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A 6-Year Statistical Study of Systemic Sclerosis in the Region of Casablanca-Settat, Morocco

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Systemic sclerosis is a non-organ-specific autoimmune disease of the connective tissue, characterized by excessive production of collagen leading to fibrosis of the skin as well as organs such as the lung, it is responsible for aesthetic discomfort, an alteration of the functional prognosis and potentially life-threatening due to damage to the heart, lungs and kidneys. We, therefore,

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decided to carry out a retrospective study extending over 6 years at the Internal Medicine Department and Geriatrics Unit of the Ibn Rochd University Hospital Center in Casablanca that concerned the medical files of 2164, in order to see if systemic scleroderma in our region presented any particularities. We noted that scleroderma was relatively rare in our context with only 42 patients in whom the diagnosis was made in 06 years with a female predominance (the sex ratio in our studies was 4.25 women for 1 man), we noticed that the provinces the most concerned are Casablanca, El Jadida and Settat with a predominance in urban areas, that the family history of scleroderma or autoimmune disease is weakly present in our context, the main profession at risk found in our context is automobile sheet metal work and it concerned 3 male patients (7.14%), exposure to tobacco was however present in 11 patients or 26.9%. We also noted that the first symptoms were diverse (arthralgia, myalgia, Raynaud's phenomenon) and often appeared between 1 and 5 years (in 59.6% of patients) before the diagnosis to be made. The clinical picture is classic with varied skin involvement in 100% of our patients with abnormalities on capillaroscopy in 95.2% of our patients, orofacial involvement in 54.8% of patients, muscular involvement in 57.1%, joint damage in 64.3%, bone damage in 23.8%, lung damage in 61.9%, heart damage in 23.8%, kidney damage in 26.2%, digestive damage in 54.8%, and urogenital involvement in 33.3% of patients. 7 patients died (16.66%), 3 patients (7.14%) had progression of the disease leading to complications, and 20 patients (47.61%) reported improvement while the disease remained stationary in 11 patients (26.19%).

Keywords: Systemic scleroderma; autoimmune disease; connective tissue; microcirculation.

1. INTRODUCTION

Systemic scleroderma is a non-organ-specific autoimmune disease of the connective tissue characterized by damage to the microcirculation leading to Raynaud's Phenomenon and excessive collagen production resulting in fibrosis of various organs. It is a rare condition with a poorly known prevalence and predominantly affecting women, with a female-male ratio ranging from 3:1 to 8:1. This condition not only impacts aesthetic and functional aspects but also vital due to the potential involvement of the lungs, heart and kidneys [1].

Our work consists of a retrospective study reporting the different particularities of scleroderma in the Casablanca-Settat region.

2. MATERIALS AND METHODS

Our work consists of a retrospective study over 6 years extending from January 1 of 2018, to December 31 of 2023, carried out in the Internal Medicine and Geriatrics Unit of the Ibn Rochd University Hospital Center in Casablanca and which drains patients from the region of Casablanca-Settat and which concerned the medical files of 2164 patient with 42 patients in whom scleroderma was newly diagnosed. The objective of our study is to determine the different epidemiological particularities of scleroderma, the different visceral damage, the response to different treatments and the evolution of this condition, as well as the impact of this condition on the fertility of patients. For this we used the following operating sheet created using Google Forms.

3. RESULTS

During the period of 06 years from January 1, 2018 to December 31, 2023 we welcomed 2164 patients to the Internal Medicine and Geriatrics Unit of the Ibn Rochd University Hospital Center in Casablanca for different reasons and the diagnosis of Systemic Scleroderma was retained according to the ACR/EULAR 2013 criteria in 42 patients, which represents 1.94% of all admissions to the service during this period, of which 8 were men and 34 were women.

The skin manifestations observed in patients included Raynaud's phenomenon in 95.2%, pulp ulceration in 35.7%, pulp scarring in 61.9%, sausage-like fingers in 54.8%, skin sclerosis not extending beyond the MCP joints in 45.2% and extending beyond the MCP joints in 45.2%, thinning of the lips and nose in 40.5%, loss of forehead wrinkles in 23.8%, exaggerated perioral folds in 14.3%, skin hypopigmentation in 11.9%, telangiectasia in 28.6%, and calcinosis in 4.8%.

4. DISCUSSION

Scleroderma is a non-specific autoimmune disease of connective tissue, which makes it a systemic disease. It is characterized by damage

to the microcirculation, the most classic of which is Raynaud's phenomenon, as well as excessive production of collagen leading to organ fibrosis, the most common of which is pulmonary fibrosis. It has an aesthetic and functional prognosis and can be life-threatening due to damage to the kidneys, lungs and heart. The pathophysiological mechanism is partially understood, and the etiology is unknown. [1]

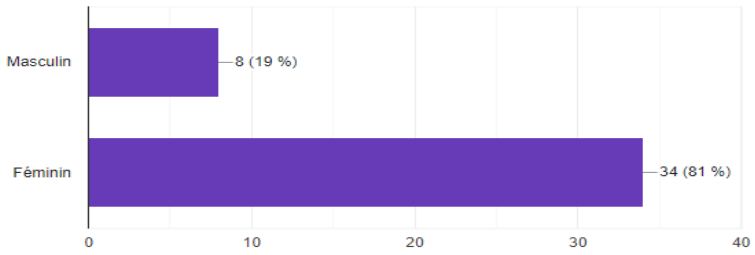

Fig. 1. Distribution of patients according to gender

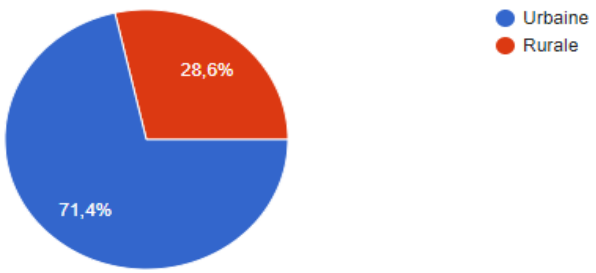

Fig. 2. Distribution of patients according to rural/urban origin

71.4% (n=30) were of urban origin, while 28.6% (n=12) were of rural origin.

