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DE MEDICINĂ ȘI FARMACIE
VICTOR BABEȘ | TIMIȘOARA

Circulating Kidney Injury Molecule-1 and chronic inflammation as risk factors of mortality in hemodialysis patients

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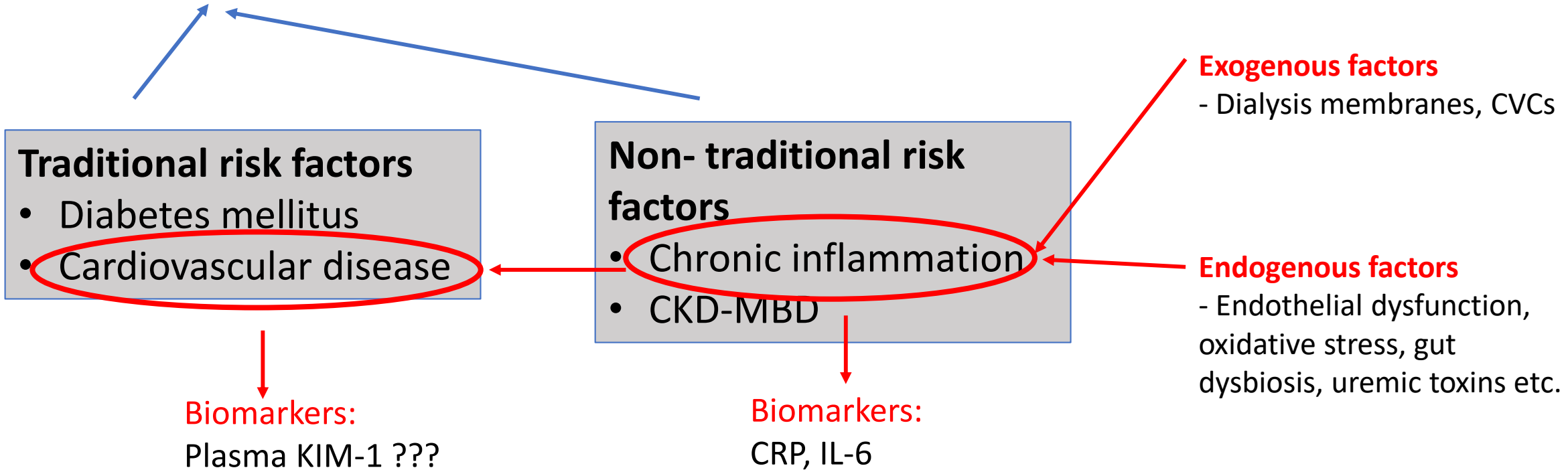
BACKGROUND

Hemodialysis dependent CKD patients have an increased risk of cardiovascular morbidity and mortality, but also a higher susceptibility to infections and malignancies, that are also contributing

→ **increased mortality**.



The aim of this study is to to assess the level of plasma Kidney Injury Molecule- 1 (KIM-1) and chronic inflammation as risk factors of mortality. .

Methods

Study group (CKD G5D)

63 patients

- Dialysis vintage 3.3+/- 1 years (1-5 years)
- Arterio-venous fistula 51: central venous catheter 12

Exclusion criteria: HFrEF (patients with EF<40%)

Control group (CKD)

52 patients

- CKD G1-5,
- mean eGFR 64.76+/- 32.69ml/min)

Baseline assessment

- Informed consent
- Medical history (medical records)
- Blood specimen collection (predialysis, fasting)
- Echocardiography (intradialytical)
- ECG (intradialytical)

- **Markers of inflammation** (CRP, IL-6)
- **Plasma KIM-1**

[Enzyme-linked immunosorbent assay (Elabscience, USA: Human KIM-1(Kidney Injury Molecule 1) ELISA Kit, Cat.no. E-EL-H6029]

- **Usual data**

Markers of anemia (complete blood count, serum ferritin, transferrin saturation- TSAT)
Serum Albumin

Mean values	Baseline patients under HD	Control group	p
Age (years)	60.1+/- 11.8	59.03+/- 14	0.65
Female: Male	21:42	32:29	NA
Plasma KIM1 (pg/ml)	403.8 +/- 546.8	217.48 +/- 267.10	0.02
IL-6 (pg/ml)	10.8 +/- 0.9	9.5+/- 7.6	0.18
CRP (mg/dl)	1.0+/- 0.9	1.28+/- 2.97	0.47

