

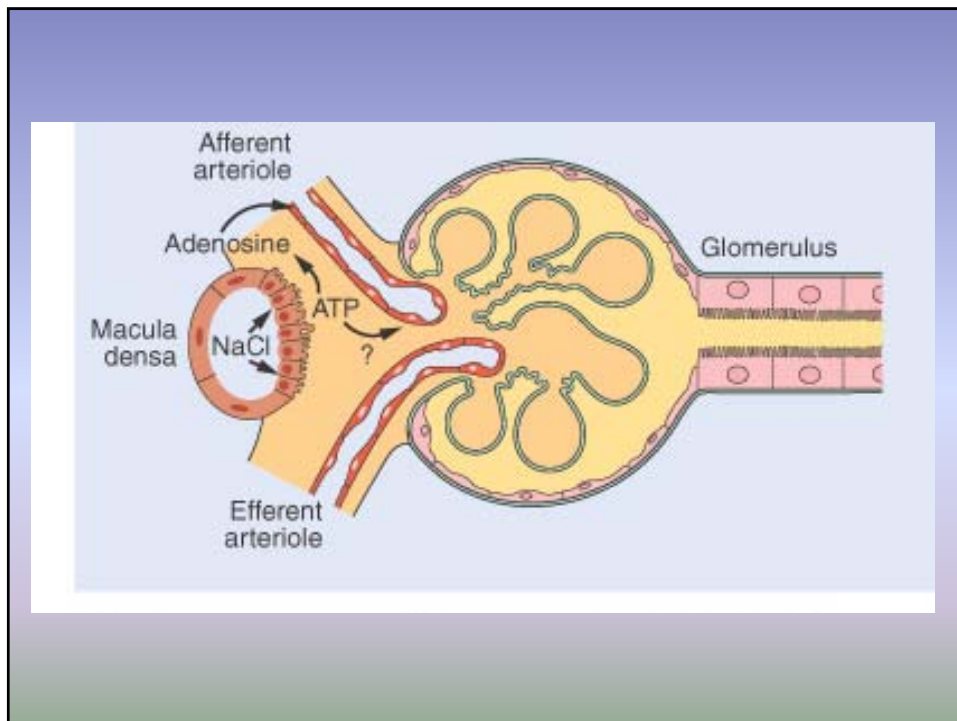
***Should I Continue ACE-
I/ARBs Prior to Surgery
or Intravenous Contrast
Studies?***

