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# Plasma endocan level as a predictor of the cardiovascular risk in patients with end-stage renal disease

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**Objectives:** Endocan, a potential biomarker of endothelial dysfunction, has been shown to be associated with an increased cardiovascular risk. We investigated the utility of plasma endocan in predicting the cardiovascular risk of patients with end-stage renal disease (ESRD) on hemodialysis.

**Methods:** Adult patients with ESRD undergoing hemodialysis were prospectively enrolled in K-cohort (CRIS no. KCT0003281) that is comprised of 6 tertiary hospitals of South Korea from June 2016 to May 2018. Plasma level of endocan of these patients were measured at enrollment day and their clinical characteristics were checked. Then, the development of the composite cardiovascular outcomes was monitored until December 2018.

**Results:** A total of 352 patients with ESRD on hemodialysis were enrolled. The composite cardiovascular outcomes were occurred in 50 patients (14%). In multiple linear regression analysis, plasma endocan level was associated with higher body mass index and pre-dialysis systolic blood pressure, lower serum albumin level, and previous history of acute coronary syndrome (ACS) and stable angina. Cox proportional-hazard analysis showed that diabetes, ACS, arrhythmia, lower HDL, and higher plasma endocan were independently associated with increased cardiovascular composite outcomes. The patients with level of endocan > 3.2 log pg/mL showed significantly higher cumulative incidence of the composite cardiovascular events (hazard ratio 4.5) ($p < 0.001$).

**Conclusions:** Plasma endocan level is associated with multiple cardiovascular risk factors and may be a useful biomarker for macrovascular endothelial dysfunction in patients with ESRD on hemodialysis.

Table 1 Clinical characteristics of ESRD patients with or without cardiovascular composite outcomes.

**Table 1 Clinical characteristics of ESRD patients with or without cardiovascular composite outcomes.**

| Variables | All (n = 352) | ESRD Patients with cardiovascular composite outcomes (n = 50) | ESRD Patients without cardiovascular composite outcomes (n = 302) | *P* value |
|---|---|---|---|---|
| Age, mean years ± SD | 62 ± 13 | 64 ± 13 | 62 ± 13 | 0.60 |
| Male gender | 235 (67) | 32(64) | 203(67) | 0.78 |
| BMI ± SD | 23 ± 3.9 | 23.5 ± 3.5 | 22.9 ± 3.9 | 0.34 |
| Follow up duration, months ± SD | 15.7 ± 7.9 | 9.1 ± 6.43 | 16.8 ± 7.6 | < 0.001 |
| **Underlying disease** | | | | |
| Diabetes | 195 (55) | 37 (74) | 158 (52) | 0.01 |
| HbA1c,% ± SD | 6.6 ± 1.4 | 6.6 ± 1.1 | 6.6 ± 1.4 | 0.76 |
| Hypertension | 257 (85) | 44 (88) | 301 (86) | 0.75 |
| Heart disease | 113 (32) | 30 (60) | 83 (27) | < 0.001 |
| Previous history of ACS | 49(14) | 18 (36) | 31 (10) | < 0.001 |
| Angina pectoris | 27 (8) | 2 (4) | 25 (8) | 0.44 |
| Valvular heart diseases | 2 (0.6) | 0 (0) | 2 (0.7) | 1.00 |
| Heart failure | 20 (6) | 6 (12) | 14 (4.6) | 0.08 |
| Arrhythmia | 37 (11) | 11 (22) | 26 (9) | < 0.001 |
| Peripheral vascular diseases | 7 (2) | 1 (2) | 6 (2) | 0.94 |
| Cerebrovascular diseases | 75 (21) | 13 (26) | 62 (21) | 0.49 |
| Solid tumor or hematologic malignancy | 41 (12) | 7 (14) | 34 (11) | 0.75 |
| Chronic liver disease | 35 (10) | 4 (8) | 31 (10) | 0.81 |
| Chronic pulmonary disease | 10 (3) | 1 (2) | 9 (3) | 0.97 |
| Rheumatoid diseases | 8 (2) | 1 (2) | 7 (2) | 0.95 |
| **Cytokines** | | | | |
| Log endocan/ESM-1, log pg/mL ± SD (Endocan/ESM-1, pg/mL ± SD) | 3.03 ± 0.19 (1185 ± 637) | 3.08 ± 0.20 (1340 ± 615) | 3.02 ± 0.19 (1159 ± 637) | 0.02 |
| IL-6, pg/mL ± SD | 4.65 ± 7.08 | 4.64 ± 3.08 | 4.66 ± 7.54 | 0.99 |
| TNF-alpha, pg/mL ± SD | 9.67 ± 5.39 | 10.76 ± 5.55 | 9.48 ± 5.35 | 0.12 |
| **Laboratory findings** | | | | |
| WBC, mean /mm$^3$ ± SD | 5.92 ± 2.01 | 6.45 ± 2.49 | 5.83 ± 1.92 | 0.02 |
| Platelet, x 10$^3$ /mm$^3$ ± SD | 175 ± 55 | 181 ± 56 | 174 ± 55 | 0.39 |
| Hemoglobin, g/dL ± SD | 10.43 ± 1.22 | 10.26 ± 1.03 | 10.46 ± 1.26 | 0.29 |
| hs-CRP, mg/dL ± SD | 3.78 ± 7.80 | 5.03 ± 10.53 | 3.58 ± 7.29 | 0.20 |
| Albumin, g/dL ± SD | 3.81 ± 0.34 | 3.72 ± 0.37 | 3.82 ± 0.33 | 0.06 |
| Ca x P, mg$^2$/dL$^2$ ± SD | 40.54 ± 12.68 | 43.71 ± 10.97 | 40.96 ± 12.50 | 0.10 |
| Total cholesterol, mg/dL ± SD | 136.86 ± 31.21 | 126.66 ± 29.37 | 138.43 ± 31.23 | 0.03 |
| LDL, mg/dL ± SD | 77.71 ± 26.81 | 76.74 ± 28.42 | 77.87 ± 26.60 | 0.78 |
| HDL, mg/dL ± SD | 45.34 ± 13.45 | 40.55 ± 10.73 | 46.08 ± 13.69 | 0.01 |
| **Hemodialysis informations** | | | | |
| Dialysis duration, mean months ± SD | 58 ± 65 | 53 ± 52 | 58 ± 66 | 0.57 |
| Pre-dialysis SBP, mmHg ± SD | 144 ± 20 | 145 ± 17 | 144 ± 21 | 0.55 |
| spKt/V ± SD | 1.57 ± 0.30 | 1.51 ± 0.30 | 1.58 ± 0.30 | 0.13 |

Data are number (%) of patients unless indicated otherwise.

SD, standard deviation; BMI, body mass index; ESM-1, Endothelial cell-specific molecule 1; IL-6, Interleukin-6; TNF-alpha, Tumor necrosis factor; WBC, White blood cell; hs-CRP, Highly sensative C-reactive protein; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, Systolic blood pressure; spKt/V, Single pool Kt/V.

Fig. 1. Competitive cardiovascular risk of endocan level over time.

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