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Long-Term Systemic Outcomes of Sarcoidosis in Patients with Uveitis

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Abstract

Background

Prognostic factors for systemic outcomes and mortality of sarcoidosis in patients with uveitis have been poorly studied.

Methods

Multicenter retrospective cohort study of sarcoidosis patients with uveitis. Sarcoidosis diagnosis was established according to the recommendations of the American Thoracic Society. Sarcoid uveitis diagnosis was based on the Standardization of Uveitis Nomenclature classification criteria. Systemic relapse-free survival (RFS) and sequelae-free survival (SFS) were analysed using Kaplan-Meier curves and Cox proportional hazards models.

Results

336 patients were included, of whom 208 (61.9%) were female. Median age at sarcoidosis diagnosis was 52 years (range, 10–89 years). Median follow-up was 7.8 years. Systemic relapses occurred in 129 of 334 (38.6%) patients. Shorter systemic RFS was associated with Sub-Saharan African ethnicity (HR, 3.65, 95% CI, 2.26–5.90, $P < .001$) and anterior uveitis (HR, 1.95, 95% CI, 1.25–3.03, $P = .007$). Sequelae occurred in 46 of 334 (13.8%) patients. Shorter systemic SFS was associated with neurologic involvement (HR, 5.05, 95% CI, 2.46–10.34, $P < .001$) and anterior uveitis (HR, 3.10, 95% CI, 1.45–6.66, $P = .002$). All-cause mortality was 7.7% (24/312) with no sarcoidosis-related deaths.

Conclusions

Relapses occurred in approximately 40% of patients and were associated with Sub-Saharan African ethnicity and anterior uveitis. One in seven patients developed sequelae of sarcoidosis, which were associated with neurologic involvement and anterior uveitis. These characteristics may help identify patients who could benefit from closer follow-up and consideration of more intensive immunosuppressive therapy. Mortality was approximately 8%, with no sarcoidosis-related deaths.

Summary Box

What is already known on this topic:

- Female sex and panuveitis have been associated with systemic relapse in sarcoid uveitis, but prognostic factors for systemic sequelae and mortality remain poorly characterized

What this study adds:

- This multicentre cohort of 336 patients with sarcoid uveitis found that systemic relapse occurred in 39% of patients and was associated with Sub-Saharan African ethnicity and anterior uveitis.

- Systemic sequelae occurred in 14% and were associated with neurologic involvement and anterior uveitis.
- All-cause mortality was 8%, with no deaths directly attributable to sarcoidosis.
- These findings may help identify patients who could benefit from closer systemic surveillance and individualized treatment strategies.

Introduction

Most patients with sarcoidosis have a benign course,[1] but the disease can sometimes be protracted and chronic with numerous inflammatory relapses.[1,2] Identifying risk factors for systemic relapse could therefore improve individualized patient care.[3–5] Some have already been described in certain phenotypes of sarcoidosis, such as pulmonary or cardiac sarcoidosis.[4,5] Ocular sarcoidosis represents another significant subpopulation, affecting 20 to 50% of patients.[6] Female sex and panuveitis have been reported as risk factors for systemic recurrence in ocular sarcoidosis,[7] but additional data are lacking in this subpopulation.

Beyond relapses, sequelae and mortality are other major concerns, with up to 30% of patients experiencing unrelenting disease.[1] Death occurs in up to 8% of cases.[8,9] In sarcoid uveitis, data on systemic sequelae and mortality are limited, undermining our ability to counsel patients regarding systemic outcomes. However, because most patients with sarcoid uveitis have extraocular involvement, systemic outcomes are integral to long-term management.

Therefore, this study aims to identify risk factors for systemic relapse and sequelae, and characterize mortality of sarcoidosis in patients with uveitis.

Methods

Study Population

We conducted a retrospective multicentre cohort study of patients followed up for sarcoid uveitis between January 2003 and July 2024 at the Internal Medicine and Ophthalmology departments of two university hospitals in France. The minimum follow-up required for study enrolment was 6 months.

Sarcoid uveitis diagnosis was based on the Standardization of Uveitis Nomenclature classification criteria.[10] Diagnoses were established by internists and ophthalmologists specialized in uveitis. All patients fulfilled the recommendations for diagnosis of sarcoidosis published by the American Thoracic Society.[11]

This study adhered to the tenets set forth in the Declaration of Helsinki and was approved by the local Institutional Review Board. All patients provided written informed consent for publication of their anonymized medical data. Participant ancestry was classified from demographic information in medical

records. Because the study was conducted in France, ancestry categories were based on demographic classifications used in the participating centres.

