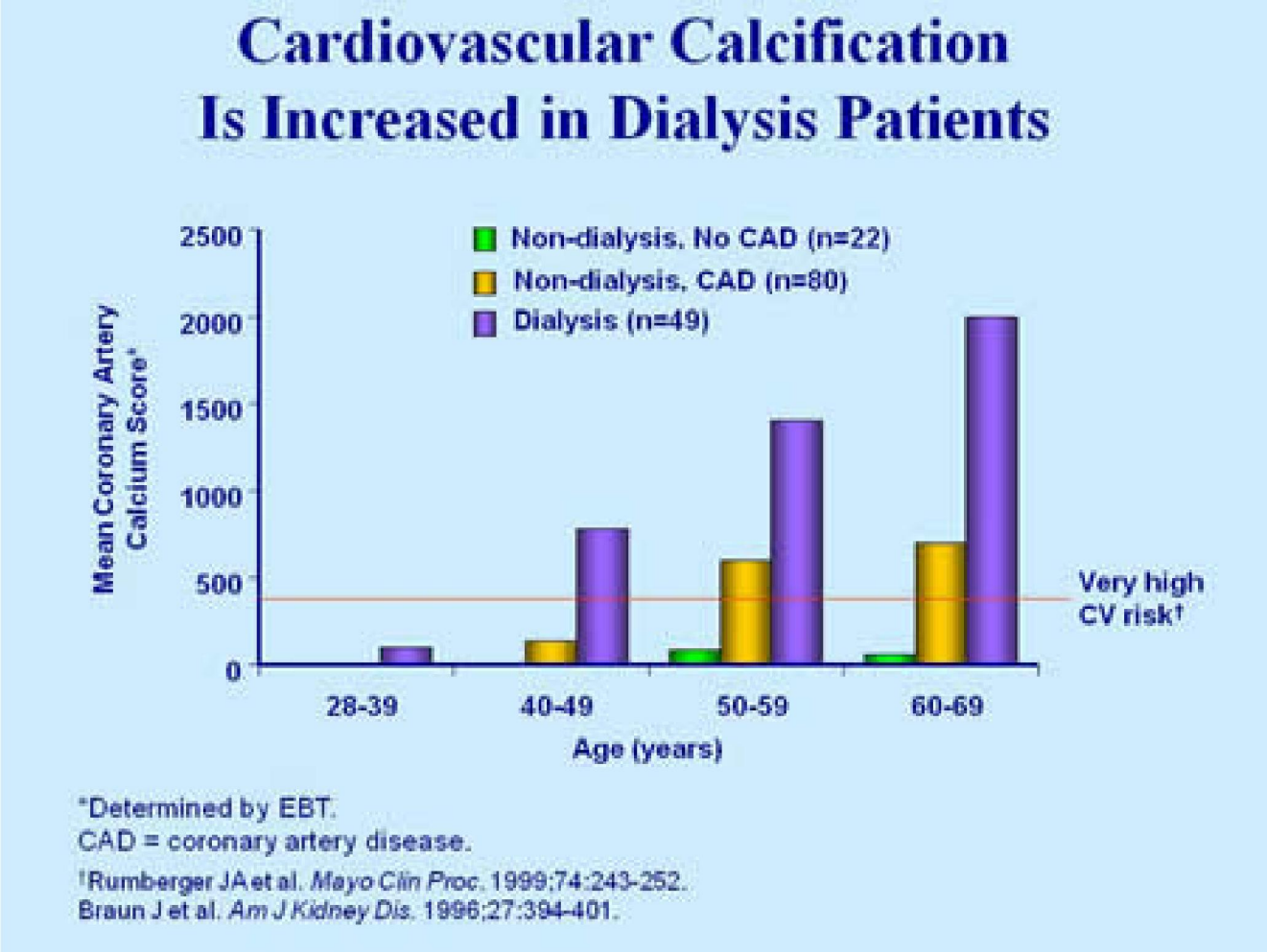
Da li je skrining vaskularnih kalcifikacija jednostavna priča?

Nada Dimković

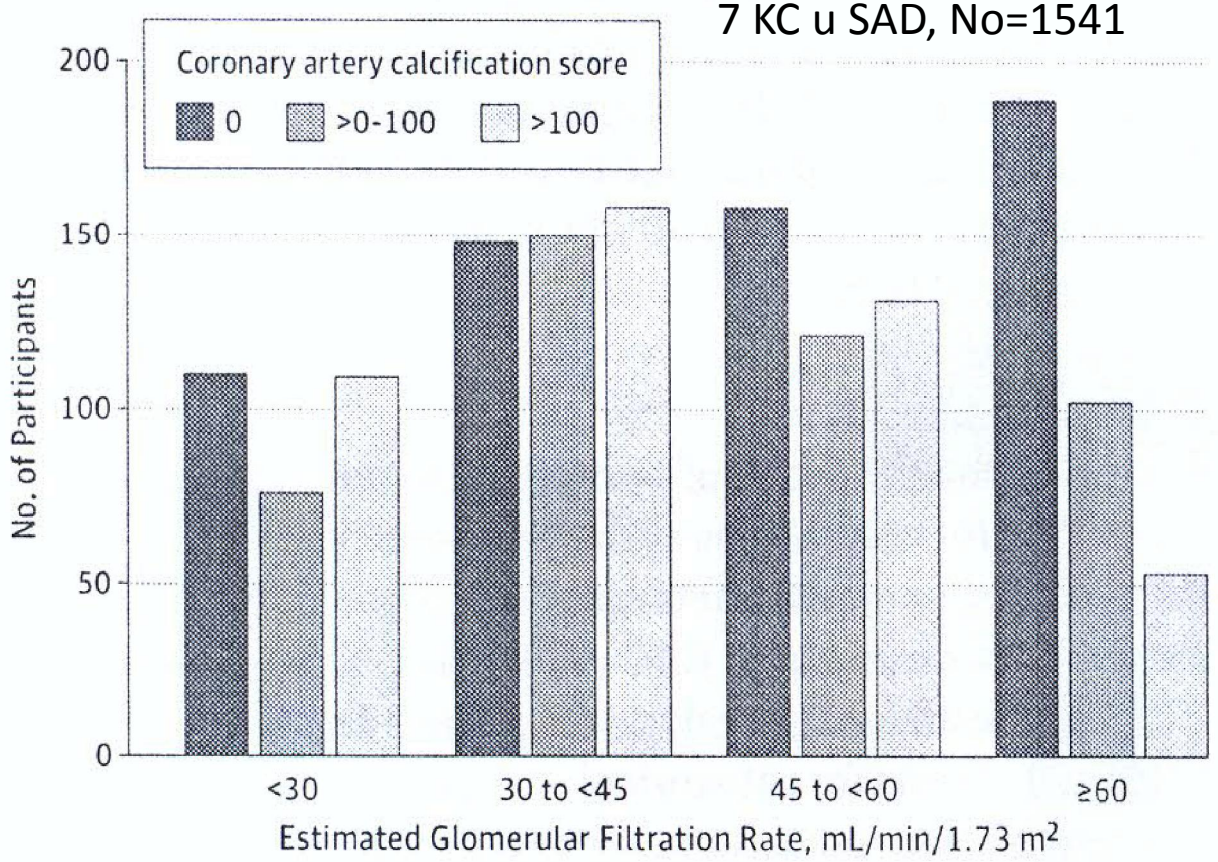
Kardiovaskularne kalcifikacije: ‘Hot topic’ od 1996



