherapists, pharmacists and podiatrists as the main healthcare providers for patients. These healthcare professionals are also mentioned in the national guidelines for healthcare management recently published by French authorities HAS (Haute Autorite de Sante) but not available when our survey was conducted.(6) Nurses were not mentioned by PL patients even though they are listed in these national guidelines/protocols. Other healthcare professionals that were not mentioned by our patients and that are listed in the French guidelines are patient's education team, surgeons, dieticians, psychologists, and social workers. Such national guidelines/protocols do not exist in the case of PTS.

Regarding the specific role of each healthcare professional according to the disease considered, our survey underlines the central role of VMP in initiating and modifying compression therapy in patients with PTS and PL. Similar results were reported by Almosni et al. in their study on the management of DVT by GP and VMP.(7) In this study, VMP also

managed initiation and determined the duration of anticoagulant treatment, whereas GP was more likely to perform anticoagulation monitoring.

Physiotherapists were more involved in the management of patients with PL than PTS (85% vs. 25%, p<0,01) probably because PL patients were more likely to benefit from manual lymphatic drainages and multilayer compression bandages.(3)

In contrast, patients with PTS were more likely to benefit from the regular care of a nurse (30% vs. 0%, p=0,02). It is possible for PTS patients that benefited from nursing care are those with severe PTS with venous ulcer requiring local wound care or complex bandages.(8) Absence of nurses involved in the management of patients with PL may seem surprising. Nursing care is necessary for those patients who require complex bandages or in case of ulcers. Exclusion of patients with obesity or chronic primary venous insufficiency may have selected healthier patients in our study that did not require such treatments.

Regarding the patient's diagnostic pathway, diagnosis was most often made by the VMP and in higher proportion in case of PTS than PL (72% vs. 60%). Time between development of CE and PL/PTS diagnosis was shorter in the case of PTS than PL and is explained by the natural history of these 2 diseases. Furthermore, PTS is more frequent and develops in patients that are usually already followed by VMP for their DVT. PL is less frequent, often less burdensome leading to greater delays in diagnosis.(9–12)

Regarding the therapeutic management, all patients from the survey wore a compression. However, the strength of the compression differed according to the disease. In the case of PL, compression strength was at least a class III. This choice follows the international guidelines for lymphedema management which suggest a compression of at least Class III of strength and the use of multilayer bandages.(3) Guidelines from the HAS also suggest a compression of at a least class III in the case of a chronic edema. (13)

In the case of PTS, compression strength was lighter than the one recommended by HAS and the one prescribed to PL patients (50% vs. 0% class II, 40% vs. 60% class 3). This is in line with what is usually practiced in French routine clinical practice .(3,13–15) Thus, Ouvry et al. had already reported in a survey conducted among French VMP members of the French Society of Vascular Medicine, that most VMP prescribed class II compression in case of DVT or PTS (64 % Class II, vs. 36 % Class III).(14) By prescribing lighter compression VMP expected to favor better compliance, Achille's heel of compression therapy.

In terms of compliance to compression therapy, there was no statistical difference between patients with PL and those with PTS (55% vs. 40%, p=0,34). These data on compliance could seem disappointing comparing to those reported in clinical trials (> 85 %).(16) They are however better than those reported in some studies on chronic venous disease where compliance varied between 20 and 25%, (17,18) and are similar to the compliance reported in the SOX trial and the EDITH study (compliance 56% at 2 years in patients who stated wearing compression at least 3 days a week and 47% respectively).(19,20) This this is

consistent with the fact that in case of chronic disease, lack of compliance to treatment is frequent (21)

Therefore, it is important to explain to PL and PTS patients how critical it is to be compliant to compression in order to prevent disease progression. That is why, the French Academy of pharmacy recommend that office based pharmacists increase and strengthen their education messages to patients wearing compression in order to improve compliance.(22)

