

Predictive Factors of Chronic Venous Disease: A Clinical Study

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ABSTRACT

Objective: The aim is to analyze the combination of factors that may be related to chronic venous disease in order to develop future prevention policies.

Material and Methods: The study is based on a medical examination of patients treated in the Department of Angiology, Vascular and Endovascular Surgery of the Hospital de la Santa Creu i Sant Pau in Barcelona. In addition, an exhaustive podiatric study was carried out and a large number of variables were collected. The study tries to determine which factors may cause chronic venous disease and to derive association rules to predict it. First, a numerical and graphical descriptive study of the data is carried out using standard statistical methods. Data mining techniques are then applied using WEKA software to find and describe structural patterns that explain and predict what might happen in similar scenarios. WEKA helps with tasks such as clustering, classification, regression and association rules.

Results: It is possible to determine which factors are significant for chronic venous disease. WEKA applies different mathematical algorithms of selection methods and establishes a ranking of the predictor variables that have intervened in this process. Factors such as age, gender, obesity or the number of toes affected by onychodystrophy are variables that, depending on the values reached, imply a risk of suffering from chronic venous disease.

Conclusions: A podiatric examination can detect a possible chronic venous disease. In case of suspicion of this pathology, the patient should consult a specialist in the circulatory system to confirm the podiatric diagnosis.

Keywords: Onychodystrophy; Chronic Venous Disease; Clinical Diagnosis; Data Mining Techniques; WEKA

Introduction

Chronic venous disease refers to a range of conditions that affect the veins in the legs, usually caused by poor venous blood flow. Normally, veins carry blood from the limbs back to the heart, and they have valves that prevent blood from flowing backward. The VEIN-TERM document [1], an interdisciplinary consensus of the main scientific societies, defines the concept of chronic venous disease as any alteration of the venous system, both from a morphological and hemodynamic point of view. Chronic venous disease (CVD) has been defined as any hemodynamic and morphological disturbance of the venous system, of long evolution, in the form of signs and/or symptoms that require investigation and/or treatment. Chronic venous in-

sufficiency would only include advanced degrees of chronic venous disease, i.e. those that represent a functional impairment of the venous system and are manifested in the form of oedema, skin changes or venous ulcers. More specifically, this condition can manifest in various forms, such as

1. Spider veins: small, thin veins that appear as red, blue, or purple webs on the skin's surface.
2. Varicose veins: enlarged, twisted veins visible under the skin.
3. Chronic venous insufficiency: a more severe condition where the veins fail to return blood efficiently, leading to swelling, skin changes, and sometimes ulcers, or

4. Leg ulcers: open sores, often on the lower leg, that result from long-standing venous insufficiency.

Varicose veins not only cause a loss of quality of life for the patient but also represent a significant cost to the healthcare system. Symptoms of CVD include swelling in the legs and ankles, pain or aching, especially after standing for long periods, heaviness or fatigue in the legs, skin discoloration or hardening, itching or burning sensations and in severe cases, ulcers or sores. However, the symptoms can be very different, and the prevalence of the disease increases significantly with age, especially in the female population.

Prevalence studies show different results depending on the type of population chosen, the variables and the methodology used to detect and diagnose venous insufficiency. According to [2] it is estimated that 60% - 80% of the world's adult population suffers from chronic venous disease. However, a study carried out in France found a prevalence of up to 50% in women compared to 30% in men [3], while other studies, such as the Edinburgh study, found the opposite, a higher prevalence of venous pathology in men compared to women, 40% compared to 32% [4]. It is essential to consider the prevention of potential triggering and aggravating factors, such as being overweight, chronic constipation, sedentary lifestyle, and prolonged standing, among others, and to reduce the consequences of repeated pregnancies and hormone therapy [5]. Constipation could be due to many plausible and synergic effects, including the pro-inflammatory status generally associated to the increased adiposity, and other factors, such as an augmented intra-abdominal pressure, which may lead to greater reflux, increased vein diameter, and venous pressure. Venous ulcers affect 20.7% of the elderly older than 80 years, compared with 0.3% of those between 41 and 50 years. Within the clinical signs we find telangiectasias, varicose veins (the most frequent), oedema, skin changes, or ulcers. The Edinburgh Vein Study [6], the Detect-IVC-2000 [7], and the Vein Consult Program [8], are some of

the epidemiological studies of reference. The CEAP (Clinical-Etiology-Anatomy-Pathophysiology) classification is the most widely used by experts to classify and establish the diagnosis of chronic venous disease. Venous circulation disorders of the lower extremities group have a wide range of clinical signs arranged in seven clinical categories from C0 to C6 [2].