Hronična bubrežna slabost i CAC skor

Figure 1. Chronic Renal Insufficiency Cohort Study Participants by Coronary Artery Calcification Score and Estimated Glomerular Filtration Rate

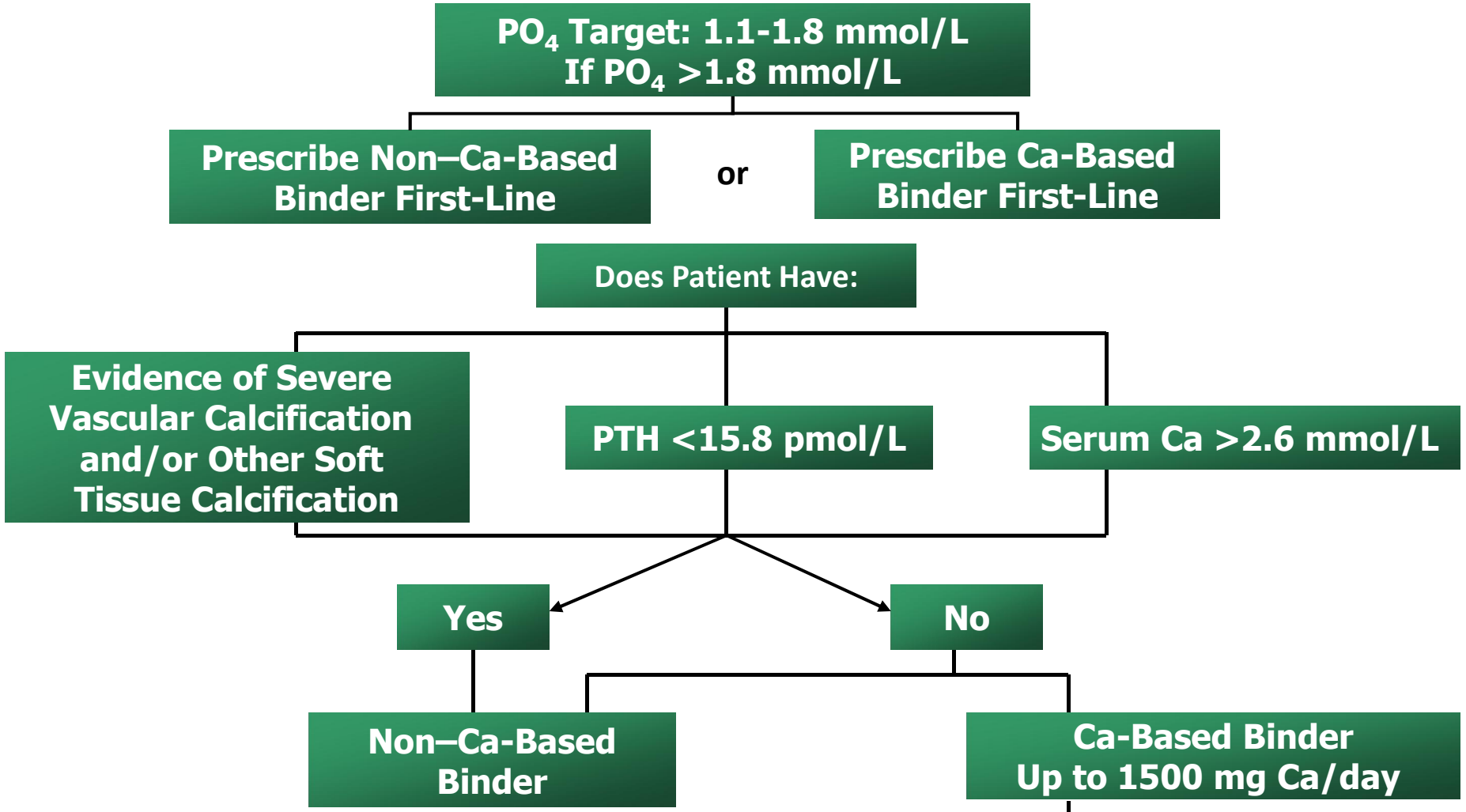
7 KC u SAD, No=1541



Chen J et al, JAMA Cardiology 2017; DOI: 10.1001/jamacardio.20170363

calcification, hemodialysis	= 3141 referenci
calcification, peritoneal dialysis	= 448 "
calcification, chronic renal failure	= 2937 "
calcification, renal transplantation	= 828 "

K/DOQI Recommendations:



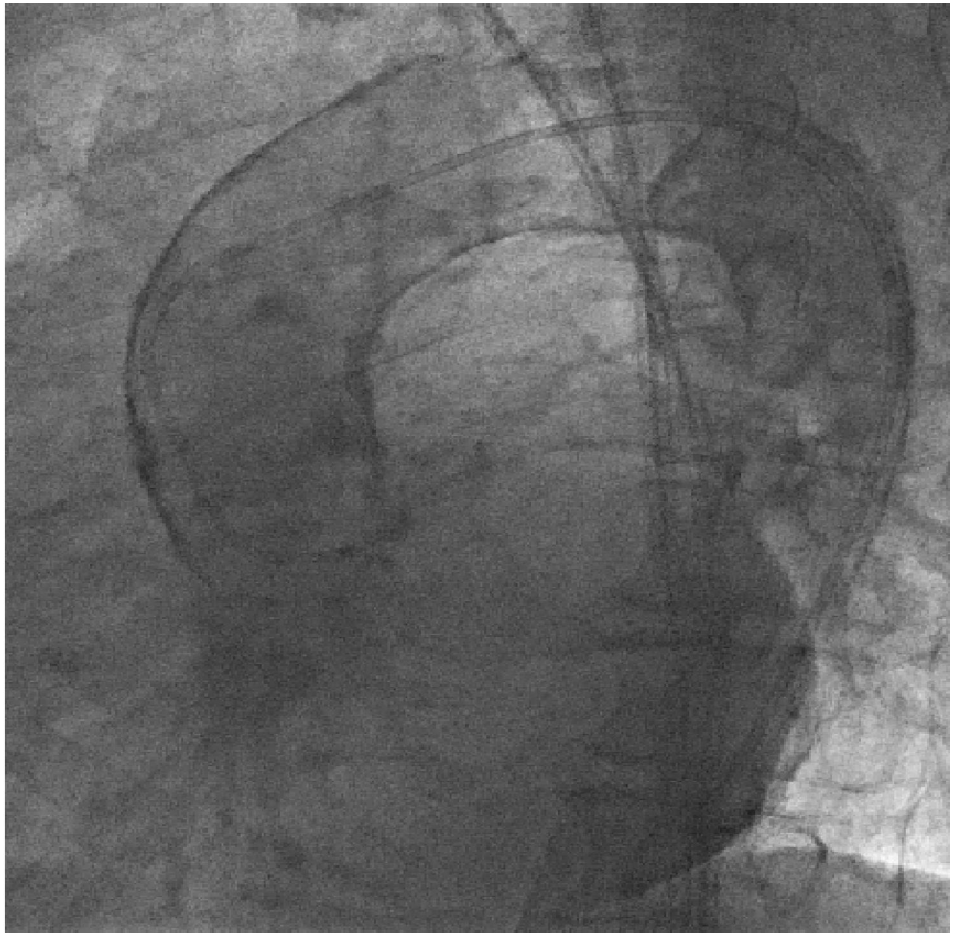
Am J Kidney Dis. 2003;42(suppl 3):S1-S201.

