

Biomarkers in the Assessment of Congestive Hear**t** Failure

Mid-Regional pro-Adrenomedullin (MR-proADM) vs BNP & NT-proBNP as Prognosticator in Heart Failure Patients:

Results of the BACH Multinational Trial

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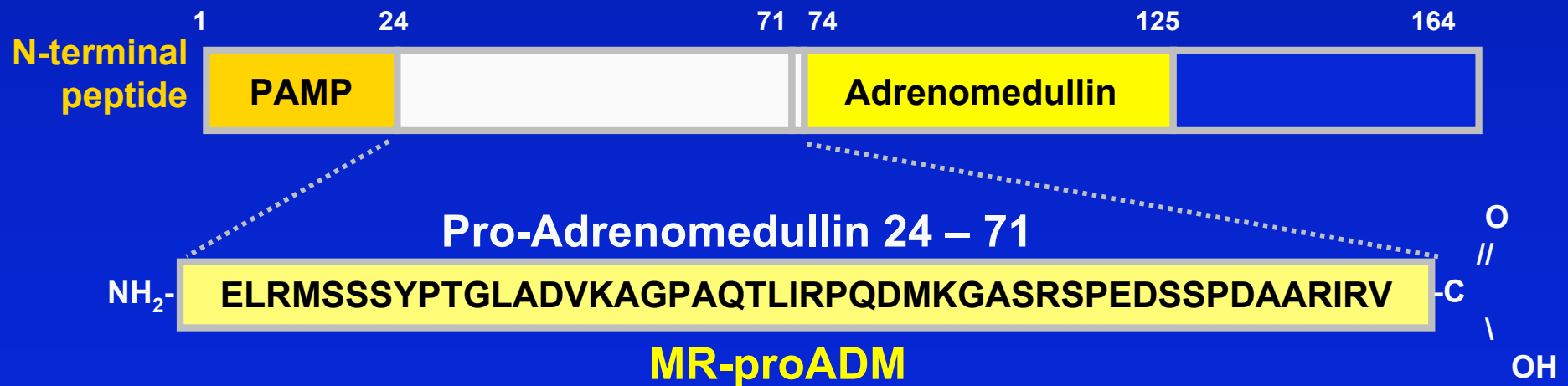
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Disclosure Stefan D Anker:

Consulting: BRAHMS Aktiengesellschaft
Research Support: BRAHMS Aktiengesellschaft, Biosite/Inverness

Adrenomedullin:

- Peptide hormone consisting of 52 amino acids
- vasodilator, important for microcirculation & endothelial (dys)function
- quantification of ADM could be helpful in cardiac diseases (CHF, MI, ACS,...) as well as in others (like infections & kidney disease)
- ADM measurement is not suitable for clinical routine diagnosis assessment due to its *ex vivo* instability (immediate binding to receptors, 22min half-life time)
- mid regional pro-ADM (MR-proADM) is a stable and reliable surrogate marker for ADM release

