

Contribution of Imaging to the Diagnosis of Non-Traumatic Tendinopathies of the Thoracic Limb in a Resource-Constrained Country

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Abstract

Introduction: Tendinopathy of the thoracic limb (TMT) is frequent, and is responsible for an important socio-professional handicap. Medical imaging, in particular, ultrasound has a major role in contributing to the diagnosis. As the use of ultrasound is recent in osteoarticular pathology, especially in Africa, we proposed to determine the contribution of imaging in the diagnosis of tendinopathy of the thoracic limbs in a country with limited resources. **Patients and Method:** A descriptive and analytical cross-sectional study of patients with tendinopathy of the thoracic limb who consulted the rheumatology department of the CNHU-HKM of Cotonou from August 6, 2019 to October 6, 2019. We evaluated the concordance of thoracic limb tendinopathy between imaging (radiography and ultrasound) and the clinic on the one hand and then between radiography and ultrasound on the other hand. The analysis of the collected data was carried out with the Epi-info software version 7.2.1.0. Then the concordance was evaluated by the kappa coefficient. **Results:** Fifty-two (52) patients with 104 joints were evaluated. The average age was 54.92 ± 3.40 years. Clinically, rotator cuff tendinopathy was the most frequent abarticular pathology (45.19%). The clinical-ultrasound agreement was strong ($k = 0.7527$) for the shoulders, very strong ($k = 0.9360$) for the elbows and moderate for the wrists ($k = 0.6695$). The clinical-radiographic agreement was weak ($k = 0.2316$) at the shoulder level and very weak ($k = 0.2087$) at the elbow level. The radio-ultrasound agreement was very low in the shoulders ($k = 0.1522$), elbows ($k = 0.1859$) and wrists ($k = 0.0001$). **Conclusion:** The contribution of imaging in the diagnosis of TMT remains certain even in a country with lim-

ited resources like ours. Ultrasound is a reliable examination for the diagnosis of non-traumatic tendinopathy of the thoracic limb with a good clinical-ultrasound concordance and a weak radio-clinical and radio-ultrasound concordance.

Keywords

Tendinopathy, Thoracic Limb, Radio-Clinical Concordance, Clinical-Ultrasound Concordance, Benin

1. Introduction

Tendinopathy represents a frequent reason for consultation, accounting for 19% of musculoskeletal disorders and more than 30% of consultations in general and sports medicine [1] [2]. Tendinopathy of the thoracic limb (TMT) is the most common occupational pathology in many countries of the world. It is multifactorial pathology that causes a significant socio-professional handicap [3]. The most frequently encountered TMT are, in order of frequency: rotator cuff tendinopathy (shoulder), epicondylitis and epitrochleitis (elbow), De Quervain's tenosynovitis (wrist), and jerky finger (hands). Standard X-ray and ultrasound are the most accessible imaging techniques for the exploration of TMT in our resource-limited countries. Ultrasound has both diagnostic and therapeutic value in tendon pathology [4]. The use of ultrasound is recent in osteoarticular pathology in Africa. Most of the studies conducted on the use of ultrasound in the diagnosis of tendinopathy of the thoracic limb are of interest to the West, and do not take into account African realities. The aim of the present work is to determine the contribution of imaging in thoracic limb tendinopathy in Benin, a country with limited resources.

2. Patients and Methods

This was a descriptive and analytical cross-sectional study with prospective data collection over a period of two (2) months from August 2019 to October 2019. An exhaustive enrolment of all patients with thoracic limb tendinopathy was seen in the rheumatology department of the CNHU-HKM during the study period. The patients included in the study met the following criteria:

- A diagnosis of thoracic limb tendinopathy made by a rheumatologist on the basis of clinical arguments;
- Have had an X-ray and an ultrasound of the clinical lesion site;
- Have given informed consent.

A total of 104 joints were studied for the 52 included patients, as only one joint site was examined in a single patient (either shoulders, elbows, or wrists).

Socio-demographic parameters, clinical and paraclinical data (radiography and ultrasound) were studied and then the radio-clinical concordance was evaluated.