Pitanja od značaja

Koji je najmerodavniji metod skrininga i kako to menja našu dnevnu praksu

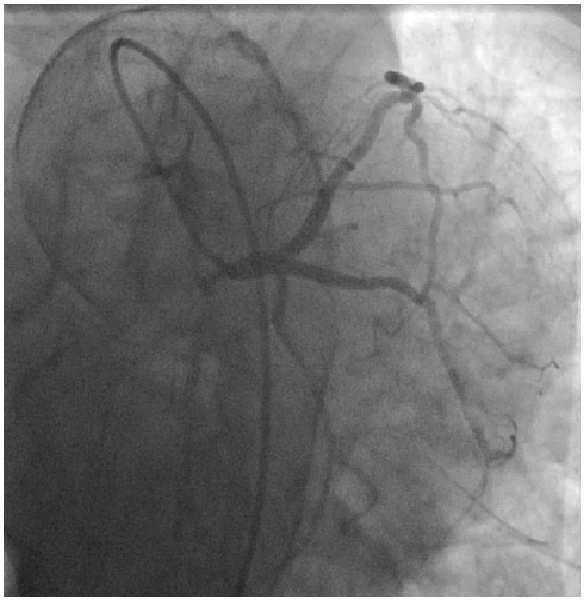
Prikaz slučaja

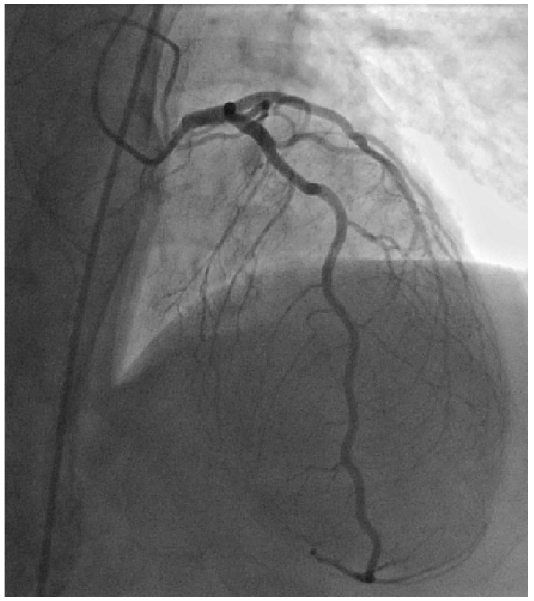
Bolesnik 68g, muškog pola, TBS/HTN, CAPD 5g, simptomi AP

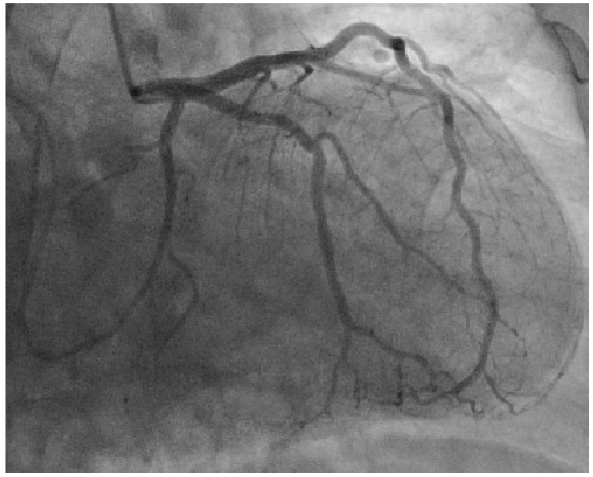


Boljević D, Kongres nefrologa Srbije, 2016.

Angiogram: normalan nalaz







Boljević D, Kongres nefrologa Srbije, 2016.

Vascular calcifications in non-diabetic prevalent HD patients

(No=194;103 male)

Site of cardiovascular calcification	Patients with calcification, No(%)
Femoral/iliacal arteries (n = 188)	95 (51%)
Wrist/finger arteries (n = 189)	56 (30%)
AV fistula (n = 186)	37 (20%)
Heart valves (n = 165)	73 (40%)
Carotid arteries (n = 189)	129 (68%)

Schlieper G et al, Kidney Blood Press Res. 2009;32(3):161-8. doi: 10.1159/000221064.

Podaci ukazuju na razliku od ~50% izmedju pojedinih krvnih sudova

Nisu sve arterije jednako kalcifikovane!

Patogeneza kalcifikacije medije se razlikuje izmedju pojedinih arterija

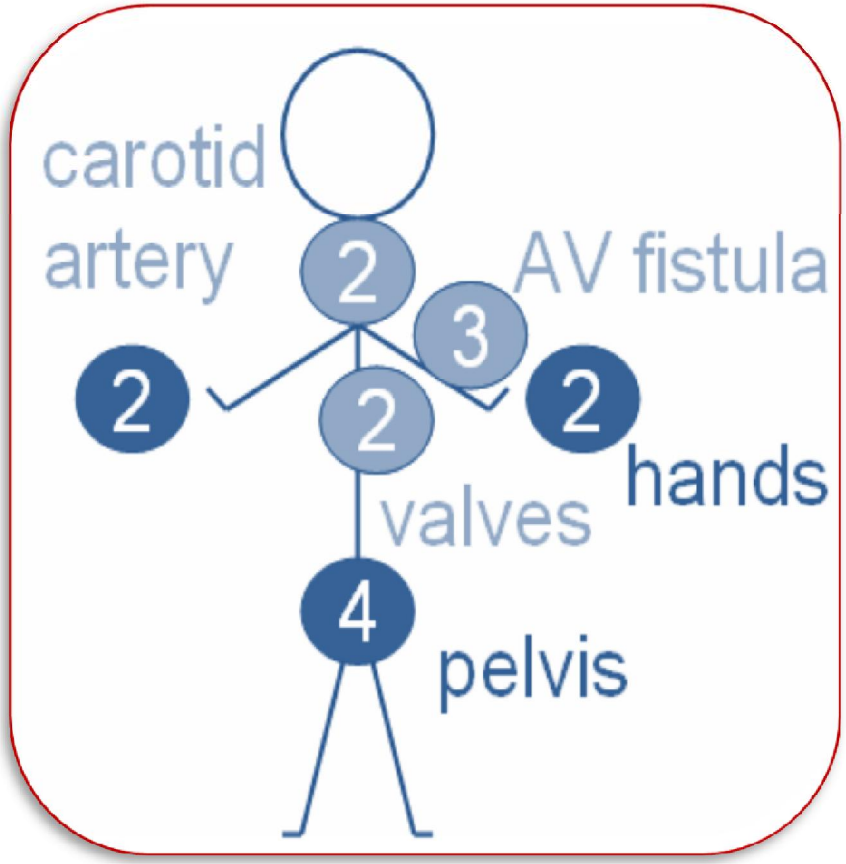
- ‘Epigenetic programminga’
- Veličine arterija
- Sadržaja elastičnih vs. mišićnih vlakana
- Laminarnog vs. turbulentnog protoka krvi
- Sresa na zid krvnog suda
- Amplitude krvnog pritiska
- Aterosklerotičnih oštećenja
- ……

