Ocular Immunology and Inflammation

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/ioii20

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To cite this article: Caroline Borciuch, Thomas El-Jammal, Laurent Kodjikian, Loïc Boussel, Nicolas Romain-Scelle, Mikail Nourredine, Mathieu Gerfaud-Valentin & Pascal Sève (2023): Value of Chest X-Ray and Chest Computed Tomography for Systemic Sarcoidosis Diagnosis in Undifferentiated Uveitis, Ocular Immunology and Inflammation, DOI: 10.1080/09273948.2023.2226203

To link to this article: https://doi.org/10.1080/09273948.2023.2226203

OCULAR IMMUNOLOGY AND INFLAMMATION
https://doi.org/10.1080/09273948.2023.2226203

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ORIGINAL ARTICLE

Value of Chest X-Ray and Chest Computed Tomography for Systemic Sarcoidosis Diagnosis in Undifferentiated Uveitis

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ABSTRACT

Background: To evaluate the contribution of chest X-ray and chest CT for the diagnosis of sarcoid uveitis.
Methods: Retrospective study on consecutive patients with uveitis of unknown etiology, who underwent both chest X-ray and CT during uveitis diagnosis workup in a tertiary French university hospital.
Results: A total of 914 patients were included. Systemic sarcoidosis was identified in 23.1%. The probability of discordance between chest X-ray and CT increased with age at diagnosis ($p < 0.001$). In patients 30 years of age and younger, the probability of discordance was 5% or less, and 0.8% if the ACE level was normal. After 78.3 years of age, the probability of discordance was 20% or more.
Conclusion: We recommend not to perform CT in patients under 30 years of age with a normal chest X ray and ACE level, and suggest performing chest CT first in the elderly.

ARTICLE HISTORY
Received 8 February 2023
Revised 17 May 2023
Accepted 12 June 2023

KEYWORDS
Chest imaging; chest X-ray; CT scan; sarcoidosis; uveitis

Background

Uveitis is defined as an intra-ocular inflammation affecting the iris, ciliary body, vitreous, choroid, or retina; up to 35% of patients with uveitis have a significantly impaired visual function, and it is responsible for 5–10% of cases of blindness worldwide.[1] The determination of uveitis etiology is a challenge because there are about 80 causes reported and there is a lack of specific signs for each etiology.[2] These can be grouped into infectious diseases, inflammatory diseases, specific ocular syndromes, drug-induced uveitis, and pseudo-uveitis (that includes mainly post-traumatic causes and lymphoma),[3] however, according to the location of uveitis, 26 to 45% of cases remain idiopathic.[4–6] The recommendations for etiological diagnosis strategy are mostly based on clinical experience and the evaluation of each exam separately rather than a global diagnostic strategy.[3,7] However, the prospective study ULISSE found that a standardised strategy was neither inferior nor non-inferior to an open strategy for the etiological diagnosis of uveitis.[8]

As mediastinal and parenchymal abnormalities may support sarcoidosis in the diagnostic workup, chest imaging (X-ray or computed tomography [CT]) is part of the first-line examinations in undifferentiated uveitis.[9,10] Nevertheless, there is currently no recommendation as to which imaging modality to use for a particular patient. While the superiority of chest CT in detecting signs of sarcoidosis has been reported,[11,12] chest X-ray is often performed first because of its lower cost and radiation dose. Also, some studies suggest that CT may be more useful than X-ray in specific populations such as elderly patients.[13,14]

In the present study, we therefore assessed and compared the value of chest X-ray and chest CT in the etiological diagnosis of uveitis in a large cohort of patients. We also aimed to establish the predictive demographic, clinical, and laboratory characteristics associated with the contribution of each exam, with a focus on sarcoidosis diagnosis.

