Reviewer's report

Title: Ocular fundus pathology and chronic kidney disease in a Chinese population

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Reviewer: Line Kessel

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Major Compulsory Revisions:

Methods:
Recruitment: The authors should be more precise on how where the subjects recruited – where they invited from the local area using door-to-door screening or were they recruited amongst patients attending the hospital for other reasons or? In other words – is this study based on the background population or on a specific (perhaps sick) population?

Why did 7% not have fundus examination?

Fundus examination: an undilated fundus examination is not as precise as the standard dilated, photographic fundus examination that has been used in most epidemiologic studies for the last couple of decades. Did the authors check the validity of their examination procedure by dilating and photographing a subset of the population and grading fundus abnormalities to check how many were missed using the undilated procedure? It does not appear that the authors used standardized grading systems – so how did the authors ensure that what one ophthalmologist said was normal or abnormal would not by another ophthalmologist be graded as the reverse? Eg. how many microaneurisms or drusen was need to grade the fundus abnormal? Why was the funduscopic examination not compared to standardized systems.

Definition of chronic kidney disease: the authors used eGFR and proteinuria (measured by dipstick). The prevalence of eGFR<60ml/min was 3.8% but CKD was found in 13.9% meaning that the majority of patients were diagnosed with CKD because of the urine dipstick. A urine dipstick is not very accurate and there may be many false positives (infection, menstruation, poor hygiene etc). Did you check the urine dipstick on a separate day? The authors should justify that their method is accurate and that the subjects were not incorrectly classified as having chronic kidney disease due to false positives on the dipstick. Did you measure the urinary albumin excretion ratio in a subset of the population to validate your diagnosis?

Other conditions: did you use a specific questionnaire or did you simply ask if the participants were healthy?

Diabetes definition: how many hours of fasting were required? Surely, the
authors have not examined nearly 10,000 subjects in the morning.

Cardiovascular disease: which disease entities were included?

Why did the authors analyse for the risk of retinopathy and not for whether retinopathy was a risk factor for CKD? Do the authors think that CKD can cause retinopathy? I would expect that retinopathy was a risk indicator for common etiologies leading to CKD and turn the analysis around.

Results:

Prevalence of retinopathy in subjects with or without CKD. Using the more reliable method of eGFR, I do not find an overrepresentation of subjects with glaucoma (Chi-Sq 0.15) or AMD (Chi-Sq 0.25).

Table 1: What is retinopathy compared to? Why did the authors not show the no-retinopathy column? If I read the table correctly nearly 80% of those with retinopathy did not have diabetes – so why did they have retinopathy? According to the table 967 of the total study population had diabetes but only 359 had diabetes and retinopathy. Thus, 62% of those with diabetes did not have retinopathy. Is this what you would expect or was your method of estimating retinopathy not accurate? Why did you not include the number of subject with chronic kidney disease in the Table?

Secondary analysis: why do you not show these results in detail? And why did you not perform a subset analysis only including those with diabetes?

Discussion:

There is a well-established association between diabetes, diabetic kidney disease and diabetic retinopathy. I do not understand why the authors did not use their data to stratify for diabetes and perform the analyses for subjects with or without diabetes. How many of the subjects with diabetes had CKD (see my comments previously for definition of CKD) and were they more likely to have retinopathy and was retinopathy a risk factor for having kidney disease as a diabetic? Those are the interesting questions. Secondly, you can look for other reasons for CKD and then look at whether retinopathy or other types of retinal abnormalities are risk factors for CKD in non-diabetics.

The authors conclude that the prevalence of retinopathy was increased in subjects with CKD and that may be what the authors found when proteinuria was used to diagnose CKD. When the analyses were restricted to eGFR in the multivariate analysis the authors did not find an effect of retinopathy or ocular pathology and this is quite an important remark that should at least be included in the conclusion.

Minor Essential Revisions:

Table 1: Plasma UA should most likely be Plasma UA

“Diabetic nephropathy, age-related macular degeneration and glaucoma are important cause of blindness in United States” – do you really mean that diabetic
nephropathy is a cause of blindness?

Concluding remarks:
The topic is interesting. The manuscript would benefit from editing of English language. The work has serious methodological flaws. I do understand that conducting research in developing nations and developed nations may not be the same and that the authors had their reason to use unconventional methods of assessing the two primary outcome measures – chronic kidney disease and retinopathy. I do not think that grading retinopathy unundilated pupils without using a standard grading system (at least an agreement between graders of how many microaneurism or hard exudates were sufficient to categorize a subject as having retinopathy or whether this diagnosis was only made on proliferative retinopathy) is a valid method. I do not think that using a urinary dipstick to diagnose CKD is sufficient (how was the overlap between being diagnosed with CKD on eGFR and dipstick?). The conclusion does, in my opinion, not hold since the authors only found an increased OR for retinopathy when the dipstick was used to diagnose CKD but not when the more robust measurement of eGFR was used.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests