Prognostic Value of FGF23 among patients with End-Stage Renal Disease: a systematic review and Meta-Analysis

Hongliu Yang[1], Ping Fu[2], Xi Tang[2], Xiaoxi Zeng[2]

[1]West China Medical School, Sichuan University; [2]West China Hospital, Sichuan University

Background and Objectives:

Fibroblast growth factor 23 (FGF23) is a circulating peptide that secreted by bone osteocytes and osteoblasts that acts on kidney to regulate phosphate and vitamin D metabolism[1]. Patients with end-stage renal disease (ESRD) have increased FGF23 concentrations due to phosphate retention and decreased clearance[2].Prognostic value of FGF23 in ESRD patients is controversial[3-9]. To resolve this uncertainty of FGF23 as a prognostic biomarker, a systematic review was conducted to quantify the association between elevated FGF23 and overall mortality among ESRD patients.

Methods:

MEDLINE, EMBASE, PubMed and article reference lists were searched for relevant studies. The quality of the included studies was evaluated using Newcastle-Ottawa Scale (NOS) checklist. Pooled effects were calculated as hazard ratio (HR) using fixed-effect models and chi-square test was used for heterogeneity testing.

Results:

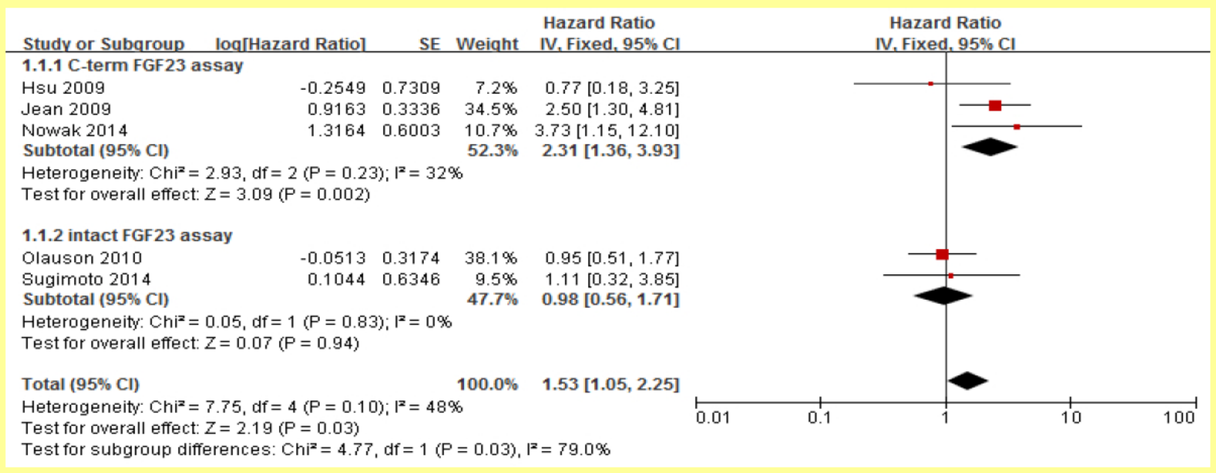

Figure 1. Total HR for the association between FGF23 and all-cause mortality and subgroup analysis in FGF23 assays

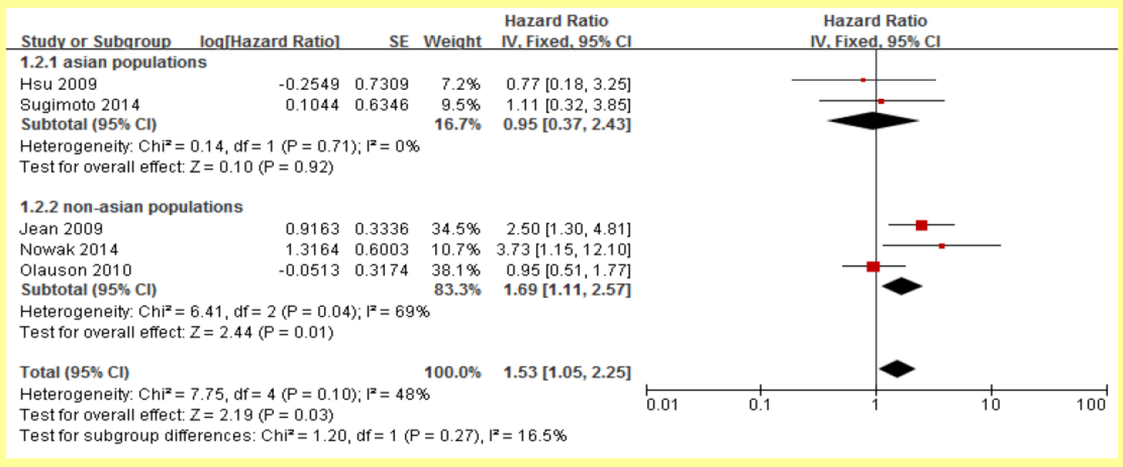

Figure 2. Total HR for the association between FGF23 and all-cause mortality and subgroup analysis of population.

There were 7 included studies[3-9] (1406 patients); 5 studies contributed data. Patients were included with mean age of 62.3 and mean follow-up of 29.4 months. 123(8.7%) of patients were receiving peritoneal dialysis while the rest of them receiving hemodialysis. From the pooled analysis, elevated FGF23 was significantly associated with increased all-cause mortality (HR, 1.53, 95% CI: 1.05-2.25) (Fig1, 2). P value for heterogeneity was at the critical point (P=0.10) with I^2=48% in fixed-effect model. The heterogeneity is acceptable.