Patients and methods

Patients

This retrospective, observational cohort study included patients with uveitis referred by the department of ophthalmology (Lyon university hospital, Lyon, France) or by non-hospital ophthalmologists to the department of internal medicine (Lyon university hospital, Lyon, France) between January 2003 and March 2021 for a diagnostic workup. All uveitis diagnoses were confirmed by ophthalmological examination. The Standardisation of Uveitis Nomenclature (SUN) criteria were used for the anatomical location of uveitis.[15] The present study received approval from the local ethics committee (CPP Sud Est IV) in February 2019 (N° 19–31) and was registered on www.clinicaltrials.gov (NCT03877575).

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Supplemental data for this article can be accessed online at https://doi.org/10.1080/09273948.2023.2226203

Diagnostic workup and definitions

Included patients underwent the standard screening protocol for uveitis of our medicine department, including a C-reactive protein test, a complete blood cell count, a serological syphilis test, and a chest X-ray. Patients with chronic or granulomatous uveitis had a blood angiotensin-converting enzyme (ACE) test, a QuantiFERON®-TB Gold Plus test (Biron, Brossard, Canada), and a chest CT. The physician could also decide to perform these tests if the initial workup was negative. If there were clinically suggestive signs of sarcoidosis, conjunctival or skin biopsies were performed. Patients could undergo a minor salivary gland biopsy (MSGB), a transbronchial lung biopsy, a bronchoalveolar lavage fluid (BALF) analysis, and an ^{18}F-Fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET). Serum ACE levels were considered elevated if they exceeded the reference value of the laboratory[16] and a lymphocyte count of 1.0 G/L or less was considered low.[17] We excluded patients who did not undergo both a chest X-ray and a CT, or in whom the interval between the examinations was more than three months. Patients with uveitis occurring during the course of a previously diagnosed disease were excluded.

Biopsy-proven sarcoidosis was defined as histological demonstration of non-caseating granuloma and exclusion of other diseases, according to the World Association for Sarcoidosis and Other Granulomatous Disorders/American Thoracic Society/European Respiratory Society (WASOG/ATS/ERS) criteria.[18] In the absence of histological proof, the diagnosis of presumed/probable sarcoidosis was based on Abad's modified criteria, which include ^{18}F-FDG PET scan instead of ^{99m}Tc scintigraphy.[19] Patients were presumed to have sarcoid uveitis if they met at least two out of the following four criteria: typical changes on chest X-ray or CT; alveolitis with a predominance of CD4+ lymphocytes on BALF analysis; an elevated ACE level; or ^{18}F-FDG uptake on PET scan. Subjects were judged to have probable sarcoidosis when only one criterion was met. Zajicek's classification was used for the definition of neurosarcoidosis.[20] Moreover, we used the most recent SUN classification criteria for sarcoidosis-associated uveitis.[21]

Chest imaging

Included patients underwent standard chest X-ray and chest CT following a routine protocol on a 16-detector-row CT scanner (Lightspeed Pro, General Electric, Boston, MA, USA), a 64-detector-row CT scanner (Brilliance CT 64; Philips, Amsterdam, the Netherlands) after 2007, a 128 or 256-detector-row CT scanner after 2017 (Brilliance ICT Elite 256 or Ingenuity CT 128, Philips). Intravenous contrast was injected in all patients to improve the visualisation of lymph nodes.

Chest X-rays were evaluated by two internal medicine physicians (CB and PS, the latter is an expert in the field of sarcoidosis). The analysis of chest CT was performed by a radiologist aware of uveitis history only. The CT was reviewed by the internal medicine physician in charge of the patient.

Scadding classification was used for the analysis of chest X-rays.[22] Exams were divided into negative, positive for sarcoidosis, and contributory for other diagnoses. Chest CT was defined as normal or consistent with sarcoidosis according to the following criteria: non-compressive and non-necrotic hilum bilateral and mediastinum lymph nodes with a short-axis diameter greater than 1 cm, perilymphatic pulmonary nodules, and other features compatible with parenchymal sarcoidosis.[23,24] Chest CT could also be abnormal and contributory for a diagnosis different from sarcoidosis.