In Figure 1 we can see photographs of the lower limbs of patients suffering from chronic venous disease, taken in the Department of Angiology, Vascular and Endovascular, which reflect the degree of affection according to the CEAP scale. In fact, from grade or level C1 to C6 the patient is considered to suffer from chronic venous disease (CVD) and from level C3 to C6 the patient is considered to suffer from chronic venous insufficiency (CVI). Each CEAP clinical class is characterized by morphological changes and functional abnormalities of the veins manifested by signs and/or symptoms. According to the etiology, chronic venous diseases are classified as primary, secondary, and angiodysplasia. The etiology of CVD is divided into congenital, primary and secondary. Primary CVD is the result of a combination of factors, the share of heredity in its manifestation is not predominant. It occurs as a result of internal pathological processes not associated with trauma, thrombosis or congenital disorders. The secondary causes, in 30% of cases, are deep vein thrombosis, its sequelae being the so-called post-thrombotic syndrome. Hypoplasia or malformations constitute a minor group of cases [2]. The diagnosis of venous circulation disorders in the lower extremities is established on the basis of clinical signs which are confirmed by hemodynamic examination. This examination was performed with Doppler ultrasound and spectral analysis of venous flow. Modification of lifestyle habits, elastic compression of the limb, venotonic drugs, exercises that improve venous return, or surgery to eliminate venous reflux are some of the treatments recommended for patients with chronic venous disease [2]. However, all these diagnostic methods and subsequent treatments are not often timely [9,10].



Figure 1: Different grades or levels of CVD affection according to the CEAP scale.

Chronic venous disease is a progressive and disabling disease with a high prevalence in the world population. Prolonged exposure to genetic and environmental risk factors can lead to important biophysical and biochemical changes in the venous system, implying a complex vascular response. An increasing number of studies focusing on CVD demonstrate the relevance of this vascular pathology, especially in the more advanced stages (CVI). More studies are needed to gain a better understanding of CVD and to explore new medical and translational approaches to improve the quality of life of these patients. Society should be aware of the real impact of the disease and try to take measures to prevent the development and/or progression of CVD to CVI, e.g. by increasing physical activity or through dietary and lifestyle interventions. An integrative perspective on this condition would have immediate benefits for the clinical management of these patients, especially those most at risk. In addition, the costs of diagnosis and treatment are really high for the public health system [2]. For all these reasons, this study proposes easier, cheaper, and non-invasive indirect diagnostic methods for CVD detection based solely on an onychodystrophy study and some other basic information of the patients.

Onychodystrophy is understood as an abnormality or deformity of the nails, whether it is in color, shape, texture, or thickness. It can affect both fingernails and toenails, and the causes can vary widely, including trauma, infections, systemic diseases, or certain dermatologic conditions. Common causes of onychodystrophy include

- (1) Fungal infections (onychomycosis),
- (2) Psoriasis or other skin conditions,
- (3) Trauma or injury to the nail or nail bed,
- (4) Nutritional deficiencies,
- (5) Autoimmune diseases like lichen planus or lupus,
- (6) Genetic disorders like nail-patella syndrome or
- (7) Circulatory issues, which is the objective of this study.

Usually, it causes discomfort when wearing shoes, especially in the more extreme degrees of the disorder (see Figure 2A). This disease is associated with chronic venous insufficiency, since CVI is characterized by impaired blood circulation in the foot with possible consequences such as metabolic, skin, or systemic, as well as the appearance of tumors in the nail region. Onychodystrophy is also related to subungual pathology, nail cosmetics, trauma, tics, sweating disorders, and onychopathy [11,12]. The elementary lesions caused by onychodystrophy, as far as nail morphology is concerned, can be classified according to changes in shape, size, thickness, surface, consistency, color, relationship between the plate and the bed, and in the alterations of the periungual tissue. Around 50% of the cases of onychodystrophies are caused by onychomycosis [13] the most frequent condition (see Figure 2B). In recently published epidemiological studies, the global prevalence of nail fungal infection was estimated to be 5.5%. Fungal nail infection affects more than 10% of the population aged 40 to 60, a percentage that rises to more than 60% in the toenails of the elderly.



Figure 2:

- A. Foot affected by onychodystrophy.
- B. Foot affected by onychomycosis.