Methods

Study group
(CKD G5D)
63 patients

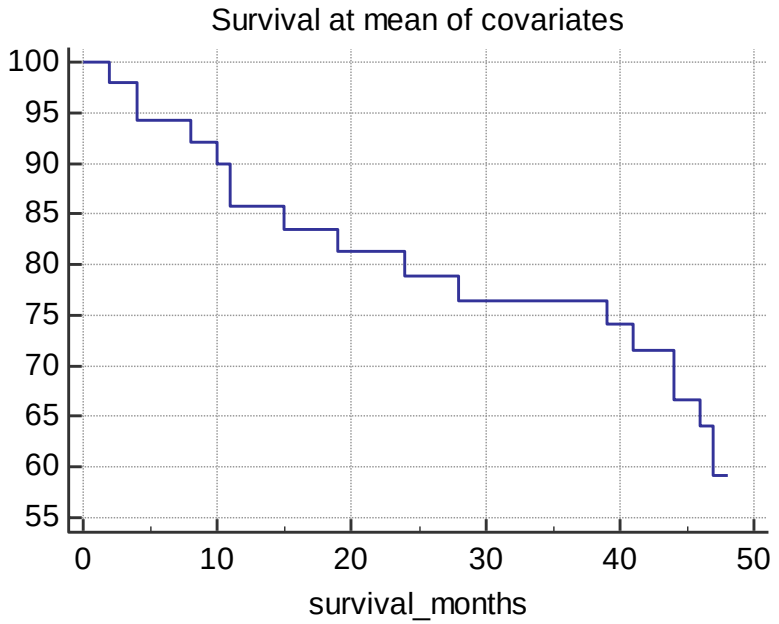
Follow up
31 patients

Follow-up at 48 months

- Reconsent
- Medical history (medical recods)
- Blood specimen collection (predialysis, fasting)
- Echocardiography (intradialytical)
- ECG (intradialytical)

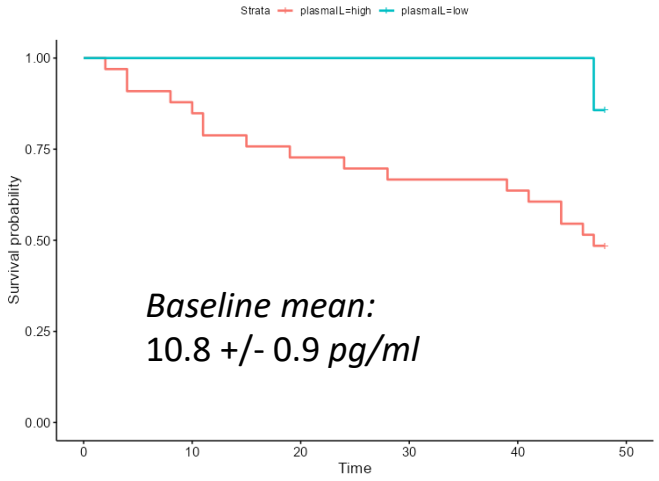
Retrospective mortality assessment at 24 and 48 months

After 24 months of follow up we found a mortality rate of 22.23%, while after 48 months the mortality rate was of 50.73%.