This study is part of a companion work addressing risk factors for ocular relapse and visual prognosis in sarcoid uveitis.[12]

Clinical Data

Data collected included demographic characteristics (age, sex, ethnicity), smoking status, uveitis phenotype, systemic involvement, laboratory results (e.g., angiotensin-converting enzyme, soluble interleukin-2 receptor), imaging results (e.g., chest computed tomography [CT] scan), and treatments. Chest CT scans staging was adapted from the Scadding classification.[13]

Definitions

For baseline evaluation, manifestations present at diagnosis or developing within 3 months thereafter were considered part of the initial disease presentation. Ocular phenotype was classified according to the initial uveitis presentation regardless of the timing of onset. Systemic relapses were defined as disease flare or progression in previously involved organs at least 90 days after the previous flare, or as involvement of new organ systems. Flare and progression were defined respectively as recurring or worsening clinical, functional, or radiologic indicators, e.g., cough, pulmonary function tests, chest CT scan. Sequelae of sarcoidosis were defined as persistent symptoms or lesions attributable to sarcoidosis in the absence of patent active disease, e.g., dyspnoea, cutaneous papules.

Outcomes

The main outcome measure of systemic relapses was the time to systemic relapse, and Kaplan-Meier systemic relapse-free survival (RFS) curves were constructed accordingly. Secondary outcome measures were the number of relapses per relapsing patient, and the number of simultaneous ocular and systemic relapses. In keeping with the method used for systemic relapses, time to systemic sequelae was measured and Kaplan-Meier curves for systemic sequelae-free survival (SFS) were constructed. The inclusion date for Kaplan-Meier analyses was the time of systemic sarcoidosis onset. For sarcoidosis-related mortality, we evaluated the cause of death for possible relation to sarcoidosis.

Statistical Analysis

Statistical analyses were performed using R version 4.0.1 (R Foundation for Statistical Computing, Vienna, Austria). Data were described as frequencies and percentages for categorical variables, and as means and standard deviations or medians with interquartile range (IQR) for continuous variables.

Analyses were performed using complete-case data, with patients excluded from individual analyses when relevant variables were unavailable.

Factors associated with systemic relapses and sequelae were evaluated by performing univariable analyses for selected variables on systemic RFS and systemic SFS curves. Multivariable Cox proportional hazards models were constructed using variables with *P* values < .10 in univariable analysis. Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated for each variable in the univariable and multivariable analysis. Statistical significance was set at the *P* < .05 level.

The variables selected for univariable analysis of systemic RFS were age at diagnosis, sex, ethnic background, smoking status, initial uveitis anatomic subtype, CT stage at baseline, and multiorgan involvement at baseline; variables selected for systemic SFS were the same except for the addition of neurologic involvement at baseline. These variables were preselected for clinical relevance, reported associations with sarcoidosis prognosis, and availability at the initial evaluation.

Results

Baseline Characteristics

Among 336 patients, 208 (61.9%) were women. The median follow-up was 7.8 years. The main ethnic groups were Caucasian (62.2%), North African (21.7%), and Sub-Saharan African (9.8%). Anterior uveitis was the most frequent initial uveitis subtype, found in 116 (34.5%) patients. Uveitis onset occurred > 3 months after onset of systemic symptoms in 42 (12.5%) patients. Sarcoidosis was histologically proven in 279 (83.0%) patients. Complete baseline characteristics are shown in Table 1. Additional data are provided in Supplemental Table 1.

Table 1
Baseline Characteristics

Characteristic	**Patients**[a]
Demographic data	
Age at sarcoidosis diagnosis, median (range), years	52 (10–89)
Female sex, *n* (%)	208 (61.9)
Ethnic background, *n* (%)	
Caucasian	209 (62.2)
North African	73 (21.7)
Sub-Saharan African	33 (9.8)
Other[b]	21 (6.3)
Smoking status, *n* (%)	
Never-smokers	212 (63.1)
Former smokers	67 (19.9)
Active smokers	57 (17.0)
Uveitis anatomical subtype, *n* (%)	
Anterior	116 (34.5)
Anterior and intermediate	58 (17.3)
Intermediate	35 (10.4)
Posterior	23 (6.8)
Panuveitis	104 (31.0)
Chest CT staging, *n* (%)[c]	
Stage 0	63/323 (19.5)
Stage 1	127/323 (39.3)
Stage 2	108/323 (33.4)
Stage 3	21/323 (6.5)
Stage 4	4/323 (1.2)
Systemic involvement, *n* (%)	
General symptoms	71/333 (21.3)

Characteristic	Patients[a]
Lymph nodes[d]	267/333 (80.2)
Lungs	133/333 (39.9)
Skin	55/333 (16.5)
Joints	34/333 (10.2)
Nervous system[e]	34/333 (10.2)
Multiorgan involvement	190/333 (57.1)

[a] If the number of patients with data available differs from the total population (i.e., 336), data are expressed as number/total number (percentage) of patients with data available.