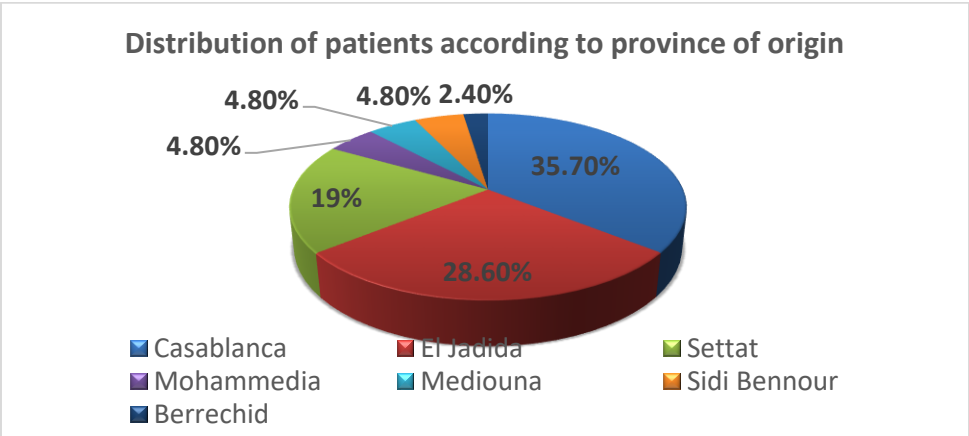

Fig. 3. Distribution of patients according to province of origin

35.7% (n=15) were from Casablanca, 28.6% (n=12) from El Jadida, 19% (n=8) from Settat, 4.8% (n=2) from each of Mohammedia, Médiouna, and Sidi Bennour, and 2.4% (n=1) from Berrechid

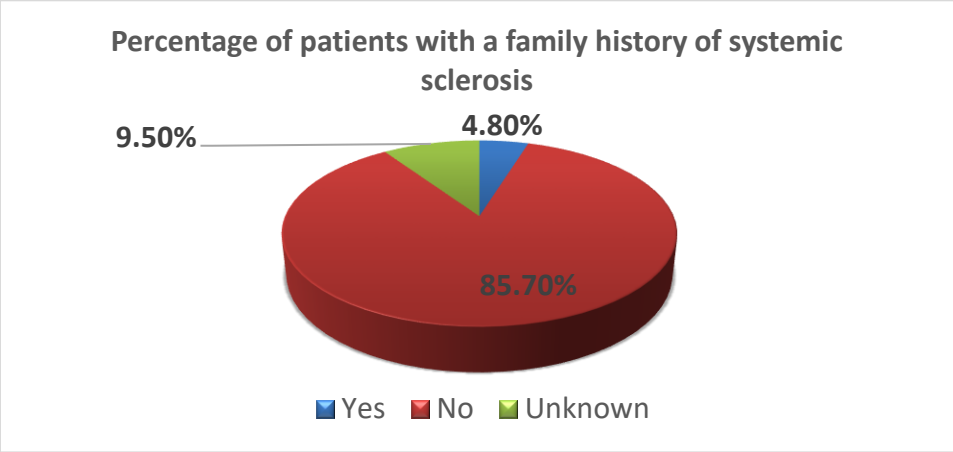

Fig. 4. Percentage of patients with a family history of systemic sclerosis

85.7% (n=36) had no family history of systemic scleroderma, 9.5% (n=4) were unaware if they had any, and 4.8% (n=2) reported a family history of scleroderma

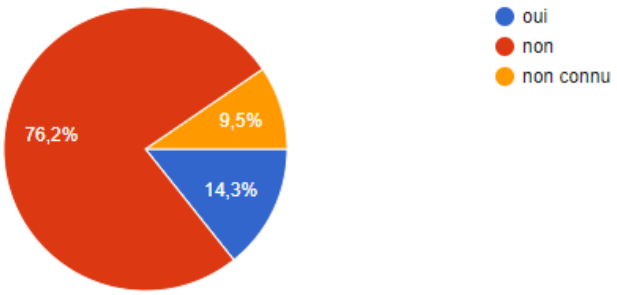

Fig. 5. Percentage of patients with a family history of autoimmune disease other than scleroderma

76.2% (n=32) had no family history of autoimmune disease, 14.3% (n=6) had at least one family member with an autoimmune disease, and 9.5% (n=4) were unaware if they had a family history of autoimmune disease

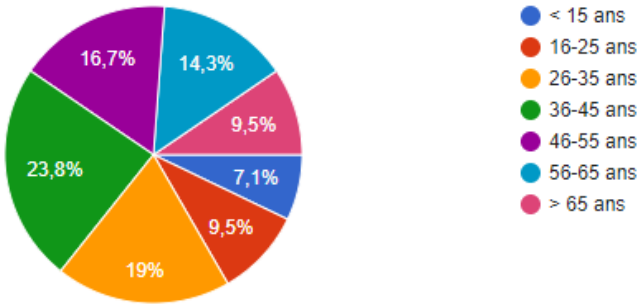

Fig. 6. Distribution of patients according to age of onset of first symptoms

The age of onset of the first symptoms was below 15 years in 7.1% of patients, between 16 and 35 years in 28.5% of cases, between 36 and 55 years in 40.5% of cases, between 56 and 65 years in 14.3%, and over 65 years in 9.5% of cases

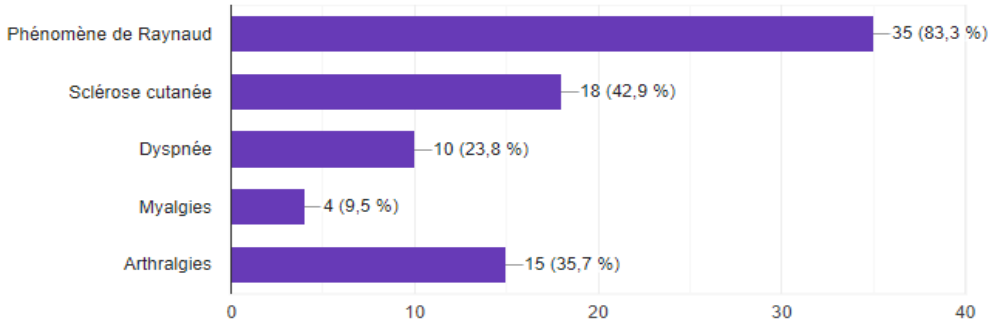

Fig. 7. Summary diagram of the initial symptoms of systemic scleroderma in our patients
The initial symptoms included Raynaud's phenomenon in 83.3% of cases, skin sclerosis in 42.9%, dyspnea in 23.8%, myalgia in 9.5%, and arthralgia in 35.7%