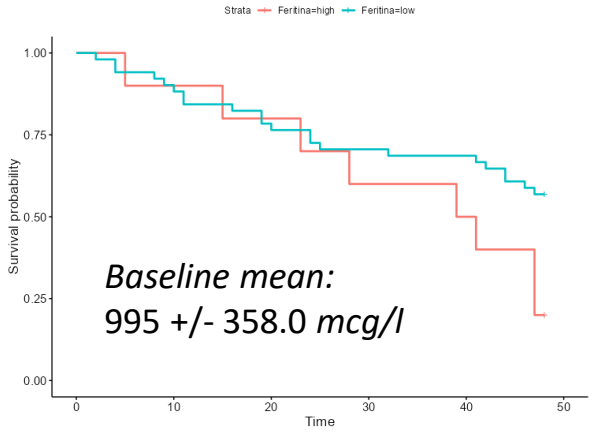


Results

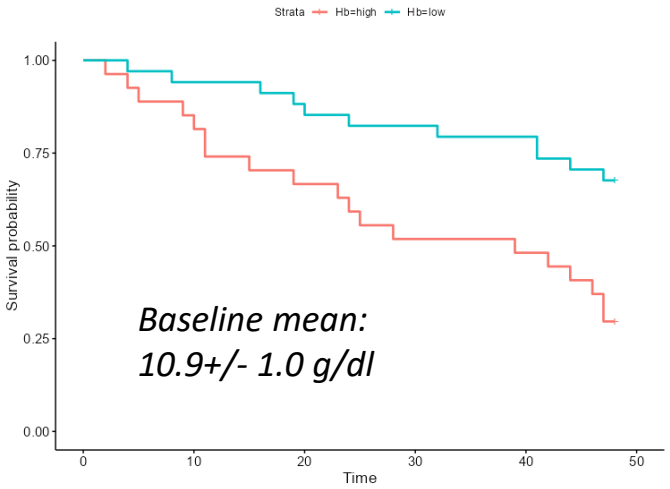
Factors associated with a significantly decreased survival in HD patients



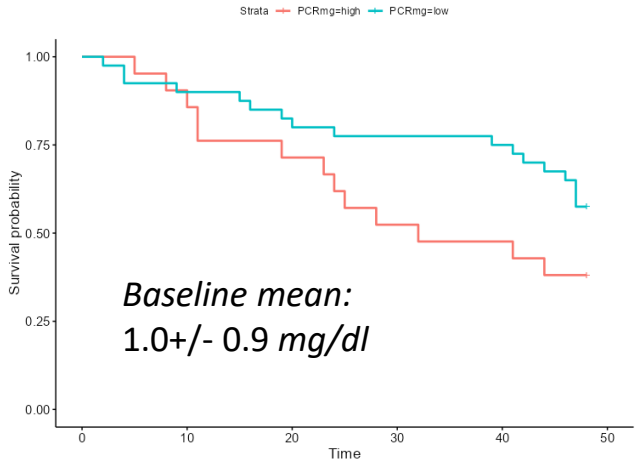
IL-6 >9.8 pg/ml (p=0.079)



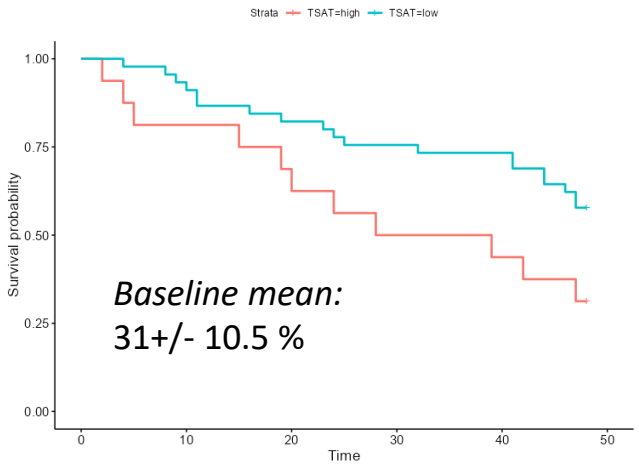
Ferritin>1360 mcg/l (p=0.063)



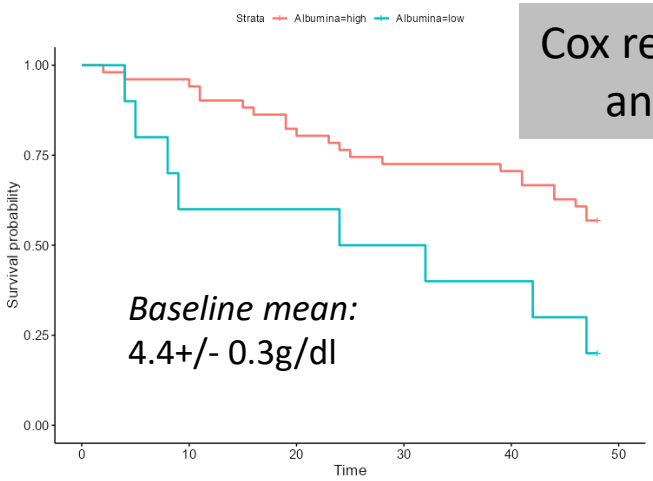
Hg>11g/dl (p=0.002)