[b] Other ethnicities (number of patients): Asian (8), Afro-Caribbean (7), Middle Eastern (4), South American (2).

[c] Adapted from the Scadding classification.

[d] All lymph nodes, including intrathoracic.

[e] Central and peripheral nervous systems.

Systemic Relapses, Sequelae and Mortality

Among 334 patients with systemic involvement, 304 systemic relapses occurred in 129 (38.6%) patients, with a median of 2 (IQR, 1–3) relapses per relapsing patient. Relapses increasingly occurred in previously involved organ systems, as shown in Fig. 1. Among first systemic relapses, 37% (47/128) occurred in previously affected organs, compared with 86% (12/14) of fifth systemic relapses. Simultaneous ocular and systemic relapses occurred in 49 of 222 patients (22.1%). Additional relapse data are provided in Supplemental Table 2.

Sequelae were identified in 46 of 334 (13.8%) patients; they occurred mainly in the nervous system in 11 (23.9%), the lungs in 10 (21.7%), and the skin in 9 of 46 (19.6%) patients. Cardiac sequelae and sarcoidosis-associated pulmonary hypertension occurred in 5 (10.9%) and 3 of 46 (6.5%) patients, respectively. In the entire cohort, one implantable cardioverter defibrillator was implanted, and no organ transplants were performed.

An all-cause mortality rate of 7.7% (24/312) was observed, with none of the 21 evaluable immediate causes of death directly attributable to sarcoidosis. The median age at death was 77 years (IQR, 69–81 years). Three of 24 (12.5%) patients were excluded from cause-of-death analysis due to unavailable cause-of-death data (n = 2) or absence of systemic sarcoidosis (n = 1). Thirty percent (3/10) of patients with combined pulmonary and cardiac sarcoidosis died during follow-up, with no deaths directly

attributable to sarcoidosis. Supplemental Fig. 1 shows the 15-year censored Kaplan-Meier curve for overall survival.

The main immediate causes of death were cardiovascular (37.5%), oncological (25.0%), and infectious (16.7%). Deaths from infectious causes occurred exclusively in patients receiving oral corticosteroids (4/4, 100.0%), with one (25.0%) patient also treated with methotrexate. Additional sequelae and mortality data are provided in Supplemental Tables 3 and 4.

Factors Associated with Systemic Relapse-Free Survival

Figure 2A shows the 10-year censored Kaplan-Meier curve for systemic RFS. At 1, 3, and 5 years, 39 of 315 (12.4%), 73 of 289 (25.3%), and 99 of 251 (39.4%) patients had experienced a first systemic relapse, respectively. Among relapsing patients, 56 (43.4%) and 30 of 129 (23.3%) relapsed for the first time after 3 and 5 years, respectively.

In univariable analysis, shorter systemic RFS was associated with Sub-Saharan African ethnicity (HR, 4.00, 95% CI, 2.48–6.43, $P < .001$) and anterior uveitis at initial presentation (HR, 2.01, 95% CI, 1.31–3.07, $P = .002$). Multivariable analysis confirmed shorter systemic RFS with Sub-Saharan African ethnicity (HR, 3.65, 95% CI, 2.26–5.90, $P < .001$) and anterior uveitis at initial presentation (HR, 1.95, 95% CI, 1.25–3.03, $P = .007$) (Fig. 2B, C).

Factors Associated with Systemic Sequelae-Free Survival

Figure 3A shows the 15-year censored Kaplan-Meier curve for systemic SFS. At 1, 3, and 5 years, 12 of 315 (3.8%), 18 of 289 (6.2%), and 24 of 251 (9.6%) patients had developed a first sequela, respectively. Among affected patients, 28 (60.9%) and 22 of 46 (47.8%) developed sequelae for the first time after 3 and 5 years, respectively. By 15 years, 42 of 46 (91.3%) patients had developed sequelae.

In univariable analysis, shorter systemic SFS was associated with baseline neurologic involvement (HR, 4.10, 95% CI, 2.05–8.21, $P < .001$) and anterior uveitis at initial presentation (HR, 2.28, 95% CI, 1.10–4.71, $P = .035$). Former smoking (HR, 2.20, 95% CI, 1.11–4.36, $P = .081$) was also included in the multivariable model.

