

## Deoxycholic Acid and the Risk of Death and Cardiovascular Events among Patients with Advanced Chronic Kidney Disease

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**Purpose:** Circulating levels of the secondary bile acid, deoxycholic acid (DCA), are elevated in chronic kidney disease (CKD) and may contribute to vascular calcification in CKD patients. Whether circulating DCA levels are associated with death and cardiovascular events (CVE) among advanced chronic kidney disease patients is unknown.

**Methods:** The Homocysteine Study was a randomized double-blind trial evaluating the effects of high doses of folic acid and B vitamins on all-cause mortality (ACM) and CVE in subjects with advanced CKD and elevated serum homocysteine levels. Fasting serum DCA levels were measured in stored serum samples obtained at 3 months in 1,054 patients with mainly stage 4 CKD (mean eGFR  $18.1 \pm 6.5$  mL/min/1.73m<sup>2</sup>) in this cohort. The study population was divided into quartiles according to plasma DCA levels. We used Cox proportional-hazards models to examine the association between DCE levels with ACM and a composite of CVE (combining myocardial infarction, stroke and amputation).

**Results:** Participants had a mean age of  $69 \pm 11$  years. The median DCA level was 119 [63-232] ng/mL. During a median follow-up of 3.0 years, 445 (42%) patients died from any cause and 210 (20%) had a CVE. Higher DCA levels were not directly associated with higher risks of death. Compared to the first (lowest) quartile, the HR (95% CI) for death were as follows: second quartile, 0.89 (0.74-1.06); third quartile, 0.98(0.82-1.18) and fourth quartile, 0.88 (0.73-1.06) after adjustment for potential confounders available in the database. Similar results were obtained when DCA was examined as a continuous variable: 0.97 (0.93-1.02). Compared to the lowest quartile, the two highest quartile of DCA were also not associated with a significantly elevated risk of CVE (HR 0.98, 95% CI 0.82-1.78) and (HR 0.87, 95%CI 0.73-1.05), respectively after multivariate adjustment.

**Conclusions:** Among HOST participants, DCA was not associated with death and cardiovascular events in patients with advanced CKD not requiring dialysis.