CRP >1.22 mg/dl (p= 0.093)



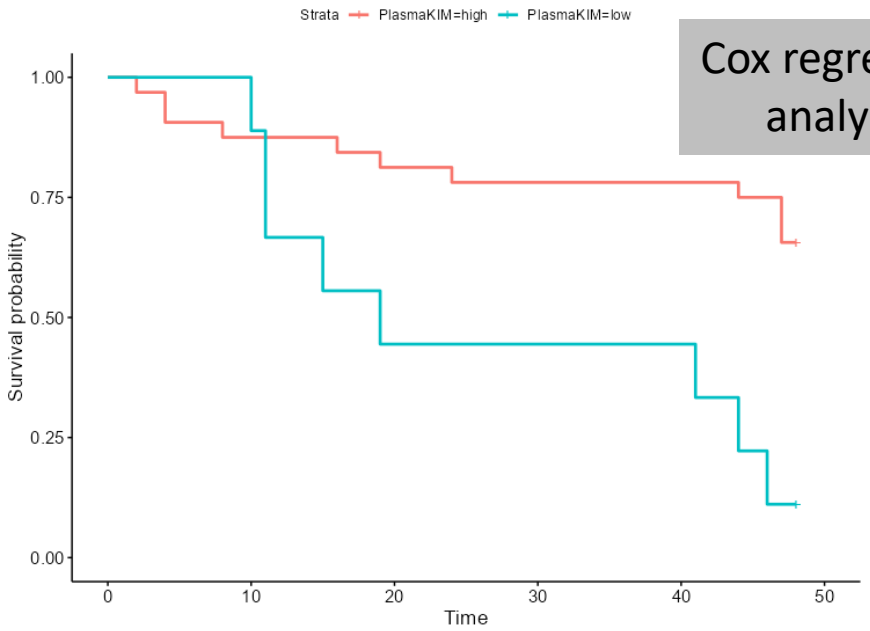
TSAT>35 % (p=0.038)



Albumin <4.04 g/dl (p=0.01)