Multivariable analysis confirmed all three variables were independently significant: baseline neurologic involvement (HR, 5.05, 95% CI, 2.46–10.34, $P < .001$), anterior uveitis at initial presentation (HR, 3.10, 95% CI, 1.45–6.66, $P = .002$) (Fig. 3B – C), and former smoking (HR, 2.62, 95% CI, 1.30–5.28, $P = .032$). Full results are shown in Table 2.

Table 2
Factors Associated with Systemic Relapse-Free and Systemic Sequelae-Free Survival

A. Systemic Relapse-Free Survival				
Variable[a]	**Univariable HR (95% CI)**	***P* value**	**Multivariable HR (95% CI)**[b]	***P* value**
Age ≥ 65 years	0.82 (0.53–1.28)	.384	–	–
Male sex	0.95 (0.65–1.38)	.791	–	–
Ethnic background		< .001		< .001
North African	1.44 (0.93–2.23)		1.14 (0.72–1.81)	
Sub-Saharan African	4.00 (2.48–6.43)		3.65 (2.26–5.90)	
Other[c]	0.82 (0.33–2.03)		0.68 (0.27–1.70)	
Smoking status		.531	–	–
Former	0.83 (0.50–1.37)			
Active	1.17 (0.73–1.87)			
Uveitis subtype		.002		.007
Anterior	2.01 (1.31–3.07)		1.95 (1.25–3.03)	
Anterior and intermediate/intermediate	1.11 (0.68–1.82)		1.16 (0.71–1.92)	
CT stage		.638	–	–
1	0.77 (0.46–1.30)			
2	1.01 (0.60–1.69)			
≥3	0.89 (0.41–1.93)			
Multiorgan involvement	1.36 (0.94–1.98)	.099	1.42 (0.97–2.06)	.067
B. Systemic Sequelae-Free Survival				
Age ≥ 65 years	0.58 (0.24–1.38)	.189	–	–
Male sex	1.05 (0.56–1.98)	.882	–	–
Ethnic background		.103	–	–
North African	0.93 (0.41–2.09)			
Sub-Saharan African	2.77 (1.27–6.03)			
Other[c]	1.37 (0.41–4.57)			

A. Systemic Relapse-Free Survival				
Variable[a]	**Univariable HR (95% CI)**	***P* value**	**Multivariable HR (95% CI)**[b]	***P* value**
Smoking status		.081		.032
Former	2.20 (1.11–4.36)		2.62 (1.30–5.28)	
Active	0.96 (0.39–2.36)		1.01 (0.40–2.51)	
Uveitis subtype		.035		.002
Anterior	2.28 (1.10–4.71)		3.10 (1.45–6.66)	
Anterior and intermediate/intermediate	1.03 (0.43–2.49)		0.98 (0.39–2.42)	
CT stage		.737	–	–
1	0.78 (0.33–1.85)			
2	0.69 (0.28–1.68)			
≥3	1.16 (0.38–3.56)			
Multiorgan involvement	1.40 (0.73–2.67)	.302	–	–
Neurologic involvement	4.10 (2.05–8.21)	< .001	5.05 (2.46–10.34)	< .001

Abbreviations: CI, confidence interval; CT, computed tomography.

[a] Reference categories: <65 years, female sex, Caucasian ethnicity, never smoker, posterior/panuveitis, CT stage 0, no multiorgan or neurologic involvement.

[b] Multivariable models include variables with $P < .10$ in univariable analysis.

[c] Other ethnicities (number of patients): Asian (8), Afro-Caribbean (7), Middle Eastern (4), South American (2).

Sensitivity Analysis Excluding Delayed-Onset Uveitis

In a sensitivity analysis excluding the 42 patients with delayed-onset uveitis, the main findings remained unchanged. Sub-Saharan African ethnicity (HR, 4.15, 95% CI, 2.51–6.85, $P < .001$) and anterior uveitis at initial presentation (HR, 1.85, 95% CI, 1.15–2.96, $P = .022$) remained associated with systemic RFS, while neurologic involvement (HR, 5.29, 95% CI, 2.52–11.09, $P < .001$) and anterior uveitis at initial presentation (HR, 2.89, 95% CI, 1.28–6.51, $P = .022$) remained associated with systemic SFS. However, former smoking lost significance as a predictor of systemic SFS. Complete results of the sensitivity analysis are shown in Supplemental Table 5.

Discussion

This study describes the systemic outcomes of sarcoidosis in 336 patients with uveitis followed up over a median of 7.8 years. Among patients with systemic involvement, the relapse rate was approximately 40%. Relapses impair quality of life, increase healthcare costs, and may lead to hospitalization or death.[14] Identifying high-risk patients early may support closer monitoring and consideration of treatment intensification.