Statistical analysis

Quantitative variables were expressed as median [interquartile range, IQR], and categorical data were presented as frequency (percentage). Categorical variables were compared using the Fisher's exact test or the Chi-squared test as appropriate, and quantitative variables using Kruskal-Wallis rank sum test. Factors associated with a positive chest X-ray and/or CT were investigated in a multivariate analysis by logistic regression after determining the factors of interest in univariate analysis. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were estimated by age category. Punctual estimates without precision estimates are shown for indicative purposes only. The probabilities of discordance between chest X-ray and CT were modelled using a multivariate logistic regression, with the following features as candidate covariates: age at diagnosis, sex, ethnicity, anatomical type of uveitis, lymphopenia, ACE level. In subgroups with a low probability of discordance, we investigated for additional factors associated with the probability of discordance. A sensitivity analysis was performed considering alternative diagnostic criteria. Alpha risk for statistical significance was set at 0.05. Analysis were conducted using the R software (4.2.1).[25]

Results

Patient characteristics

A total of 1588 patients were referred to the department of internal medicine with uveitis. After excluding 411 patients because uveitis occurred during the course of a previously diagnosed disease, and 263 patients who did not undergo both chest X-ray and CT, 914 patients were included. The characteristics of excluded patients are presented in supplemental Tables S1 to S4. The median [IQR] age at onset was 52 [37–67] years. The male/female ratio was 0.68, and 708 (77.5%) patients were Caucasian. Patients had mostly chronic (76.6%, $n = 700$) and bilateral (66.4%, $n = 607$) disease (Table 1).

Uveitis was considered idiopathic in 446 (48.8%) patients. Sarcoidosis was identified in 211 (23.1%) patients; Among patients with sarcoidosis, it was biopsy proven in 108/211 (51.2%) patients, presumed in 53 (25.1%) patients, and probable in 47 (22.3%) patients (Table 1). Uveitis was associated with systemic manifestations in 55/211 (26.1%) patients diagnosed with sarcoidosis. The most recent SUN classification criteria (21) for sarcoidosis-associated uveitis were fulfilled by 198 (93.8%) sarcoidosis patients. A total of eight patients with sarcoid uveitis were excluded because of the lack of chest X-ray or CT scan (supplemental Table S3). Among them, only one patient had a chest X-ray alone and it was normal. Characteristics of patients diagnosed with sarcoidosis are reported

Table 1. Patient characteristics.

	Total population, n = 914
Age at onset - years, median [IQR]	52 [35–67]
Male/female ratio	372/542 (0.69)
Ethnicity, n (%)	
Caucasian	708 (77.5)
North African	146 (16.0)
Sub-Saharan	45 (4.9)
Asian	15 (1.6)
Anatomical type, n (%)	
Anterior	237 (25.9)
Intermediate	120 (13.1)
Posterior	138 (15.1)
Anterior + Intermediate	54 (5.9)
Intermediate + Posterior	39 (4.3)
Panuveitis	326 (35.7)
Chronic, n (%)	700 (76.6)
Bilateral, n (%)	607 (66.4)
Granulomatous, n (%)	295 (32.2)
Hypertensive, n (%)	79 (8.6)
Etiology	
Idiopathic, n (%)	446 (48.8)
Specific ocular syndromes, n (%)	45 (4.9)
Vogt-Koyanagi-Harada disease	7 (15.6)
Birdshot chorioretinitis	16 (35.6)
Pars planitis	5 (11.1)
Fuchs heterochromic cyclitis	3 (6.7)
Sympathetic ophtalmia	1 (2.2)
Acute retinal necrosis	1 (2.2)
Punctate inner choroidopathy	3 (6.7)
Post-chirurgical	2 (4.4)
Multifocal choroiditis	6 (13.3)
White dots syndromes	1 (2.2)
Infectious disease, n (%)	91 (10.0)
Tuberculosis	65 (71.4)
Syphilis	4 (4.4)
Herpes	2 (2.2)
Lyme	11 (12.1)
Toxoplasmosis	2 (2.2)
Toxocarosis	2 (2.2)
Infectious uveomeningitis	2 (2.2)
Leptospirosis	2 (2.2)
Bartonellosis	1 (1.1)
Inflammatory disease, n (%)	296 (32.4)
Sarcoidosis, n (%)	211 (71.3)
Proven	108 (51.2)
Presumed	53 (25.1)
Probable	47 (22.3)
HLA-B27-related uveitis	30 (10.1)
Behçet's disease	26 (8.8)
Multiple sclerosis	17 (5.7)
Crohn's disease and hemorrhagic rectocolitis	4 (1,4)
TINU syndrome	2 (0.7)
Blau disease	1 (0.3)
Horton	2 (0.7)
Auto-inflammatory syndrome	1 (0.3)
APECED	1 (0.3)
Immune reconstitution inflammatory syndrome	1 (0.3)
Other, n (%)	36 (3.9)
Lymphoma	22 (61.1)
Iatrogenous	8 (22.2)
Atrophic polychondritis	2 (5.6)
Granulomatosis with polyangiitis	2 (5.6)
Leukocytoclastic vasculitis	2 (5.6)