Cox regression analysis

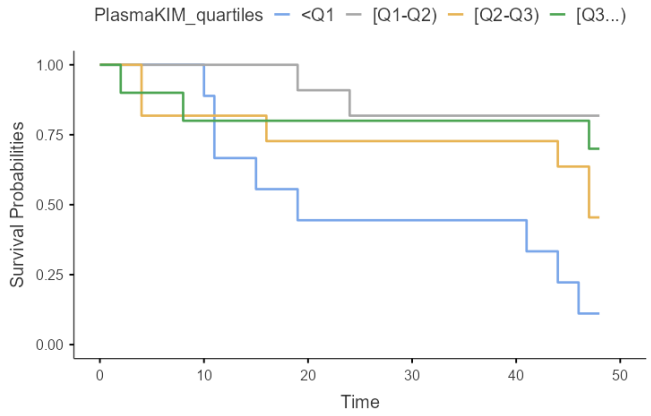
Plasma KIM-1

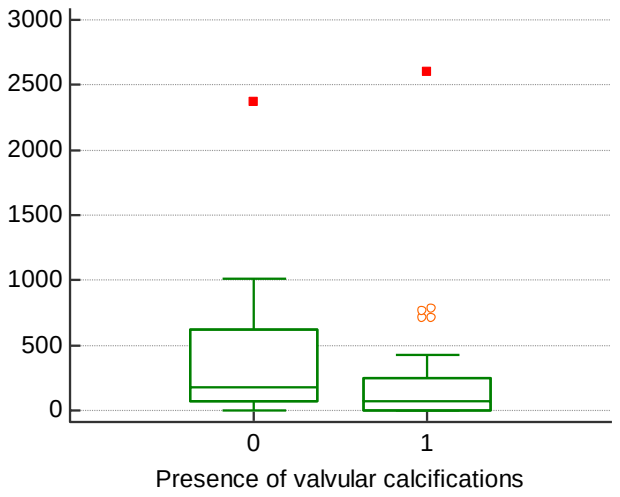


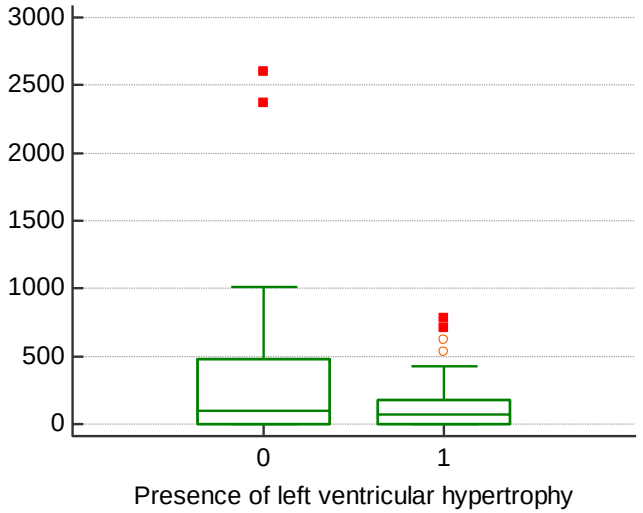
Cox regression analysis

	Plasma KIM-1
Hemoglobin	R=-0.5; p=0.01
Hematocrit	R=-0.5; p=0.01
CRP	R=0.28; p=0.02
IL6	R=0.35; p=0.005
Valvular calcifications (absence vs. presence)	462.5+/- 648.8 vs. 210.0 +/- 414.1 (NS)
Left ventricular hypertrophy (absence vs. presence)	432.1+/- 690.2 vs. 155.5 +/- 214.0 (p=0.02)
Ejection fraction	NS

Significantly decreased survival in patients with low KIM-1<81.98 pg/ml (p<0.001)