In recent years, the diagnosis and prevalence of onychodystrophy has increased, reaching a higher incidence among the elderly population. We can say, from a medical point of view, that chronic venous disease contributes to onychodystrophy by reducing the blood supply to the nail beds. The toenails become thickened and darker in color and also increased risk of secondary infections [11]. Managing the underlying venous disease can help prevent or reduce these nail abnormalities. The treatment depends on the underlying cause and may involve topical or systemic medications, lifestyle changes, or treatments aimed at managing associated conditions. Diagnosis usually requires a clinical examination and sometimes additional tests such as cultures, biopsies, or blood tests to determine the exact cause. Data mining is an excellent tool to extract information, find patterns, trends, or associations rules that explain the behaviour of certain data in a specific context [14]. In fact, the ultimate goal is the ability to describe and predict, that is, the identification of patterns. The application of data mining technology has been a fundamental field in medical research, as it has proven to be an excellent tool for assessing patient risks, helping clinical decision-making, and enabling the construction of prediction models. In this study, data mining techniques have been applied to patients with chronic venous disorder to identify high-risk patients, define causal factors of CVD, and show the relationship between factors so that these relationships are easy to identify.

There are few published works that relate onychodystrophy, obesity, and chronic venous pathology, simultaneously. On the contrary, there is a substantial amount of literature and specialized studies that treat these conditions separately [15]. Multiple linear regression, decision tree analysis, and association rules have been used successfully in clinical medicine for predictive modelling of diseases [16], medical or dermatological diagnosis [17], lung cancer disease [18] or classification of medical data [19]. Good results have also been obtained when applied to occupational risk prevention [20-23]. The objective of the study is to determine an early diagnosis of chronic venous pathology through onychodystrophy in the feet. Thus, the final intention of the study has been to offer a previous diagnosis, establish greater prevention and provide more effective and precise treatment of chronic venous disease.

Methodology

The study was observational, analytical, inferential and single centre. The information was collected from a population made up of patients who visited the Angiology, Vascular and Endovascular Surgery Service of the Hospital de la Santa Creu i Sant Pau in Barcelona during the days when the study was carried out in 2015-2017. The hospital is a tertiary referral centre and covers a population of 403,951 inhabitants in a defined area of Barcelona, according to information provided by CatSalut (Catalan Health Service). Patients were selected and attended on a consecutive and voluntary manner, following an a priori exclusion process. The Hospital de la Santa Creu i Sant Pau of Barcelona has a Clinical Research Ethics Committee of the Research

Institute, which approved and supervised the research (ethical approval EC/15/260/4382). The study was carried out in accordance with international ethical recommendations for medical research involving human subjects, guaranteeing compliance with the Declaration of Helsinki, in accordance with the standards of Good Clinical Practice, the information sheet and the informed consent form. With regard to the confidentiality of the study data, the provisions of Organic Law 15/1999, of 13 December, on Protection of Personal Data were observed. Patients with chronic venous disease were examined and asked to undergo venous Doppler ultrasound. They were then scheduled for a second visit to assess their toenails. The researcher analyzed the nails independently, without knowledge of the doctor's previous diagnosis or the Doppler ultrasound result.

The study of the variables were recorded in a specially adapted data collection notebook, along with the historical information obtained from the vascular examination and anamnesis. All nails were described and compared according to the parameters considered for a normal nail. This included any changes that might indicate a structural abnormality, such as changes in shape, size, thickness, surface, consistency, color, relationship between plate and nail bed, and periungual tissue (not statistically represented in this study). Inspection of the nail plate and adjacent soft tissues began with a visual examination of the twenty nails, both hand and foot, under a light reflector. By examining the nails, we were able to gather information to make a diagnosis of nail-specific pathologies. A certified digital caliper was used to compare thickness in the most advanced cases of nail disease, if present. For better clinical diagnosis, onychoscopy (dermoscopy) [11] was performed during nail examination using a 10x manual dermatoscope. Photographs of both feet were taken using an Olympus FE-4030 digital camera. A matte black background was chosen to highlight the altered nails and to try to eliminate or minimize the formation of reflections. The anterior part of the foot was photographed so that all the nails could be viewed together and, if necessary, a macro photograph of the nail to be highlighted was taken. The identification number of each patient's photograph corresponded to the number assigned to each patient's medical history in the study.

In the differential diagnosis of onychomycosis, the following clinical features or dermoscopic patterns in the observed nails were considered: the presence of spikes (nailing) and longitudinal striations, the line of the free edge of the nail, and the irregular distal end of the nail body, i.e., slits with distal separation of the plate and bed. When using this examination method to exclude tinea unguium, the following clinical manifestations were also considered: Alteration of the normal pink color of the nail, subungual hyperkeratosis, thickening, production of subungual debris and malodour, splinter haemorrhages in the nail bed, periungual inflammation and purulent drainage. In our analysis, patients with a history of onychomycosis of the feet were excluded. Dermoscopy is a non-invasive diagnostic tool for pigmented lesions, skin diseases and adnexa such as hair and nail (onychoscopy).