IQR: interquartile range; TINU : Tubulointerstitial nephritis and uveitis; HLA: Human leucocyte antigen; APECED: Autoimmune polyendocrinopathy candidiasis ectodermal distrophy.

in supplemental Table S5. Among the 58 patients with sarcoidosis who had both normal chest X-ray and CT, 31 (53.4%) had an ^{18}FDG PET compatible with systemic sarcoidosis, 14 (24.1%) had a positive MSGB, skin, bronchial or lymphadenopathy biopsy, and five (8.6%) had lymphocytic alveolitis on BALF. Six patients had elevated serum ACE level only and two patients met Zajicek's criteria for neurosarcoidosis.

Chest imaging results

The chest X-ray was abnormal in 89 (9.7%) patients. The results of the chest X-rays are shown in the Table 2.

Chest CT was abnormal in 353 (38.6%) patients. Changes considered equivocal for sarcoidosis were found in 165/353 (46.7%) patients with abnormal chest CT. Of these, 153/165 (92.7%) patients with CT scans suggestive of sarcoidosis were found to have systemic sarcoidosis on further investigations. The results of the chest CT are shown in the Table 3.

In 88/211 (41.7%) patients diagnosed with sarcoidosis, chest CT contributed to sarcoidosis diagnosis after a normal chest X-ray, while 58/211 (27.4%) patients with systemic sarcoidosis had both normal chest X-ray and CT. A total of 68 (7.4%) of chest X-rays and 153 (16.7%) CT scans contributed to the diagnosis of sarcoidosis.

Patients were classified into four groups according to the chest imaging results for sarcoidosis: X-ray and CT both negative (-/-), X-ray and CT both positive (+/+), X-ray positive only (±), CT positive only (-/+) (Table 4).

One patient had an X-ray compatible with stage 2 of the Scadding classification, while CT showed an interstitial syndrome suggestive of tuberculosis. According to the univariate analysis, the distribution of age, anatomical type, bilateral uveitis, granulomatous uveitis, lymphopenia and ACE level were significantly different between the four groups. Patients in the +/+ group appeared to be younger, with more bilateral and granulomatous uveitis, and more lymphopenia and elevated ACE level. Characteristics that were not significant in univariate analysis are shown in Supplemental Table S5. Characteristics of sarcoidosis patients are shown in Supplementary Table S6.

Factors associated with X-ray and CT results in multivariate analysis and exams reliability

After determining the significant covariates in the univariate analysis, the multivariate analysis found that the probability of positivity of chest X-ray was higher in patients of non-Caucasian ethnicity than of Caucasian ethnicity (OR = 2.11, 95% CI 1.24 to 3.53, $p = 0.005$); it was 6.1% (95% CI 4.6 to 8.2) among Caucasians, and 12.1% (95% CI 8.3 to 17.3) among non-Caucasians.

