

IL-33 and ST2 levels in chronic kidney disease: associations with inflammation, vascular abnormalities, cardiovascular events, and survival



Ozkan Gungor¹, Hilmi Umut Unal², Aydin Guclu³, Mustafa Gezer², Tayfun Eyiletten², Altunoren¹, Ertugrul Erken¹, Yusuf Oguz², Ismail Kocyigit⁴, Mahmut Ilker Yilmaz²

1 Department of Nephrology, Sütçü İmam University, Kahramanmaraş, Turkey .e-mail:ozkan.gungor@yahoo.com
2 Department of Nephrology, Gulhane School of Medicine, Ankara, Turkey
3 Department of Nephrology, Ahi Evran University, Kirsehir, Turkey
4 Department of Nephrology, Erciyes University, Kayseri, Turkey

Introduction

Increased inflammation, associated with the increase in chronic kidney disease (CKD) stage, has a very important influence in vascular injury and cardiovascular diseases. In this study, we aimed to investigate the levels of IL-33 and ST2 in the different stages of CKD and to determine their effect on vascular damage and cardiovascular events (CVE).

Methods

This was an observational cohort study in which serum IL-33 and ST2 were obtained from 238 CKD (stages 1-5) patients. We examined the changes in IL-33/ST2 levels in CKD patients, as well as the association with a surrogate of endothelial dysfunction. Fatal and non-fatal CVE were recorded for a mean of 24 months. We also performed a COX regression analysis to determine the association of IL-33/ST2 levels with CVE and survival.

Results

IL-33 and ST2 levels were significantly increased and estimated glomerular filtration rates (eGFR) were decreased. Flow-mediated dilatation (FMD) was significantly decreased from stage 1 to stage 5 CKD (**Table**). IL-33 and ST2 levels were associated with FMD, and ST2 was a predictor. Multivariate Cox analysis showed that the presence of diabetes mellitus, smoking, and proteinuria and haemoglobin, Hs-CRP, IL-33, and ST2 were associated with the risk of CVE. Kaplan-Meier survival curves showed that patients with IL-33 and ST2 levels below the median value (IL-33=132.6 ng/L, ST2=382.9 pg/mL) had a higher cumulative survival compared with patients who had IL-33 and ST2 levels above the median value (log-rank test, p=0.000)

Parameters	Control	Stage 1 (≥90 ml/min) n:47	Stage 2 (60-89 ml/min) n:50	Stage 3 (30-59 ml/min) n:50	Stage 4 (15-29 ml/min) n:47	Stage 5 (0-14 ml/min) n:44	p
Age (years)	48(26-66)	48(26-69)	53(28-67)	49(27-69)	49(29-69)	49(26-69)	0,075
eGFR(ml/min/1.73 m ²)	120(115-129)	95(91-107)	68(61-82)	44(30-89)	21(15-29)	5,5(1-14)	0,001
Triglyceride, mg/dl	137(115-167)	137(103-179)	139,5(106-159)	137(107-168)	138(124-202)	134(93-168)	0,03
Total Cholesterol (mg/dl)	192(159-265)	194(160-254)	193(170-235)	193,5(171-235)	194(159-253)	192(149-235)	0,065
Hemoglobin (g/l)	15(12-17)	13,4(7,4-17)	12,0(8-16,9)	12,3 (7,4-16)	11,5(8,8-16,8)	10,7(7-16,6)	0,001
Hs-CRP (mg/l)	2(1-4)	7,6(3,2-16)	10(5-24)	16(5-35)	23(4,7-46)	27,5 (4-64)	0,001
IL33	39(26-168)	72,82(28-168)	109,71(27,7-199)	281,2(57,2-528)	400(31,3-1226)	526,19(44,71230)	0,001
ST2	245(115-469)	341(170,580)	355,25(187-590)	389,5(247-780)	540(324,4-1130)	718,3(220,1320)	0,001
Homa-IR index	1,34(.90-2,06)	1,380(95-3,28)	1,465(1,01-2,92)	1,52(.97-7,45)	1,72(1,9-1,62)	1,71(1,14-5,68)	0,003
FMD, %	9(7,5-11,2)	8,2(7,2-9,7)	7,2(6,2-8,3)	6,8(5,8-8,2)	6,2(4,1-8,2)	5,35(4-7,2)	0,001

Conclusion

In this prospective study, we found that IL-33 and ST2 levels increased with increasing stage of CKD in patients with chronic renal failure and IL-33, ST2, hs-CRP, diabetes and smoking history, proteinuria and Hb level were associated with vascular dysfunction and were also a predictor of fatal–nonfatal cardiovascular events and survival.