These data were collected on a survey form after a structured individual interview with each patient, followed by the rheumatological examination. Each patient received radiographs of the pathological joint and then a comparative and bilateral ultrasound of the joint site. The ultrasound scans were subsidized by the hospital. Only one joint site was examined comparatively in a single patient (either shoulders, elbows, or wrists). In addition, several tendon abnormalities could be found in the same subject.

Data analysis was performed with Epi-info software version 7.2.1.0. Graphs and frequency tables were made with Excel 2010. Statistical significance was established by a p-value less than or equal to 5%, with a 95% confidence interval. Cohen's Kappa (k) nonparametric test was used to estimate the rate of agreement or concordance between clinical and para-clinical findings (radiography and ultrasound). The Landis and Koch classification was used to qualitatively assess the agreement rate [5]. Observations were considered to be in agreement when the Kappa coefficient was statistically different from 0. Agreement was either very poor (k = 0 - 0.20), poor (k = 0.21 - 0.40), moderate (k = 0.41 - 0.60), strong (k = 0.61 - 0.80) or very strong (k = 0.81 - 1) [5].

3. Results

3.1. General Characteristics of the Population

A total of 104 joints were studied (because only one joint site was examined in a single patient, either the shoulders, elbows, or wrists) for the 52 included patients.

The mean age of the patients was 54.92 ± 3.40 years with extremes of 21 and 83 years.

There was a predominance of women (40 patients or 76.92%) with a sex ratio of 0.33.

3.2. Clinical Data

Table 1 summarizes the physical examination data of the patients.

In the shoulder, the Jobe's maneuver was the most frequent tendon test for tendinopathy and the Hakwins sign was the most frequent test for subacromial impingement (37.50%).

Elbow injuries were revealed by pain on pressure of the lateral or medial side, which was the most frequent palpatory sign in 13 (12.50%) cases and the Middle finger test was the most frequent test in 8 (7.69%) cases.

As for the wrist, the extension of the wrist was the most frequent painful counter movement 10 (09.61%) and the Finkelstein test was the most frequent tendon test 12 (11.53%) cases.

Table 2 shows the distribution of patients according to the clinical diagnosis. Rotator cuff tendinopathy was the most frequent abarticular pathology 47 (45.19%) cases, followed by De Quervain's tenosynovitis 12 (11.54%) cases and lateral epicondylitis 6 (5.77%) cases.

Table 1. Distribution of patients according to the results of the physical examination of shoulders, elbows and wrists, CNHU/HKM rheumatology department, N = 104.

Physical examination time	Shoulders		Elbows		Wrists	
	N	%	N	%	N	%
Inspection						
Swelling	1	0.96	0	0	12	11.54
Bone relief abnormality	2	1.92	-	-	-	-
Amyotrophy of the supraspinous fossa	2	1.92	-	-	-	-
Palpation						
Pain on passive stretching	10	9.62	3	2.84	5	4.80
Pain when stretching against resistance	8	7.69	6	5.77	8	7.69
Pain on local palpation	36	34.62	-	-	-	-
Local heat	1	0.96	1	0.96	4	3.84
Palpatory pain	-	-	13	12.50	22	21.15
Painful counter movements						
Flexion	18	17.30	2	1.92	9	8.65
Extension	8	7.69	1	0.96	10	9.61
Abduction	42	40.38	-	-	6	5.69
Adduction	7	6.73	-	-	4	3.84
Pronation	-	-	6	5.69	-	-
Supination	-	-	9	8.65	-	-
Internal rotation	31	29.80	-	-	-	-
External rotation	15	14.42	-	-	-	-
Positive tendon tests						
Palm up test	18	17.30	-	-	-	-
Paw test	24	23.07	-	-	-	-
Jobe maneuver						
Lift off or Gerber maneuver	33	31.73	-	-	-	-
Neer's maneuver	15	14.42	-	-	-	-
Yocum's sign	36	34.61	-	-	-	-
Hawkins sign						
Positive middle finger						
Grip test	-	-	8	7.69	-	-
Finkelstein test	-	-	-	-	12	11.53
Brunelli's test	-	-	-	-	6	5.76

3.3. Radiographic Data

Table 3 illustrates the distribution of radiographic abnormalities of the thoracic limbs.