Schlieper G, KI 2014; 85: 501-503
O'Neill WC, **Adams** AL, KI2014; 85(3):668-76

Skrining vaskularnih kalcifikacija deluje jednostavno ali još uvek ne znamo najpouzdaniju metodu

Kompozitni skor KV kalcifikacija

Adragao skor (8) + AVF skor (3) + obe CCA (2) + valvularni skor (2)= total skor do15



Composite score:

Both CCA= 2

AVF = 3

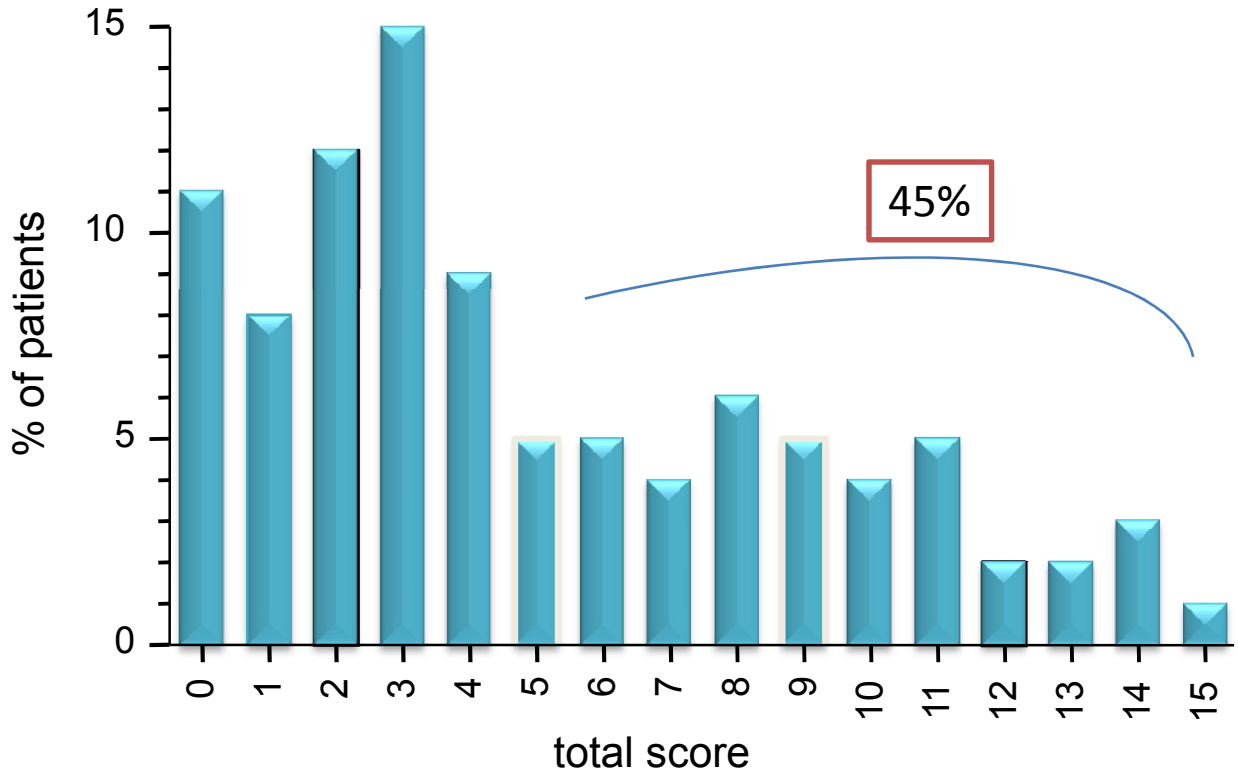
Valves = 2

Hands = 4

Pelvis = 4

Total=15

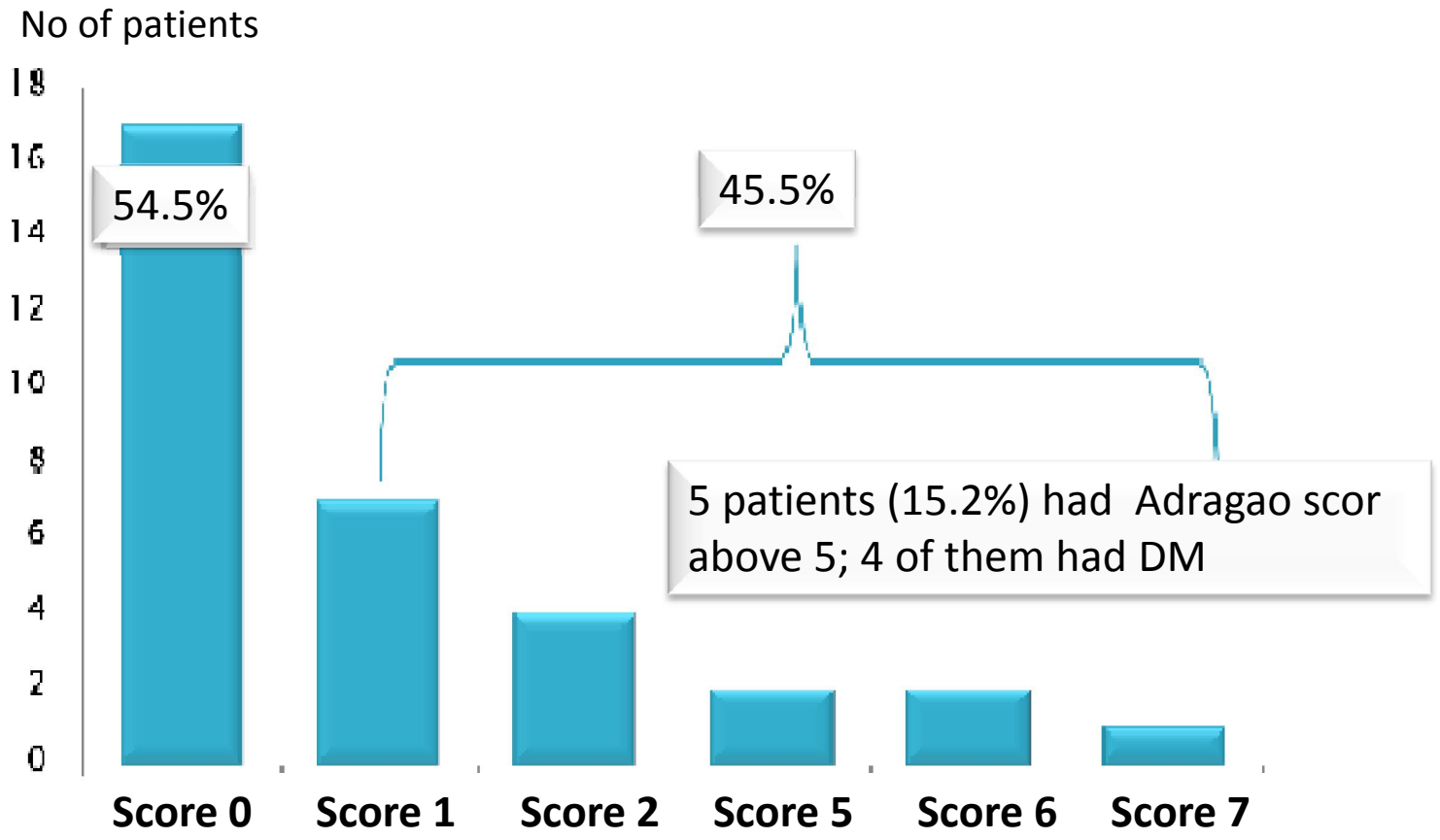
Distribution of Total calcification score* in cohort of HD patients