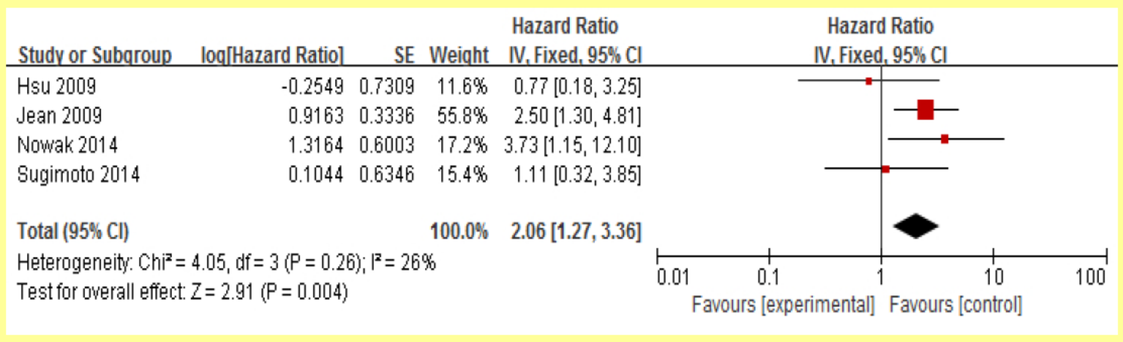

Figure 3. Pooled HR for the association between FGF23 and all-cause mortality when Olauson's study was excluded.

Subgroup analysis on different FGF23 assays suggest the association between elevated FGF23 level and all-cause mortality was absent in terms of C-term FGF23 assay (HR=0.98, 95%CI: 0.56-1.71), while elevated FGF23 was highly associated with all-cause mortality for intact FGF23 assay (HR=2.31, CI:1.36-3.93) (Fig1). Furthermore, the pooled HR was 0.98 (95%CI: 0.37-2.43) for Asian population and 1.69 (95% CI: 1.11-2.57) for non-Asian population respectively (Fig2). In addition, the exclusion of study on patients of 'incident' hemodialysis and peritoneal dialysis strengthen the association between elevated FGF23 and all-cause mortality (HR=2.06, 95% CI: 1.27-3.36) (Fig3).

Conclusions:

FGF23 predicts poor prognosis in patients with ESRD. Individuals with elevated FGF23 concentration have high risk of death. This finding suggests that FGF23 may be a promising risk prediction biomarker and may help to guide clinical practice.

References:

1. Gutierrez O, Isakova T, Rhee E, Shah A, Holmes J, Collerone G, Juppner H, Wolf M: Fibroblast growth factor-23 mitigates hyperphosphatemia but accentuates calcitriol deficiency in chronic kidney disease. Journal of the American Society of Nephrology : JASN 2005, 16(7):2205-2215.
2. Imanishi Y, Inaba M, Nakatsuka K, Nagasue K, Okuno S, Yoshihara A, Miura M, Miyauchi A, Kobayashi K, Miki T *et al*: FGF-23 in patients with end-stage renal disease on hemodialysis. *Kidney international* 2004, 65(5):1943-1946.
3. Nowak A, Friedrich B, Artunc F, Serra AL, Breidthardt T, Twerenbold R, Peter M, Mueller C: Prognostic value and link to atrial fibrillation of soluble Klotho and FGF23 in hemodialysis patients. *PloS one* 2014, 9(7):e100688.
4. Hsu HJ, Wu MS: Fibroblast growth factor 23: a possible cause of left ventricular hypertrophy in hemodialysis patients. *The American journal of the medical sciences* 2009, 337(2):116-122.
5. Olauson H, Qureshi AR, Miyamoto T, Barany P, Heimburger O, Lindholm B, Stenvinkel P, Larsson TE: Relation between serum fibroblast growth factor-23 level and mortality in incident dialysis patients: are gender and cardiovascular disease confounding the relationship? *Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association* 2010, 25(9):3033-3038.
6. Sugimoto H, Ogawa T, Iwabuchi Y, Otsuka K, Nitta K: Relationship between serum fibroblast growth factor-23 level and mortality in chronic hemodialysis patients. *International urology and nephrology* 2014, 46(1):99-106.
7. Jean G, Terrat JC, Vanel T, Hurot JM, Lorriaux C, Mayor B, Chazot C: High levels of serum fibroblast growth factor (FGF)-23 are associated with increased mortality in long haemodialysis patients. *Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association* 2009, 24(9):2792-2796.
8. Holden RM, Beseau D, Booth SL, Adams MA, Garland JS, Morton RA, Collier CP, Foley RN: FGF-23 is associated with cardiac troponin T and mortality in hemodialysis patients. *Hemodialysis international International Symposium on Home Hemodialysis* 2012, 16(1):53-58.
9. Gutierrez OM, Mannstadt M, Isakova T, Rauh-Hain JA, Tamez H, Shah A, Smith K, Lee H, Thadhani R, Juppner H *et al*: Fibroblast growth factor 23 and mortality among patients undergoing hemodialysis. *The New England journal of medicine* 2008, 359(6):584-592.

52 ERA 408--FP

J5) Chronic Kidney Disease. Bone disease.

Hongliu Yang

DOI: 10.3252/pso.eu.52era.2015

ePosters supported by F. Hoffmann- La Roche Ltd.

52nd ERA-EDTA CONGRESS London2015 UNITED KINGDOM MAY 28th-31st

PosterSessionOnline.com