The examination of nail changes is a technique that allows us to assess various characteristics of the nails and it is a very useful tool in the diagnosis of onychomycosis. The history recorded in the data collection notebook was compared with the electronic clinical history that each patient has in the hospital computer system to verify their medical data, especially their morbid history and current medication. Patients were asked to complete a questionnaire, their height and weight were measured, varicose veins and chronic venous insufficiency were classified, venous blood samples were taken and the duration of venous reflux was measured.

Some of the information requested from patients, such as ethnicity, social class, dietary habits, drug or alcohol consumption, other previous medical interventions, medications they usually take, type of work or sport they regularly do, were not used in this study because they were not considered by medical professionals to be directly related to chronic venous disease. However, they may be included in future studies if deemed necessary. Once all the expected information was obtained from the patients, a descriptive and inferential statistical study was carried out using various statistical tools and methods. The statistical and inferential calculations were carried out using Minitab v22 and the behavioral patterns by means of WEKA software.

Population Study and Factors

The participants were 83 patients between 40 and 84 years old, randomly selected in the medical consultation of the Angiology, Vascular and Endovascular Surgery of the Hospital de la Santa Creu i Sant Pau in Barcelona. Almost all patients had chronic venous pathology in at least one lower extremity, with a clinical grade of C1 to C6 on the CEAP scale, and manifested venous reflux. In addition, the visit was used to carry out an exhaustive podiatric examination as described in the previous section. Data from both specialists were collected in order to cross-reference the information and to establish a possible interrelationship between both pathologies. Previous studies by the authors have clearly demonstrated a relationship between onychodystrophy and chronic venous disease [24]. Volunteers attending the medical consultation, with chronic venous disease of the reflux on Doppler ultrasound examination, were included in the study. They also had to be between 40 and 84 years old and sign the informed consent document. Patients with congenital onychopathies, nail or cosmetic prostheses, lower limb amputations, or toenail surgery in the past year were excluded, as were patients with onychodystrophy that was clearly and directly related to biomechanical problems, nail infections, medications, tumors, toe deformities, advanced degenerative joint disease, onychodystrophy due to surgical iatrogenesis, habitual use of inappropriate or ill-fitting footwear, presence of a second toe longer than the first, and dermatological diseases with nail manifestations. Patients with post-thrombotic syndrome and those who had undergone invasive lower limb surgery were also excluded.

Patients were also excluded if, despite meeting the eligibility cri-

teria, they refused to participate in the study or sign the informed consent document, or if, due to any medical condition or psychiatric disorder, the medical specialist considered that they did not understand the reason for their selection or were unable to give their informed consent to participate in the study [24,25]. Of the variables of interest, we can point out gender, age, smoker/non-smoker, weight, height, number of fingers affected by onychodystrophy, and degree of chronic venous disease. Although some variables are numeric, they have been previously transformed into nominal or categorical and discretized into a small number of different ranges to be treated with WEKA. From the variables height and weight, the variable body mass index (BMI) was obtained, which will be an important factor for CVD and CVI, as seen in previous works [25]. Chronic venous disease is the target variable or response in the present study. Thus, the following factors were considered in this work:

- a) Gender (G):** A categorical variable with two possibilities, F=female, M=male.
- b) Age (A):** Age of the patients in years. This variable has been grouped into nine categories:
1= [40,44], 2= [45,49], 3= [50,54], 4= [55,59], 5= [60,64], 6= [65,69], 7= [70,74], 8= [75,79], 9= [80,84].
- c) Smoker (S):** Two categories are established, 0=no smoker, 1=smoker.
- d) Height (H):** Height of the patients measured in meters.
- e) Weight (W):** Weight of the patients measured in kilograms.
- f) Left foot (LF):** The number of toes on the left foot affected by onychodystrophy, which can take the values {0, 1, 2, 3, 4, 5}.
- g) Right foot (RF):** The number of toes on the right foot affected by onychodystrophy with the values {0, 1, 2, 3, 4, 5}.

The average of the left and right foot affected by onychodystrophy, provides a new variable, that is:

- h) Left-right toes (LRT):** The average of toes of both feet affected by onychodystrophy can be classified into the six following categories, 0= {0}, 1= {0.5, 1}, 2= {1.5, 2}, 3= {2.5, 3}, 4= {3.5, 4}, 5= {4.5, 5}.