Table 2. Distribution of patients by clinical diagnosis, CNHU/HKM rheumatology department, N = 104.

Clinical diagnosis retained	Numbers (N)	Percentages (%)
Rotator cuff tendinopathy	47	45.19
Lateral epicondylitis	6	5.77
Medial epicondylitis	2	1.92
De Quervain's tenosynovitis	12	11.54
No diagnosis/normal clinical examination	37	35.58
Total	104	100.00

Table 3. Distribution of thoracic limb abnormalities on radiography, CNHU/HKM rheumatology department, N = 104.

Radiographic abnormalities	Shoulders		Elbows		Wrists	
	N	%	N	N	%	N
Anomaly of the supraspinatus	7	6.73	-	-	-	-
Calcifying tendinopathy	5	4.80	-	-	-	-
Calcifying enthesopathy	2	1.92	-	-	-	-
Calcifying tendinopathy of the subscapularis	2	1.92	-	-	-	-
Anomaly of the infraspinous	6	5.76	-	-	-	-
Calcifying enthesopathy	1	0.96	-	-	-	-
Calcifying tendinopathy	5	4.80	-	-	-	-
Calcifying enthesopathy of the deltoid	3	2.88	-	-	-	-
Calcifying enthesopathy of the brachial triceps	-	-	1	0.96	-	-
Associated lesions						
Morphological abnormality of the acromion	25	24.03	-	-	-	-
Omarthrosis	14	13.46	-	-	-	-
Acromioclavicular osteoarthritis	13	12.50	-	-	-	-
Humero-ulnar osteoarthritis	-	-	1	0.96	-	-

At the shoulder level, radiographs were normal in 60 cases or 57.69%.

The supraspinatus was the most affected tendon with 5 cases of calcific tendinopathy (04.80%) and 2 cases of calcific enthesopathy (1.92%).

X-rays of the elbow and wrist were normal in all patients with pain and clinical suspicion of tendinopathy.

3.4. Ultrasound Data

We recorded 58 (55.76%) pathological shoulders on ultrasound with 159 tendon abnormalities (**Table 4(a)**). The supraspinatus was the most affected tendon (64 cases or 61.53%) in the shoulder (**Figure 1**) and calcific tendinopathy was the most common tendon disorder (27 cases or 25.96%).

Table 4. (a) Distribution of abarticular shoulder anomalies on ultrasound, CNHU/HKM rheumatology department, N = 58; (b) Distribution of abarticular abnormalities of the elbows on ultrasound, CNHU/HKM rheumatology department, N = 104; (c) Distribution of abarticular wrist abnormalities on ultrasound, CNHU/HKM rheumatology department, N = 104; (d) Distribution of ultrasound lesions associated with abarticular anomalies of the thoracic limbs, CNHU/HKM rheumatology department, N = 104.

(a)		
Topography and type of tendon injuries	Numbers (N)	Percentages (%)
Supra-spinous	64	61.53
Tendinopathy	9	8.65
Fissural tendinopathy	15	14.42
Calcific tendinopathy	27	25.96
Enthesopathy	7	6.73
Rupture	6	5.77
Infraspinous	53	50.96
Fissural tendinopathy	13	12.50
Calcific tendinopathy	22	21.15
Enthesopathy	7	6.73
Rupture	11	10.58
Subscapular	31	29.80
Tendinopathy	1	0.96
Fissural tendinopathy	7	6.73
Calcific tendinopathy	12	11.54
Enthesopathy	3	2.88
Rupture	8	7.69
Long biceps	11	10.57
Tendinopathy	2	1.92
Fissure tendinopathy	3	2.88
Rupture	3	2.88
Subluxation	3	2.88
(b)		
Ultrasound abnormalities	Numbers (N)	Percentages (%)
Lateral epicondylar tendons	11	10.57
Non-calcific tendinopathy	5	4.80
Enthesopathy	5	4.80
Fissural tendinopathy	1	0.96
Medial epicondylar tendons	7	6.73
Calcific tendinopathy	3	2.88
Non-calcific tendinopathy	2	1.92
Enthesopathy	2	1.92