* Adragao score (8)+ of both carotid arteries (2), + AV fistula with neighbouring arteries (3) + aortic and mitral heart valves (2)

Vaskularne kalcifikacije u incidentnih HD bolesnika

Incident HD patients, period 17 months (01.01.2013. to 01.05.2014):
No 33 (25 males, 8 females), mean age 62.3±11.3 years

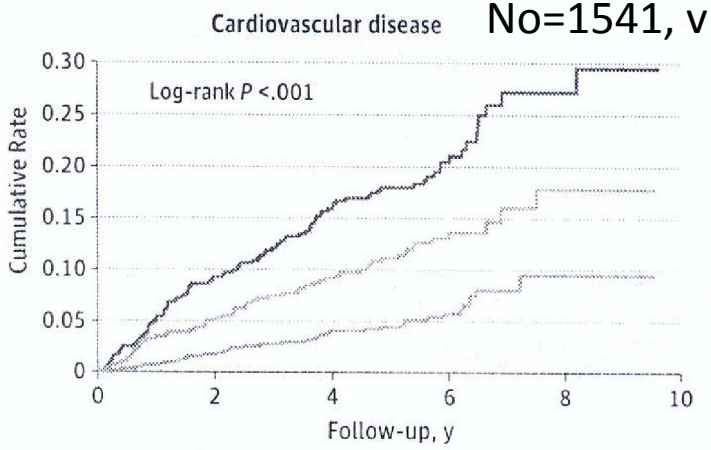


Klinički značaj vaskularnih kalcifikacija

HBS i CAC skor i rizik od CV Mb i Mt

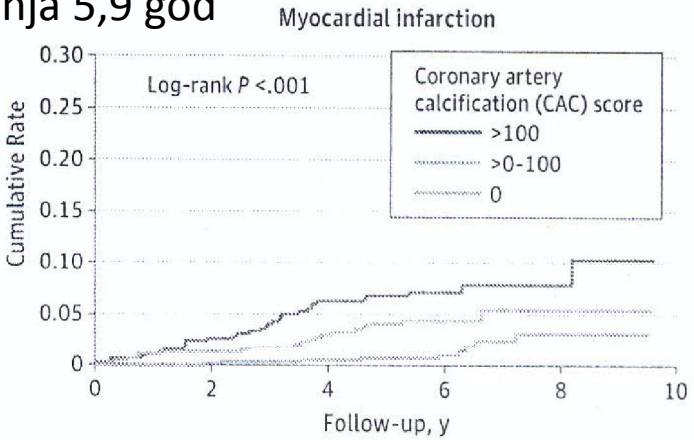
Figure 2. Kaplan-Meier Cumulative Event Rate of Cardiovascular Disease, Myocardial Infarction, Heart Failure, and All-Cause Mortality According to Coronary Artery Calcification Score Among Chronic Renal Insufficiency Cohort Participants Without a History of Cardiovascular Disease

No=1541, vreme praćenja 5,9 god



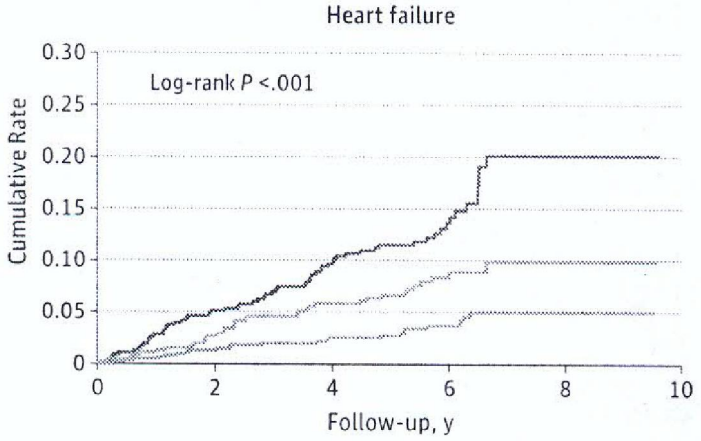
No. at risk

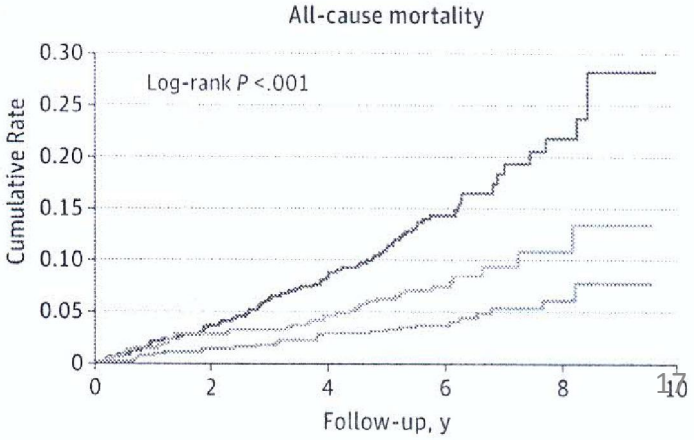
CAC score >100	463	402	338	142	41
CAC score >0-100	460	409	352	158	36
CAC score 0	618	579	506	270	70



