

Response to Reviewer 1

Summary

Magnetic resonance imaging findings corresponding to vasculitis as defined by [18F] FDG positron emission tomography or ultrasound. This manuscript discusses an important and hot topic for the rheumatologists. However, some points need to be addressed.

Response: Thank you very much for taking the time to review our manuscript. Please find the detailed responses below and the corresponding revisions in track changes in the resubmitted file.

Questions for General Evaluation	Reviewer's Evaluation	Response and Revisions
Does the introduction provide sufficient background and include all relevant references?	Can be improved	We added information on the studies comparing MRI with different imaging modalities (see Comment Nr. 3).
Are all the cited references relevant to the research?	Can be improved	We have checked all references and added information on the studies comparing MRI with different imaging modalities (Refs. 12, 13, 15) in the introduction section to clarify the relevance of the cited references.
Is the research design appropriate?	Can be improved	We edited the methods section to clarify that the study design was cross-sectional (see Comment Nr. 4) and mentioned in the limitations that our study is exploratory.
Are the methods adequately described?	Can be improved	We edited the methods section and added information about the interpretation of the ultrasound images, the study design, and statistical analysis.
Are the results clearly presented?	Can be improved	We have edited the text so that the results are presented chronologically according to the methods.

Are the conclusions supported by the results?	Can be improved	We added a recommendation at the end of the conclusion as suggested in Comment Nr. 9.
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Point-by-point response to comments and suggestions for authors

Comment 1: p.1, l.18; “tomography (PET/CT) or ultrasound”, The authors mean and not or

Response 1: Thank you for pointing this out. P.1, l.18; we changed “or” to “and”.

Comment 2: p.1, l.25; “MRI showed mural thickening in”, The results should be arranged chronologically according to the methods.

Response 2: Thank you for pointing this out. To keep the order consistent, we have changed section 2.2, page 2 from:

“Pathological MRI findings (i.e., mural thickening, late mural enhancement and mural oedema) were assessed by a board-certified radiologist (G.S., 8 years of experience) subspecialized in cardiovascular imaging, blinded for the clinical data, PET/CT scan and ultrasound results. Mural thickening was scored as: 0 (no mural thickening), 1 (mild mural thickening, 2-3 mm for aorta, 1-2 mm for the subclavian/axillary artery), or 2 (strong thickening, >3 mm for aorta, >2 mm for the subclavian/axillary artery). Mural contrast enhancement was subjectively scored as 0 (no mural enhancement), 1 (mild mural enhancement), 2 (strong mural enhancement and/or perivascular enhancement) using static and dynamic T1w sequences pre and post contrast. Mural oedema was subjectively scored as 0 (no mural oedema), 1 (mild mural oedema), 2 (strong mural oedema) using T2w BLADE and Diffusion-weighted sequences (Supplementary Table S2).”

To

“Pathological MRI findings (i.e., mural thickening, mural oedema and late mural enhancement) were assessed by a board-certified radiologist (G.S., 8 years of experience) subspecialized in cardiovascular imaging, blinded for the clinical data, PET/CT scan and ultrasound results. Mural thickening was scored as: 0 (no mural thickening), 1 (mild mural thickening, 2-3 mm for aorta, 1-2 mm for the subclavian/axillary artery), or 2 (strong thickening, >3 mm for aorta, >2 mm for the subclavian/axillary artery). Mural oedema was subjectively scored as 0 (no mural oedema), 1 (mild mural oedema), 2 (strong mural oedema)

using T2w BLADE and Diffusion-weighted sequences. Mural contrast enhancement was subjectively scored as 0 (no mural enhancement), 1 (mild mural enhancement), 2 (strong mural enhancement and/or perivascular enhancement) using static and dynamic T1w sequences pre and post contrast (Supplementary Table S2). ”

Comment 3: p.2, l.50; “Furthermore, studies comparing MRI”, It will be better of the authors give short notes about these studies and the nature of the comparison.

Response 3: *Thank you for this comment. We agree and we changed the section p.2, l.53 from “Furthermore, studies comparing MRI with other imaging modalities are sparse and have limitations due to different approaches for MRI interpretation and heterogenous patient populations including patients with Takayasu arteritis (12,13,15). ”*

To

“Furthermore, studies comparing MRI with other imaging modalities are sparse and used different approaches for MRI interpretation. In a study comparing a visual, semi-quantitative 4-point PET score with findings on CT-angiography and MR-angiography (MRA) in patients with GCA or Takayasu arteritis (TAK), an increasing PET score was associated with the synchronous presence of wall thickening (12). In a study comparing MRA with FDG-PET in patients with GCA or TAK, vascular involvement on MRA was defined by the presence of either wall thickening, oedema, stenosis, occlusion, or aneurysm. The authors found an association between vessel wall oedema and thickening in MRA with PET scans consistent with active vasculitis. However, the agreement between MRA and PET for the extent of the disease was only 60% (13). Yip et al. compared MRI to ultrasonography findings in patients with GCA and defined vasculitic changes on MRI as mural thickening using a 4-point ranking scale. In this study, the agreement between ultrasound and MRI for disease extent was 72.1% (15). ”

Comment 4: p.2, l.62; “PET/CT underwent a prospective thoracic study MRI in the frame of our local Ethics”, This is not a prospective, this is still a cross sectional. it is better to be edited as it is confusing.