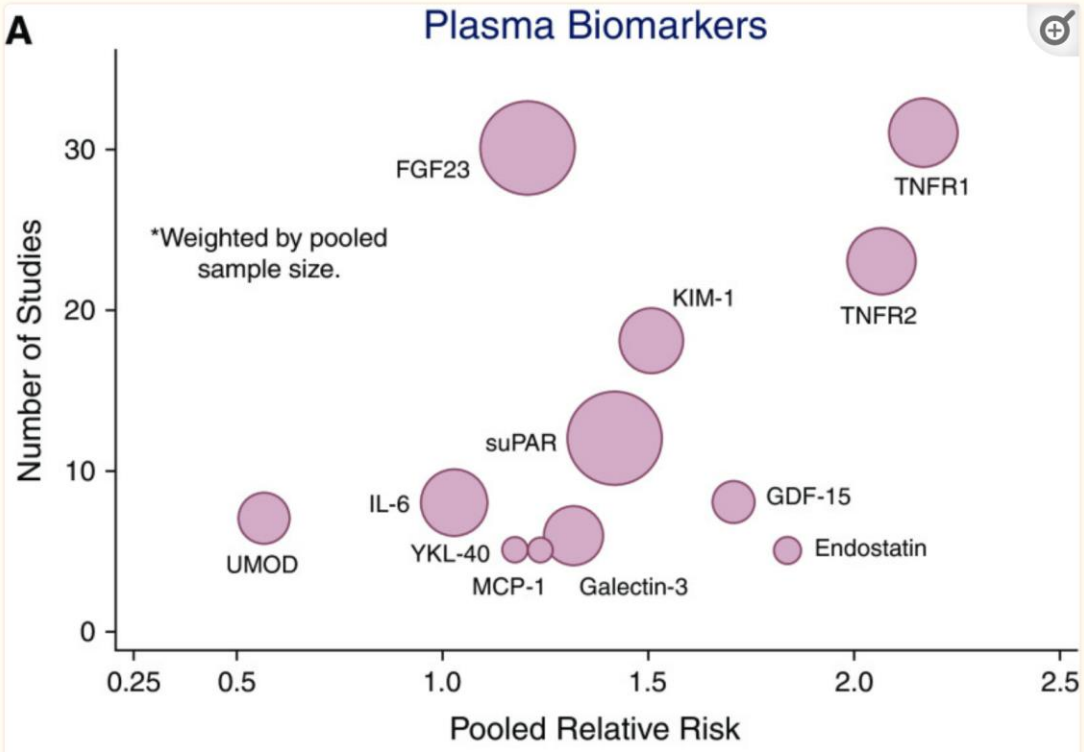


Discussion- The importance of plasma KIM1

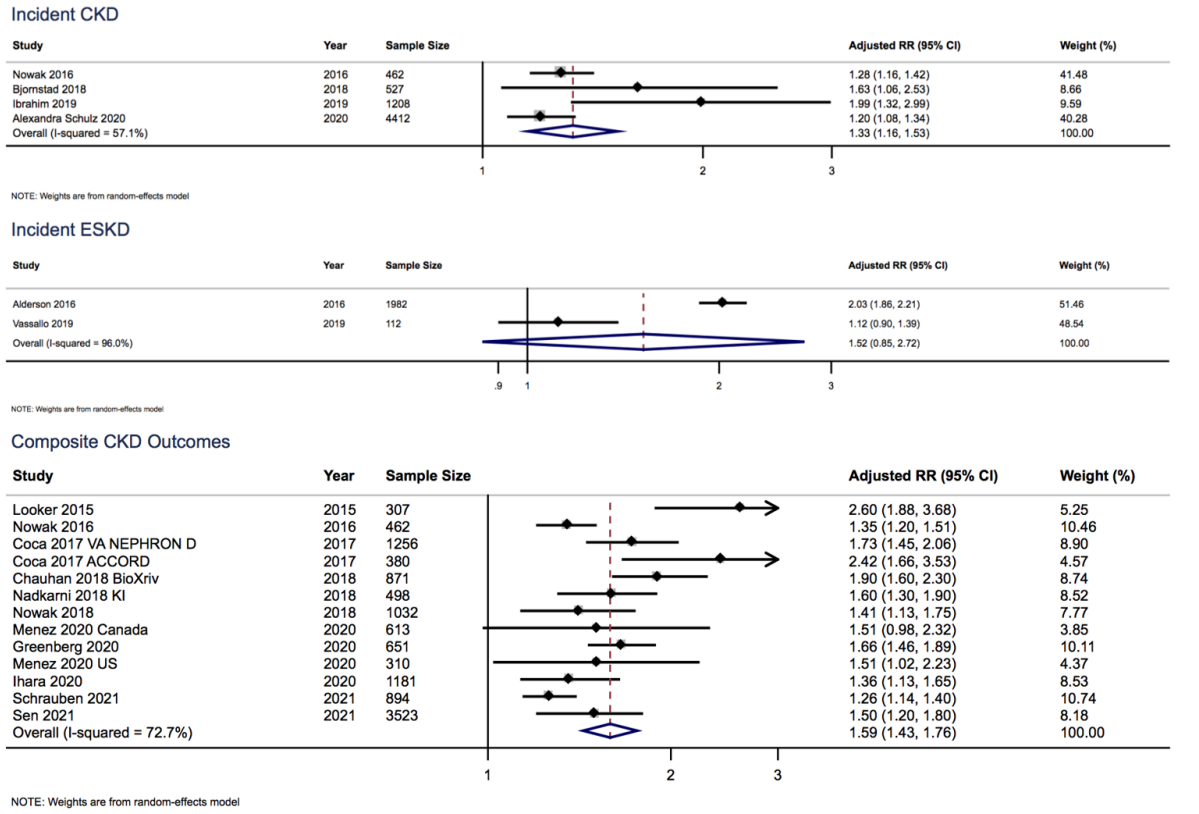
- **Urinary KIM-1 –** *marker of tubular injury*
- **Plasma KIM-1- ???**

- associated with glomerular function→ association with decreasing GFR

- associated with heart failure, higher BMI, diabetes, dyslipidaemia, and hypertension.