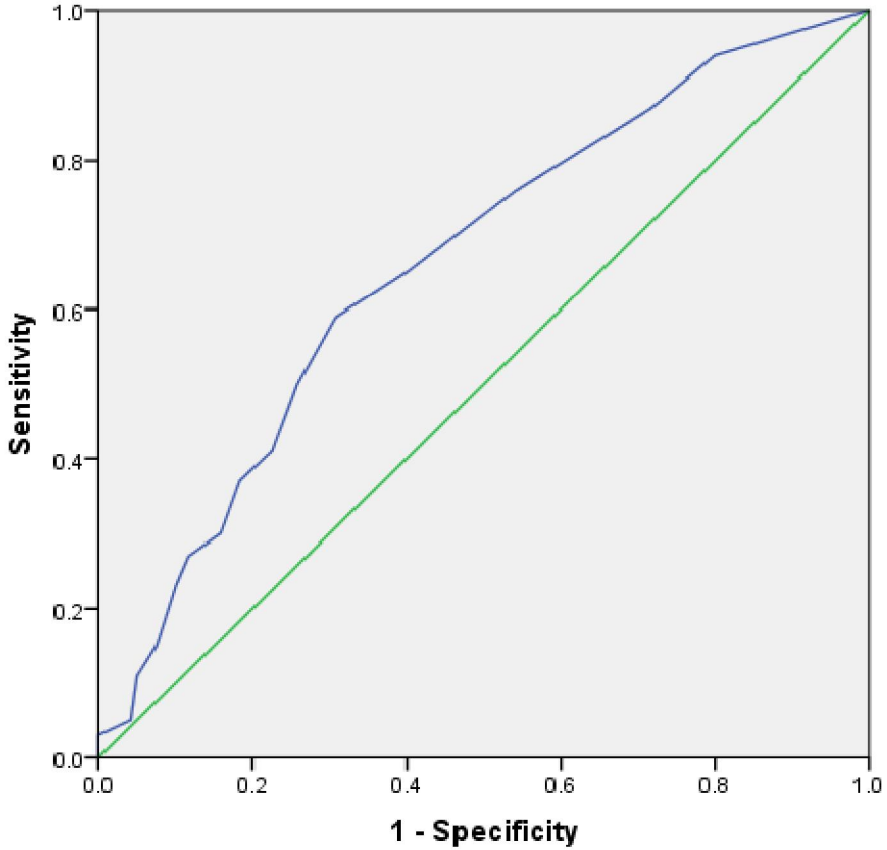
No. at risk

CAC score >100	463	428	368	165	47
CAC score >0-100	460	425	376	176	40
CAC score 0	618	584	520	283	74





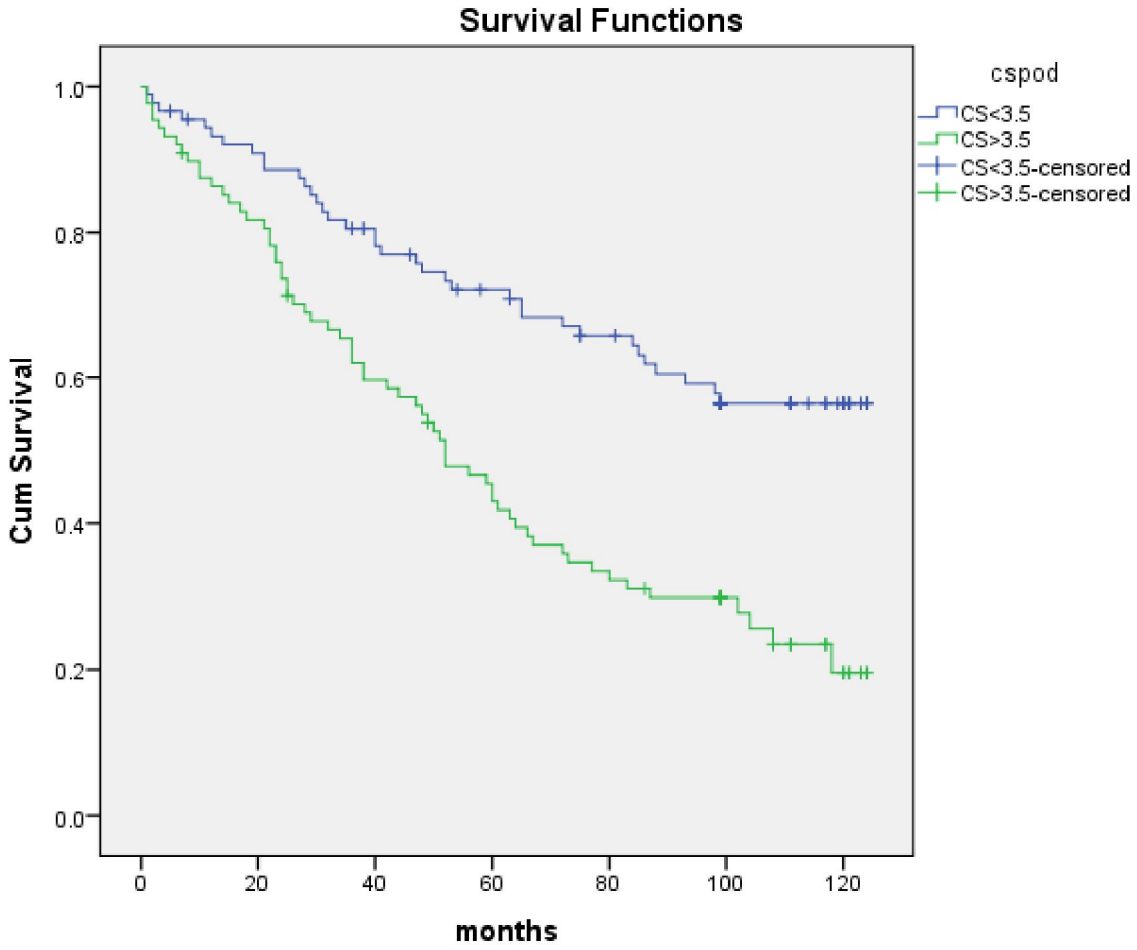
Receiver operating characteristic (ROC) kriva kompozitnog skora CV kalcifikacija i CV Mt



Cut-off: 3.5, Sensitivity 65.0 % , Specificity 68.8 %, AUC: 0.709 (0.632 - 0.786); p = 0.000;

Dugotrajno preživljavanje bolesnika u odnosu na kompozitni skor CV kalcifikacija

(cut off value – 3,5)



Kalcifikacije vaskularnog pristupa

Vascular access calcification was found in 49 of **212 hemodialysis patients** as measured by **plain X-ray** (arteriovenous fistula or synthetic graft) in two dimensions