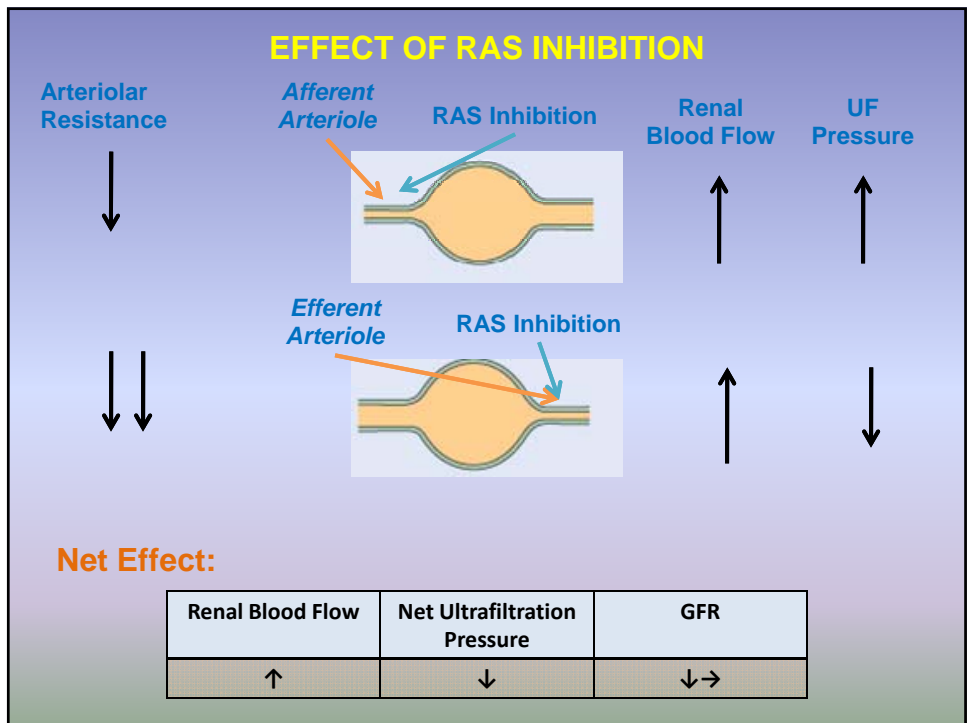
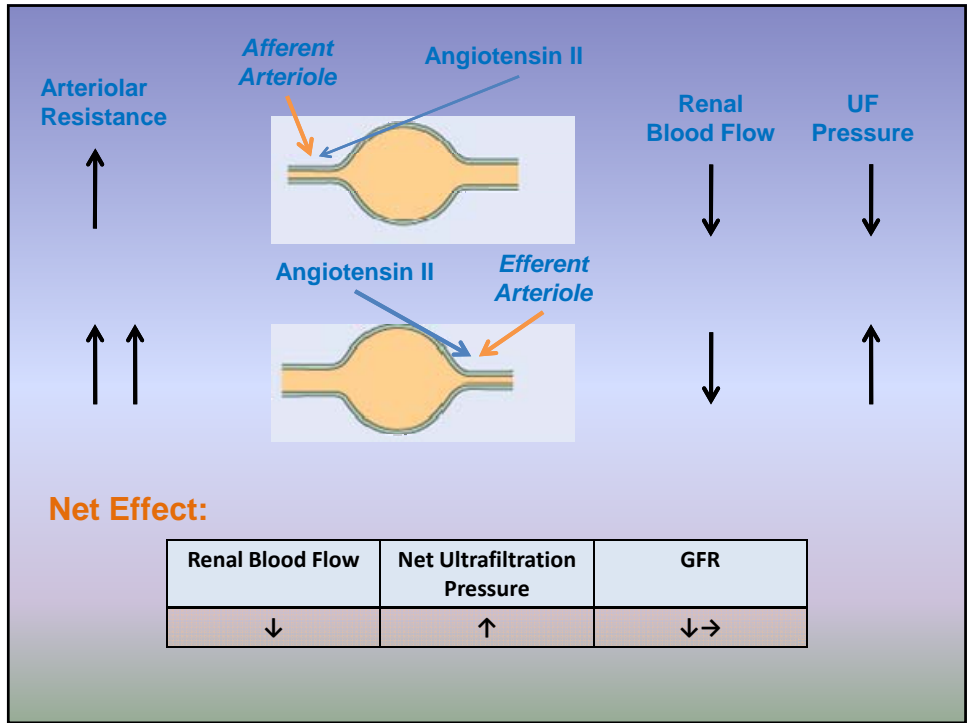
ASN
Tomas Berl, MD
November 18, 2010

Outline

- **The physiology underlying the question**
- **What is the data?**
- **Conclusions**

**Effect of Angiotensin II and
angiotensin II inhibition on
glomerular hemodynamics and renal
blood flow**





The Data (penia)

Cardiac Surgery

Haemodynamic and renal effects of intravenous enalaprilat during coronary artery bypass graft surgery in patients with ischaemic heart dysfunction

Ryckwaert F, et al. *Br J Anaesth* 86: 169-175, 2001

Results

	ACEI Group n=7	Control Group n=7	p
CI L/min/m ²	3.0	2.3	<0.05
RPF ml/min	605 ± 154	402 ± 87	<0.05
Ccr ml/min	142 ± 25	62 ± 11	<0.05

Conclusion:

Renal perfusion and renal function are well-maintained by ACE Inhibition

Ryckwaert F, et al. *Br J Anaesth* 86: 169-175, 2001

**Beneficial hemodynamic
and renal effects of
intravenous enalaprilat
following coronary artery
bypass surgery
complicated by left
ventricular dysfunction**

Wagner F, et al. *Crit Care Med* 31 (5):1421-1428, 2003

Who was studied?

40 patients with LVEF < 35%

How?

Placebo control double blind. Enalapril vs. placebo during CABG

Results

Creatinine Clearance (ml/min)

	Baseline	72 h	p
Placebo	76	72	
Enalaprilat	66	80	0.009

Conclusion: Renal function improved following CABG

Preoperative Angiotensin- Converting Enzyme Inhibitors and Acute Kidney Injury After Coronary Artery Bypass Grafting

Benedetto U, et al. *Ann Thorac Surg* 86:1160-1166, 2008

Who was studied?