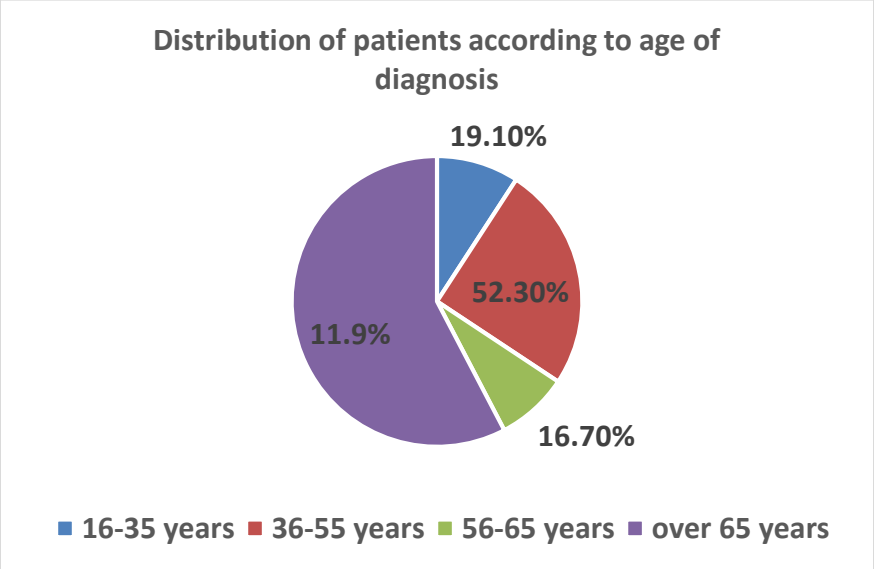

Fig. 8. Distribution of patients according to age of diagnosis
The age at diagnosis was between 16 and 35 years in 19.1% of cases, between 36 and 55 years in 52.3%, between 56 and 65 years in 16.7%, and over 65 years in 11.9%

Table 1. Results of the immunological assessment in our patients

Immunological assessment	Number of patients	Percentage
Immunological assessment not done	1	2.4%
Negative immunological test	3	7.1%
Positive Anti-Nuclear Antibodies	38	90.5%
Anti-Topo-Isomerase/Scl 70 antibodies positive	12	31.57%
Anti-RNA polymerase III antibodies positive	7	18.42%
Positive Anti-Centromere Antibodies	11	28.94%
Anti-Centromere Antibodies + Positive Anti-Scl 70 Antibodies	3	7.89%
Anti-Centromere Antibodies + Positive Anti-RNA-Olymerase III Antibodies	3	7.89%
Anti Scl 70 antibodies + Anti RNA-polymerase III antibodies positive	2	5.26%

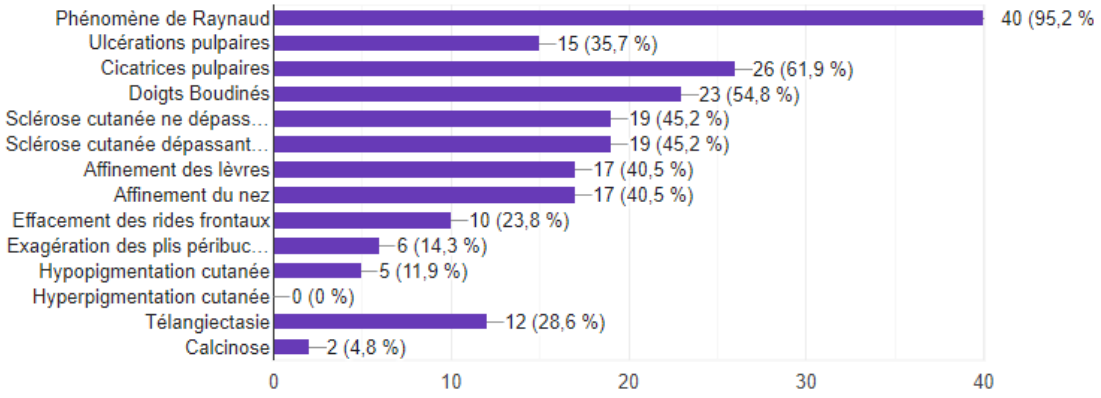

Fig. 9. Summary diagram of the different skin manifestations found in our patients

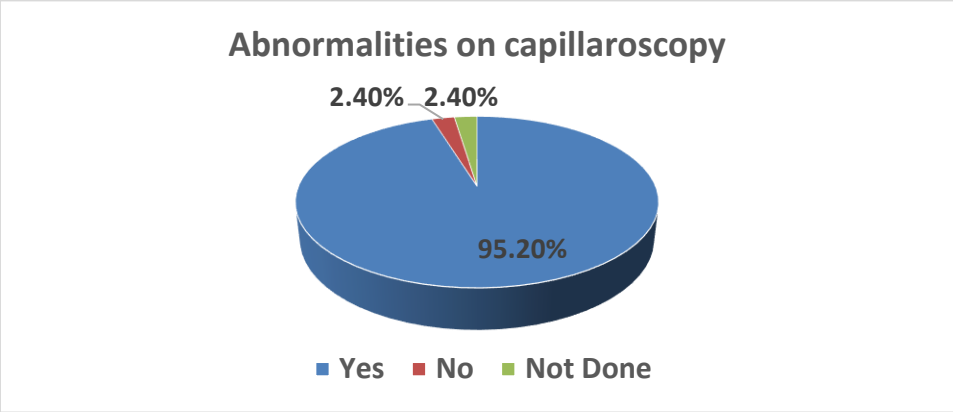

Fig. 10. Summary diagram of the presence or absence of abnormalities on capillaroscopy
95.2% of patients had abnormalities in periungual capillaroscopy, 2.4% had a normal capillaroscopy, and 2.4% did not undergo the procedure

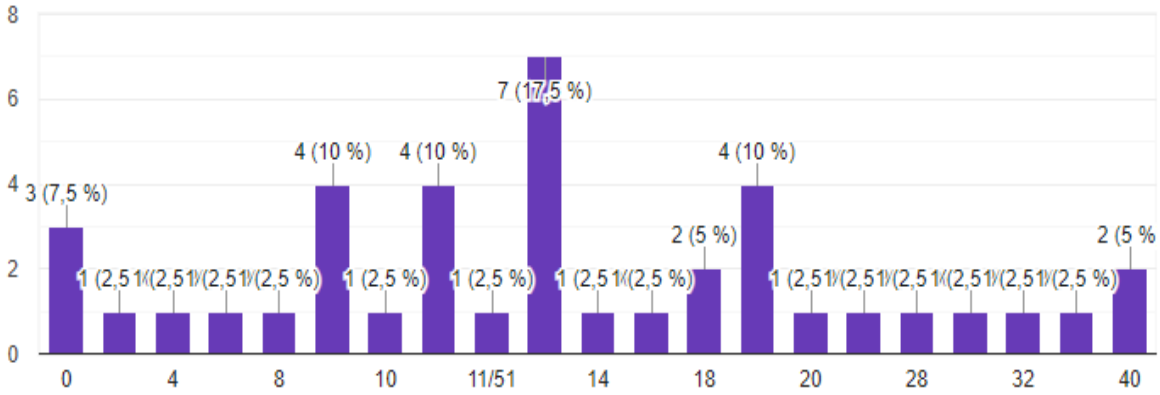

Fig. 11.Summary diagram of rodnan score at diagnosis
57.1% of patients experienced myalgia, and 4.8% had actual myositis