Relapses were associated with Sub-Saharan African ethnicity and anterior uveitis. African Americans have long been known to have a worse prognosis of sarcoidosis, whether for severity of organ involvement,[2] frequency of relapses,[15] or mortality.[16] The multiple biological, environmental, and social determinants leading to an overall worse prognosis for Black patients could contribute to the increased risk of relapse observed in our cohort. In addition, anterior uveitis segregates with some African ethnicities,[6] which could explain this association. It may also reflect that anterior uveitis is associated with an inflammatory systemic phenotype which is prone to relapse, a concept supported by studies on phenotypic clusters of sarcoid uveitis.[17]

Most relapses occurred during the first 3 years, implying that close monitoring is especially important during this time. In a study on pulmonary sarcoidosis where 31% of patients relapsed, half of the relapses occurred during prednisone tapering below 10–15 mg/day, and the other half occurred a median of 8 months after discontinuing corticosteroid therapy.[4] Other studies have found a similar trend for an early relapsing phase.[3]

Interestingly, relapses increasingly shifted toward previously involved organs, with fewer than 25% of relapses affecting new organs by the third event. This suggests that once established, sarcoidosis phenotypes may become relatively fixed over time, with decreasing progression to new organs. Alternatively, the treatments used for sarcoidosis could delay or prevent progression to new organs. In addition, systemic relapses often occurred independently of ocular flares and could also occur when the ocular inflammation was fully under control. This finding emphasizes the importance of multidisciplinary collaboration to optimize patient outcomes. In a study from Belgium, systemic relapses were found in 6 of 45 (13.3%) patients with ocular sarcoidosis.[7] Female sex (odds ratio, 6.66, 95% CI, 1.50–40.40, P = .021) and panuveitis (odds ratio, 7.23, 95% CI, 1.70–40.99, P = .013) were associated with relapses. Interestingly, they reported a 31% (5/16) rate of simultaneous relapses, consistent with our findings, suggesting that disease activity at different systemic sites may occur independently.

Sequelae were observed in every seventh patient, similar to the 10 to 20% reported in the literature.[8] In contrast to relapses, sequelae frequently developed later during follow-up, emphasizing the need for prolonged monitoring, even in case of apparent disease control. Neurologic involvement and anterior uveitis were predictive of sequelae. Interestingly, neurological sequelae predominated in our cohort, although chronic damage in sarcoidosis primarily affects the lungs.[1] Neurologic involvement has been shown to cluster with ocular sarcoidosis in other cohorts,[18–20] and it often fails to improve or even deteriorates in up to a third of patients despite multiple lines of treatment, emphasizing its poor

prognosis.[21] In a report on the systemic prognosis of sarcoid uveitis, the lung was the most commonly affected organ at uveitis onset, but over 10 years, new organ involvement occurred predominantly in the central nervous system (11% of patients), with limited new pulmonary involvement.[22] These findings highlight the close relationship between ocular sarcoidosis and neurosarcoidosis, and the worse systemic outcomes in this subgroup of patients.

To our knowledge, anterior uveitis has not been shown to segregate with neurologic or pulmonary involvement, but Niederer et al. found an association between anterior uveitis and cutaneous sarcoidosis.[23] This might explain why anterior uveitis was associated with sequelae, which were often cutaneous. Alternatively, anterior uveitis may identify a subgroup with a more inflammatory systemic phenotype.

Former smoking was significantly associated with sequelae in the survival analysis on the entire cohort (Supplemental Fig. 2), but it lost significance in the sensitivity analysis excluding patients with delayed-onset uveitis. This finding should therefore be considered exploratory. While smoking has historically been reported to reduce sarcoidosis incidence,[24] former smokers experience worse pulmonary and neurological outcomes,[3,25] likely through accumulation of damage in target organs of sarcoidosis, possibly explaining our results. In addition, although Sub-Saharan African ethnicity was not a significant predictor of sequelae, this could indicate a lack of statistical power as there was a clear trend for increased chronic damage in this subgroup as shown in Supplemental Fig. 3. Therefore, particular attention should be given to Black patients with anterior uveitis and neurologic involvement, as this subpopulation could be at higher risk of long-term organ damage. This is especially important because of the substantial long-term functional impairment and quality of life loss associated with these complications.