**536 patients who underwent CABG on
cardio-pulmonary bypass**

How?

**Prospective multivariate analysis with
propensity scoring**

AKI: 50% decrease in GFR

Results

	Not on ACE	On ACE	p
n=	255	281	
% AKI	12.2	6.4	0.02
Dialysis	6.3	2.4	0.03

Results

Multivariate Logistic Regression Analysis

	OR	95% CI	p
ACE	0.48	0.23-0.77	0.04
IABP	8.1	2.75-24.2	0.0001

Conclusion

Preoperative ACE are associated with REDUCED rate of AKI after on-pump CABG surgery

**Preoperative Angiotensin-Converting Enzyme Inhibition Can Cause Severe Post CPB Vasodilation
– Current UK Opinion**

Devbhandari MP, et al. *Asian Cardiovasc Thorac Ann* 12 (4):346-349, 2004

Who?

- **Surveyed 167 practicing UK cardiac surgeons**

- **105 replied**

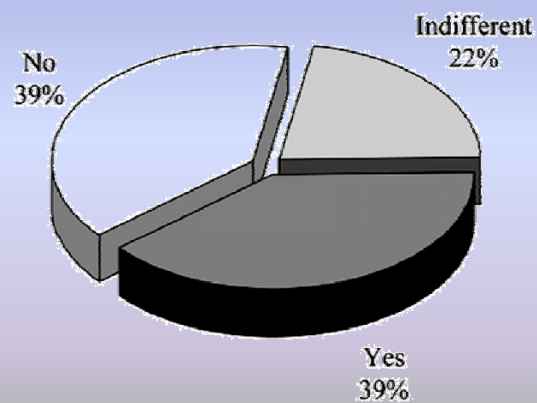
Q. Do you feel it is beneficial to stop ACEI before cardiac surgery?

Yes

No

Makes no difference

Q. Do you feel it is beneficial to stop ACEI before cardiac surgery?



Preoperative Use of Angiotensin-Converting Enzyme Inhibitors / Angiotensin Receptor Blockers is Associated with Increased Risk for Acute Kidney Injury after Cardiovascular Surgery

Arora P, et al. *CJASN*
3:1266-1273, 2008

Who was studied?

**1358 adults who underwent cardiac surgery
(Mostly CABG)**

How?

**Retrospective – Bivariate models and
propensity scoring**

AKI – RIFLE criteria

Results

Univariate Analysis

	NOT ON ACE/ARB	ON ACE/ARB	p
n	652	706	
AKI %	36.7	43.4	0.0006

Results

Multivariate Regression + Matching Propensity Score

	Point Estimate	95% CI
ACE/ARB	1.41	1.07 – 1.85
Age	1.04	1.03 – 1.05
Diabetes	1.66	1.29 – 2.13
CABG + Valve Replacement	1.69	1.23 – 2.59
Hypotension	1.42	1.06 – 1.88
On Pump	1.89	1.38 – 2.59

Weakness

- Selection bias in a retrospective study
- Mitigated by complex statistical methods, including propensity scoring and bi-variate models

Conclusion

**There is a significant
association of pre-op
ACE/ARB use with post-op
AKI**

Acute Kidney Injury Associated with Cardiac Surgery

**“Whether ACEI and ARB
should be discontinued before
surgery is not known and is a
source of some debate.”**

Rosner M, Okusa M, *CJASN* 1:19-32, 2006

Outline

- The physiology underlying the question
- What is the data?
 - ✓ Contrast Administration
- Conclusions

Background Literature Conflicting Reports

- Risk factors for CIN in patients with CKD - Diabetics on ACE
Louis B, et al. Renal Failure. 1996
- Captopril a risk factor for CIN
Toprak O. Anadolu Kardiyol Derg. 2003
- Captopril reduced the risk for CIN by 79%
Gupta R. Indian Heart J. 1999

Impact of renin-angiotensin-aldosterone blockade by angiotensin-converting enzyme inhibitors or AT-1 blockers on frequency of contrast medium-induced nephropathy: a post-hoc analysis from the Dialysis-versus-Diuresis (DVD) trial