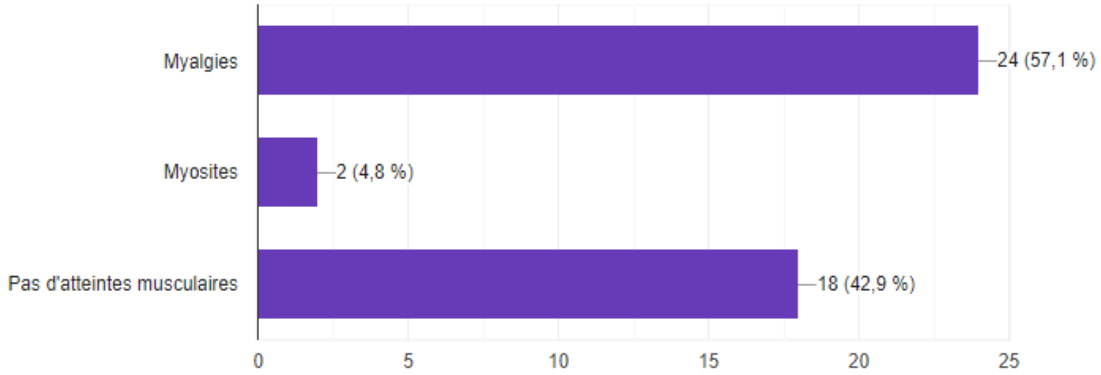

Fig. 12. Summary diagram of muscle damage
61.9% of patients experienced inflammatory arthralgia, and 4.8% had true arthritis

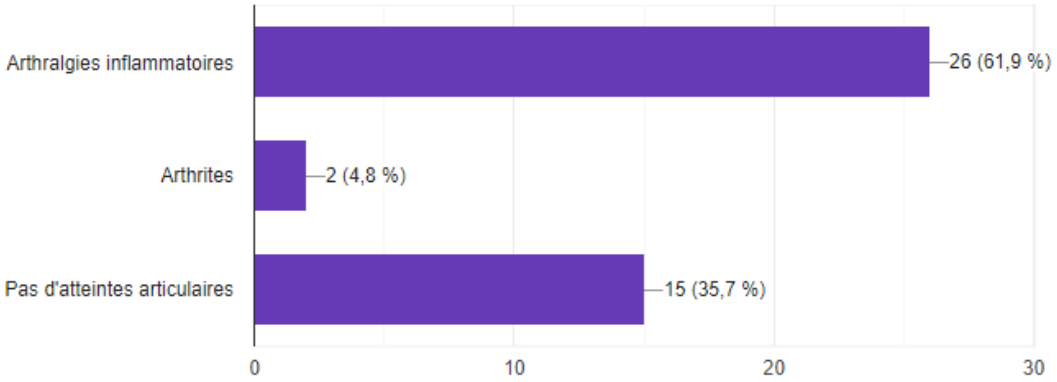

Fig. 13. Summary diagram of joint damage
19% of patients had osteoporosis, and 4.8% had acro-osteolysis