We found an all-cause mortality rate of around 8% in our cohort, with no deaths directly attributable to sarcoidosis. In a New Zealand study reporting on all-cause mortality rates in 2723 subjects with uveitis and scleritis, 129 patients with sarcoid uveitis had a mortality rate of 7%.[26] Notably, no deaths resulted from pulmonary or cardiac sarcoidosis, the leading causes of sarcoidosis-related deaths.[27] In a study on veterans with sarcoidosis, Birnbaum et al. found that ocular inflammation was associated with a lower 1-year all-cause mortality (HR, 0.35, 95% CI, 0.19–0.67, P = .013).[28] This suggests that sarcoidosis with ocular involvement may be less lethal than other phenotypes, possibly because of a lower prevalence of lung involvement in sarcoidosis patients with uveitis compared to those without uveitis.[29] Moreover, only approximately 1% of patients developed sarcoidosis-associated pulmonary hypertension in our cohort, which is low compared to predominantly pulmonary sarcoidosis cohorts reporting up to 6%.[30] In addition, 30% of patients with combined pulmonary and cardiac sarcoidosis died during follow-up, which is significantly higher than the cohort average. Nevertheless, even in this target population, immediate causes of death were not due to sarcoidosis.

The main limitation of this study is its retrospective design. In 4 patients, gaps in medical records limited reliable assessment of relapse early during the follow-up. For these patients, relapse evaluation was restricted to periods of regular follow-up to ensure accuracy. Importantly, the baseline time origin for survival analyses was not modified. In addition, selection bias related to the tertiary referral centre setting may have led patients with less severe forms of sarcoidosis to not be referred, or to not have been seen at all (e.g., asymptomatic hilar lymph nodes, self-limiting bout of acute anterior uveitis), potentially leading to overestimation of relapse rates and artificially worse outcomes. Furthermore, the applicability of our findings to Asian or American populations may be limited, as the cohort consisted predominantly of individuals of Caucasian and African ancestry. Moreover, we evaluated systemic sarcoidosis as a whole rather than organ-specific phenotypes. Refining risk factor analyses to specific phenotypic subgroups could be of interest. Treatment effects on relapses were not evaluated because of the heterogeneity of systemic sarcoidosis phenotypes. Future analyses focusing on more homogeneous phenotypic subgroups could better clarify the impact of treatments on relapse risk. Finally, we relied on in-house definitions of relapses and sequelae as there are no consensual definitions for these in the literature. This limits the reproducibility of our findings in case other definitions are used.

Strengths include the large sample size and long follow-up period. In addition, to our knowledge, this is one of the first large studies specifically evaluating risk factors for systemic outcomes of sarcoidosis in patients with uveitis, analysing relapses, sequelae, and mortality simultaneously. Our findings support a framework wherein selected patients can be offered closer follow-up and more intensive immunosuppression to optimize systemic outcomes.

Future studies should focus on confirming these factors in independent multiethnic cohorts, ideally using prospective designs. In addition, clear and standardized definitions of relapse and sequelae across all organ systems affected by sarcoidosis are needed to improve comparability between studies and enhance data reproducibility between centres. Further work should also explore organ-specific phenotypes, the role of biomarkers (e.g., angiotensin-converting enzyme, soluble interleukin-2 receptor) and imaging (e.g., ^{18}F-fluorodeoxyglucose positron emission tomography/CT),[31] and the impact of treatment strategies on long-term systemic outcomes.

Conclusions

Systemic relapses occur in approximately 40% of sarcoidosis patients with uveitis and are associated with Sub-Saharan African ethnicity and anterior uveitis. Systemic sequelae of sarcoidosis occur in every seventh patient and are associated with neurologic involvement and anterior uveitis. These characteristics may help identify patients who could benefit from closer follow-up and consideration of more intensive immunosuppressive therapy. Mortality was approximately 8%, with no sarcoidosis-related deaths.

Abbreviations

CIs
confidence intervals
CT
computed tomography
HRs
hazard ratios
IQR
interquartile range
RFS
relapse-free survival
SFS
sequelae-free survival

Declarations

Ethics approval: This study adhered to the tenets set forth in the Declaration of Helsinki, and was approved by the Institutional Review Board of the Hospices Civils de Lyon in February 2019 (N° 19-31).

Consent for publication: All patients signed a written informed consent agreement upon entering the Lyon Sarcoid Uveitis Cohort dataset (**NCT03863782**), allowing for publication of their anonymized medical data.

Availability of data and materials: Deidentified participant data underlying the findings of this study are available from the corresponding author upon reasonable request.