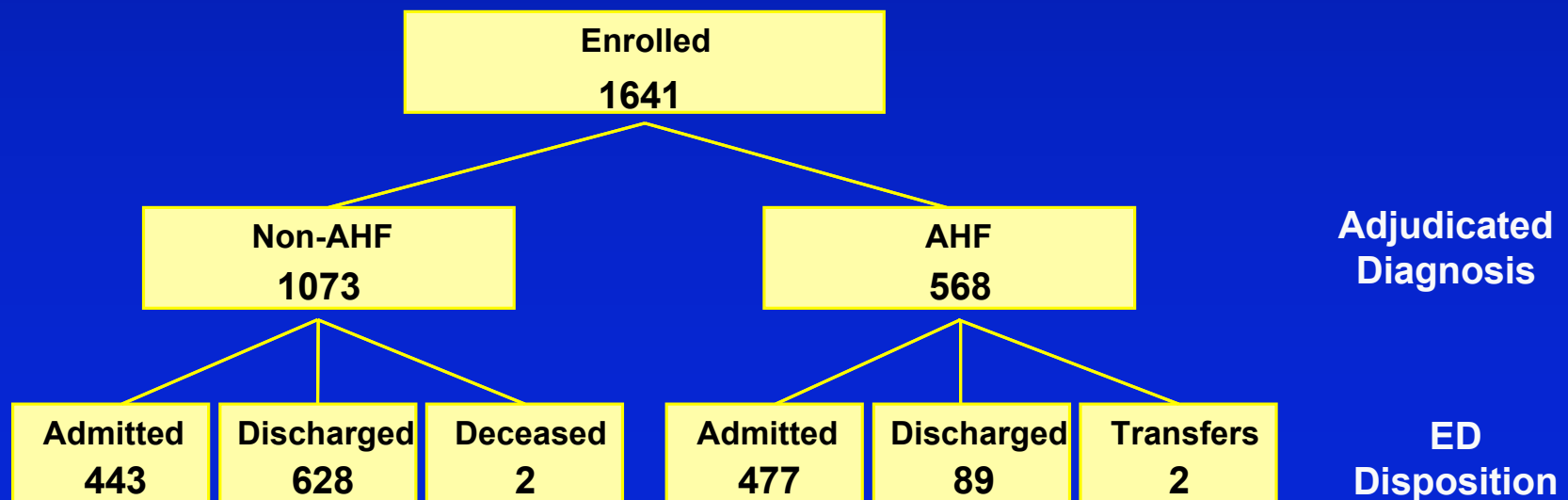


QUESTIONS:

- What is the preferred (best) clinical tool for prognostication in HF?
- Does measuring of MR-proADM, better predict prognosis than BNP or NT-proBNP?
- **1° endpoint:** Is MR-proADM superior in predicting 90-day mortality compared to BNP?

PATIENTS & FOLLOW-UP

- Patients included who presented to ED with SOB not from trauma, or obvious MI & not on dialysis – then MD assessment for heart failure
- Follow-up for 90 days for survival, main outcome “All cause mortality within 90 days”
- 15 enrolling centers (US, Europe, NZL), recruiting 1641 patients.
- **N=1641, Age 64±17 yrs, Female 48%, History of HF 36%, prior AMI 19%, Diabetes 29%, BMI 29±8 kg/m²**



Prognostic Accuracy: MR-proADM 73.5% vs BNP 60.8% (p<0.001)
 vs NT-proBNP 63.6% (p<0.001)

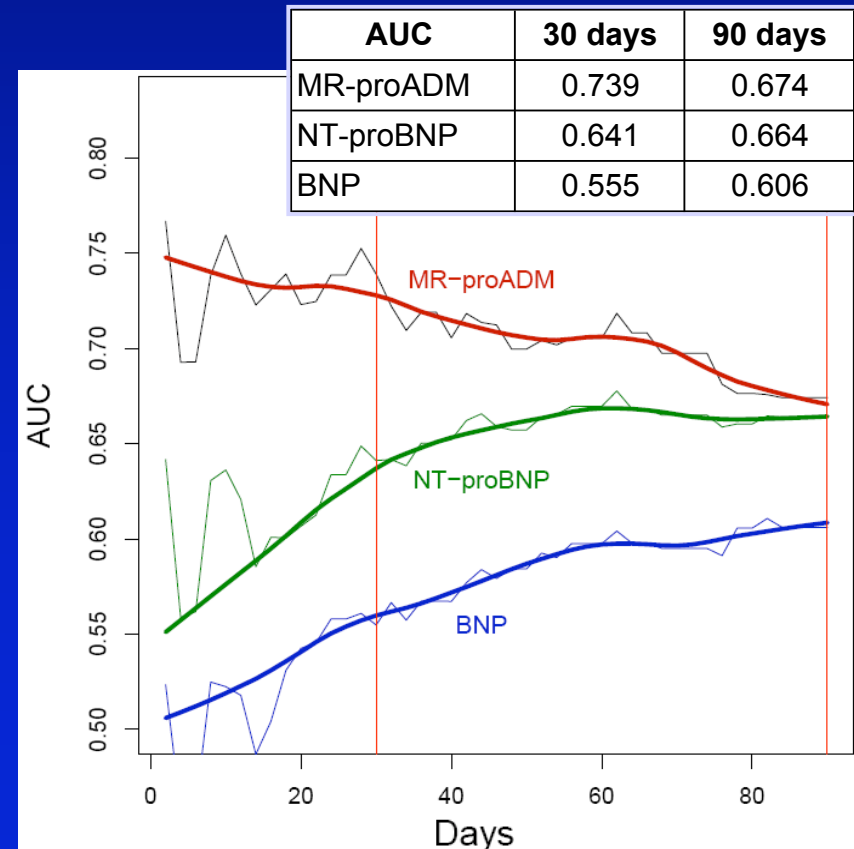
Results of Cox regression with continuous predictors:

MR-proADM is superior to BNP and NT-proBNP for predicting 90-day mortality (Cox regression).