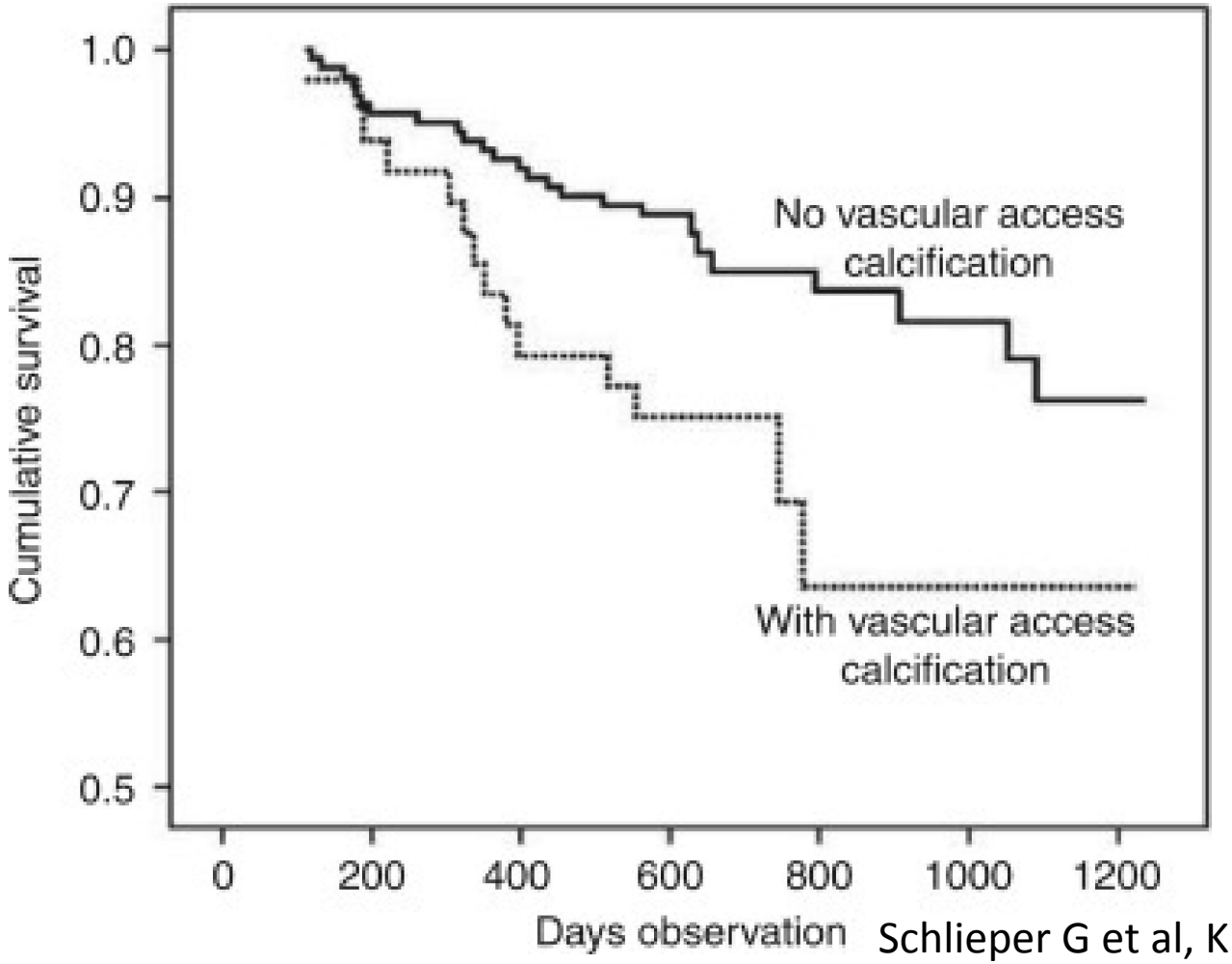
In the multivariate analysis (logistic regression), only **male gender** (OR 5.08, 95% CI 2.18–11.86, *P*=0.00016), **DM** (OR 4.57, CI 1.75–11.95, *P*=0.0019), and **dialysis vintage** (OR 1.15, CI 1.06–1.25, *P*=0.0012) remained significant predictors for VAC

Serum parameters were not independently related to access calcification

Schlieper G et al, KI 2008, 1582–1587

Kaplan–Meier analiza preživljavanja bolesnika u odnosu na kalcifikacije vaskularnog pristupa

Hazard ratio 2.14; 95% confidence interval 1.11–4.12; P=0.023



Schlieper G et al, KI 2008, 1582–1587

Efekat kalcifikacija vaskularnog pristupa na ukupan Mt (univarijantna i multivarijantna Cox regresiona analiza)

Vascular access calcification	HR	95% CI	P
Univariate analysis	2.14	1.11–4.12	0.023
Multivariate analysis	2.15	1.05–4.39	0.036

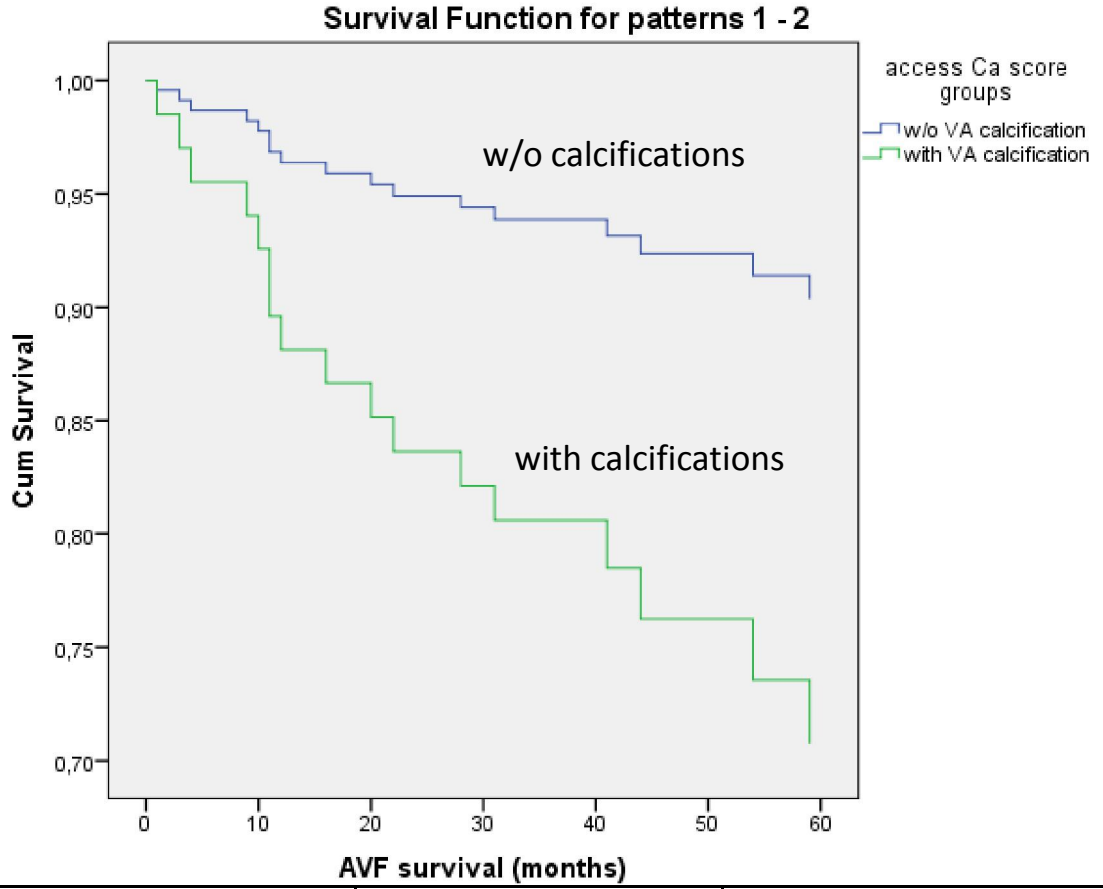
The hazard ratio of VAC for cardiovascular mortality was 1.79 (95% CI 0.81–3.97, *P*=0.14).