Conflict of interest: No conflicting relationships exist for any author

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Figures

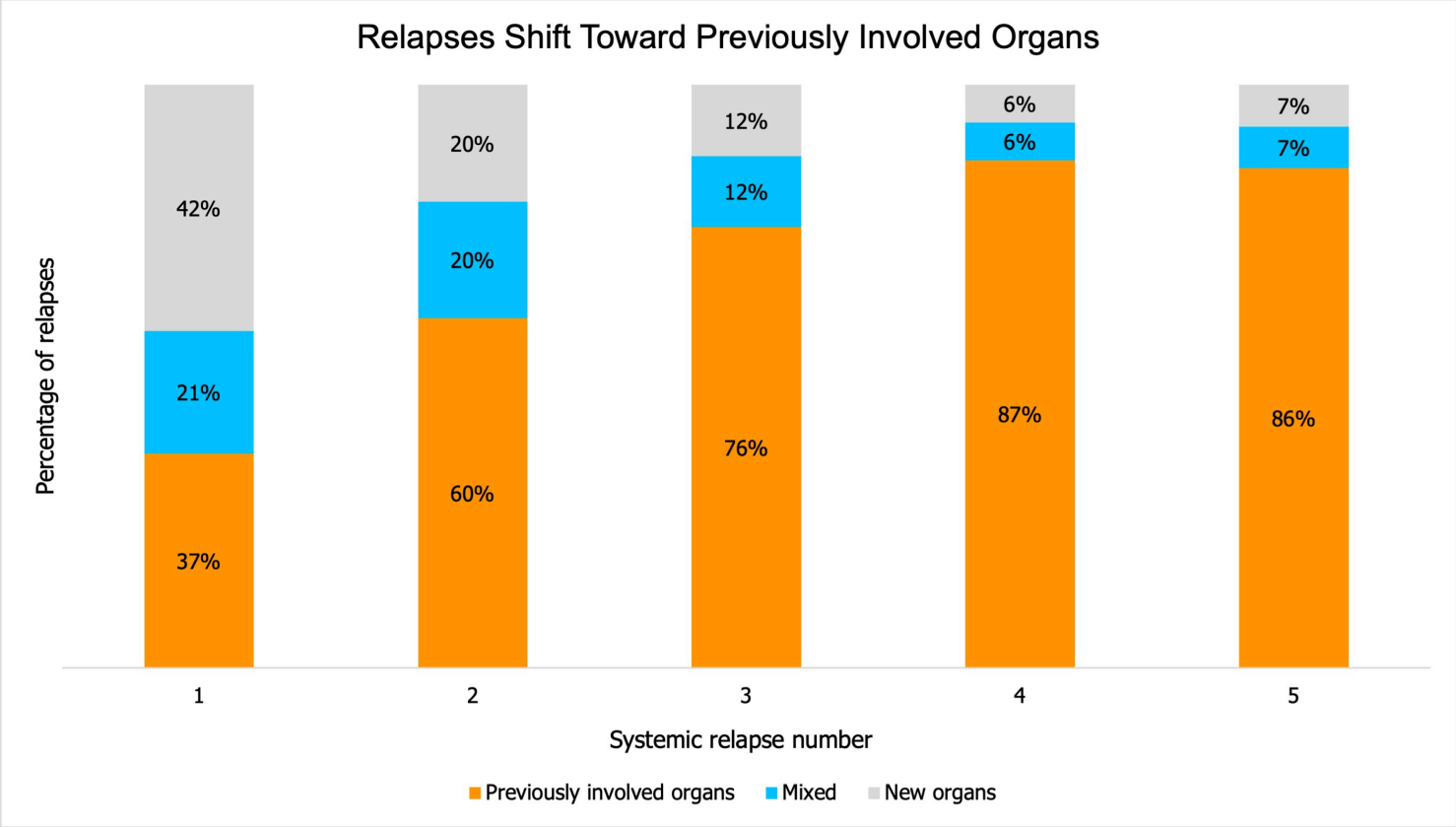

Figure 1

Relapses increasingly shift toward previously involved organ systems

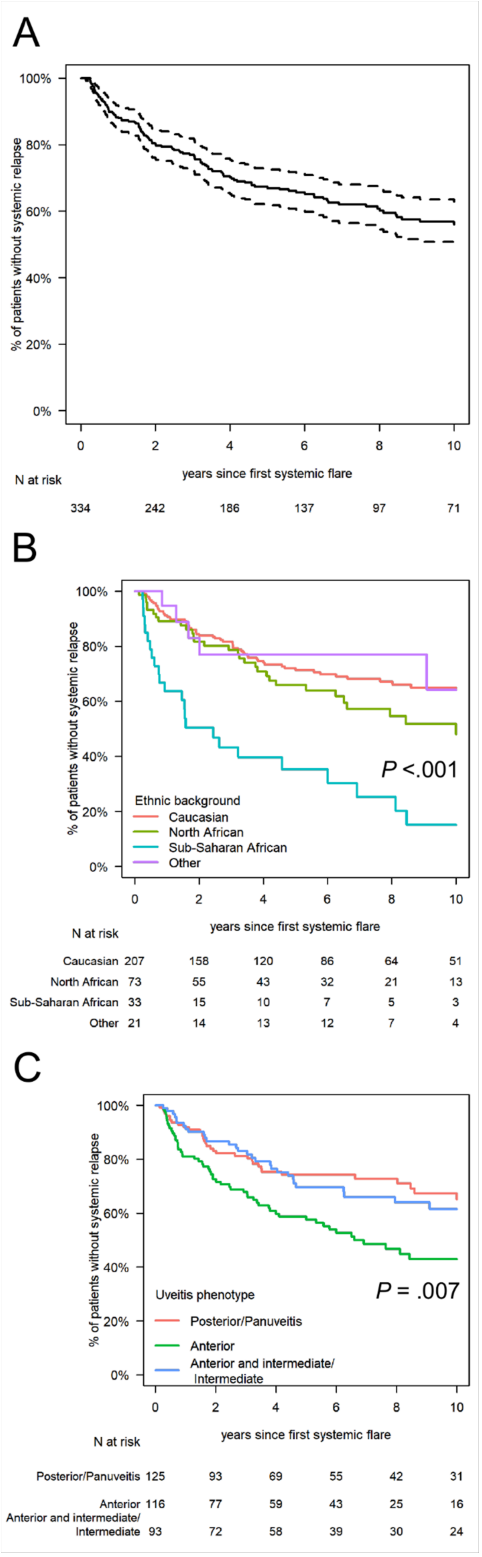

Figure 2

A, The 10-year censored Kaplan-Meier systemic relapse-free survival (RFS) curve. B, Systemic RFS is poorer in patients of Sub-Saharan African