The Role of Vitamin D in Heart Disease

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Conflict of Interest

- None

What is Vitamin D

- Produced predominantly by the kidney 1,25(OH)2D functions as a hormone
- Similar in structure to steroid hormone
- Both vascular smooth muscle and endothelial cells also convert vitamin D affecting a wide range of effects on numerous organs including the CV system

- JACC 2011:58:1547-56

Function of Vitamin D

- Vitamin D regulates numerous genes including
  - Renin production in the kidney
  - Insulin production by beta cells in the pancreas
  - Growth and proliferation of vascular smooth muscle cells and cardiac cells
  - Lymphocytes and macrophages

JACC 2011:58;1547-56

Forms of Vitamin D

- **Vitamin D2 – (ergocalciferol)**
  - **Found in some plants and**
  - **Fortified foods and also supplements**
  - **Prescription**

- **Vitamin D3- (cholecalciferol)**
  - **Produced in the skin – UVB radiation from sun**
  - **Animal sources – fatty fish (wild or farm salmon, mackerel, tuna, sardines, cod liver oil); egg yolks; liver**
  - **Supplements**
  - **Fortified foods (dairy products, cereals, margarines, flour, OJ)**

- **Both D2 and D3 can be used in fortification.**
- **Both undergo identical metabolism.**
- **Some evidence indicates D2 may be more rapidly metabolized than D3 but daily intake considered bioequivalent.**

Mayo clin Proc. 2011;86(1):50-60
JACC 2011:58;1547-56

Current Definition of Vitamin D

Serum 25 Hydroxyvitamin D, ng/ml	Vitamin D Status
<10	Severe deficiency
10-20	Deficiency
20-30	Mild-moderate deficiency
≥30	Sufficient
40-50	Ideal
50-150	Indeterminate data
>150	Toxicity
Institute of Medicine Definition (IOM)	
<12	At risk of deficiency
12-19	At risk of inadequacy
20-50	Sufficient
>50	Possibly harmful

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CV Effects of Vitamin D

Hypertension

- Vitamin D deficiency – up regulation of the RAAS and hypertrophy of both smooth muscle cells and the left ventricle.
- LVH
- Vitamin D regulates endothelial cell dependent vasodilation

- JACC 2011;58:1547

Type II Diabetes Mellitus

- Pancreatic β-cell dysfunction
- Peripheral tissue resistance to insulin
- Chronic inflammation

- Am J Cardiol 2010;106:798-805

Lipids

- Increase peripheral insulin resistance contributing to metabolic syndrome
- Increased vessel free radicals lead to oxidation of low density lipoprotein (LDL) and increased foam cell formation in macrophages

- Am J Cardiol 2010;106:798-805

Hyperparathyroidism

- Chronic vitamin D deficiency causes secondary hyperparathyroidism (↑PTH) – may cause severe CV effects
- ↑ arterial pressure and myocardial contractility leads to apoptosis, fibrosis and vascular smooth muscle cell hypertrophy as well as LVH
- Predisposes to mitral annular calcification, valvular sclerosis/calcification and calcification of the myocardium
- Also contributes to chronic kidney disease-CV risk

JACC 2011;58:1547

Inflammation

- Low levels of vitamin D and increases in PTH result in elevated C-reactive protein (CRP) and interleukin-10.
- Treatment with vitamin D showed down regulation of biomarkers

JACC 2011;58:1547

Vitamin D, CV Disease and Mortality

- Framingham Offspring Study
  - 1,739 free of CVD at baseline
  - Rate of CV events 53 to 80% higher among those with low vitamin D levels
  - Increased risk magnified with those with HTN
  - Slightly higher risk at higher vitamin D levels
- NHANES III
  - 13,331 followed for median 8.7 years
  - Mortality inversely associated with vitamin D levels
  - <17.8 ng/ml had 26% increased mortality compared with highest quartile
  - Also suggested U-shaped relationship with slight increased mortality at high >50 ng/ml
  - Circulation 2008;117(4):503-11
  - Arch Intern Med 2008;168(15):1629-37

Vitamin D, CV Disease and Mortality

- Intermountain Healthcare System analyzed >27,000 patients
  - >60% of patients had levels of vitamin D ≤30 ng/ml
  - Highly significant increases in Type II DM, HTN and dyslipidemia
  - Vitamin D deficiency highly associated with CHD, MI, CHF, CVA as well as total mortality.
- Health Professionals F/U Study
  - 10 yr. f/u free of CVD
  - 18,225 men – 454 men – nonfatal MI's or fatal CHD
  - Low levels of vitamin D (<15 ng/ml) assoc. with higher risk of MI even after controlling for other CHD risk factors when compared to those with >30 ng/ml.
  - Am J Cardiology 2010;106:963-8
  - Arch of Intern Med 2008;168:1174-80