Continued

Triceps tendon	3	2.88
Fissural tendinopathy	1	0.96
Calcific tendinopathy	1	0.96
Enthesopathy	1	0.96

(c)

Ultrasound abnormalities	Numbers (N)	Percentages (%)
1st compartment	20	19.23
Tenosynovitis of the abductor pollicis longus	6	5.77
Enthesopathy of the abductor pollicis longus	4	3.84
Tenosynovitis of the extensor pollicis brevis	4	3.84
Tendinopathy of the extensor digitorum brevis	3	2.88
Tendinopathy of the abductor pollicis longus	3	2.88
2nd compartment	6	5.77
Tenosynovitis of the extensor carpi radialis longus	2	1.92
Tenosynovitis of the extensor carpi radialis brevis	2	1.92
Tendinopathy of the extensor carpi radialis brevis	1	0.96
Tendinopathy of the extensor carpi radialis longus	1	0.96
3rd compartment	1	0.96
Tenosynovitis of the extensor pollicis longus	1	0.96
4th compartment	1	0.96
Tenosynovitis of the extensor digitorum and extensor indicis	1	0.96
5th compartment	2	1.92
Tendinopathy of the extensor digiti minimi	1	0.96
Tenosynovitis of the extensor digiti minimi	1	0.96
6th compartment	1	0.96
Extensor carpi ulnaris tenosynovitis	1	0.96

(d)

Ultrasound lesions associated	Shoulders		Elbows		Wrists	
	N	%	N	%	N	%
Degenerative bone lesions	29	27.88	1	0.96	1	0.96
Intra-articular fluid effusion	25	24.03	1	0.96	1	0.96
Pathology of the SASD*	24	23.08	-	-	-	-
Acromioclavicular osteoarthritis	23	22.11	-	-	-	-
Fatty involution	14	13.46	-	-	-	-
Synovitis	-	-	-	-	13	12.50
Amyotrophy	6	5.76	-	-	-	-
Presence of impingement	6	5.76	-	-	-	-
Bone erosion	-	-	-	-	2	1.92
Radio carpal osteoarthritis	-	-	-	-	2	1.92

*SASD = subacromial-subdeltoid bursa.

Nine (9 or 8.65%) of the elbows were pathological on ultrasound with 21 tendon abnormalities (**Table 4(b)**). The lateral epicondylar tendons (**Figure 2**) were the most affected (11 cases 10.57%) and non-calcific tendinopathies were the most common tendon condition of the elbow. Doppler activity was positive in two patients.

Tendinopathies found on wrist ultrasound were 31 (**Table 4(c)**) for 08 (07.69%) pathological wrists. De Quervain's tenosynovitis (abnormality of the 1st compartment of the wrist) was the most frequent abnormality with 20 cases (19.23%) and a Doppler hyperemia in one patient (**Figure 3**).



Figure 1. Oblique coronal section of the right and left supraspinatus tendons showing erosion of the trochlea with a left non-calcific tendinopathy, in a patient of the series.