From the weight and height, the Body Mass Index (BMI) is obtained by using the following formula:

$$BMI = \frac{Weight(kg)}{Height^2(m^2)} \quad (1)$$

After calculating the BMI given in (1), the values are classified into the usual four categories as follows:

i) Body Mass Index (BMI): Underweight (U) < 18.5, Normal weight (N)= [18.5, 24.9], Overweight (O)= [25.0, 29.9], Obesity (Ob) ≥ 30.0.

j) Chronic Venous Disease (CVD): Level that indicates the degree of chronic venous disease of a patient, which is classified into seven groups {C0, C1, C2, C3, C4, C5, C6} from the lowest C0 (no affection) to C6 the highest degree of affection, according to CEAP classification.

Statistical Methodology

Data mining consists of extracting potentially useful information from data that has not yet been processed, using the technique of machine learning. The goal is to find and describe structural patterns in the data to explain and predict what might happen in similar scenarios. One tool for finding structural patterns is WEKA, a popular open source data mining and machine learning software, developed at the University of New Zealand. It is designed to provide a comprehensive set of tools for data analysis and predictive modelling. WEKA is particularly in academic and research environments due to its flexibility and ease of use. It is designed to help with tasks such as clustering,

classification, regression and association rules. Renowned for its versatility and reliability, WEKA offers a wealth of features that make it a popular choice among data scientists and researchers. In general, a data mining process is divided into several steps:

- (1) Selection of the database according to the purpose of the investigation,
- (2) Data cleansing and transformation, removing incorrect data, filling in missing data, generating new variables, converting data formats and ensuring data consistency. Extraction of numerical and graphic descriptive study of the data through the usual methodology,
- (3) Selection of the target variable and obtention of the best predictor variables by means of machine learning algorithms,
- (4) Generation of association rules using Apriori algorithm, with prior setting of parameters, and
- (5) Evaluation of the results through the association rules to make predictions.

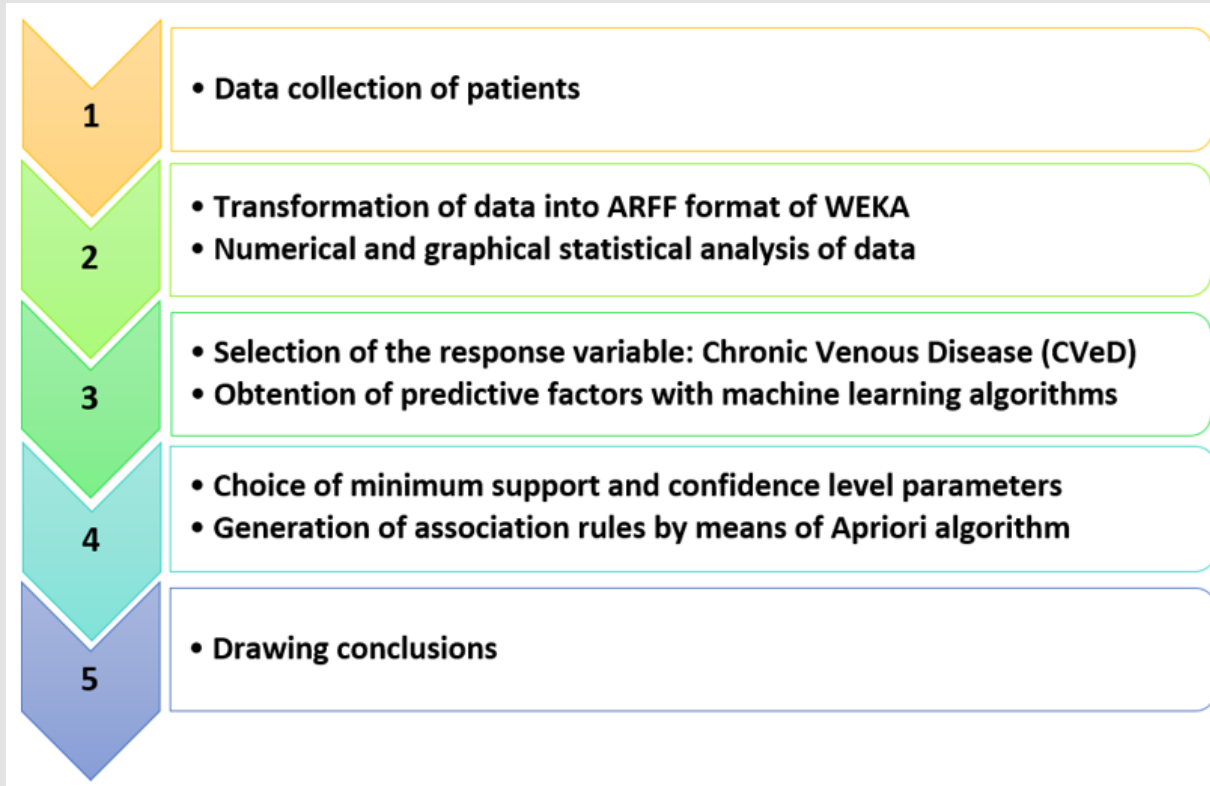


Figure 3: Diagram of the process developed in this study.

