Association between plasma pentraxin-3 levels and risk of all-cause mortality in Japanese hemodialysis patients with nutritional risk

Tetsu Miyamoto[1], Mika Matsumoto[3], Hiromichi Ueno[1], Ken Otsuji[1], Emi Hasegawa[1], Akihiro Kuma[1], Yoko Nakano[1], Kenichiro Bando[1], Yumi Furino[1], Ryota Serino[2], Akira Yashiro[4], Hiroshi Tanaka[5], Yutaka Otsuji[1], Masahito Tamura[2]

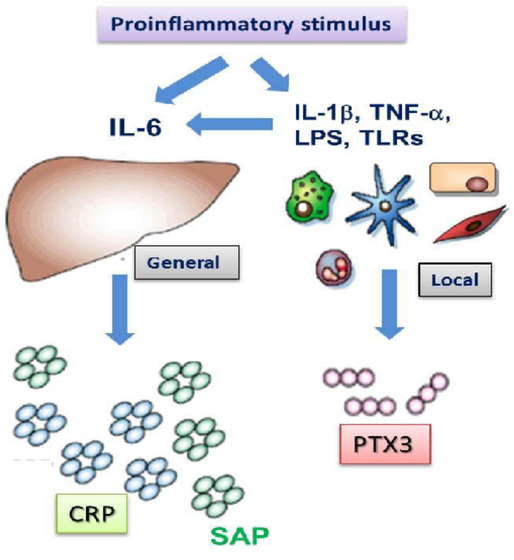
[1] Second Department of Internal Medicine and [2] Kidney Center, University of Occupational and Environmental Health

[3] Yukuhashi Clinic, [4]Kurate Hospitall, [5]Iseigaoka Clinic, Japan

Background

Persistent inflammation is an important cause of protein-energy wasting, which is a potent predictor of mortality. Therefore, regular monitoring of inflammatory biomarkers may be clinically useful for estimating mortality risk in dialysis patients. Pentraxin-3 (PTX3), a new candidate marker for inflammation, belongs to the same pentraxin superfamily of acute-phase reactants as C-reactive protein (CRP). PTX3 has been reported to be associated with all-cause mortality in Caucasian patients with end-stage kidney disease. However, uncertainty remains regarding PTX3 in relation to nutritional status, and no data are available on PTX3 in Asian hemodialysis patients, of which inflammatory profile is different from Caucasian dialysis patients .

Pentraxin3 (PTX3)



Pentraxin3 is a multifunctional soluble pattern recognition receptor that modulates immune inflammatory responses. In contrast to C-reactive protein (CRP), a systemic inflammation marker that is primarily generated by hepatocytes, PTX3 is produced at sites of inflammation by a wide range of various cell types. PTX3 is produced in response to IL-1 and TNF-α by vascular smooth muscle cells, endothelial cells, macrophages, fibroblasts, etc.

Design & Methods

◆ **Participants** : 380 maintenance hemodialysis patients (38% female; median age: 66 years (range, 21-92 years) , median dialysis duration: 7.6 years (range, 1.1-33.7 years))

◆ **Study Design**: Prospective cohort study

◆ **Mortality**: Cox proportional hazards models were used to estimate mortality risk after median 32 months of follow up.

◆ **Nutritional risk**: Geriatric nutritional risk index (GNRI) was used to assess nutritional risk.

GNRI : [1.489 × albumin(g/dL)] +[41.7 × (BW/IBW*)]
BW/IBW is set to 1 when the patient's BW exceeded the IBW
*** IBW(Ideal body weight) : Body height (m) × Body height(m) × 22**

Results

Table 1. Baseline characteristics of 380 hemodialysis patients grouped according to highest tertile of plasma PTX3 levels.

	Low PTX3 PTX3 ≤ 6.29 ng/mL, n=253	High PTX3 PTX3 > 6.29 ng/mL, n=127	P-value
Age (years)	66 (44-82)	68 (54-80)	0.36
Sex (female, %)	86 (34%)	60 (47%)	0.01
Diabetes Mellitus (%)	102 (40%)	34 (27%)	0.01
Cardiovascular disease (%)	80 (32%)	35 (28%)	0.41
Dialysis vintage (years)	6.0 (0.8-21.2)	10.2 (2.4-26)	< 0.001
Body weight (kg)*	55.4 (43-73)	51.1 (39-63)	< 0.001
Body mass index (BMI, kg/m^2)	22.5 (18.9-28.3)	21.1 (18.2-26.3)	< 0.001
Geriatric Nutrition Risk Index (GNRI)	98.1 (84.0-103)	91.5 (82.3-100.5)	0.01
CRP (mg/dL)	0.14 (0.05-1.1)	0.16 (0.03-1.9)	0.58
Interleukin-6 (pg/mL)	5.0 (1.3-20.5)	5.3 (1.7-17.8)	0.73
Albumin (g/dL)	3.6 (3.2-4.2)	3.6 (3.0-4.12)	0.65
Urea (mg/dL)	67 (47 - 85)	66 (48-85)	0.50
Creatinine (mmoL/L)	11.0 (7.3-13.0)	10.3 (6.9-14.1)	0.02
LDL-Cholesterol (mg/dL)	90 (58-132)	94 (58-135)	0.32
HDL-Cholesterol (mg/dL)	48 (33 - 74)	55 (34-83)	0.002
Triglyceride (mg/dL)	100 (57 - 200)	85 (47 -152)	0.003
Tissue iron binding capacity (mg/dL)	266 (188 -341)	261 (190-351)	0.82
Hemoglobin (g/dL)	10.5 (9.4 - 11.7)	10.3 (8.9-11.7)	0.14