IOM Recommendations

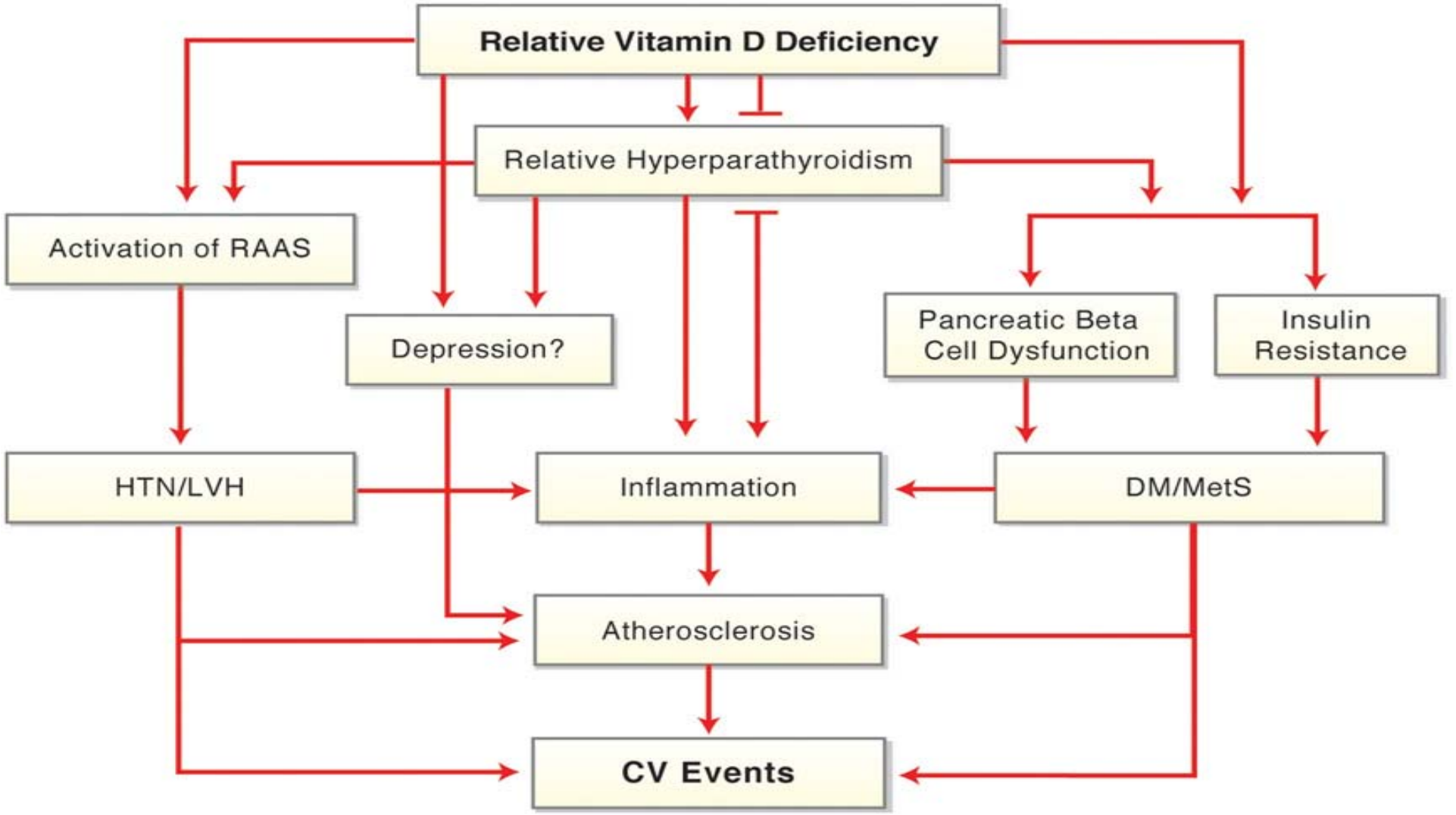
Age	Ave. Daily Requirement	Recommended dietary allowance	Upper Intake level
0-6 months			1000 iu/d
6-12 months			1500 iu/d
1-3 years	400 iu/d	600 iu/d	2500 iu/d
4-8 years	400 iu/d	600 iu/d	3000 iu/d
9-13 years	400 iu/d	600 iu/d	4000 iu/d
14-18 years	400 iu/d	600 iu/d	4000 iu/d
19-30 years	400 iu/d	600 iu/d	4000 iu/d
31-50 years	400 iu/d	600 iu/d	4000 iu/d
51-70 yrs men	400 iu/d	600 iu/d	4000 iu/d
51-70 yrs females	400 iu/d	600 iu/d	4000 iu/d
> 70 years	400 iu/d	800 iu/d	4000 iu/d
14-18 pregnant/lact	400 iu/d	600 iu/d	4000 iu/d
19-50 pregnant/lact	400 iu/d	600 iu/d	4000 iu/d

Ongoing Trials

Brigham and Women's Hospital	Est. Completion
• Vitamin D & Omega 3 Trial (VITAL)	June 2016
If supplements ↓ risk of Cancer, Heart Ds, and Stroke	
• Study of Vitamin D & Omega 3 Supplementation Preventing Diabetes	?
• Vitamin D & Omega 3 Hypertension Trial (VITAL Hypertension)	June 2016
Massachusetts General Hospital	
• Impact of Vitamin D supplementation on Cardiac Structure and Function (VITAL-ECHO)	June 2016
University of Guelph Ontario Canada	December 2013
• Vitamin D and Omega 3 Inhibit Metabolic Syndrome	

Clinical Trials.gov

Potential Mechanisms for CV Effects of Vitamin D Deficiency



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