

Reviewer A**Comments to the authors:**

The authors are to be congratulated for tackling this long-debated and contentious aspect of dermatomyositis -- the need for screening for internal malignancy. There are several points concerning this manuscript that I would ask the authors to consider.

There is a growing consensus that the designation “dermatomyositis” should be used as an umbrella designation for the four clinically-distinct major subtypes of dermatomyositis: 1) adult-onset classic dermatomyositis, 2) adult-onset clinically-amyopathic dermatomyositis, 3) juvenile-onset classic dermatomyositis and 4) juvenile-onset clinically-amyopathic dermatomyositis. Throughout the manuscript the authors use only the umbrella designation “dermatomyositis” when discussing the need for internal malignancy surveillance. I did not see a reference to either juvenile- or childhood-onset dermatomyositis in the manuscript. This is not surprising as it is widely believed that juvenile-onset classic dermatomyositis and juvenile-onset clinically amyopathic dermatomyositis do not carry an increased risk for internal malignancy.

We thank **Reviewer A** for this insightful comment. We agree it is important to be specific that evidence suggests adult subtypes of dermatomyositis, and not juvenile-onset subtypes, may be related to underlying malignancy. We have added a sentence in the first paragraph of the “results” section to clarify that risk of underlying malignancy is specific to adult subtypes of dermatomyositis.

In addition, I saw only a single reference in the manuscript to clinically-amyopathic dermatomyositis on line 114 where it is stated that *“Importantly, current evidence supports that the risk of malignancy in the clinically amyopathic DM population is similar to that of the classic DM population (3-6).”* Recent data from an academic dermatology practice-ascertained dermatomyositis population suggest that risk of internal malignancy in adult-onset clinically amyopathic DM was 1.7%, a figure that was much lower than earlier studies have reported (*Bowerman K, Pearson DR, Okawa J, Werth VP. Malignancy in dermatomyositis: A retrospective study of 201 patients seen at the University of Pennsylvania. J Am Acad Dermatol. 2020;83(1):117-122. doi:10.1016/j.jaad.2020.02.061*). I would ask the authors of the manuscript to address these more recent observations.

Thank you for this suggestion. We have added a sentence detailing that the above study noted an incidence of malignancy in their clinically amyopathic dermatomyositis patients that is noticeably lower than most other reported cohorts.

I would also suggest that the authors make it clear as a caveat at the outset of the manuscript that their review of the literature is focused primarily on the risk of internal malignancy in adult-onset classic dermatomyositis patients.

We agree with Reviewer A that it is important to state that our review of the literature is primarily focused on adult-onset DM. We have clarified this in the first sentence of the second paragraph in the results section.

As our data in the review does include multiple cohorts with clinically amyopathic dermatomyositis (or presumably so based on inclusion criteria; references 3, 4, 7, 8, 13, 14, etc.) we believe it would be more accurate to avoid mentioning the review is primarily focused specifically on adult-onset classic DM. However, if the reviewers and editors strongly feel this should be specified as such, the authors are amenable to this change.

I applaud the authors' concluding recommendation that "high-value" recommendations for internal malignancy screening in dermatomyositis patients be developed preferably by a consortial effort of all involved stakeholders.

We thank Reviewer A for this compliment. We do believe that involving all pertinent stakeholders in the development of malignancy screening recommendations would result in guidelines with the highest value for clinicians.

Reviewer B

Comments to the authors:

This is an incredibly thoughtful and important piece of work that clearly makes the point that malignancy screening is not only associated with benefits but instead needs to be a process that first requires physician education and then careful discussion with involved parties before the malignancy screen is embarked upon. The article is incredibly complete and detailed, and very well-written.

We thank Reviewer B for this generous compliment.

--It might be helpful to clearly organize out the potential pitfalls of malignancy screening:

- 1) finding cancers that ultimately do not impact patient morbidity/mortality;**

- 2) false “positives” that require further followup;
- 3) cost and patient morbidity associated with screening

I mention this because, it is confusing why the authors ultimately suggest (line 337) restricting screening to “high cancer risk” patients when the same main issue of #1 still exists (although of course it minimizes #2 and #3). Perhaps the authors could reconcile this issue, since it was clearly pointed out in the text of the paper? How is “cancer overdiagnosis” to be mitigated?

We thank Reviewer B for these very thoughtful and very important suggestions and agree it is important to address them in this manuscript. These underscore the challenges and complexity of the research required to truly develop “high-value” malignancy screening guidelines.

To address these suggestions we have added a section to our discussion titled “*What future work needs to be done to define ‘high-value’ malignancy screening guidelines for DM patients?*” and detailed the importance of evaluating for the above-mentioned screening pitfalls, as well as the challenges that likely will exist to accurately evaluate for them. Furthermore, we propose a strategy (in the form of a prospective, international registry) to collect data that may allow for such evaluations.

--I think one important concept that needs to be stressed here is the fact that it will not be a one size fits all algorithm, as alluded to. Combinations of many factors are likely very important (e.g. race and antibody) and will provide further precision regarding cancer risk, and, likely even cancer morbidity/mortality risk. (may be worth mentioning, for example, the very important Japanese paper by Ogawa-Momohara that anti-TIF1g patients--at least in Japan--present with cancers at higher stage than non-TIF). This may help inform the first issue I mentioned as well, and suggests, as the authors so clearly state, that more research is required and there might be hope that we can risk stratify patients, not only with regards to overall risk of diagnosis, but additionally risk of mortality/morbidity from their cancer.

--as per above, the idea of “top 12 cancers” may not make sense but perhaps instead, given the patient characteristics (race, geography, antibody, other?) then perhaps the clinician could have a list of the most likely cancers that would be

present, and screen appropriately. When you group everybody together, you lose very important information. For example, table 1 does not mention gastric cancer, which is probably the #2 or #3 cancer in Japanese patients with DM.

We again thank Reviewer B for these excellent comments and citation recommendations and have addressed these in our new discussion section, titled “*What future work needs to be done to define ‘high-value’ malignancy screening guidelines for DM patients?*”