

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Nephrology

ESPS manuscript NO: 25629

Title: Vascular calcification: When should we interfere in chronic kidney disease patients and how?

Reviewer's code: 00503199

Reviewer's country: Greece

Science editor: Shui Qiu

Date sent for review: 2016-03-19 15:24

Date reviewed: 2016-03-26 19:46

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

The review is interesting. However some modification is needed before a recommendation can be given. Comments of this reviewer are: 1. Provide the actual words of the abbreviations the first time they appear. 2. ... "Hemodialysis (HD) patients have higher calcification scores than either peritoneal dialysis (PD) or CKD G4. More heavily calcified patients were significantly older and mostly male [23]" ... I 'm not sure that HD pts have more calcification than PD pts. If you have additional comparative studies that prove this, provide the relative references. You cannot generalize that HD patients have more calcification than PD pts, based only in one study. Otherwise, you can change the above sentence to..."In one study, HD patients had higher..." 3. The legends of the figures need to be more explanatory 4. "Increased FGF23 level is associated with increased risk for mortality among incident HD patients, during their first year of treatment [127]. This association was also confirmed in prevalent dialysis patients [128]. Neutralization of FGF23 in CKD rats was found to accelerate V.C. and increases mortality [129]"In this paragraph you mention two, at first glance, contradictory effects of FGF-23 in VC and mortality. You need to be more specific and explanatory, in

order to highlight the different effects. 5."We recommend small dose of vitamin D or vitamin D analogues to be given daily as prophylaxis against V.C. in spite of the lack of clinical trials favoring the use of either native or active vitamin D analogues to prevent V.C. progression. The rarity of vitamin D toxicity in general and the privileged survival benefits offered by VDRA's administered in small doses even in cases suffering hyperparathyroidism and/ or increased calcium and phosphorus levels supports this concept."....How do you define small doses? In which patients? Even in those with low iPTH levels? You need to give precise doses and target population as this is your "recommendation". However, I do not agree with such a recommendation as there are no prospective controlled trials that support any survival benefit from any vitamin D compound in CKD patients, especially the VDRA's. Using data from retrospective studies are not enough even for suggestions. In addition several experimental and prospective clinical data and RCTs (for example from transplant patients) may have harmful effects on patients. 6. Check the title in ref 129

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Nephrology

ESPS manuscript NO: 25629

Title: Vascular calcification: When should we interfere in chronic kidney disease patients and how?

Reviewer's code: 00225280

Reviewer's country: Greece

Science editor: Shui Qiu

Date sent for review: 2016-03-19 15:24

Date reviewed: 2016-03-30 01:56

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

Vascular calcification is a hot topic in nephrology literature these days. A recent literature research in Pub Med releases more than 1600 articles. This review is a well-written and organized manuscript which aims to sum up everything known so far about this subject. In general, the authors prefer to quote a large number of references relevant to the subject than to analyze critically the literature. Major comments 1. The title of the review implies that the review will focus on the clinical aspects of the vascular calcification (who and when to treat). The main text is disproportionally divided; half of the pages are focused eg on pathogenesis. I would prefer a more extended reference to the clinical aspects of VC. 2. Regarding the clinical implications of VC, I believe that the authors should insist more on analyzing the current debate about a) VC as a marker and prognostic factor of the kidney disease but not as a relevant etiological factor in the arterial disease b) the necessity of screening for VC or not c) lack of trials based on VC as a clinical end point. (Zoccali C and London G, Nephrol Dial Transplant, 2015 and Zoccali C et al, Hypertension, 2015;66:3-9). 3. Moreover all the related clinical trials which the authors refer to, should be critically reviewed (pitfalls, end points and surrogate end

points, discrepancies etc) 4. The pathogenesis section should be re-written in a more concise and precise way. For example FGF23-klotho section is too long with too many references. On the contrary, there is no clear description of the sequence of the mechanisms involved from the early to late stages eg inflammation-associated osteogenesis, cytokines, transcription factors, conversion of VSM cells, micro RNAs etc. I suggest reference to excellent reviews like Neil J. Palioian and Cecilia M. Giachelli. A current understanding of vascular calcification in CKD *Am J Physiol Renal Physiol* 307: F891-F900, 2014. 5. Conclusion section should be shorter with clear suggestions 6. Too many pointless references. For example, the authors illustrate the high CVD mortality of CKD patients (a common knowledge) and cite 5 references. They describe FGF-klotho association with VC and cite 50 references (this is not a review for klotho!) Minor comments 1. Plain definition of VC in the beginning of the manuscript. 2. In the introduction section, is the definition of ESAD valid? (where and when used?reference?) 3. Put the ideal strategy...The verb develop is better. 4. Large instead of big vessels. 5. I would prefer explanatory tables about eg treatment strategies instead of the images