In Figure 3, a diagram of the process is shown. Some details of the established process in this study are presented below.

- Analysis of the variables by means of numeric and graphic statistical methods as a first evaluation of the data. Chronic venous disease is chosen as the response variable and the remaining variables are used as possible predictors or causal factors.
- Machine learning algorithms are designed to select the most appropriate attributes to use in decision making. To find the most significant predictors, several attribute methods have been applied. Specifically, CfsSubEval, ClassifierSubsetEval and WrapperSubsetEval as attribute subset evaluators that, combined with the BestFirst, GreedyStepwise, and Ranker search methods, provide a ranking of the best predictor variables. Clearly, each classification method gives a solution that does not usually coincide with the others since they use different methodologies. How each method works can be found in [26]. The position of each predictor variable in each classification method is calculated and averaged. At the end of this process, a ranking of the significant attributes related to the response variable is obtained.
- Once the best attributes have been selected, the Random Tree classifier is used along with an attribute selection mode called cross validation, with n=10 folds. Thus, the data set is ran-

domly reordered and then divided into 10 folds of approximate size. A fold is used for testing and the other (n-1) folds are utilized to train the classifier. After this process, a confusion matrix (commonly called contingency table) shows how many instances have been correctly assigned to each class. Another important parameter, Kappa statistic, measures the correlation between the predicted and observed categorizations of the data set.

- Association rules discover associations and correlations in large data sets. Data mining identifies association rules in a two-step process:
 - 1) All high-frequency items in the collection are enumerated, and
 - 2) Association rules are generated based on the high-frequency items.

Therefore, before the association rules can be obtained, the frequent elements must be selected using certain algorithms. In fact, the Apriori algorithm is used for this purpose. The confidence level indicates how likely an association rule is true. Thus, for example, the first association rule that appears in Table 1 must be interpreted as follows: An overweight patient with an average of 3.5 - 4 toes affected by onychodystrophy has a probability of 0.95 of suffering from chronic venous disease with clinical grade C5.

Table 1: The eight best association rules for the response variable chronic venous disease.

Rule	Predictor	Predictor	Predictor	Predictor	Response Variable	Confidence Level
1			BMI=O	LRT=4	CVI=C ₅	0.95
2	A=5		BMI=Ob		CVI=C ₅	0.9
3		G=F		LRT=4	CVI=C ₅	0.87
4	A=1	G=M	BMI=Ob		CVI=C ₅	0.85
5	A=4		BMI=Ob		CVI=C ₅	0.85
6			BMI=Ob	LRT=1	CVI=C ₅	0.8
7		G=M	BMI=O		CVD=C ₂	0.78
8	A=8		BMI=O		CVD=C ₂	0.75

Note: A: Age; G: Gender (F: Female, M: Male); BMI: Body Mass Index (O: Overweight, Ob: Obesity); LRT: Left-Right average of affected toes; CVI: Chronic Venous Insufficiency; CVD: Chronic Venous Disease.

Statistical Results

Following the steps detailed in the previous section, the statistical results that emerge from this study are presented. The graphics of the four predictor variables, gender, age, left-right toes, and body mass index can be observed in Figures 4A-4D, respectively. These are characteristics of the group studied in the sample and cannot be extrapolated to the general population. Finally, the graphic of the response attribute chronic venous disease is given in Figure 4E. Figure 4A shows that the proportion of women in the sample, 72.3%, is almost three times higher than that of men, 27.7%. In Figure 4B, we can observe that an important group of patients, 20.5%, are in the age range between 55 and 59 years and the remaining are distributed in more

homogeneous groups. Interestingly, 49.4% of patients have a slight average of toes on both feet affected by onychodystrophy, with category 1= {0.5,1}, as seen in Figure 4C. In addition, Figure 4D indicates that 43.4% of the patients are overweight. Finally, in Figure 4E it is observed that 43.4%, almost half of the patients, suffer from chronic venous disease at a C5 level, which means that the sample is dominated by patients without ulcers. In step 3 shown in Figure 3, WEKA uses a set of predictor factors to determine which of them are significant for the response variable, which in our case is CVD. To do this, it applies various mathematical algorithms or factor selection methods and establishes a ranking of the predictor variables that have intervened in this process as possible causal factors.