An analysis of the relative risk for different biomarkers for the prognosis of **CKD outcomes** (CKD incidence, progression, or incident ESKD)



Meta-analysis: plasma KIM-1→ 18 studies/ 20,905 pooled study participants

[Liu C. et al. JASN 2022]

Discussion- Plasma KIM1 as a cardiovascular risk/ mortality marker

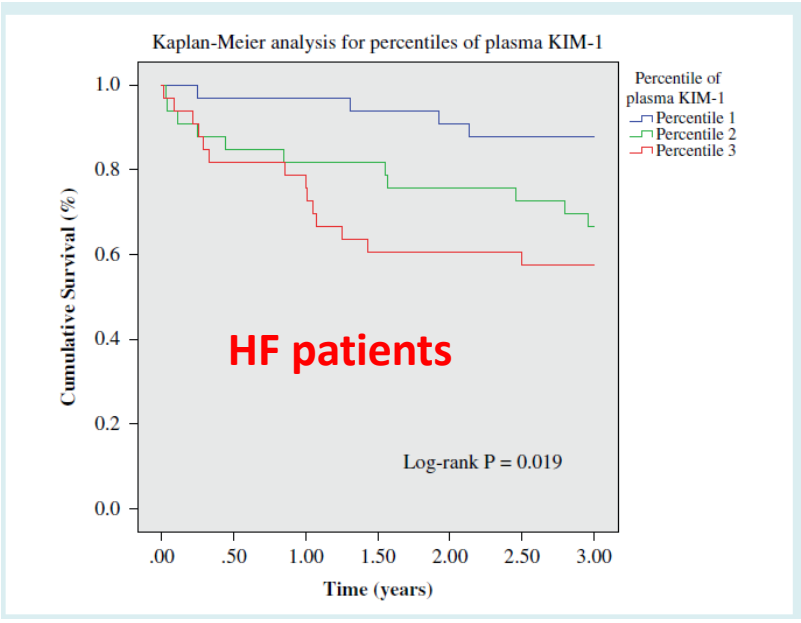
European Journal of Heart Failure (2016) 18, 641–649
doi:10.1002/ejhf.426

RESEARCH ARTICLE

Plasma kidney injury molecule-1 in heart failure: renal mechanisms and clinical outcome

Johanna E. Emmens[1], Jozine M. ter Maaten[1], Yuya Matsue[1], Marco Metra[2], Christopher M. O'Connor[3], Piotr Ponikowski[4], John R. Teerlink[5], Gad Cotter[6], Beth Davison[6], John G. Cleland[7], Michael M. Givertz[8], Daniel M. Bloomfield[9], Howard C. Dittrich[10], John Todd[11], Dirk J. van Veldhuisen[1], Hans L. Hillege[1,12], Kevin Damman[1], Peter van der Meer[1], and Adriaan A. Voors[1]*

120 stable outpatients with systolic heart failure- from the PROTECT study



JACC: HEART FAILURE VOL. 3, NO. 10, 2015
© 2015 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION ISSN 2213-1779/$36.00
PUBLISHED BY ELSEVIER INC. http://dx.doi.org/10.1016/j.jchf.2015.06.006

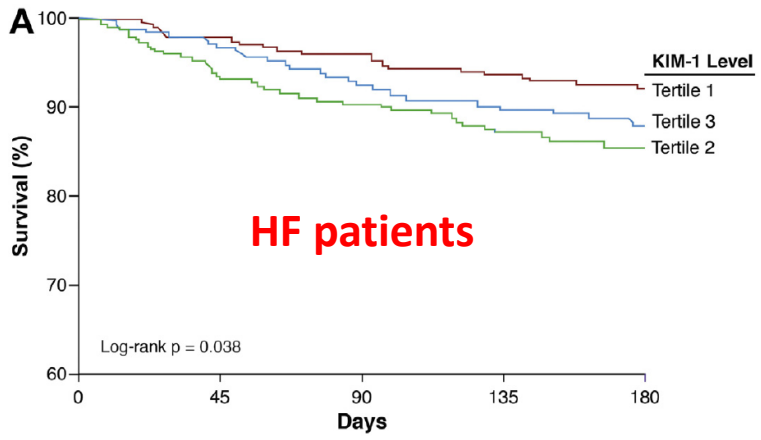
Circulating Kidney Injury Molecule-1 Levels in Acute Heart Failure

