### Title

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## VITAMIN D RECEPTOR ACTIVATION AND A NOVEL CLASSIFICATION OF CARDIO-RENAL SYNDROME

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Due to increasing survival rate of cardiac and renal disease patients, Cardiorenal syndrome (CRS), a combination of these two is becoming an important problem. Some classifications have been proposed for CRS but for clinical approach, it would be more appropriate to emphasize the pathophysiologic pathways to classify CRS into: 1\ hemodynamic, 2\ atherosclerotic, 3\ uremic, 4\ neurohumoral, 5\ anemic-hematologic, 6\ inflammatory-oxidative, 7\ vitamin D receptor (VDR) related, and 8\ multi-factorial CRS. Recently, it has been revealed that vitamin D and its receptor play an important role in the CRS. Decreased 1-α-hydroxylase activity, nutritional deficiency, decreased Megalin receptors, and increased 1-24-hydroxylase activity are major causes for vitamin D depletion in CKD. Decrease in GFR, renal mass and 1-α-hydroxylase expression along with phosphate retention, increased FGF-23, and loss of both 1-α-hydroxylase and 25(OH)vitamin D are important factors for decreased 1-α-hydroxylase activity. Suboptimal or defective VDR activation may play a role in causing or aggravating CRS. Newer VDR activators such as vitamin D mimetics (e.g. paricalcitol and maxacalcitol) are promising agents. Some studies have confirmed the survival advantages of D-mimetics as compared to non-selective VDR activators. Higher doses of D-mimetic per unit of PTH (paricalcitol to PTH ratio) are associated with greater survival, and the survival advantages of African American dialysis patients could be explained by higher received doses of paricalcitol. More studies are needed to verify these data and to explore additional avenues for CRS management via modulating VDR pathway.

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