Table 2. Chest X-ray results.

X-ray result	Total, *n* = 914
Normal, n (%)	**825 (90.3)**
Evocative of sarcoidosis according to Scadding classification, n (%)	**68 (7.4)**
Stage 1	54
Stage 2	8
Stage 3	4
Stage 4	2
Evocative of tuberculosis, n (%)	**3 (0.3)**
Abnormal but non-contributory chest X-rays, n (%)	**18 (2.0)**
Cardiomegaly	7
Isolated parenchymal nodule	5
Small calcified mediastinal lymph nodes	3
Already known pulmonary neoplasia	2
Heart failure	1

Table 3. Chest CT results.

CT result, n (%)	Total, *n* = 914
Normal, n (%)	**561 (61.4)**
Evocative of sarcoidosis, n (%)	**165 (18.1)**
Lymphadenopathy	159
Both hilar and mediastinum lymphadenopathy	116
Exclusive mediastinum lymphadenopathy	38
Exclusive bihilar lymphadenopathy	5
Associated-to-isolated parenchymal involvement	51/5 = 10.2
Evocative of other diagnosis, n (%)	**27 (3.0)**
Tuberculosis	23
Lymphoma	2
Behçet disease	1
Granulomatosis with polyangiitis	1
Abnormal but non-contributory CT, n (%)	**161 (17.6)**
Aspecific pulmonary nodules	74
Aspecific lymphadenopathy	22
Emphysema	25
Pulmonary atelectasis	16
Infectious pneumonia	8
Thymus abdnormalities	6
Bronchiectasis	5
Thyroid nodule	3
Pulmonary neoplasia	2

The positivity of chest CT was associated with older age (OR = 1.02, 95% CI 1.01 to 1.03 for each additional year, $p < 0.001$) and anatomical type (in case of panuveitis, OR = 2.19, 95% CI 1.41 to 3.48 compared to anterior uveitis, $p < 0.001$) in multivariate analysis. The sensitivity of chest X-ray interpreted as typical of sarcoidosis was 30.8%, and for CT this was 72.5% (Table 5). In the study sample, the sensitivity of chest radiography was lower in patients older than 60 years of age compared to younger patients. The sensitivity of CT scanning also tended to decrease in patients over 60 years of age but remained above 70%. Specificity exceeded 98% in all age categories.

The probability of discordance increased with age, exceeding 20% in patients aged 78.3 years and over (Figure 1). In patients under 30 years of age, the probability of discordance was less than 5% (95% CI 3.0 to 7.0). In this subgroup, elevated ACE was associated with discordance (OR = 27.8, 95% CI 3.85 to 560 $p = 0.004$), which was 0.8% (95% CI 0.1 to 5.4) in case of normal ACE.

Discussion

In the present study, the sensitivity of chest X-ray was lower in patients over 60 years of age, while the decrease in sensitivity of chest CT with age appeared to be less important. We also found that the probability of discordance between chest X-ray and CT for sarcoidosis diagnosis increased with age. Because of the low frequency of occurrence of a negative CT after a positive chest X-ray (herein, only one patient had a negative chest CT after a positive chest X-ray), the probability of discordance between the two exams is a good approximation of the probability of having a positive CT in case of a negative chest X-ray. The probability of discordance between CT and X-ray was low in the young patients, in particular if the level of ACE was normal. In clinical practice, a chest CT is often performed whether the X-ray is positive or negative for sarcoidosis. Even if new low-dose CT are showing non-inferior results to standard CT,[27] it is important to avoid unneeded healthcare cost and unnecessary irradiation, the latter appearing especially risky in young patients.[28] According to the results presented herein, we can recommend not to carry out a thoracic CT in case of a negative X-ray in a patient <30 years of age with normal ACE. Additionally, we found that the probability of discordant results on chest CT and X-ray reached levels over 20% after the age of 78.3 years. This suggests that the performance of CT exceeds that of radiography, and that chest CT may be recommended as a first-line examination in patients after the age of 78 years. The study reported by Febvay et al included 83 patients with proven sarcoidosis,[29]

Table 4. Patient characteristics according to chest imaging results.

