## Peer Review File

**Article Information:** https://dx.doi.org/10.21037/jtd-21-1760

**Reviewer A**

We thank the reviewer for the effort he made and the time he spent to review this manuscript and for his comments. Our point-to-point answers are as follow:

**1. There is nothing new for the readers of journal in this study.**

To our knowledge, our study is the first that correlates specific characteristics, usually assessed at initial patient evaluation in a Sarcoidosis Clinic, to newly defined clinical phenotypes. The above classification was very recently published by sarcoidosis experts.

**2. The authors screened 350 patients and enrolled 147 cases for this study on basis of consecutive visits for at least twice a year during a 5-year period. Are there any other inclusion or exclusion criteria for study or not, if so need to mention it?**

Patients were excluded if they missed an appointment or refused to provide informed consent. We modified our text as advised (page 3, line 48)

**3. It is mentioned that all the patients were biopsy proven and figure 1 shown that 65 cases also have extrapulmonary sites. However, it is not clear that how many patients are of single site disease and how many with multiple organ involvement. Are all the patients had pulmonary involvement?**

All our patients admitted to the clinic had pulmonary involvement. 82 had only pulmonary involvement and 65 had also other organ involvement.

**4. More than 20% cases were smoker. This may be affecting the PFT and CT findings. Is this a confounding factor.**

None of our patients suffered from clinical, spirometry and imaging features of COPD or emphysema in CT at initial assessment. Furthermore, according to previous evidence, smoking was not clearly related to sarcoidosis. [Ramos-Casals, M., Kostov, B., Brito-Zerón, P., Sisó-Almirall, A., & Baughman, R. P. (2019). How the Frequency and Phenotype of Sarcoidosis is Driven by Environmental Determinants. Lung. doi:10.1007/s00408-019-00243-2]. Moreover, smoking was not reported as a confounding factor in recent sarcoidosis phenotype related literature.

5. **Figure 1 shown that renal involvement in 0,7 and no numbers against spleen. Correct it.**

Thank you. We apologize for this oversight error. There was no spleen involvement. We modified figure 1 as advised.

**6. Table 2 shown that the enlargement of Lymph nodes are seen in 88-95% cases. However the details of site and numbers are missing even in text. It is better to mention it.**

That was omitted in the context of text shortening. But you are right. We modified our text as advised (page 5, line 102)

**7. The table 2 showing that 58(39.5%) are asymptomatic, while same table shown that 19 cases with fever, 13 cough, 9 Erythema nodosum and 58 dyspnoea amongst the asymptomatic group and the table 1 also showing that dyspnoea in 97 cases. How it is possible and needed the explanation.**

The term ‘asymptomatic’, used in table 2, refers to the phenotype as it was stated by the DELPHI consensus, where we based our study.

**8. The period of treatment in months was negatively correlated to DLCO%. Is it correlated with others parameters**.

There was not any significant correlation between other PFTs than DLCO% and each one of the other parameters analyzed. The above correlation is apparently due to disease severity and longer treatment duration.

**9. None of the patients were treated with any second line drug with 49 cases of advanced disease. Needed a justification.**

There was not any need for second line treatment, as all patients treated responded well and had disease control only with oral steroids.

**10. The extrapulmonary site mentioned in figure 1 and table 2 is not matching. The table 2 also showed involvement of extrapulmonary sites in asymptomatic group. Needed a explanation**.

We modified the table as advised. The term 'asymptomatic', used in table 2, refers to the phenotype as it was stated by the DELPHI consensus, where we based our study.

**11. The data of extrapulmonary site is not matching in figure 1, table 2 and table3.**

In figure 1 we mentioned extrapulmonary manifestations found in our cohort. Tables 2 and 3 mention extrapulmonary manifestations according to the DELPHI consensus.

**12. The author just summarized the findings of study without any conclusive advantage of the study. As most of the findings are already known.**

We agree with the reviewer that some of our findings are already reported in other cohorts. However, we strongly believe that our work adds new information to the field, as it is the first study that correlates clinical, PFTs and imaging findings with recently published phenotypes.

**13. What is the strength of study for readers?**

The strength of the study is that our results come from an extended follow up period and by using the latest recommendations, also by the fact that our results could be easily assessed in everyday clinical practice.

**14. There is no any clear conclusion of study.**

We feel that we have provided robust and clear conclusions in a concise manner.