After adjustment for age, diabetes, dialysis vintage, *Kt*/*V*, and vascular disease

Schlieper G et al, KI 2008, 1582–1587

Efekat kalcifikacija u predelu AVF na njihovo preživljavanje

(Cox proportional analysis, censored for death and transplantation)

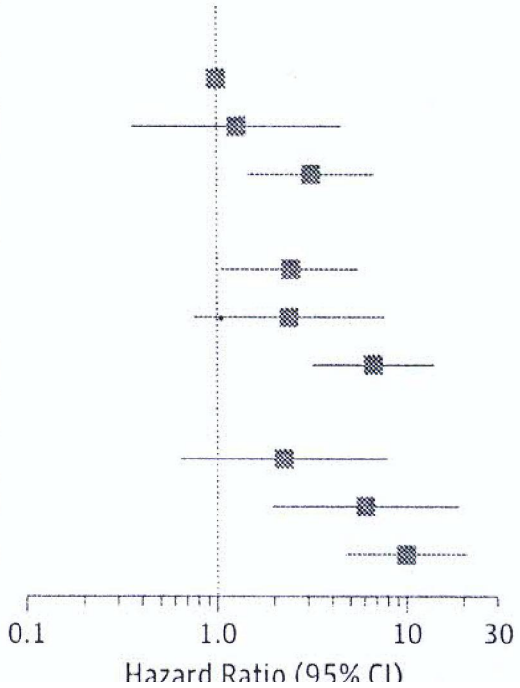


No of patients with functional AVF	Beginning of study	After 5 years follow-up
Group w/o VA calcification	**36**	**32**
Group with VA calcification	54	41

ACC/AHA aterosklerotic CVD risk score+ CAC skor = poboljšana predikcija CVD u HBS

Figure 3. Multivariable-Adjusted Hazard Ratios of Cardiovascular Disease by ACC/AHA Atherosclerotic Cardiovascular Disease Risk Score and CAC Score Among Chronic Renal Insufficiency Cohort Participants Without a History of Cardiovascular Disease

ACC/AHA Atherosclerotic Cardiovascular Disease Risk Score Category	Hazard Ratio (95% CI)
<5.0%	
CAC score 0	1 [Reference]
CAC score >0-100	1.28 (0.36-4.60)
CAC score >100	3.16 (1.46-6.84)
5.0%-7.5%	
CAC score 0	2.45 (1.05-5.71)
CAC score >0-100	2.41 (0.76-7.64)
CAC score >100	6.70 (3.18-14.10)
>7.5%	
CAC score 0	2.25 (0.64-7.93)
CAC score >0-100	6.09 (1.94-19.10)
CAC score >100	10.00 (4.76-21.00)



Chen J et al, JAMA Cardiology 2017; DOI: 10.1001/jamacardio.20170363

Nephrol Dial Transplant (2016) 31: 31–39
doi: 10.1093/ndt/gfv111
Advance Access publication 26 April 2015

Vascular calcification in chronic kidney disease: an update

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death.

In daily practice, assessment of cardiovascular calcifications in CKD patients cannot be recommended as routine diagnostics on a regular basis and should be reserved for particular situations (e.g. ultrasound of the iliac arteries for transplant listing, echocardiography to detect calcific aortic valve stenosis or when patients want to know their individual cardiovascular risk). In addition, we feel that in many patients a diagnostic workup for calcifications has little clinical consequence. Thus, in old dialysis patients with a relatively short life expectancy, the detection of cardiovascular calcifications usually does not alter their treatment. Vice versa in younger dialysis patients, in particular those waiting for a kidney transplant, every measure should be undertaken to prevent the development of calcification rather than wait for them to become detectable and to act only then.

Šta smo naučili

- Incidentni i prevalentni bolesnici pokazuju visok stepen kalcifikacija krvnih sudova
- Stepen kalcifikacija zavisi od vrste arterija i metode pregleda
- Skrining metoda(e) još uvek nisu standardizovane kao ni indikacije
- Pri skriningu u obzir treba uzeti:
  - Godine bolesnika i očekivani životni vek
  - Dijagnostičko/Terapijski target
  - Ugrožene (fokus grupe)

Šta smo naučili

- Na osnovu stečenih znanja, kalcifikacije utiču
  - Povećano KV oboljevanje
  - Smanjeno preživljavanje bolesnika
  - Skraćen vek vaskularnog pristupa
  - CVI? PVB?
- Terapijska strategija?
  - Ca u dijalizatu (1,25 i 1,375 mmol)
  - Vezivači P bez Ca
  - Kalcimimetici
  - Izbegavanje Vit K antagonista (Vit K2)
  - NaTS
- Preventivna strategija?

Značajne razlike izmedju preživelih i umrlih bolesnika

	Umrli od KVB No=100, 45 %	Preživeli No=120, 55 %	P
Composite VC score	6.2 ± 4.3	3.4 ± 3.6	p = 0.000
Adragao score	2 ± 6	1 ± 3	p = 0.003
PWV, m/s	10.2 ± 1.9	9.1 ± 1.98	p = 0.001
AGE, years	63. ± 9.8	53.9 ± 10.5	p = 0.000
Hypertension, yes	93	63	p = 0.023
HD, hours/week	12.0 ± 1.4	12.6 ± 1.3	p = 0.005
Kt/V	1.2 ± 0.15	1.34 ± 0.21	p = 0.001
CRP, mg/L	13.76 ± 23.57	4.95 ± 7.54	0.002
Fetuin A, g/L	0.51 ± 0.13	0.58 ± 0.12	0.002
uc MGP, nmol/L	176.48 ± 91.45	206 ± 109	0.048
Hemoglobin, g/dL	9.22 ± 1.55	9.71 ± 1.62	0.043

Od spektakulanog početka – 20 godina očekivanja rešenja