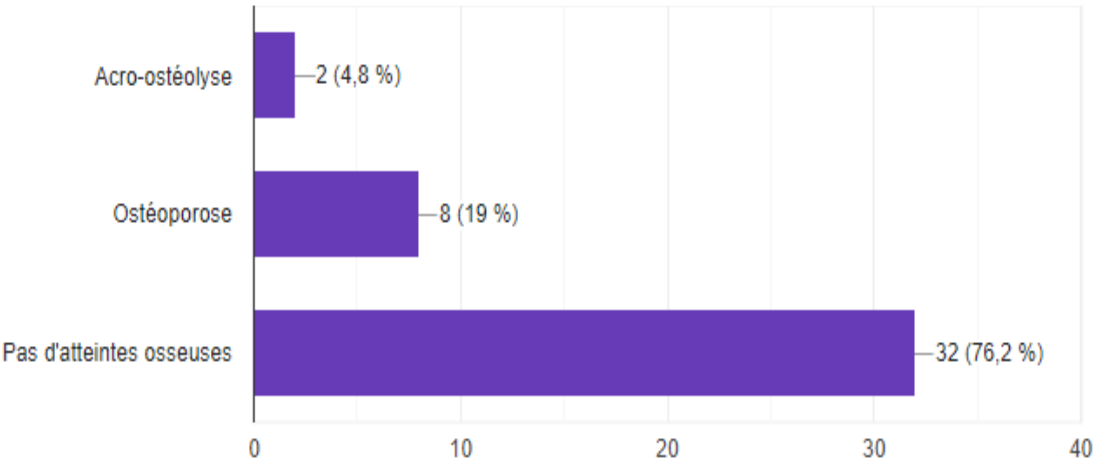

Fig. 14. Summary diagram of bone damage

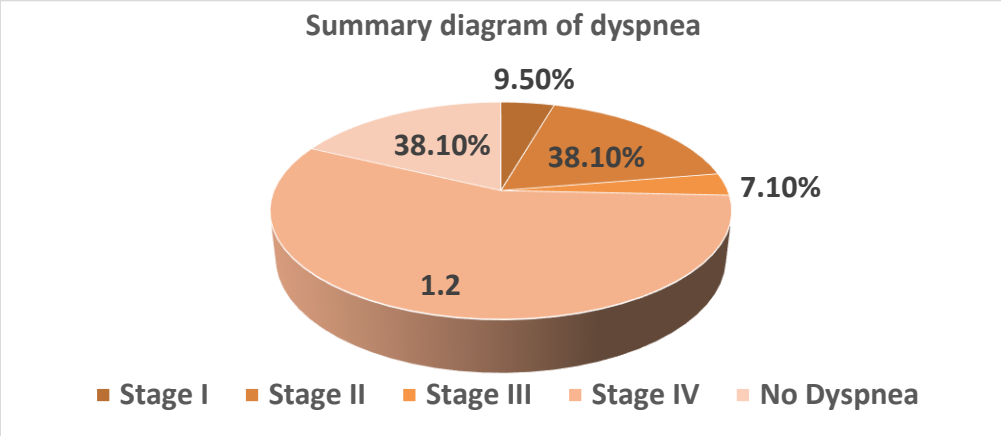

Fig. 15. Summary diagram of dyspnea present

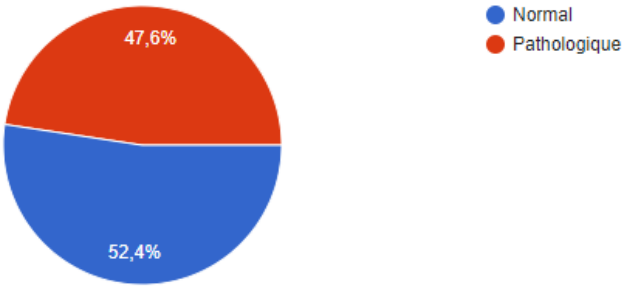

Fig. 16. 6-minute Walk Test result

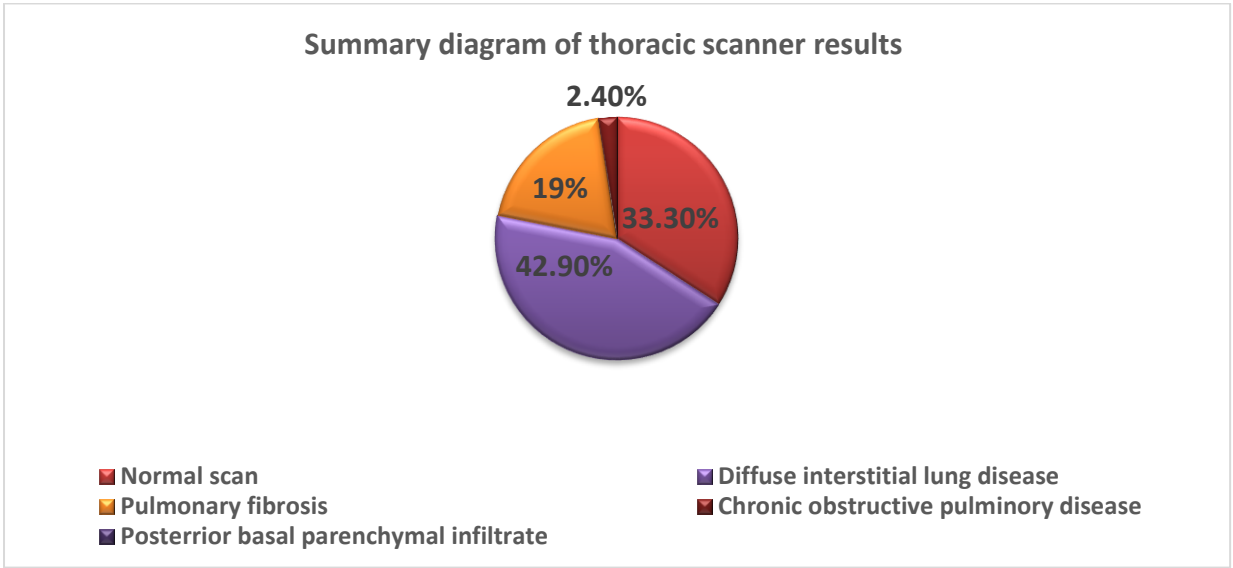

Fig. 17. Summary diagram of thoracic scanner results

42.9% of patients had diffuse interstitial lung disease on chest CT, 33.3% had a normal scan, 19% had pulmonary fibrosis, 2.4% had chronic obstructive pulmonary disease, and 2.4% had a posterior-basal parenchymal infiltrate

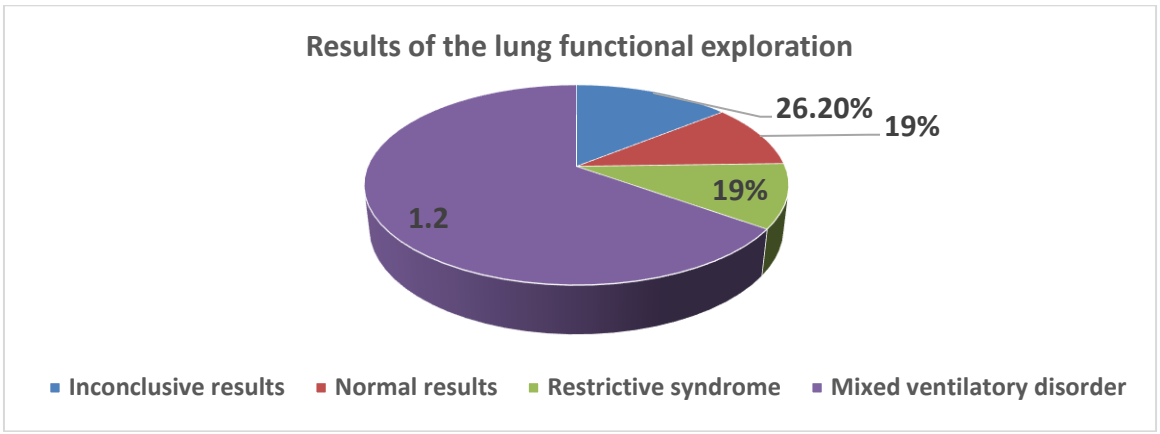

Fig. 18. Summary diagram of the results of the lung functional exploration

66.6% of patients underwent pulmonary function tests. Among them, 26.2% had inconclusive results, 19% had normal results, 19% had a restrictive syndrome, and 2.4% had a mixed ventilatory disorder

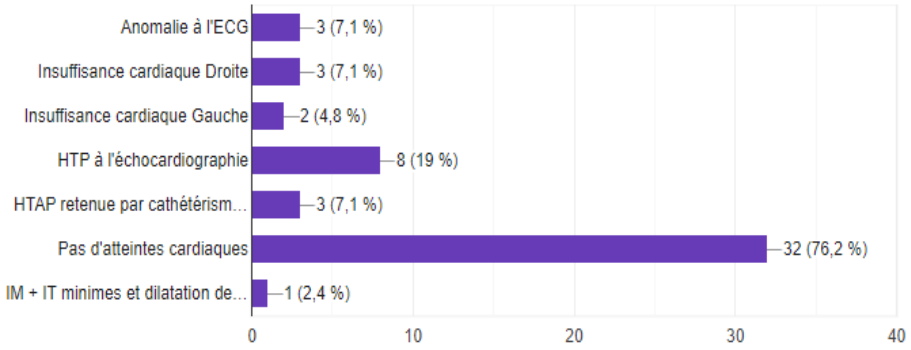

Fig. 19. Summary diagram of cardiac damage

7.1% of patients had conduction disturbances on EKG, 7.1% had left heart failure, 19% had pulmonary hypertension on echocardiography, 2.4% had mitral insufficiency with tricuspid insufficiency and dilation of the inferior vena cava, and 7.1% had pulmonary arterial hypertension detected by catheterization