Our study has a number of strengths and limitations that need to be underlined. First, as it was conducted in the hospital setting, there is a recruitment bias that has certainly influenced our patient's pathways. For example, we are not able to have an exact idea of the role of community-based VMP. Prescription of compression in our study was done by VMP, but it is likely that not all the patient with PTS and in a lesser extent with PL are followed by a VMP. It is likely that for those patients who do not have a VMP, prescription of compression is done by GP. Compliance to compression was defined on an empirical manner in our study. However, given the complexity of the diseases and of the management of multilayer compression garments in case of PL, lack of compliance has probably a different meaning in the case of PTS or PL. Given the pairing of patients with PL on patient with PTS, our observed sex ratio does not reflect the reality of the distribution by sex in patients with PL. Lastly, our small sample size limits the interpretation of the results. However, this small sample size is the direct consequence of the number of patients in our CHROEDEM study. To the best of our knowledge, our study is the first one to compare PTS and PL patients' therapeutic management pathways. If our hospital-based recruitment does not allow us to have a definitive idea of patient's ambulatory pathway in case of lymphedema or post thrombotic syndrome it is likely to provide important information on how patients perceive the complementarity between hospital and the ambulatory care setting.

Conclusion

Among a population of patients followed in a University Hospital, management of lower limb PL and PTS are multidisciplinary. GP and VMP play a key role, as well as physiotherapist in case of PL. Nurses and pharmacists are involved but to a lesser extent. Our data suggest that in the event of development of a standardized patient's pathway in case of PTS, these five health care professionals should be strongly involved. Finally, some important efforts should be made in order to improve compliance to compression.

Disclosure of interest:

The authors declare that they have no competing interest.

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Legends :

Figure 1 : Out-hospital patient's pathway with primary lymphedema of a lower limb

Figure 2 : Out-hospital patient's pathway with post-thrombotic syndrome of a lower limb

Table 1 : Population characteristics

Table 2 : Therapeutic management according to pathology



Figure 1 : Out-hospital patient's pathway with primary lymphedema of a lower limb

- § : Health-care professionals involved in patient's pathway : % (n)
- ‡ : Frequency of visits : % (n)



Figure 2 : Out-hospital patient's pathway with post-thrombotic syndrome of a lower limb

- § : Health-care professionals involved in patient's pathway : % (n)
- ‡ : Frequency of visits : % (n)

Table 1 : Population characteristics

	PRIMARY LYMPHEDEMA	POST THROMBOTIC SYNDROME	
	n=20	n=20	
Age : mean (SD) (years)	53.75 (± 16.61)	55.65 (± 19.27)	
Age : median (Q1;Q3) (years)	51.50 (51.50;65.50)	60.50 (36.50;73.00)	
Male : n (%)	12 (60)	11 (55)	
Female : n (%)	8 (40)	9 (45)	
BMI : median (Q1;Q3) (Kg/m2)	26.74 (22,02;31.33)	24.98 (23.00;28.50)	

	PRIMARY LYMPHEDEMA n=20	POST THROMBOTIC SYNDROME n=20	р
Elastic compression using : Yes vs. No, n (%)	20 (100)	20 (100)	/
Class II : n (%)	0 (0)	10 (50)	0.0003
Class III : n (%)	12 (60)	8 (40)	0.2059
Class IV : n (%)	2 (10)	0 (0)	0.4872
Compressive orthesis association to reach class > IV or multi-layer bandaging : n (%)	6 (30)	2 (10)	0.2351
Other treatments : Yes vs. No, n (%)	15 (75)	7 (35)	0.0110
Lymphatic drainage: n (%)	15 (75)	5 (25)	0.0016
Other method of physiotherapy : n (%)	0 (0)	3 (15)	0.2308
Phlebotonic drug : n (%)	1 (5)	4 (20)	0.3416
Thermal cure : n (%)	3 (15)	2 (10)	1.0000
Pressure therapy : n (%)	2 (10)	1 (5)	1.0000

Table 2 : Therapeutic management according to pathology