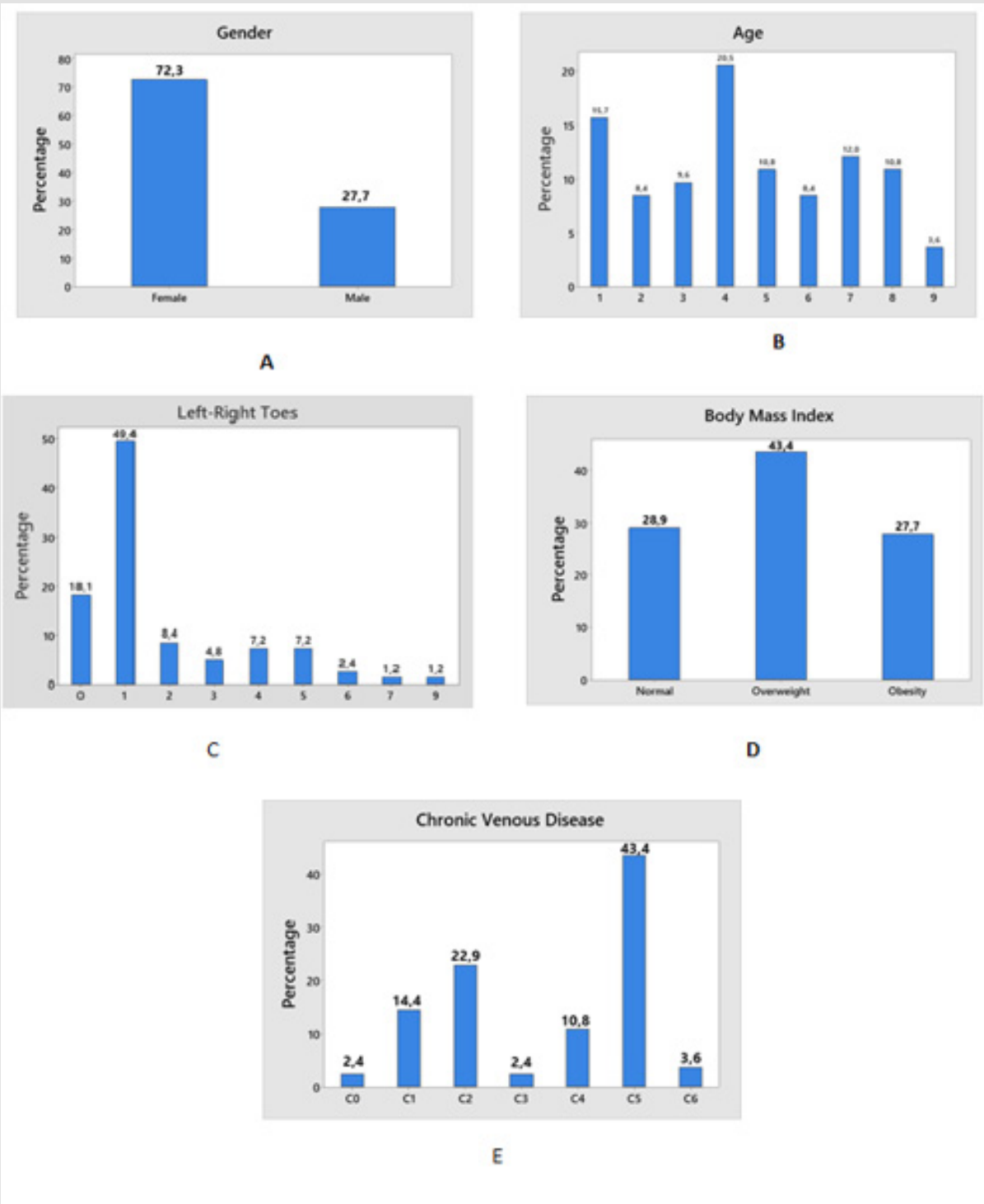


Figure 4:
A. Gender.
B. Age.
C. Left-Right Toes.
D. Body Mass Index.
E. Chronic Venous Disease.

WEKA initially used all the variables that were measured in the patients, but some of these predictive factors do not appear in the final ranking that WEKA provides, so these factors are excluded as potential causal factors when finding the association rules that appear in step 4 of Figure 3. For instance, this is the case for the smoker variable. Thus, after applying different machine learning algorithms, as commented above, the variables that should be considered as good predictors of chronic venous disease, in order of importance, are age, gender, body mass index, and number of toes affected on the left-right foot. Working only with age, gender, body mass index, and number of toes affected on the left-right foot as possible causal factors, a Random Tree classifier is searched. In this study, a cross- 369 validation classification method with n=10 folds have been used. The confusion matrix guarantees that 67 instances are correctly classified, that is, 80.72% of them. In addition, Kappa statistic is 0.73, which can be considered as a significant value because the maximum Kappa statistic value is 1. The last step is to obtain a set of association rules that allow making predictions for CVD and CVI. Table 1 shows the eight best association rules ordered by confidence level. In the Discussion section, the consequences that can be drawn from these associations are analyzed and commented.