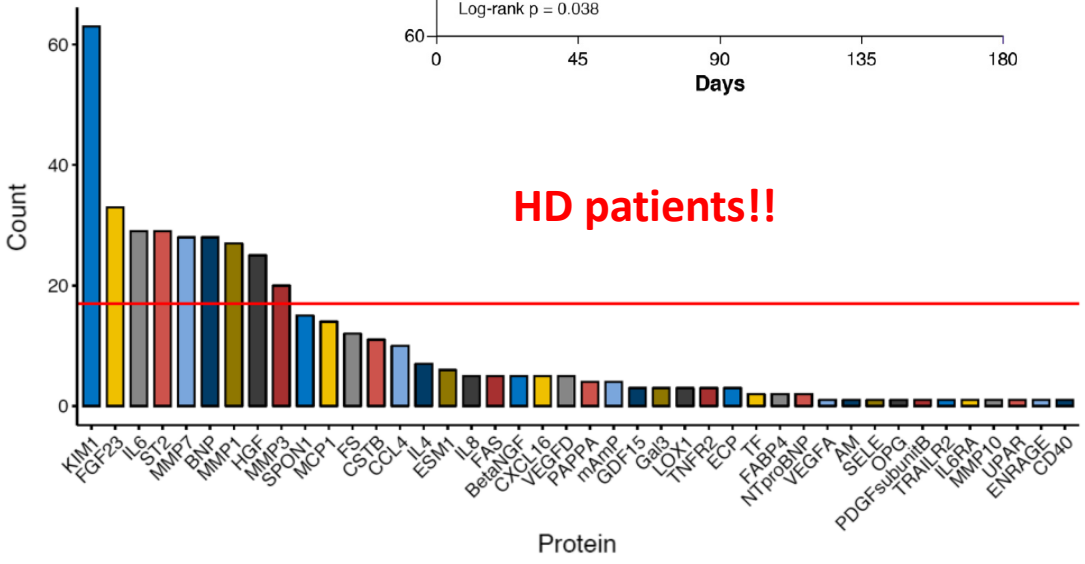
Insights From the ASCEND-HF Trial (Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure)

Justin L. Grodin, MD,* Antonio L. Perez, MD, MBA,*† Yuping Wu, PhD,‡ Adrian F. Hernandez, MD, MHS,‡ Javed Butler, MD,§ Marco Metra, MD,‖ G. Michael Felker, MD,‡ Adriaan A. Voors, MD,¶ John J. McMurray, MD,# Paul W. Armstrong, MD,** Robert M. Califf, MD,‡ Randall C. Starling, MD, MPH,† Christopher M. O'Connor, MD,‡ W.H. Wilson Tang, MD*

874 patients from the ASCEND-HF study

Circulating KIM-1 at baseline and during hospitalization was not associated with adverse clinical outcomes in acute decompensated heart failure





Journal of Nephrology (2019) 32:111–119
https://doi.org/10.1007/s40620-018-0556-5
ORIGINAL ARTICLE

Circulating proteins as predictors of cardiovascular mortality in end-stage renal disease

Tobias Feldreich[1,2,3] · Christoph Nowak[2] · Tove Fall[3] · Axel C. Carlsson[2,3] · Juan-Jesus Carrero[4] · Jonas Ripsweden[5] · Abdul Rashid Qureshi[6] · Olof Heimbürger[6] · Peter Barany[6] · Peter Stenvinkel[6] · Nicolas Vuilleumier[7,8] · Philip A. Kalra[9,10] · Darren Green[9,10] · Johan Ärnlöv[1,2]

Received: 7 February 2018 / Accepted: 10 September 2018 / Published online: 29 November 2018

Analysis of three cohorts of HD patients- plasma KIM1 – as top predictor of cardiovascular mortality

Conclusion

- Similar inflammation in the HD patients and in the ND CKD patients control group
- In our study, increased **inflammation** in hemodialysis patients was associated to a significantly higher risk of mortality. Consistent with previous studies: *Biomarkers of inflammation IL-6 and CRP show a great predictive power for all-cause and CV death in ESRD patients*.
- Statistically significant correlation between inflammation and plasma KIM1
- **Plasma KIM1** was significantly higher compared to the control group (ND CKD patients)
- Surprisingly, low levels of **plasma KIM1** were associated with some cardiovascular changes and also to an increased risk of mortality (*at 4 years, not after one year*).
- Additional studies are needed to establish the utility of the biomarker plasma KIM1 in hemodialysis patients

Thank you!