Response 4: *Thank you for pointing this out. We edited the following section accordingly: p.2, section 2.1, from: “This is a cross-sectional analysis of a prospective MRI study (ClinicalTrials.gov identifier: NCT04204876) of patients diagnosed with LV-GCA between*

January 2019 and March 2023 at the University Hospital Basel, Switzerland. Patients with suspected LV-GCA are routinely screened by ultrasound of the supra-aortic vessels and PET/CT. Eight patients with newly diagnosed LV-GCA on PET/CT underwent a prospective thoracic study MRI in the frame of our local Ethics committee approved MRI study (EKNZ Project-ID 2019-02161). In addition, we included 4 patients from our local GCA cohort that underwent all three imaging modalities but were not prospectively included (Basler Riesenzellarteriitis Kohorte [BARK EKNZ, #239/09]).

To:

“This is a cross-sectional analysis of patients diagnosed with LV-GCA between January 2019 and March 2023 at the University Hospital Basel, Switzerland. Patients with suspected LV-GCA are routinely screened by ultrasound of the supra-aortic vessels and PET/CT is performed to assess aortic involvement. This study included newly diagnosed GCA patients who were found to have large vessel involvement on PET/CT and who underwent an additional MRI scan at diagnosis.”

Comment 5: p.2, 1.64; “In addition, we included 4 patients from our local GCA cohort that underwent all three imaging modalities but were not prospectively included (Basler Riesenzellarteriitis Kohorte [BARK EKNZ, #239/09]).” Unnecessary details which may be confusing to the readers.

Response 5: *Thank you for this comment. We agree with the reviewer and we edited this section accordingly and removed this sentence (see comment and response Nr. 4).*

Comment 6: p.3, 1.100; “Ultrasound examination and assessment”; We need more idea about the operator and his /her experience and how the interpretation of the images done and if it depended on only one or two readers.

Response 6: *We agree with this comment. Therefore, we changed the following section (p.3, section 2.4) from*

“Vascular ultrasound was done using EPIQ 7 duplex devices with a linear 12-3 MHz and 18-5 MHz transducer (both from Philips, Best, The Netherlands). An experienced angiologist (M.A.) blinded to the clinical data, MRI and PET/CT results evaluated all ultrasound images. LVV was defined as circumferential homogenous hypoechoic wall thickening, well-delineated towards the luminal side and without arteriosclerotic lesions (17).”

To

“Vascular ultrasound was done using EPIQ 7 duplex devices with a linear 12-3 MHz and 18-5 MHz transducer (both from Philips, Best, The Netherlands). All ultrasound images were evaluated by an experienced angiologist (M.A., 30 years of experience) blinded to the clinical data, MRI, and PET/CT results. The subclavian/axillary segments were bilaterally categorised as ‘normal’ or ‘vasculitis’. Vasculitis was defined as circumferential homogenous hypoechoic wall thickening, well-delineated towards the luminal side and without arteriosclerotic lesions, as previously described (17).”

Comment 7: p.3.; 1.113; “2.6. Statistical analysis”, More details are needed here.

Response 7: Thank you for this comment. We edited the following section (p.3., section 2.6) from

“Continuous variables are expressed as medians with interquartile ranges (IQR). Categorical variables are presented as numbers with percentages. All statistical analyses were performed in R version 4.1.1 (2021-08-10) (19).”

To

“As this study was exploratory, the study sample was not calculated, and the analyses presented in this manuscript are descriptive. Continuous variables are expressed as medians with interquartile ranges (IQR). Categorical variables are presented as numbers with percentages. All statistical analyses were performed in R version 4.1.1 (2021-08-10) (19).”

Comment 8: p.3, 1.119; “with newly diagnosed LV-GCA”, It is better to determine what is meant by “newly” and if the authors determine a specific period from the diagnosis.

Response 8: Thank you for pointing this out. The period from the diagnosis (start of treatment) to the time of imaging examination is found in section 3.1. To clarify what is meant by “newly diagnosed” we edited the methods section (p.2, section 2.1) from:

“All three imaging modalities were performed at diagnosis.”

To

“This study included newly diagnosed GCA patients who were found to have large vessel involvement on PET/CT and who underwent an additional MRI scan at diagnosis. All three imaging modalities were performed within 4 weeks of starting treatment.”

Comment 9: p.6, l.196; “Conclusion”, It is better to add the recommendations.

Response 9: We would like to thank the reviewer for this comment. We added a recommendation at the end of the “Conclusion”:

“Our results support the use of a second imaging modality in cases of suspected GCA but ambiguous clinical, laboratory or histological findings.”

Comments on the Quality of English Language: Moderate editing of English language required.

Response: English language was edited further within the manuscript.