	Chest X-ray and CT results combination					
	Overall, N = 914	-/-, N = 748	-/+, N = 98	±, N = 1[1]	+/+, N = 67	p-value
Age at onset - years, median [IQR]	52 [35–67]	50[26–] 66]	64 [53–75]	80 [80–80]	49 [40–61]	<0.001
Anatomical type, n (%)						0.002
Anterior	237 (26)	205 (27.4)	14 (15)	-	18 (27)	
Intermediate	120 (13)	104 (14)	10 (10)	-	6 (9.0)	
Posterior	138 (15)	123 (16.4)	11 (11)	-	4 (6.0)	
Anterior + Intermediate	54 (6)	45 (6)	5 (5)	-	4 (6.0)	
Intermediate + Posterior	39 (4)	31 (4.1)	6 (6)	-	2 (3.0)	
Panuveitis	326 (36)	240 (32.1)	52 (53)	-	33 (49)	
Bilateral, n (%)	607 (66)	479 (64)	76 (78)	-	51 (76)	0.009
Granulomatous, n (%)	295 (32)	216 (29)	43 (44)	-	35 (52)	<0.001
Lymphocytes count, n (%)						<0.001
Normal	836 (91)	706 (94.4)	82 (84)	-	48 (72)	
Lymphopenia < 1 G/L	65 (7.1)	31 (4.1)	14 (14)	-	19 (28)	
Lymphocytosis > 4 G/L	5 (0.5)	5 (0.7)	0 (0)	-	0 (0)	
Missing data	8 (0.9)	6 (0.8)	2 (2.0)	-	0 (0)	
ACE, n (%)						<0.001
Normal	707 (77)	630 (84)	51 (52)	-	25 (37)	
Elevated	190 (21)	102 (14)	46 (47)	-	42 (63)	
Missing data	17 (2)	16 (2)	1 (1)	-	0 (0)	

IQR: interquartile range.
+/+ : Chest X-ray and CT both negative for sarcoidosis.
-/+ : Normal chest X-ray, CT positive for sarcoidosis.
+/- : Chest X-ray positive for sarcoidosis, normal CT.
+/+ : Chest X-ray and CT both positive for sarcoidosis.
1Patient data has been censored for anonymity.

Table 5. Reliability of chest X-ray and CT for systemic sarcoidosis ($n = 914$).

	Sensitivity, %	Specificity, %	PPV, %	NPV, %
Chest X-ray				
Overall	30.8%	99.6%	95.6%	82.7%
Age at diagnosis				
<40 years	44.7%	100%	100%	92.1%
40–60 years	40.8%	99.6%	96.9%	83.4%
>60 years	17.5%	99.1%	89.5%	74%
CT scan				
Overall	72.5%	98.3%	92.7%	92.3%
Age at diagnosis				
<40 years	81.6%	98.4%	88.6%	97.2%
40–60 years	77.6%	98.2%	95.6%	92.9%
>60 years	70.1%	98.3%	94.5%	88.6%

Those results are solely indicative, and unfit for statistical inference beyond this study's sample.
PPV: positive predictive value.
NPV: negative predictive value.