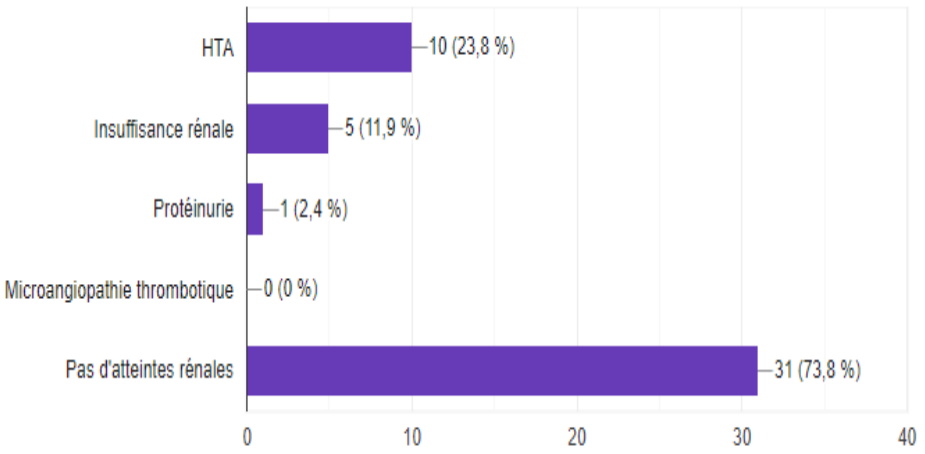

Fig. 20. Summary diagram of renal damage

23.8% of patients had hypertension, 11.9% had renal insufficiency, and 2.4% had proteinuria

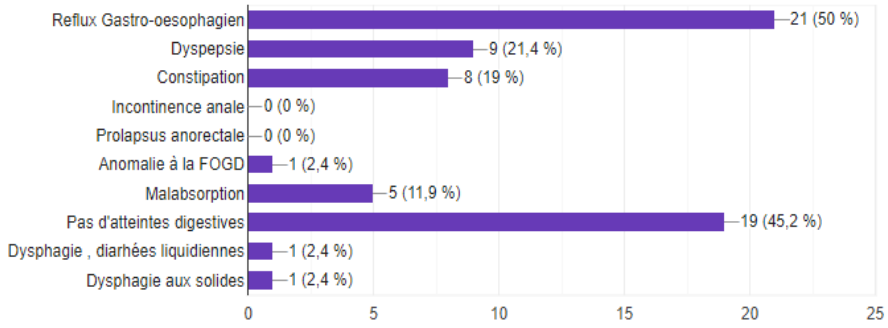

Fig. 21. Summary diagram of digestive damage

50% of patients had gastroesophageal reflux, 21.4% had dyspepsia, 19% had constipation, 11.9% had malabsorption, 2.4% had dysphagia with solids, 2.4% had dysphagia with liquid diarrhea, and 2.4% had abnormalities on esogastroduodenoscopy.

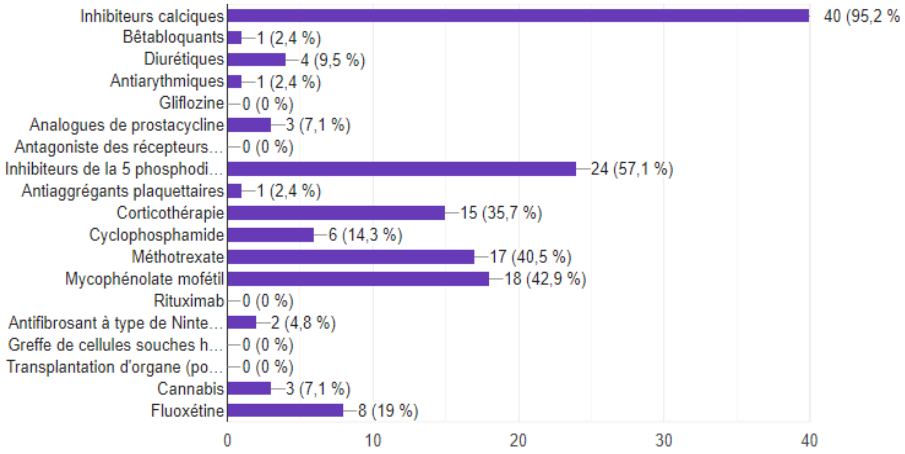

Fig. 22. Summary diagram of the different treatments adopted

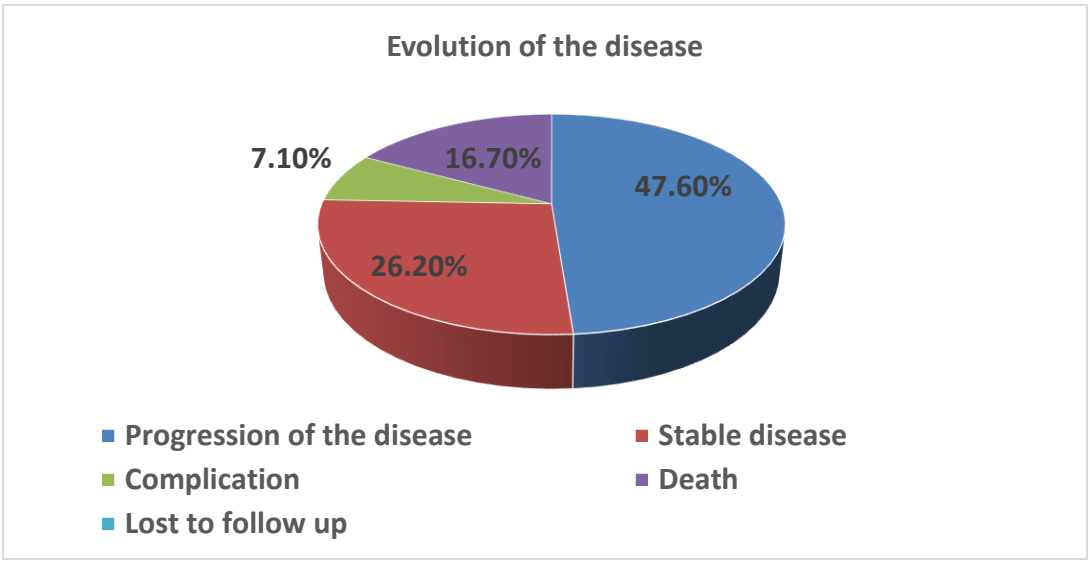

Fig. 23. Summary diagram of the different modes of evolution of the pathology in our patients