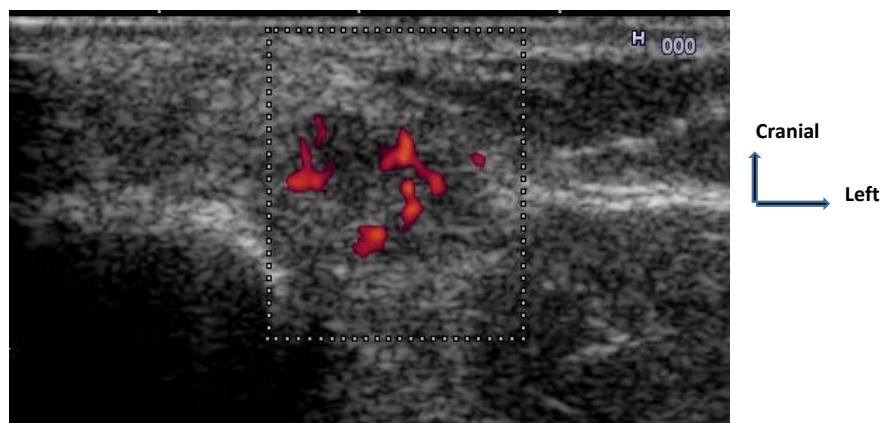


Figure 2. Longitudinal section of the common tendon of the lateral epicondyles illustrating a right lateral epicondylitis, active in a patient of the series.

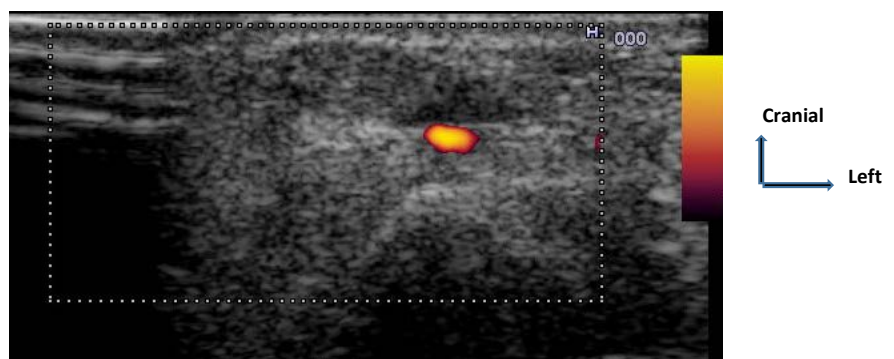


Figure 3. Axial section of the 1st dorsal compartment of the left wrist showing De Quervain's tenosynovitis in a patient of the serie.

Apart from tendon abnormalities, ultrasound allowed us to find some associated lesions summarized in **Table 4(d)**. The most frequent were, in order of frequency, degenerative bone lesions followed by intra-articular fluid effusion, particularly in the shoulders.

3.5. Analytical Data

The radio-clinical concordance study at the level of the shoulders, elbows and wrists is summarized in **Table 5**.

The study of the radio-clinical concordance at the level of the shoulders, elbows and wrists revealed that: the concordance between the clinical results and those of the ultrasound was strong ($k = 0.7527$) at the level of the shoulders, very strong ($k = 0.9360$) at the level of the elbows and moderate at the level of the wrists ($k = 0.6695$). The agreement between clinical and radiographic findings was low ($k = 0.2316$) at the shoulder level and very low ($k = 0.2087$) at the elbow and the wrists ($k = 0.0001$).

Table 6 shows the concordance between radiography and ultrasound in the diagnosis of tendinopathy in the shoulders, elbows and wrists, which is very low.

Table 5. Radio-clinical concordance of tendinopathy in the shoulders, elbows and wrists; CNHU/HKM rheumatology department, N = 104.

Radiology	Clinical		Total	k	Interpretation of the concordance
	Tendinopathy (+)	Tendinopathy (-)			
Shoulder					
Radiography					
Tendinopathy (+)	11	1	12	0.2316	Low
Tendinopathy (-)	36	56	92		
Total	47	57	104		
Ultrasound					
Tendinopathy (+)	46	12	58	0.7527	High
Tendinopathy (-)	1	45	46		
Total	47	57	104		
Elbow					
Radiography					
Tendinopathy (+)	1	0	1	0.2087	Very low
Tendinopathy (-)	7	96	103		
Total	8	96	104		
Ultrasound					
Tendinopathy (+)	8	1	9	0.9360	Very high
Tendinopathy (-)	0	95	95		
Total	8	96	104		

Continued

Wrist					
Radiography					
Tendinopathy (+)	0	0	0	0.0001	
Tendinopathy (-)	12	92	104		Very low
Total	12	92	104		
Ultrasound					
Tendinopathy (+)	7	1	8	0.6695	
Tendinopathy (-)	5	91	96		High
Total	12	92	104		

Table 6. Concordance between radiography and ultrasound in the diagnosis of tendinopathy, CNHU/HKM Rheumatology Department, N = 104.