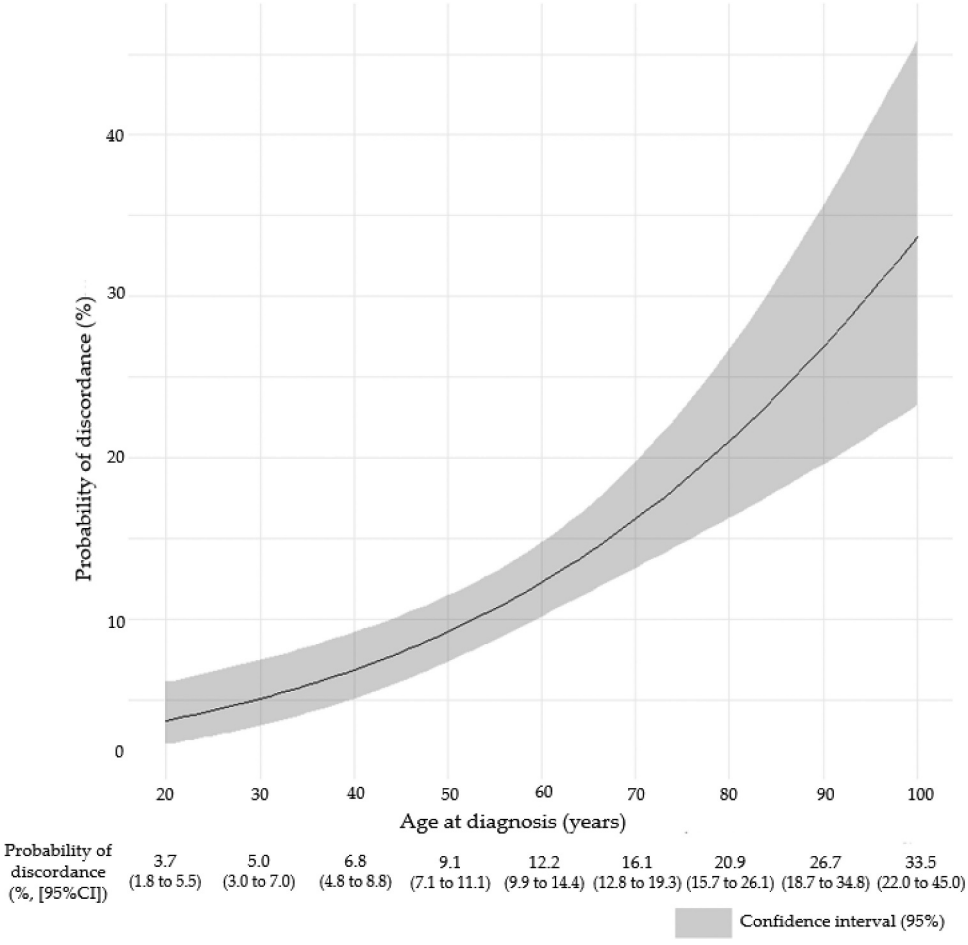

Figure 1. Predicted probability of discordance between chest X-ray and CT according to age at diagnosis.

and found that there were almost half as many positive chest X-rays among patients over 50 years of age than among younger patients, while the proportion of positive scans was similar in both groups. These results suggest that chest X-ray is of poor value compared to CT in elderly patients, which is consistent with the increase in the probability of discordance with age herein. In patients with undifferentiated uveitis and normal chest CT, Chauvelot et al. found that PET scan enabled intraocular sarcoidosis diagnosis in 19/67 (28.4%) patients[30]; older age was associated with PET scan positivity, suggesting that CT may miss lymphadenopathy in elderly patients, which are better visualised on PET scan in this population. Taken together, these findings and those reported herein are consistent with the hypothesis that granulomatous burden is less important in late-onset sarcoidosis or after a long chronic course, and therefore more precise examinations such as CT or even PET scan are needed to identify mediastinal involvement in the elderly,[29–31] as opposed to young patients in whom a chest X-ray is sufficient to find granulomatous infiltration. Nevertheless, chest imaging was normal in over a quarter of patients

with sarcoidosis herein, which serves to underline that sarcoidosis is a polymorphic disease with no definitive diagnostic marker and that negative imaging does not rule out the diagnosis; in cases of clinical suspicion and negative chest imaging other examinations should be considered as these can lead to a sarcoidosis diagnosis, such as PET scan or biopsy.