47.6% of patients reported progression of the disease, 26.2% had stable disease, 16.7% died, 7.1% reported complications, and 2.4% were lost to follow-up

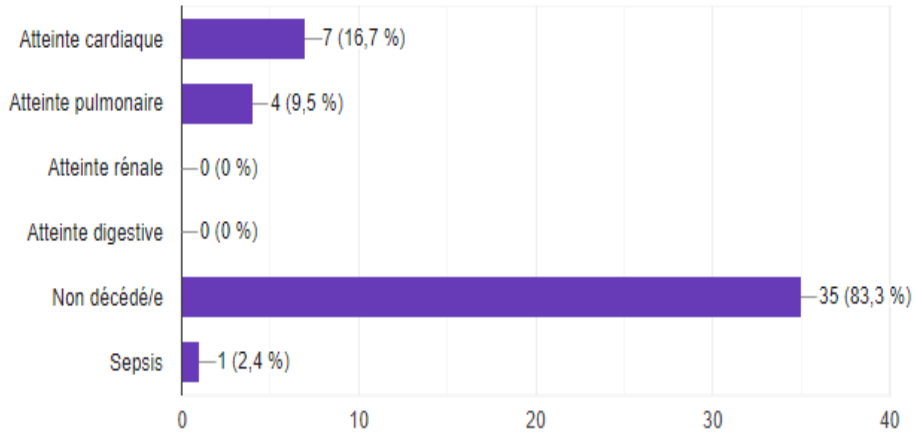

Fig. 24. Summary diagram of the different causes of death
4 patients died from cardiorespiratory failure, 1 patient died from cardiac arrest due to septic shock, and 2 patients died from cardiac decompensation

We therefore carried out a retrospective study spanning 06 years from January 1, 2018 to December 31, 2023 in the Internal Medicine department and geriatrics unit of the Ibn Rochd University Hospital Center in Casablanca during which we highlighted the following particularities:

- **On the Epidemiological level:**

This is a rare condition in our context, of 2164 patients hospitalized in our department, the diagnosis of systemic sclerosis was only retained in 42 patients or 1.94%. We noticed a strong female predominance with 34 female patients for 8 male patients, i.e. a sex ratio of 4.25 women for 1 man, which is consistent with data from the French literature [1].

71.4% of our patients were of urban origin compared to 28.6% who were of rural origin, dominated by the province of Casablanca from which 35.7% originated, followed by the province of El Jadida from with 28.6% than the province of Settat in 3rd position from which 19% of patients came, totaling 83.3% of patients.

Several studies have highlighted the physiopathological role of certain organic solvents such as aliphatic hydrocarbons, halogenated aliphatic hydrocarbons, white spirits or naphtha solvents; toluene, xylenes, trichloroethylene and aromatic hydrocarbons, which made it possible to identify so-called risky professions such as car painting, sheet metal work and textiles [2]. During our study only 3 patients, all male, i.e. 7.1% of patients had occupations known to be at risk and worked in automobile sheet metal, while 71.4% of our patients were without a profession and finally 21.4% had occupations not known to be at risk.

The genetic component has been suggested in the bibliography about the pathophysiology of systemic scleroderma, evoking some familial cases of scleroderma or even an area of familial autoimmunity although specific genomic studies attempt to precisely identify the genomic actors. incriminated are still ongoing. [3,4] We only found a family history of systemic sclerosis in 4.8% of our patients while a family history of autoimmune diseases other than systemic sclerosis was found in 14.3% of type patients including Systemic Lupus Erythematosus, Rheumatoid Arthritis and Immunological Thrombocytopenia.

It has been noted in the French literature that the peak frequency of scleroderma is between the age of 45 and 64 years [1], but in our study the peak frequency was between 36 and 55 years in 52.3% of our patients, however we noted that the onset of symptoms was way before with a delay between the appearance of the first symptoms and the diagnosis varying between 2 to 5 years in 42.9% of patients, greater than 5 years in 21.4% of patients while it was equal or less than to 1 year in 35.9% of patients.

- **On the Clinical level:**

The first clinical symptoms related to the disease were essentially cutaneous (made of Raynaud's

phenomenon and cutaneous sclerosis found respectively in 83.3% and 42.9% of patients), joint (type of arthralgia found in 33.7% of patients), respiratory (type of Dyspnea found in 23.8% of patients) and muscular (type of Myalgia found in 9.5% of patients). It should be noted that patients in whom the pathology first appeared in the respiratory system were able to be diagnosed quickly in less than a year, while patients with joint, muscular and skin involvement could'nt be diagnosed quickly with a delay between the appearance of symptoms and the making of the diagnosis which can exceed 5 years, which can be explained by the severity of the condition with a rapid manifestation of sufficient classification criteria when the pulmonary involvement is inaugural, while the diagnostic delay in patients showing isolated cutaneous, muscular or joint symptoms does not allow the diagnosis to be made quickly, especially since patients in the Moroccan context only consult late after prolonged and often random self-medication.

At the time of diagnosis of systemic sclerosis in our patients, the clinical picture was dominated by skin involvement with Raynaud's phenomenon found in 95.2% of patients, followed by pulp scars found in 61.9% of patients, then curled fingers found in 54.8%, of cutaneous sclerosis not exceeding the MCP in 45.2% and exceeding the MCP in 45.2%, then refinement of the lips and nose found in 40.5% of patients, then pulpal ulcerations found in 35.7%, telangiectasias in 28.6%. The Rodnan scores at the time of diagnosis varied between 0 for scleroderma sin scleroderma and 40 in patients with extensive sclerosis, with a majority Rodnan score at 13. Orofacial involvement was present in 54.8% of patients with limitation of the mouth opening in these and calcinosis of the facial in only 2 of them. Muscular damage mainly due to myalgia was found in 57.1% of patients, only 2 of whom presented true myositis with a clinical muscle deficit, biological rhabdomyolysis and a myogenic trace on the electro-neuro-myogram. Joint damage was found in 61.9%, mainly suffering from arthralgia, of which only 2 patients presented true arthritis. Bone damage was found in 23.8% of patients with 2 patients having presented acro-osteolysis and 8 having presented osteoporosis (a frequent manifestation of scleroderma [1]); In a study conducted jointly by the Rheumatology Department of Pasteur Hospital in Nice and the Nephrology Department of CHU Nîmes on 102 patients, the incidence of osteoporosis was 35%. In contrast, another study conducted at the Internal Medicine Department of CHU Tunis in Tunis found an incidence of acro-osteolysis at 37.03% [5,6].

