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PEER-REVIEW REPORT

Name of journal: World Journal of Radiology

Manuscript NO: 54819

Title: Multi-modality imaging of cardiac amyloidosis: a contemporary update

Reviewer's code: 03366276

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Turkey

Author's Country/Territory: United States

Manuscript submission date: 2020-02-20

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-02-21 03:44

Reviewer performed review: 2020-02-22 22:53

Review time: 1 Day and 19 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

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It was a pleasure to review the article on multimodality imaging of cardiac amyloidosis. I have a few minor /major revision comments. Presentation section: Reduced EF or impaired systolic function is also a common presentation and not mentioned at all. Differential diagnoses: DCM should also be included. Non imaging investigations: Other possible blood tests and biopsy from other sites need to be mentioned. Cardiovascular magnetic resonance: Did you mean TI (inversion time scout) with the following phrases "Standard T1 scout and T2 imaging should also be performed." "and T1 inversion scout is helpful to time delayed imaging". Please check nomenclature especially in the CMR section. CMR section "of distribution is often subendocardial (especially for AL subtype) or transmural (especially for ATTR subtype or advanced disease affecting both ventricles)(34)." Please give image examples of these patterns, not very clear in this form for the reader. Nuclear medicine section is much more detailed than the others and also explains the methodology which was not done for echo and CMR-not good for consistency. Examples for this are matrix size etc. For example you don't mention the gadolinium dose for CMR but give tracer dose for nuclear. Frame rate for echo can be another example that was not included. Please either include those for all modalities or mention in title and introduction that work focuses specifically on nuclear medicine. Table 4 "diffuse LGE" is a very vague description. Please amend. Figure 3. LGE image on left upper panel not typical and diagnostic for amyloid, parametric T1 maps should be in color with DICOM LUT chosen on CVI42 software. I think map analysis section of software may be more demonstrative.

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PEER-REVIEW REPORT

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Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [ ] No
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The authors reviewed articles regarding cardiac amyloidosis focusing on imaging techniques. Wide-ranging issues, not only cardiac imaging but also epidemiology, clinical features, diagnosis, and treatment, are comprehensively covered. This is an interesting review article elucidating current progress in cardiac imaging for the diagnosis of systemic amyloidosis. It is timely to take topics of amyloidosis, particularly light chain (AL) amyloidosis and transthyretin (ATTR) amyloidosis, because novel therapeutic options for these diseases, such as chemotherapy, TTR stabilizers, small interfering RNA, and antisense oligonucleotide, now appear one after another. The manuscript is well written, and I enjoyed reading it. I believe many physicians will be attracted to this article. Although I do not have any critical comments, minor issues to strengthen this manuscript are raised as follows: 1. ATTR amyloidosis consists of hereditary ATTR (ATTRv) amyloidosis and wild-type ATTR (ATTRwt) amyloidosis (Biomedicines 2019; 7: E11). This issue should be clarified in the introduction section from the viewpoint of terminology, citing this article. In addition, patients with ATTRv amyloidosis tend to manifest cardiomyopathy, somatic neuropathy, and autonomic dysfunctions, while those with ATTRwt amyloidosis are characterized by cardiomyopathy and carpal tunnel syndrome (Biomedicines 2019; 7: E11). As this issue is important to understand clinical spectrum of ATTR amyloidosis, it should be mentioned in the “Presentaton” section. 2. As for ATTRv amyloidosis, early-onset cases from conventional endemic foci in Portugal and Japan tend to have cardiac conduction disturbances leading to the necessity of pacemaker implantation, while late-onset cases from non-endemic areas usually manifest diastolic dysfunctions due to massive amyloid deposition (Arch Neurol 2002; 59: 1771-6). Pathological examinations revealed subendocardial amyloid deposition resulting in atrophy and degeneration of cardiomyocytes in conventional early-onset cases, whereas diffuse amyloid deposition throughout layers of myocardium unaccompanied by cardiomyocyte degeneration in

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late-onset cases, corresponding to the difference of clinical features (Neurology 2004; 63: 129-38). These issues should be incorporated citing relevant articles because they are important to understand the mechanisms of cardiac amyloidosis. 3. Previous studies of ATTR amyloidosis indicate the presence of two types of amyloid fibrils from the viewpoint of morphology (i.e., short amyloid fibrils in late-onset patients and long amyloid fibrils in early-onset patients) (J Pathol 2005; 206: 224-32; J Neurol Sci 2009; 287: 178-84). A 99mTc-3,3-diphosphono-1,2-propanodicarboxylic acid scintigraphy may discriminate these two types of amyloid deposits (PLoS One 2019; 14: e0211983). I would recommend incorporating this issue by citing these studies.

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PEER-REVIEW REPORT

Name of journal: World Journal of Radiology

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Title: Multi-modality imaging of cardiac amyloidosis: a contemporary update

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In this manuscript, the authors aimed to discuss the clinical utility of multi-modality cardiac imaging in the contemporary evaluation and management of cardiac amyloidosis. They discussed echocardiography, cardiac magnetic resonance imaging and nuclear imaging in the non-invasive diagnosis and evaluation of cardiac amyloidosis. My comments are as follows: 1) It was an up-to-date and highly scientific review article. 2) Noncompaction of the left ventricular myocardium and Loeffler endocarditis should be present among the differential diagnosis. In this respect, articles of Gulel et al (Korean Circ J. 2018;48(7):655–657. doi:10.4070/kcj.2017.0348) and Celebi et al (Int J Cardiol. 2008;128(1):e22–e24. doi:10.1016/j.ijcard.2007.04.160) should be mentioned in the text. 3) References should be rewritten according to the Journal's style.