Predictor (univariate)	Chi ² Statistic	p	c index
log MR-proADM	31.0	<0.001	0.669
log BNP	7.1	0.008	0.596
log NT-proBNP	17.1	<0.001	0.654

MR-proADM adds significantly to BNP or NT-proBNP, however neither BNP nor NT-proBNP add to MR-proADM.

	Chi ² Statistic	p
adding MR-proADM to BNP	23.9	<0.0001
adding MR-proADM to NT-proBNP	15.3	<0.0001
adding BNP to MR-proADM	0.0	0.906
adding NT-proBNP to MR-proADM	1.1	0.291



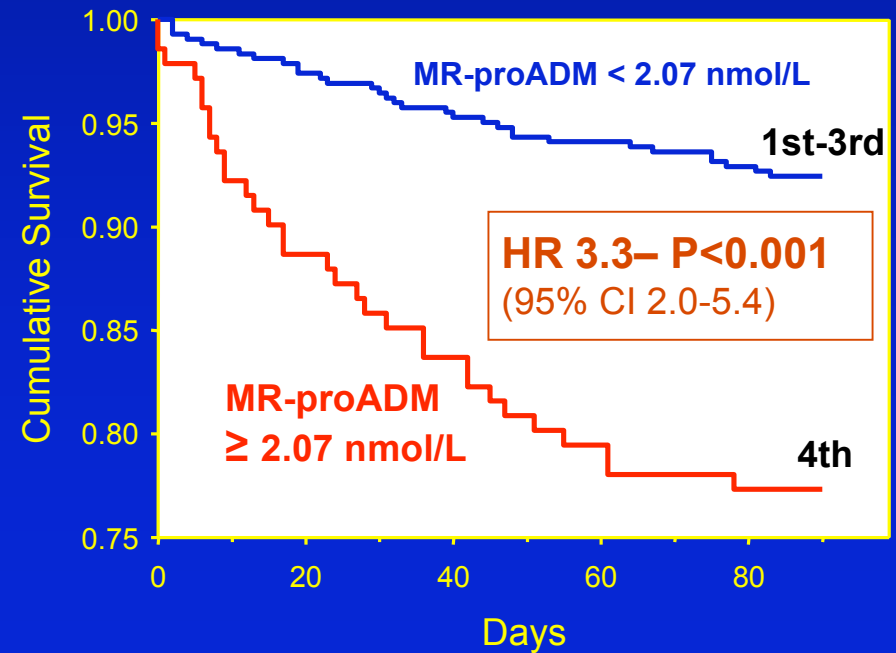
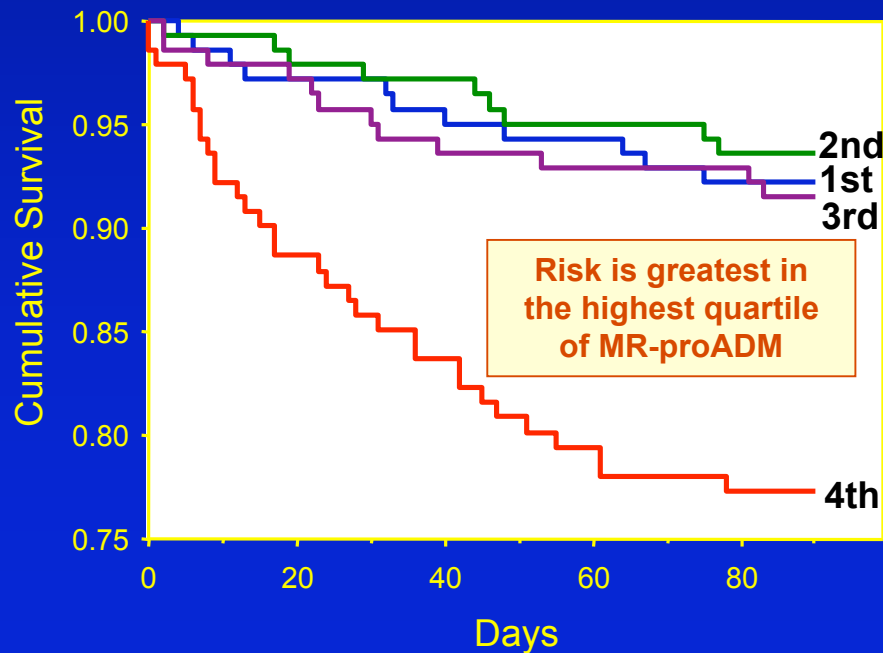
Troponin values were available in 511 of 568 HF patients – in 107 (20.9%) patients they were elevated (i.e. above local normal range). Shown are results of 3-marker models.