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All the authors declare no conflict of interest.

Results

Table 2. Cox proportional hazard model predicting all-cause mortality in total cohort.

Parameter	Hazard ratio	95% CI	P-value
Age, per 10 years of age	1.51	1.13- 2.05	0.004
Female, vs male	1.62	0.90- 2.90	0.106
Dialysis vintage, per 10 years	0.86	0.55- 1.32	0.501
Diabetes Mellitus, presense	1.26	0.66- 2.41	0.474
Cardiovascular disease, presence	2.08	1.13- 3.84	0.019
High PTX3, PTX3>6.29 ng/mL	2.73	1.52- 4.92	0.001

A total of 51 (13.4%) patients died during the observation period. When adjusting for age, sex, dialysis vintage, diabetes mellitus and cardiovascular disease, patients with high PTX3 levels, defined as the highest tertile of plasma PTX3 (> 6.29 ng/mL), had an increased mortality risk.

Table 3. Cox proportional hazard model predicting all-cause mortality, stratified for nutritional risk.

Parameter	GNRI ≤ 91.2 n=141			GNRI > 91.2 n=239		
	Hazard ratio	95% CI	P-value	Hazard ratio	95% CI	P-value
Age, per 10 years of age	1.38	0.93- 2.12	0.11	1.52	0.96- 2.53	0.08
Female, vs male	1.50	0.72- 3.17	0.28	1.88	0.67- 4.93	0.22
Dialysis vintage, per 10 years	0.66	0.39- 1.10	0.11	1.43	0.67- 2.94	0.34
Diabetes Mellitus, presence	0.80	0.35- 1.79	0.59	2.27	0.75- 7.17	0.14
Cardiovascular disease, presence	2.46	1.09- 5.43	0.03	2.53	0.94- 7.33	0.07
High PTX3, PTX3>6.29 ng/mL	4.53	2.08- 10.4	<0.001	1.01	0.31- 2.77	0.99

When patients were categorized into two groups based on nutritional risk according to the GNRI. In patients in the high nutritional risk group (GNRI<91.2, n=141), a significant correlation was evident between high PTX3 levels and mortality risk. Conversely, no association was observed in patients in the low nutritional risk group.

Table 4. Cox proportional hazard model including high PTX3 and high CRP predicting all-cause mortality, stratified for nutritional risk.

Parameter	GNRI ≤ 91.2 n=141			GNRI > 91.2 n=239		
	Hazard ratio	95% CI	P-value	Hazard ratio	95% CI	P-value
Age, per 10 years of age	1.22	0.85- 1.82	0.30	1.52	0.95- 2.53	0.08
Female, vs male	1.51	0.71- 3.21	0.28	1.87	0.67- 4.90	0.22
Dialysis vintage, per 10 years	0.81	0.48- 1.32	0.40	1.43	0.67- 2.94	0.34
Diabetes Mellitus, presence	0.80	0.36- 1.76	0.58	2.26	0.74- 7.20	0.15
Cardiovascular disease, presence	2.03	0.92- 4.33	0.08	2.53	0.94- 7.32	0.07
High PTX3 and CRP	6.82	3.35- 14.2	<0.001	1.07	0.17- 3.89	0.93

High PTX3 levels accompanied by high levels of CRP (>0.29 mg/dL) were associated with increased HRs for mortality risk only in patients with high nutritional risk. HR of High PTX3 accompanied by high levels of IL-6 (>7.7pg/mL) was 7.03 (95%CI: 2.6-18.6, P<0.001).

Conclusions

Plasma PTX3 levels may be a useful biomarker for assessing mortality risk in Japanese hemodialysis patients, especially those with high nutritional risk. Concurrent measurement of other inflammatory markers such as CRP and IL-6 is expected to improve the predictive power of PTX3.

Reference

Livija D et al. Cell Tissue Res343, 237-249, 2011
Tong M et al. CJASN 2: 889-897, 2007
Suliman ME et al. QJM 101: 397-405, 2008
Yamada K et al. Am J Clin Nutr 87: 106-113, 2008

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