

Vitamin K Status and Arterial Calcification and Stiffness in Chronic Kidney Disease: The Chronic Renal Insufficiency Cohort

Abstract

To evaluate the relationship between CAC (Coronary Arterial Calcium) and Arterial Stiffness (PWV) in adult patients with mild to moderate CKD (Chronic Kidney Disease) using Multivariable-Adjusted Generalized Linear Models (MALMs). To assess the association between CAC prevalence (CAC), CAC incidence, CAC progression (100 Agatston Units/Y increase), and PWV (Pulse Wave Velocity) in adult patients (MELD) with mild to moderate Chronic Kidney Disease (KD) (Chronic Renal Disease). A cohort of approximately 2722 participants (MELD cohort) was enrolled and two vitamin K status biomarkers (Plyllquinone and DPP) were measured (baseline and 2–4 year follow-up).

Keywords: Coronary Arterial Calcium • Arterial stiffness • Chronic kidney disease • Vitamin K • Biomarkers

Rojat Javed*

Department of Internal Medicine, Southern Illinois University, USA

*Author for correspondence:

Rajatjaved15@gmail.com

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Introduction

Atherosclerotic cardiovascular disease (CVD) is characterized by mineral imbalances that cause calcium to accumulate throughout the body's vasculature [1]. These imbalances increase the risk of cardiovascular disease and mortality (CVD). Vascular calcification occurs in two layers of the heart: the intimal layer and the medial layer. Intimal calcification (also known as coronary artery calcium (CAC)) is a subclinical form of cardiovascular disease. Medial calcification, on the other hand, is a more peripheral form of cardiovascular disease (CAC). Medial calcification contributes to the stiffening of the heart's arteries, leading to heart failure and heart fibrillation [2]. Cardiovascular stiffness is a common feature of CKD (4, 5). It is important to identify therapies that inhibit arterial calcium formation in patients with chronic kidney disease (CKD). MGP is a protein that is dependent on vitamin K. When vitamin K is present, MGP becomes carboxylated, thereby inhibiting arterial calcium formation. A diet rich in vitamin K increases MGP carboxylation and reduces arterial calcium formation and stiffness in

mice with chronic kidney disease. However, several but not all observational studies have shown GP (reflecting lower vitamin K status) was associated with increased arterial calcium formation and arterial stiffness [3]. The available studies are cross-sectional and performed in patients with end-stage renal disease, and long-term studies on vitamin K status and arterial calcium and stiffness in patients with mild-to-moderate chronic kidney disease (CKD) are not available. To fill this gap, we used data from the chronic renal insufficiency cohort (CRIC) to evaluate the relationship between plasma PHYLLQUINOON (Vitamin K1) and plasma DEPHOSPO-UNCOCKRATED MGP (DP) with CAC and AORTIC PROWORTHY WAVES (PWVs) cross-sectional and over 2–4 years of follow up. We hypothesised that lower plasma PHYELLOQUINOON and higher (DP) ucMGP will result in higher CAC and higher PWVs [4].

Methods

CRIC is a prospective study designed to identify novel risk factors for progression and cardiovascular disease (CVD) in patients with mild to moderate chronic kidney disease (CKD). The CRIC study was conducted from

2003 to 2008. 3939 patients with moderate chronic kidney disease were enrolled from clinical centres in 7 cities across the United States. At the 12-monthly follow-up visit, vitamin K status biomarkers were measured for 3402 participants in the CRIC study [5]. Of the 3402 participants, 2993 reported CAC and / or PWV measurements. We excluded 166 participants who were taking, or had missing information about, the vitamin K antagonist Anticoagulant, warfarin, and 105 participants who had missing covariate data. This left 2722 participants available for inclusion. The CRIC protocols were approved by the institutional review boards of each participating centre, and procedures followed in accordance with the principles of the Helsinki Declaration; all participants provided written informed consent, including consent to use data and bio-specimens for further research. Further information on the CRIC study design and methodology is provided elsewhere [6].

Vitamin K status

Phylloquinone concentrations were measured using an automated sandwich ELISA (commercially available) using 2 anti-MGP Monoclonal Antibodies directed against Dephosphorylated CCRM (Immunodiagnostic Systems; Interassay, 4.0%, Intra-Assay, 4.5%), Lower limit of Detection (LLD) was 300 pmol/l. Higher plasma (DP) ucMGP concentrations reflect decreased vitamin K status. Plasma Phylloquinone levels were measured by high-performance liquid chromatography (HPLC). Lower LLD was 0.1 nmol/L. Laboratory participates in vitamin K quality assurance scheme (23), consistently generates serum/plasma Phylloquinone data within acceptable expected value range (analyses are performed every 4 mo for >30 cycles verification). Intra-Assay and Interassay CV is 4.2%, 4.9%, and all plasma samples were fasted and stored at 80 °C until laboratory analysis [7,8].

