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Impact of Iron Status on Kidney Outcomes in Kidney Transplantation Patients

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Objectives: Iron deficiency is prevalent in kidney transplantation (KT) patients and is a known risk factor for cardiovascular events and death. However, there are insufficient studies on the impact of iron deficiency on kidney functions in KT patients. In this study, we investigated the association of iron status and kidney outcomes in KT patients.

Methods: We analyzed data from the KoreaN cohort study for Outcome in patients With KT(KNOW-KT). Patients were excluded who met the following criteria: 1) subjects who did not follow-up for at least 1 year after KT, 2) subjects without ferritin or transferrin saturation(TSAT) level at 1 year after KT. Based on quartiles of ferritin and transferrin saturation at 1 year after KT, iron status was categorized as "Iron replete", "Iron deficiency", "Functional iron deficiency", "High iron", and "non-classified" (Table1). Additional analysis was performed by classifying each ferritin and TSAT into 3 categories, where 25%, 35% as reference points for the TSAT, and 100ng/mL, 299ng/mL for the ferritin, respectively. Primary outcome was the composite outcome of graft failure and eGFR decline ≥ 50%. Cox regression analysis was used to analyze the association of iron status with the primary outcome.

Results: A total of 815 patients were included in the final analysis. Iron status was categorized into iron replete (n=225), iron deficiency (n=138), functional iron deficiency (n=65), high iron(n=68), and non-classified (n=319). During median follow-up of 7.1 years, primary outcome occurred in 86 patients, with an incidence rate of 19.8 per 1,000 person-years. The risk of composite outcome was higher in the high iron groups compared to the iron replete group (HR 2.37, 95% CI 1.03-5.44). The high TSAT groups also showed a trend of increased risk of the composite outcome despite statistical insignificance.

Conclusions: High iron status increased the risk of graft failure and renal progression in KT patients.

Table 1. Classification of iron status according to transferrin saturation and ferritin levels

<table>
<tr><th colspan="2" rowspan="2"></th><th colspan="4">Transferrin saturation (%)</th></tr>
<tr><th>Quartile 1
(3.4 – 18.8)</th><th>Quartile 2
(18.9 – 27.6)</th><th>Quartile 3
(27.7 – 37.5)</th><th>Quartile 4
(37.6 – 100)</th></tr>
<tr><td rowspan="4">Ferritin
(ng/mL)</td><td>Quartile 1
(3 – 28.2)</td><td rowspan="2">Iron Deficiency
(N = 138)</td><td>Non-classified</td><td>Non-classified</td><td>Non-classified</td></tr>
<tr><td>Quartile 2
(28.3 – 76.6)</td><td colspan="2" rowspan="2">Iron replete
(N = 225)</td><td>Non-classified</td></tr>
<tr><td>Quartile 3
(77.3 – 229.1)</td><td rowspan="2">Functional iron deficiency
(N = 65)</td><td>Non-classified</td></tr>
<tr><td>Quartile 4
(229.7 -3287)</td><td>Non-classified</td><td>Non-classified</td><td>High Iron
(N = 68)</td></tr>
</table>

Table 2. Hazard ratios (HR) and 95% confidence intervals (CI) for graft loss and renal functional decline ≥ 50%

	HR	95% CI	*P*
Primary Outcome			
Iron deficiency	1.02	0.48 – 2.16	0.955
Functional Iron deficiency	1.32	0.57 – 3.07	0.520
Iron-replete		*Reference*	
High Iron	2.37	1.03 – 5.44	0.043
TSAT (%)			
TSAT = 20	1.36	0.78 – 2.38	0.280
20 < TSAT = 35		*Reference*	
TSAT > 35	1.73	1.00 – 3.00	0.052
Ferritin (ng/mL)			
Ferritin = 100	0.87	0.53 – 1.41	0.561
100 < Ferritin = 299		*Reference*	
Ferritin > 299	1.33	0.63 – 2.78	0.453