Decreased natural killer cells activity in sarcopenic hemodialysis patients

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Background/Aims: Natural killer (NK) cells are lymphocytes of innate immune system that function to guard against tumors and infection. Reduced NK cell activities have been suggested in patients undergoing hemodialysis (HD) with conflicting results. Sarcopenia, a syndrome of reduction of skeletal muscle mass and function, has been reported to decrease immune system responsiveness in previous studies. The aim of this study is to determine the relationship between NK cells activity and sarcopenia in HD patients. **Methods:** We enrolled 77 HD patients between March 2015 and Feburary 2018. We excluded patients with active malignancy or those taking immunosuppressant drugs such as glucocorticoid. NK cell activity was assessed using NK Vue™ assay(ATGen Co.) that uses serum of ex vivo stimulated whole blood to detect interferon (IFN)-γ secreted from NK cells as an indicator of NK cell activity. The body composition was evaluated by bio-impedance analysis(Inbody S10) and the diagnosis of sarcopenia follows the guidelines of Asian Working Group for Sarcopenia (AWGS). **Results:** The mean age was 63.2 years and 58.4% were men. A total 22 patients(28.6%) was diagnosed as sarcopenia among 77 HD patients, and the patients with sarcopenia showed significantly older age(69.2 vs. 60.8 years, P=0.002) , lower BMI(20.73 vs. 23.44 kg/m², P=0.001), lower appendicular lean muscle mass(ALM, 8.26 vs. 9.83 kg/m², P<0.001), lower activity of NK cell (296.22 vs. 480.49 pg/mL, P=0.028). Low NK cell activity had a significant correlation with sarcopenia, and the statistical significance was maintained even after adjustment for age, sex, BMI, ALM in multivariate regression analysis. **Conclusions:** Our results showed that the activity of NK cells in HD patients with sarcopenia is significantly decreased. Further research is needed to clarify the relationship between low NK cell activity and clinical outcomes.

Table 1. Baseline characteristics of patients

Variables	Total (n = 77)		p value
	sarcopenia (n = 22)	non-sarcopenia (n = 55)	
Age, years	69.2 ± 2.16	60.8 ± 1.39	0.002
Sex(Male),%	68.2%	55.4%	0.276
DM, %	54.5%	55.4%	0.949
HTN, %	81.8%	82.1%	0.848
Height, m	1.62 ± 0.07	1.63 ± 0.08	0.604
BMI, kg/m²	20.73 ± 2.57	23.44 ± 3.09	0.001
BSA	1.13 ± 0.14	1.25 ± 0.18	0.006
Vintage, month	54.20 ± 10.37	47.46 ± 6.09	0.435
CRP, mg/L	4.05 ± 1.46	3.21 ± 1.45	0.242
Serum albumin, g/dL	3.90 ± 0.06	3.92 ± 0.04	0.750
Cholesterol,	145.1 ± 16.60	143.6 ± 5.92	0.848
ALM/ht²	8.26 ± 0.21	9.83 ± 0.19	0.000

DM, diabetes mellitus; HTN, hypertension; BMI, body mass index; BSA, body surface area; ALM, appendicular lean muscle; ht, height

Table 2. NK cell activity between sarcopenia and non-sarcopenia patients

Variables	Total (n = 77)		p value
	sarcopenia (n = 22)	non-sarcopenia (n = 55)	
NK cell , pg/mL	296.22 ± 55.77	480.49 ± 50.04	0.028

NK, natural killer

Table 3. Corrleation analysis between biochemical parameters including NK cell activity after adjusting for age and gender

Variables	NK cell activity	
	r	p value
BMI	0.324	0.004
BSA	0.200	0.081
Vintage	0.331	0.023
CRP	-0.044	0.706
Serum albumin	0.103	0.373
Cholesterol	-0.047	0.752
ALM/ht2	0.355	0.002

BMI, body mass index; BSA, body surface area; ALM, appendicular lean muscle; ht, height

Table 4. Univariate and multivariate regression between NK cell activity and biochemical parameters in all subjects