Discussion

In a large, heterogeneous population of patients with chronic obstructive cardiovascular disease (CKD), there was no consistent association between CAC prevalence (CAC), incidence (CAC), or progression across vitamin K status categories. CAC is a measure of subclinical cardiovascular disease (CVD) associated with atherosclerosis (subclinical CVD). Similar

to our previous findings that the risk of cardiovascular disease (CRIC) did not vary across plasma pharmacokinone categories (CRIC), plasma pharmacokinone (PQ) was not related to CAC. Similarly, there was no association between CAC (CAC) prevalence (CAC) and PQ (PQ) across plasma (DP) and UPMG (UPMG) categories. Overall, our results are consistent with the generally available evidence from Vitamin K supplementation RCTs, which generally do not this, suggests that vitamin K supplementation may play a protective role in improving the cardiovascular health of people with chronic obstructive cardiovascular disease (CKD) [9].

Although there was no difference in prevalence, incidence or progression of CAC across categories of plasma PHYLLAQUINO, those with plasma (DP) glucose-4-phosphonate (DPG) concentrations ranging from 300–450 ppm were 49% less likely to experience CAC progression compared to those with a plasma (DPG) concentration of 450 ppm. However, there was no difference between those with <300 ppm and 450 ppm plasma (DPG). The U-shaped relationship between CAC progression and plasma (DP) gluconephosphonate concentration decreases with increasing vitamin K status, so one would expect the lowest CAC progression rate to be in those with a lower (dp) gluconephinone concentration. As the risk for cardiovascular disease (CRIC) did not differ according to plasma (DPG)-related plasma (DPG) concentration, and neither did the incidence or prevalence of CAC. It is possible that this observation is due to chance [10].

Conclusion

In adults with mild to moderate chronic obstructive disease (CKD), vitamin K status was not consistently associated with chronic obstructive cardiovascular disease (CAC) or with chronic pulmonary disease (PWV). The prevalence of CAC, the incidence of CAC, and the progression of CAC did not vary depending on the type of plasma phylloquinone used. Those in the middle group had a significantly lower rate of progression compared to those in the highest group. However, there was no difference in CAC progression between those with and without vitamin K status at baseline or longitudinally.

References

1. Howard L, Mancuso AC, Ryan GL. Müllerian aplasia with severe hematometra: A case report of diagnosis and management in a low resource setting. *J Podiatry Adolesc Gynecol*. 132, 189-192(2019).
2. Bello AL, Acquah A, Quartey JN *et al*. Knowledge of pregnant women about birth defects. *BMC Pregnancy and Childbirth* 13, 1471-2393(2013).
3. Dolk H, Leke A Z, Whitfield P *et al*. Global birth defects app: An innovative tool for describing and coding congenital anomalies at birth in low resource settings. *Birth Defects Res*. 113, 1057-1073(2021).
4. Persani L. Central hypothyroidism: pathogenic, diagnostic, and therapeutic challenges. *J Clin Endocr*. 97, 3068-3078(2012).
5. Jomaa M.A challenging diagnosis and management of Herlyn-Werner-Wunderlich syndrome in low-resource settings: a case report complicated with hydronephrosis. *Ann Med Surg*. 70,102-843(2021).
6. Mbonda A. Diagnosis of Fraser syndrome missed out until the age of six months old in a low-resource setting: a case report. *BMC paediatrics*. 19, (2019).
7. Dimopoulos G. Cardiovascular complications of down syndrome: scoping review and expert consensus. *Circulation*. 147, 425-441(2023).
8. Melamed N. FIGO (international Federation of Gynecology and obstetrics) initiative on fetal growth: best practice advice for screening, diagnosis, and management of fetal growth restriction. *Int J Gynaecol Obstet*. 1,152 -352(2021).
9. Ballantyne A, Newson A, Luna F *et al*. Prenatal diagnosis and abortion for congenital abnormalities: is it ethical to provide one without the other?. *AJOB*.9, 48-56 (2009).
10. Timothy E. Obstetric ultrasound use in low and middle income countries: a narrative review. *Reprod health* .15, 1-26(2018).