Discussion

Table 1 summarizes the 8 best association rules that allow reliable conclusions to be drawn from the statistical point of view and translated into clinical conclusions. First, we observe that 6 out of 8 association rules imply chronic venous insufficiency with C5 degree. The BMI is a factor that appears 7 times in 8 rules, which means that obesity and overweight, combined with other variables, are potential factors of chronic venous disorders [27-29]. Thus, an overweight patient with an average of 3.5 to 4 affected toes can suffer CVI of level C5 with a probability of 0.95 (rule 1). In addition, for an obese person between 60 to 64 years of age, the probability of suffering CVI level C5 is very high, 0.9 (rule 2). From rule 3, a woman with an average of 3.5 to 4 affected toes can suffer, with a probability of 0.87 CVI of level C5. An obese young man can suffer CVI of level C5 with a probability of 0.85 (rule 4). Any obese person between 55 and 59 years old can suffer C5 level of chronic venous insufficiency with a probability of 0.85 (rule 5). From rule 6, the obesity factor together with an LRT value 1, implies that a patient can suffer CVI of level C5 with a probability of 0.80. An overweight man will probably have chronic venous disease of C2 level with a probability of 0.78 (rule 7). In addition, an elderly person between 75-79 years with over-weight, has a 0.75 probability of suffering chronic venous disease of C2 level (rule 8). In this work we limited ourselves to the study of those patients who attended the Angiology and Vascular Surgery service of the Hospital de Sant Pau in Barcelona.

The people who were considered suitable for the development of our research were only those who had been recruited during the

period of time strictly determined for the performance of our work. Therefore, neither the general population nor those patients who presented before or after the period of time defined for screening were considered. Moreover, patients who presented the exclusion criteria detailed in this work were excluded from the study. The data and conclusions obtained in this study could not be compared with the results collected in other vascular surgery services or with other similar studies. The great difficulty is the lack of specific bibliography on chronic venous disease of the lower limbs and its relationship with onychodystrophies, in order to confirm and discuss the results with those of other authors. Although we cannot contrast with similar studies, with the data obtained and after having carried out a descriptive and inferential study, along with some patterns of behaviour, we confirm the relationship between onychodystrophy and chronic venous disease [11,24,30]. The authors acknowledge that the number of patients in the sample is not very large. Therefore, we cannot categorically say that the results obtained can be extrapolated too far.

On the other hand, other factors that were not measured when the patients were examined may be triggering factors for CVD. This study is considered preliminary, and we intend to extend the research in other medical centers, with larger patient samples and with the collection of other medical factors of interest. Thus, the study of onychodystrophy by a visiting podiatrist, together with other basic information, allows a reliable prognosis of suffering from chronic venous disease and, therefore, it is possible to know with a high probability the degree of chronic venous disease that a patient has. In this case, the patient has to arrange a medical visit to the specialist to confirm the prognosis made by the podiatrist, performing more invasive and expensive tests, if necessary. In short, perhaps a simple visit to the podiatrist can be a good preventive measure to detect venous circulation problems, avoiding future health complications.

Conclusion

The importance of this study consists in establishing a diagnosis of chronic venous disease based on the clinical characteristics that prevail in onychodystrophy. From the information extracted, it has been possible to determine which factors could be the cause of chronic venous disease and to obtain association rules allowing to predict it. We have seen that factors such as age, gender, obesity, or number of toes affected by onychodystrophy are variables that, depending on the values they reach, imply a risk of suffering chronic venous disease. This way, on a visit to the podiatrist, it is possible to know the probability that a patient is affected by CVD or CVI and its risk level.

Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Comité Ético de Investigación Clínica del Hospital de la Santa Creu i Sant Pau de Barcelona, Barcelona, Spain, protocol code IIBSP-ONI-2015-67, May 31, 2017.

Author Contributions

Conceptualization, M.P.; methodology, M.P. and J.M.R.; software, J.M.R.; validation, M.P. and J.M.R.; writing-original draft preparation, M.P. and J.M.R.; writing-review and editing, J.M.R. All authors have read and agreed to the published version of the manuscript.

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Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

Data Availability Statement

Data are contained within the article.

Conflicts of Interest

The authors declare no conflicts of interest.

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