Variables	Unadjusted			Adjusted		
	β (95% CI)	Error type β p value		β (95%CI)	Error type β p value	
Age	-12.802[-21.493, -4.111]	-0.168	0.145	-	-	-
Sex	-214.006[-405.965, -22.047]	-0.128	0.268	-816.894[-1019.957, -613.264]	-0.487	0.000
DM	-16.298[-213.32, 180.724]	-0.010	0.934	-	-	-
HTN	-65.371[-319.376, 188.634]	-0.030	0.798	-	-	-
Vintage	7.470[3.961, 10.979]	0.302	0.039	-	-	-
BMI	81.535[52.751, 109.919]	0.312	0.006	-	-	-
BSA	1000.368[475.892, 1526.844]	0.214	0.061	-	-	-
CRP	4.441[-5.554, 14.236]	0.052	0.652	-	-	-
Albumin	365.097[28.053, 702.141]	0.124	0.282	-	-	-
ALM/ht²	191.758[130.947, 252.569]	0.342	0.002	349.371	0.623	0.000

DM, diabetes mellitus; HTN, hypertension; BMI, body mass index; BSA, body surface area; ALM, appendicular lean muscle; ht, height

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Analysis of infection Rate According to Natural Killer Cell Activity in Hemodialysis Patients

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Background/Aims: Natural killer (NK) cells are lymphocytes of innate immune system that play a key role in host defense against diverse range of pathogens. NK cell deficit has been suggested in patients undergoing hemodialysis (HD) with conflicting results regarding their activity and impaired antimicrobial activity in host defense. Aim of this study was to determine the susceptibility to bacterial infection according to NK cell activity in HD patients. **Methods:** Stable HD patients without malignancy or taking immunosuppressant were enrolled (N=204). NK Vue™ assay (ATGen Co.), that uses serum of ex vivo stimulated whole blood to detect interferon (IFN)-γ secreted from NK cells, was used to assess NK cell activity. NK cell activity was consecutively assessed at 6 month intervals from 2015 to 2017. We further investigated the incidence of major infections requiring intravenous antibiotics or hospitalization according to NK cell activity during the study period. **Results:** Mean age was 61.4 years and 58.8% were male. During the study, a total of 214 major infections occurred. Mean baseline NK cell activity was 586.2±540.7 pg/mL. Decreases in NK cell activity were significantly correlated with incidence of major infections. Furthermore, mean changes in NK cell activity were significantly different between periods at which infections have occurred and those periods free of infections, -71.7±875.7 pg/mL and 110.5±846.0 pg/mL, respectively (P=0.016). In univariate logistic analysis, older age[odds ratio(OR): 1.018; 95% CI, 1.004-1.032, P=0.010], higher serum C-reactive protein(CRP)[OR: 1.052; 95% CI, 1.010-1.096, P=0.014] and decreased NK cell activity[OR: 0.975; 95% CI, 0.955-0.995, P=0.017] were associated with higher incidence of infection. After adjusting for age, sex and CRP, decreased NK cell activity was independently associated with higher incidence of infection[OR: 0.976; 95% CI, 0.956-0.996, P=0.019]. **Conclusions:** Our results show higher incidence of infection during period of greater decrease in NK cell activity from baseline. NK cell activity could thus be a useful marker to predict risk of infection in HD patients
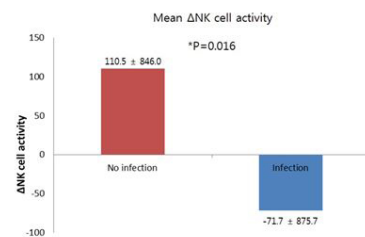

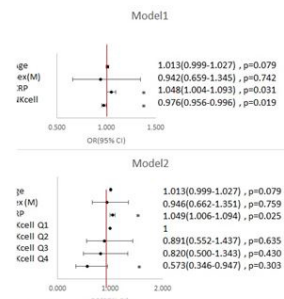**Figure 1. NK cell activity changes regarding incidence of infection**

Figure 2. Multivariate logistic regression for infection