Kiski D, et al. *Nephrol Dial Transplant*
25:759 – 764, 2010

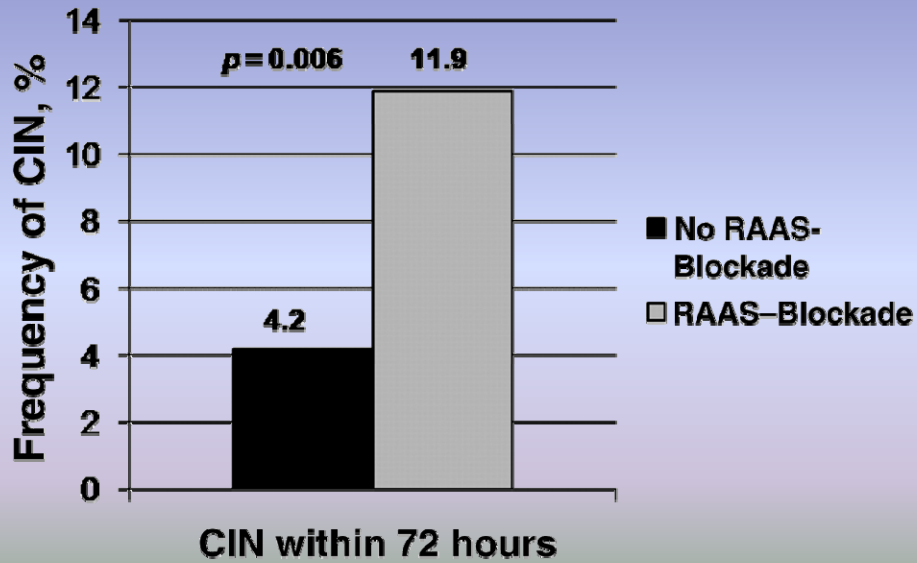
Who was studied?

412 patients who underwent coronary angiography

How?

- **Prospective Single Center**
- **CIN : Increase in serum creatinine of > 0.5mg/dl within 72 hours**

Results



Kiski D et al. *Nephrol. Dial. Transplant.* 2010;25:759-764

Baseline Characteristics

	RAAS blockade	No RAAS blockade	
	n=269	n=143	p
Hypertension %	77.8	68.5	0.027
Loop diuretics	45.9	25.2	<0.001

Results

Multivariate Analysis by Binary Logistic Regression

	OR	95% CI	p
RAAS blockade	3.1	1.23 – 7.7	0.016

Conclusion

Patients treated with RAAS blockade before exposure to CM develop significantly more often CIN within 72 h. Even after adjustment for confounding comorbidities, treatment with ACE-I or AT-1 blockers turned out to be an independent risk predictor.

Limitations

- RAAS Blockade was not the aim for randomization or intervention in this trial
- Analysis done retrospectively

In the Pipeline

A randomized control trial...

Valsartan Cardio-Renal Protection in Patients Undergoing Coronary Angiography Complicated With Chronic Renal Insufficiency (VAL-CARP) Trial

**Ikeda N, et al. *Circulation Journal*
70:548 – 552, 2006**

Who was studied?

500 Japanese with GFR between 30 – 89 ml/min
undergoing coronary angiography

How?

Single-center, open label Valsartan VS
Valsartan + ACE

Endpoint

Change in GFR by C – G equation

Outline

- The physiology underlying the question
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- Conclusions

Conclusions regarding RAS inhibitors in SURGERY from the nephrologist's perspective

- Data is scarce and conflicting
- The setting is one likely to be associated with hypotension and circulatory disturbances
- “We are simply at a crossroads”-P. McCullough
- Follow Pohl's rule: “Never trade an unknown benefit for a potential complication.”

Conclusions, cont.

- There is NO established renal benefit to continuing ACE/ARB prior to surgery
- There is possible harm to continuing ACE/ARB prior to surgery
- I would hold the drugs but would not make it a pre-op requirement

Conclusions regarding RAS inhibition in CIN

How to prevent contrast-induced nephropathy and manage risk patients: Practical recommendations

Solomon R, et al. *Kidney International*
69:551-553, 2006

“The data regarding the need to specifically discontinue angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers prior to contrast exposure is insufficient. It was the opinion of the Consensus Panel that these agents do not need to be discontinued prior to contrast exposure in stable patients receiving chronic therapy.”

•This recommendation may need modification if data of DVD trial is corroborated