The present study found that the specificity of both X-ray and CT was excellent, however, the sensitivity was lower than that reported elsewhere. For instance, Niederer et al. compared chest X-ray and CT for the diagnosis of intraocular sarcoidosis in 709 patients with undifferentiated uveitis and found that the sensitivity was 57.6% for chest X-ray and 98% for chest CT[11]; similar results were reported by Acharya et al. in 884 patients with undifferentiated uveitis.[32] This raises the question of the criteria used for the sarcoidosis diagnosis. The difference in sensitivity results described above may be explained by the use herein of the modified Abad criteria that include PET scan findings to define presumed and probable sarcoidosis. Indeed, several studies have demonstrated the value of PET scan as a second-step investigation in sarcoidosis diagnosis,[30,33] and we decided to include this examination in our diagnostic criteria choice.

Assessing the results of patients' CT, we found that 13.8% patients with proven sarcoidosis had mediastinal lymphadenopathy without hilar involvement on chest CT, although the SUN and IWOS criteria include only bilateral hilar lymphadenopathy for the diagnosis of sarcoidosis.[9,21] This suggests that mediastinal lymphadenopathy should also be considered as a diagnostic criteria for sarcoidosis.

One of the limitations of the present study is its retrospective and single-centre nature and the results need to be confirmed on an independent population. Also, the X-rays were read only by two internists, as there is no systematic reading of radiographs by radiologists in our centre, which is however close to the real conditions of X-ray reading in care centres. Also, in case of retrospective reading due to missing data, the examiner was aware of the patient's final diagnosis, generating potential interpretation bias. Furthermore, patients could be referred to the department of internal medicine by a non-hospital ophthalmologist. Then, specific ocular syndromes could be diagnosed by a trained ophthalmologist after the first consultation with the internal medicine physician, who could then prescribe a broader diagnostic workup. This explains why patients with diagnoses such as Fuchs heterochromic cyclitis, Vogt-Koyanagi-Harada disease or Birdshot chorioretinitis were included in the final analysis after undergoing both chest X-ray and CT. However, most of the patients with these diagnoses in the first cohort of 1588 patients were excluded from the final analysis. Otherwise, only 8 patients with a diagnosis of sarcoidosis were excluded because of a lack of X-ray or CT scan, limiting the risk of bias.

In addition, as mentioned above, the chosen diagnosis criteria impacted the results; chest CT was involved in the classification as proven or probable sarcoidosis according to Abad's criteria. As such, the diagnostic performance of chest X-ray and CT herein is impacted by the lack of pathological examination for all patients. Of note, 93.8% of the patients diagnosed with sarcoid uveitis fulfilled the most recent SUN criteria, considering nuclear imaging[21]; We have chosen to show the results of analysis based on the Abad's criteria, which are broader for the diagnosis of sarcoidosis. However, we found similar results in a sensitivity analysis with more stringent criteria, after excluding 7 patients who had possible sarcoidosis only on the basis of a positive ACE or BALF (data not shown). More generally, as the recently updated IWOS criteria have not yet been validated outside Asian populations, we did not use them herein.[9,26]

Conclusion

In conclusion, due to an increase in the probability of discordance with age, we recommend not to perform chest CT in patients under 30 years of age with a normal chest X ray and ACE level, while we suggest performing chest CT in first intention in the elderly. For other patients, we recommend to continue to perform a chest X-ray as the first intention examination, followed by a CT scan if it is not contributory.

Acknowledgment

We thank Philip Robinson for his editing word.

Authors' contributions

CB and PS collected the data. CB and PS contributed equally to the redaction of the manuscript. Data analysis was made by CB and NRS. PS takes responsibility for the integrity and accuracy of the data. CB, PS, MF and LK participated in the clinical management of the patients enrolled in the study. All authors revised the manuscript. All authors have read and approved the final manuscript.

Consent for publication

According to French law, written consent for this study was not required due to the retrospective nature of the study.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

The author(s) reported there is no funding associated with the work featured in this article.

Ethics approval and consent to participate

The present study received approval from the local ethics committee (CPP Sud Est IV) on February 2019 (number 19–31) and was registered on www.clinicaltrials.gov (NCT03877575).

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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