**Reviewer C**

We thank the reviewer for the effort he made and the time he spent to review this manuscript and for his comments. Our point-to-point answers are as follow:

The paper titled "Clinical, Imaging and Functional Determinants of Sarcoidosis Phenotypes in a Greek population" examined clinical phenotypes features of sarcoidosis in Greek population using WASOG Clinical Outcome Status instrument and the latest DELPHI consensus recommendations. It would significantly improve the manuscript if the below point can be considered.

1**. Page 5 Line 116 "None of our patients received second line therapy or corticosteroid sparing treatment throughout the observation period." Do the authors think whether the recurrence of sarcoidosis is related to treatment time or total dose of corticosteroid.**

It could be due to the duration of treatment, but one should also consider that oral steroids might not affect the natural course of the disease. After all the reasons for disease relapse was not an endpoint in the present study and was not further looked at.

2**. Page 4 Line 55 "Bronchial lavage analysis was also available for all the patients", How about the relationship between BALF cell classification and clinical phenotypes?**

As we are a center for BALF analysis, we used BALF analysis initially in the context of investigating data compatible with sarcoidosis. BALF analysis, as known, is not a diagnostic tool alone but it can only be assessed in combination with clinical and imaging findings. Furthermore, BALF analysis is not included in the studied phenotype classifications, and therefore correlations are not included in the aims of our study.

**Reviewer D**

We thank the reviewer for the effort and the time he spent to review this manuscript and for his comments. Our point-to-point answers are as follow:

**1. "Out of 350 individuals regularly followed up in our Clinic": clinical symptoms of sarcoidosis are not clearly described.**

We believe that clinical symptoms are sufficiently presented in Table 1.

2**. "The diagnosis of sarcoidosis had been set according to the 53 proposed criteria" – what are the criteria?**

We modified our text as advised (page 3, line 51)

3. **As one knows, the histological verification of sarcoidosis is not the gold standard of sarcoidosis.**

We had already considered that granuloma alone is not the gold standard of sarcoidosis diagnosis. We modified our text in order to clarify that histological verification is not the gold standard of sarcoidosis diagnosis, without the appropriate clinical setting. (Page 3, line 51)

**4. Inclusion and exclusion criteria are not clear.**

Patients were excluded if they missed an appointment or refused to provide informed consent. We modified our text as advised (page 3, line 48)

**5. The article does not describe specific features of sarcoidosis in the population in Greece.**

To our knowledge, there is not increased incidence of specific sarcoidosis features (eg. Löfgren syndrome, ocular involvement, cardiac involvement) in Greek patients. The published studies are scarce.

**6. References should be more recent.**

The less recent references include more classical knowledge of sarcoidosis. The main references of our study were published in the last 5 years and include the latest sarcoidosis recommendations and guidelines. Moreover, we now added a new recent reference (number 19) from 2021.

**Re-review comments:**

**1.** Response to Reviewer Comment 7. This editor understands what the author means by the term 'asymptomatic', but it really reads weird for readers at a first glance. It is advised to use ' asymptomatic sarcoidosis', 'acute sarcoidosis' and so on... when mentioning the phenotypes at the top of Table 2.

In response to your comment, we changed the titles of the parameters in table 2.

**2.** You need to keep uniform post-zero digits for a specific variable, unlike r=0.2 and r=0.523, 37% and 14.3%...but r=0.200, 37.0%…

We modified our text as advised. (Lines : 33, 71, 142, 143, 162, 169, 171, 184, 185, 188, 189, 191, 223)

**3.** Comments by reviewers should be carefully addressed and properly reflected in the paper somehow. Pertaining to Reviewer Comments 8 and 9, this editor would revise the article as follows (please kindly respond): Main-text Treatment All of our patients, even with 49 cases of advanced disease, received no second line therapy or corticosteroid sparing treatment throughout the observation period. The period of treatment in months was negatively correlated to DLCO% at the time of diagnosis (r=-0.2, p=0.015) (Figure 2b). Such a correlation was apparently due to disease severity and longer treatment duration. There was not any significant correlation between other PFT findings than DLCO% and each one of the other parameters analyzed.

Thank you for your practical modification. We included the paragraph as advised. (Line 153)

**4.** Given that this study was a scare one on new phenotype-based sarcoidosis in Greek population but not in populations of other European regions, and that the supportive data and evidence could be fairly limited, this editor recommends the author mention more about Greek population, esp when

making a conclusion or describing the patient characteristics, where appropriate. This helps add to the current literature.

Thank you for this comment. We mentioned more about Greek population in the abstract and the text as advised. (Lines 41, 43, 198, 262)