Ultrasound	Radiography		Total	k	Interpretation of the concordance
	Tendinopathy (+)	Tendinopathy (-)			
Shoulder					
Tendinopathy (+)	11	47	58		
Tendinopathy (-)	1	45	46	0.1522	Very low
Total	12	92	104		
Elbow					
Tendinopathy (+)	1	8	9		
Tendinopathy (-)	0	95	95	0.1859	Very low
Total	1	103	104		
Wrist					
Tendinopathy (+)	0	8	8		
Tendinopathy (-)	0	96	96	0.0001	Very low
Total	0	104	104		

4. Discussion

Tendinopathies are encountered above all in a context of hyper solicitation. The quality of the diagnosis depends above all on the accuracy of the clinical examination. The questioning and the physical examination with the realization of tendon tests will make it possible to reach a clinical lesion diagnosis.

Among the tendon tests performed on the shoulders in our patients, the Jobe maneuver was the most frequent (36.53%), with supra-spinous tendinopathies in the rotator cuff lesions but also in the tendinopathies of the thoracic limb. Wafa *et al.* [3] made the same observation with a frequency of 59.2%. This can be explained by the fact that during subacromial impingement, the supraspinatus is in permanent contact with the coracoacromial ligament, which predisposes it to wear

out more rapidly than the other tendons of the rotator cuff.

In patients with elbow involvement, we found much more pain in the lateral aspect as shown by the Middle finger test which was the most frequent tendon test (7.69%). These results confirm the data of the literature which had shown that tendinopathies of the lateral aspect of the elbow were the most frequent TMT of the elbow [3] [6].

In the wrists, the Finkelstein test was predominant (11.53%), testifying to the frequency of De Quervain's tenosynovitis in the wrists, thus corroborating the data in the literature [3].

In the majority of cases, after the clinical examination, it is necessary to resort to imaging to refine the diagnosis of the lesion and decide on a therapeutic strategy. Standard radiographic images are the first step in the imaging assessment, regardless of the size and apparent nature of the lesions. These images are systematically prescribed, although their contribution remains limited in tendon pathology. They are used to look for indirect signs of injury, in particular small bone changes in relation to a tendon insertion and calcifications. In the present study, we recorded 60 (57.69%) normal shoulder radiographs, 10 (9.62%) normal elbow radiographs and 13 (12.5%) normal wrist radiographs. Tendinopathy of the supraspinatus in its calcifying form was visualized in 5 cases, *i.e.*, 04.80%, followed by 2 cases of calcifying enthesopathy, *i.e.*, 1.92%. We found one (1) case of humero-ulnar osteoarthritis, one (1) case of triceps enthesopathy, one (1) radio-carpal osteoarthritis and one (1) inter-phalangeal osteoarthritis and rhizarthrosis. These observations confirm that radiography is the gold standard for the diagnosis of calcific tendinopathies [7] and the detection of chronic bone damage, but its contribution remains insignificant in non-calcific tendinopathies, hence the interest of osteoarticular ultrasound.

Technological advances and the development of consensus have considerably improved the reproducibility of ultrasound, as long as the quality of the machine and the experience of the examiner are taken into account [7]. Nowadays, ultrasound is becoming increasingly important in musculoskeletal pathology in general and in the diagnosis of tendinopathies in particular. Even if it is an examination that depends on the dexterity of the sonographer, and that the reproducibility is low, this study allowed us to describe the contribution of ultrasound in the diagnosis of tendinopathies of the thoracic limb and to evaluate the concordance between the clinical data and the imaging data (ultrasound/radiography) on the one hand, and the concordance between radiography and ultrasound on the other hand. From our results, it appears that ultrasound detects 4 times more than radiography tendinopathies of the shoulder, 8 times more those of the elbow and 7 times more those of the wrist. This could be explained by the fact that ultrasound analysis of tendon injuries is particularly easy for superficial tendons [8].