- **For visceral damage**

Dyspnea was found in 61.9% of patients at different stages, with a 6-minute walk test returning pathological in 47.6%. Parenchymal pulmonary involvement was found in 64.3% of patients, respiratory functional exploration found a restrictive syndrome in 19% of patients, and evaluation of the release of carbon monoxide found a decrease in it in 21.4% of patients, none of our patients benefited from bronchoscopy with bronchoalveolar washing, a controversial practice but which has demonstrated its effectiveness in early detection [7], other schools suggest a histological sampling in order to confirm the diagnosis, classify the lung involvement and make a prognostic assessment, however this practice is still not part of the recommendations [8]. Renal damage was found in 26.2% of patients, 23.8% presented with arterial hypertension, while 11.9% had renal failure and 2.4% of patients presented positive proteinuria. Cardiac involvement was found in 23.8% of patients with 7.1% of patients having presented abnormalities on the EKG, 7.1% had right heart failure, 4.8% had left heart failure, 19% of patients had Pulmonary hypertension on echocardiography and pulmonary arterial hypertension was found by catheterization in only 3 patients (7.1%). It has been reported in the literature that severe microcirculation abnormalities demonstrated by periungual capillaroscopy were strongly associated with pulmonary vascular damage [9], but in our study capillaroscopy was performed in 41 patients (97.6%), and revealed various abnormalities ranging from mega capillaries to vascular desertification in 95.2% of patients while PH was only found in 19% of patients. Digestive involvement was found in 54.8% of patients with gastroesophageal reflux disease (GERD) in 50% of patients, dyspepsia in 21.4%, constipation in 19%, fluid diarrhea with malabsorption in 2.4% of patients and solid dysphagia with endo-brachy-esophagus on esogastroduodenal fibroscopy. Urogenital involvement was found in 33.3% of patients, 21.4% of patients presented with urinary incontinence, 4.8% with dyspareunia and 11.9% with erectile dysfunction.

We also observed a reduction in fertility in these patients, 100% of patients who had children had them before the diagnosis of scleroderma, and

34.3% of patients attempted unsuccessfully to have children after the diagnosis of scleroderma all by natural means, we have not found any study corroborating this result and we cannot exclude the effect of different treatments which leaves the question open.

- **Therapeutically**

For Raynaud's phenomenon, 40 patients were placed on calcium channel blockers, 24 of whom required the addition of 5 phosphodiestherase inhibitors and 8 of whom required the addition of fluoxetine. For extensive skin involvement without visceral involvement, 17 patients were placed on methotrexate, 3 of whom also benefited from local treatment with cannabis oil, when this was associated with pulmonary involvement. 18 patients were placed on mycophenolate mofetil, due to lack of average 6 patients with pulmonary involvement benefited from cyclophosphamide and the 3 patients with PAH confirmed by catheterization benefited from a prostacyclin analog, and only 2 patients benefited from Nintedanib-type antifibrosis for pulmonary fibrosis.

Despite the therapeutic means made available to patients, we remain behind what is done in renowned specialized centers and in research centers, for skin damage we have demonstrated innovation by attempting to add a local treatment with Cannabis oil which has demonstrated a certain effectiveness in blocking CB2 receptors suspected in the pathophysiology of systemic sclerosis [10], the use of Hyaluronidase by local injection has also demonstrated its effectiveness without proof of toxicity and the only negative point of which remains the need for multiple injections [11] as well as non-pharmacological treatments such as sporting and physical activity which makes it possible to modulate immunity [12] or even ultrasound treatment which makes it possible to soften the skin thus making it possible to reduce functional limitation [13], with regard to the management of Raynaud's phenomenon our approach is not far from the latest recommendations developed by the Rheumatology team of Portugal in this year and which revolves around 3 main axes: patient awareness against potential triggering factors, pharmacological treatment allowing the microcirculation to dilate and finally promoting the healing of ulcerations before reaching a possible amputation [14], a Chinese team carried out a literature review in 2021 showing the effectiveness of botulinum toxin injection in the management of Raynaud's phenomenon [15]. Regarding the management of pulmonary involvement, the combination of nintedanib, mycophenolate mofetil and a low dose of corticosteroid therapy has demonstrated their superiority to other conventional treatments [16], however in our context we remain limited by the means and the difficulty of insurance procedures, moreover only 2 patients were able to benefit from nintedanib. Other studies are underway to improve the management of systemic sclerosis, such as trials of Janus Kinase inhibitors, TGF pathway inhibitors, anti-interleukins 6 and 8 and more recently transplantation especially of adipose and mesenchymal stem cells and which remains the most promising therapy [17,18, 19,20].

- **Evolution**

20 patients reported an improvement (47.6%), 11 patients (26.3%) remained stable, 3 patients (7.1%) reported various complications, 7 patients (16.7%) died while only 1 patient was lost to follow-up (2.4%).

The improvement reported by patients concerned cutaneous sclerosis in 6 patients, Raynaud's phenomenon in 9 patients, lung damage in 8 patients, digestive damage in 3 patients and joint and muscle damage respectively in 4 patients.

Regarding the complications, 13 patients presented progression of the pathology, 4 patients manifested a new autoimmune disease, and only 1 patient presented a secondary respiratory infection.

For the deceased patients, 3 were aged between 56 and 62 years at their death, while the other 4 were over 65 years old at their death. The causes of death were dominated by cardiac decompensation secondary to pulmonary failure in 4 patients, followed by cardiac failure in 2 patients and 1 patient who had septic shock.

5. CONCLUSION

Systemic sclerosis is an autoimmune disease that is certainly rare but bothersome on an aesthetic and functional level, and can be life-threatening due to its various visceral damage affecting the lung, heart and kidney. It has an unknown cause and a complex and poorly understood physiopathological mechanism but is increasingly better understood thanks to progress made in genetics. The diagnosis is

based on the ACR/EULAR classification criteria based on clinical, biological and radiological criteria and the management of which, although codified with clear recommendations, is no less complicated and costly and always makes the object of research with the need for global and multidisciplinary care.

In the context of the Casablanca University Hospital, although the frequency of the disease is relatively low, we find no difficulty in making the diagnosis and detecting the various visceral disorders, the real challenge remains on the therapeutic level which requires a simplification of administrative procedures. and easier access to different therapeutic molecules.

ANNEXE

Annexe is available in the following link: https://journalaji.com/index.php/AJI/libraryFiles/downloadPublic/8

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that generative AI technologies such as Large Language Models, etc have been used during writing or editing of manuscripts. This explanation will include the name, version, model, and source of the generative AI technology and as well as all input prompts provided to the generative AI technology

Details of the AI usage are given below:

1. ChatGPT 4 o of Open AI
2. Used for translating the text from french to english

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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