Conclusion: MR-proADM provides independent prognostic utility, but BNP & NT-proBNP do not.

Predictor (multivariable)	HR	95% CI	p
log MR-proADM	8.5	2.7-26.5	<0.001
log BNP	0.9	0.5-1.9	0.812
Elevated Tn	2.6	1.5-4.5	<0.001

Predictor (multivariable)	HR	95% CI	p
log MR-proADM	7.5	2.1-26.4	<0.001
log NT-proBNP	1.1	0.6-2.2	0.295
Elevated Tn	2.6	1.5-4.4	<0.001

Analysis of MR-proADM quartiles:



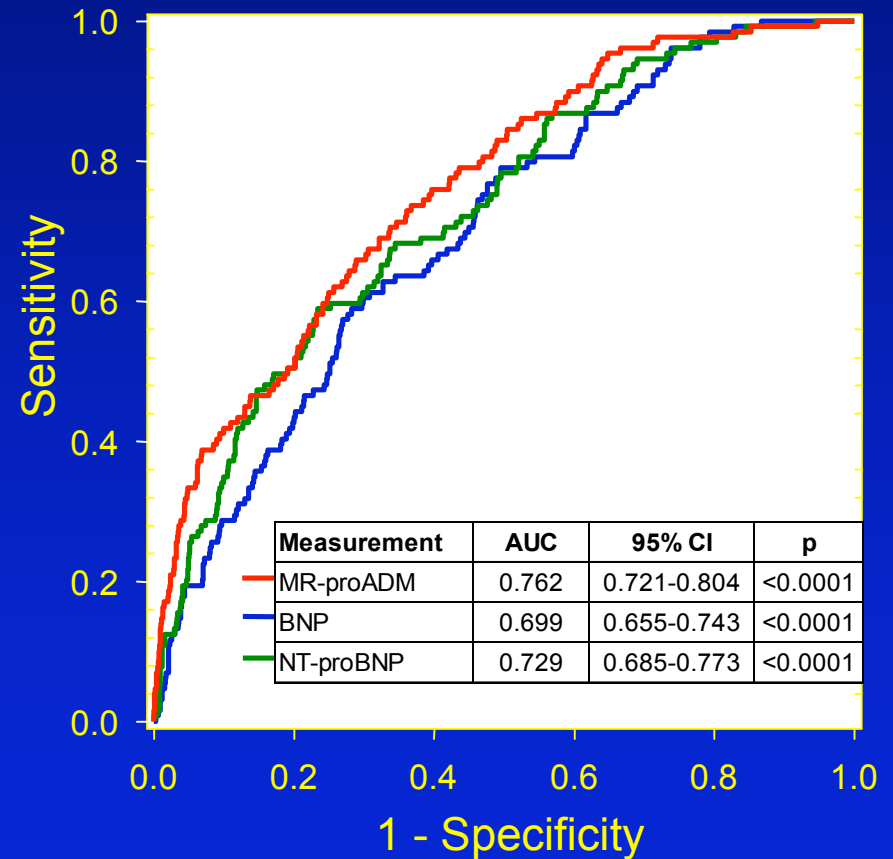
Cox Regression Analysis:

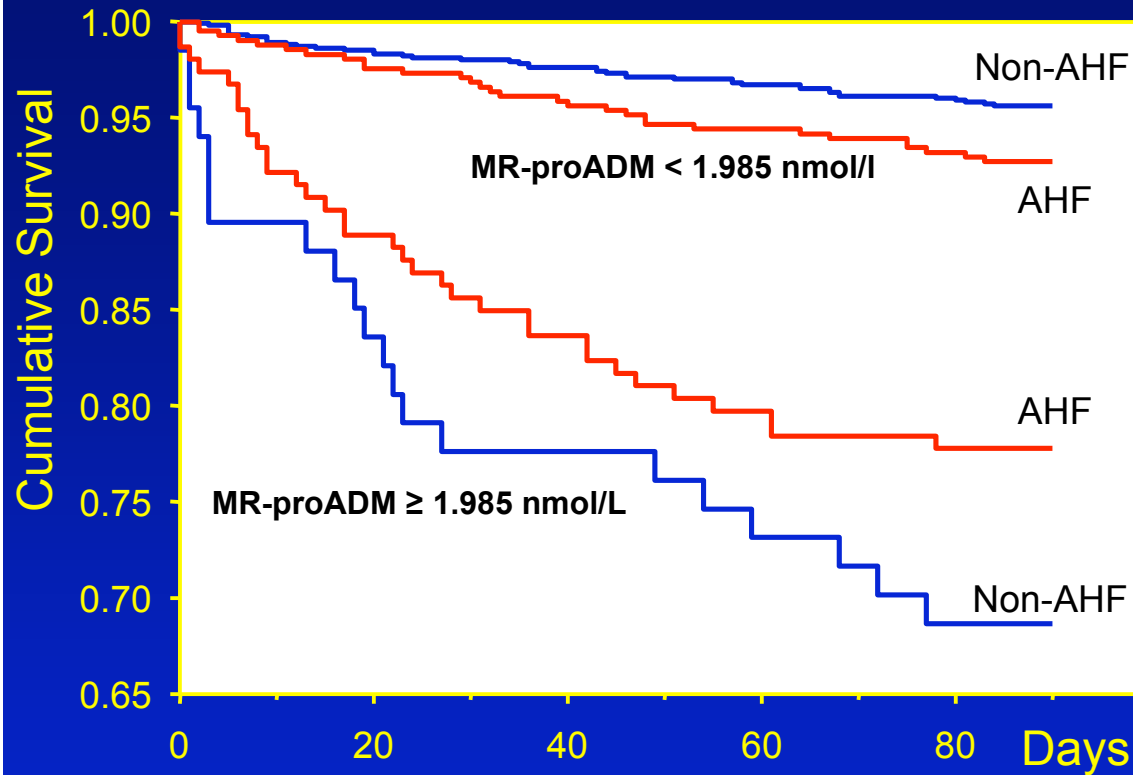
MR-proADM performs well in all SOB patients.

Predictor (univariate)	Chi ² Statistic	p	c index
log MR-proADM	129.5	<0.0001	0.755
log BNP	60.1	<0.0001	0.691
log NT-proBNP	83.7	<0.0001	0.721

MR-proADM is superior to BNP and NT-proBNP.

	Chi ² Statistic	p
adding MR-proADM to BNP	69.4	<0.0001
adding MR-proADM to NT-proBNP	46.6	<0.0001
adding BNP to MR-proADM	0.1	0.731
adding NT-proBNP to MR-proADM	1.5	0.229





AHF patients		
	AUC (90 days)	optimal cut point from ROC
MR-proADM	0.674	1.985 nmol/l

Elevated MR-proADM is strongly prognostic in patients with and without AHF – even more so in non-AHF than in AHF (interaction p=0.005).

Diagnosis	MR-proADM	HR	95% CI	p
Non-AHF	low < 1.985	1	reference	
	high ≥ 1.985	8.6	5.1-14.4	<0.001
AHF	low < 1.985	1.7	1.1-2.7	0.027
	high ≥ 1.985	5.7	3.6-8.9	<0.001

- MR-proADM is a strong prognosticator in patients with AHF and in patients presenting with SOB.
- MR-proADM is superior to BNP or NT-proBNP for predicting 90-day mortality, both in AHF as well as in all ED pts with SOB.
- All these results are unaffected by adjustment for Troponin.
- MR-proADM is particularly strong in predicting short-term prognosis within 4 weeks after assessment.
- MR-proADM can significantly improve risk stratification over BNP or NT-proBNP.
- Assessment of MR-proADM can help to identify patients who should “move to the front of the line” of medical care.