Indeed, several studies have confirmed the good sensitivity and specificity of ultrasound to detect rotator cuff damage [8] [9] [10]. These studies also noted

that there was no significant difference between the performance of ultrasound and Magnetic Resonance Imaging (MRI) in the detection of rotator cuff injuries [8] [9] [10]. Ultrasound thus appears to be a reliable tool of choice for the evaluation of rotator cuff tendon injuries. It is more sensitive than MRI and radiography for the identification of calcifications [8]. At the elbows, the lateral epichondylar tendons were the most affected (10.57%). This is consistent with the literature [6]. Non-calcific tendinopathy was the most common type of abnormality and sometimes associated with intra-tendinous Doppler activity. These results reinforce the usefulness of ultrasound for the accurate assessment of the affected tendons and the type of tendon abnormality [8]. The tendons of the 1st dorsal compartment of the wrist were the most affected (19.23%) and De Quervain's tenosynovitis was the most frequent tendinopathy. These data are consistent with the literature [3].

The agreement between clinical and ultrasound findings was high ($k = 0.7527$) in the shoulders and wrists ($k = 0.6695$) but was very high ($k = 0.9360$) in the elbows. The agreement between clinical and radiographic findings was low ($k = 0.2316$) at the shoulder, and very low ($k = 0.2087$) at the elbow and the wrists ($k = 0.001$). This could be explained by the fact that the diagnosis of tendinopathies is primarily clinical and ultrasound would be used to confirm the clinical diagnosis, but especially to assess the injury [8] [11]. Ultrasound allows a better exploration of the large joints than the smaller ones (wrists and hands) which require the dexterity of the operator but also adapted probes like the golf probe which was not available in our context.

In countries with limited resources such as ours, a good clinical examination thus allows us to make an almost certain diagnosis of tendon pathology. However, imaging remains useful because, apart from tendinopathy, ultrasound can reveal other abnormalities such as bursitis and synovitis, and joint effusions, which are a source of pain and which go unnoticed in the clinic as well as in the radiograph. Finally, ultrasound also has a therapeutic role in guiding infiltrations or the evacuation of effusions.

The concordance between radiographic and ultrasonographic findings was very low in the shoulders ($k = 0.1522$), elbows ($k = 0.1859$) and wrist ($k = 0.0001$). This low radio-ultrasound concordance can be explained by the fact that radiography only detects calcifications and chronic bone abnormalities such as osteophytes, enthesophytes and erosions in the majority of cases and does a very poor job of analysing the tendon. In addition to these lesions, ultrasound detects and analyses the tendon better. It can easily identify tendon ruptures, whether they are partial or complete with a loss of continuity of the tendon and retraction. Calcification or, more rarely, an intra tendinous tophus can also be seen. At the level of the tendon insertion (enthesis), ultrasound may reveal calcifications, called enthesophytes [8].

5. Conclusion

The contribution of imaging in the diagnosis of TMT remains definite even in a

country with limited resources such as ours. Ultrasound is a reliable examination for the diagnosis of non-traumatic tendinopathy of the thoracic limb with a good clinical-ultrasound concordance and a poor radio-clinical and radio-ultrasound concordance. Therefore, it is necessary to make it more available and more accessible in our current practice, for better diagnostic accuracy and adequate management of the patients. However, its reliability depends on the quality of the machine and the experience of the examiner.

Limitation of the Study

The main limitation of this work is the small sample size and the fact that the study is monocentric. These biases do not allow us to extrapolate our results to the rest of the population. This does not detract from the validity of our results. An extension of the study with a larger number of patients should be considered to determine more precisely the diagnostic values of the different clinical tests in relation to ultrasound and, if possible, to MRI.

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Author Contributions

All authors contributed to the design of the paper, the drafting of the article, its critical revision and the final approval of the version to be published.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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