ethnicity. C, Systemic RFS is poorer in patients with anterior uveitis at initial presentation.

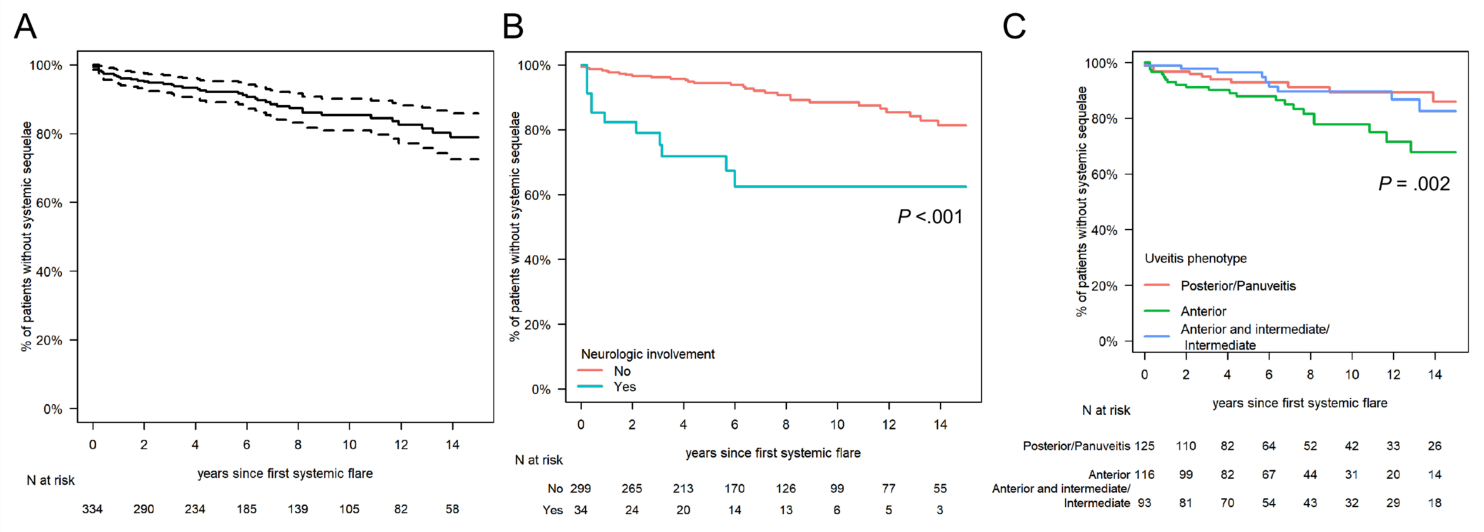

Figure 3

A, The 15-year censored Kaplan-Meier systemic sequelae-free survival (SFS) curve. B, Systemic SFS is poorer in patients with neurologic involvement at baseline. C, Systemic SFS is poorer in patients with anterior uveitis at initial presentation.

Supplementary Files

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