Intradialytic stunning

The role of systemic circulatory stress in uraemic complications

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and

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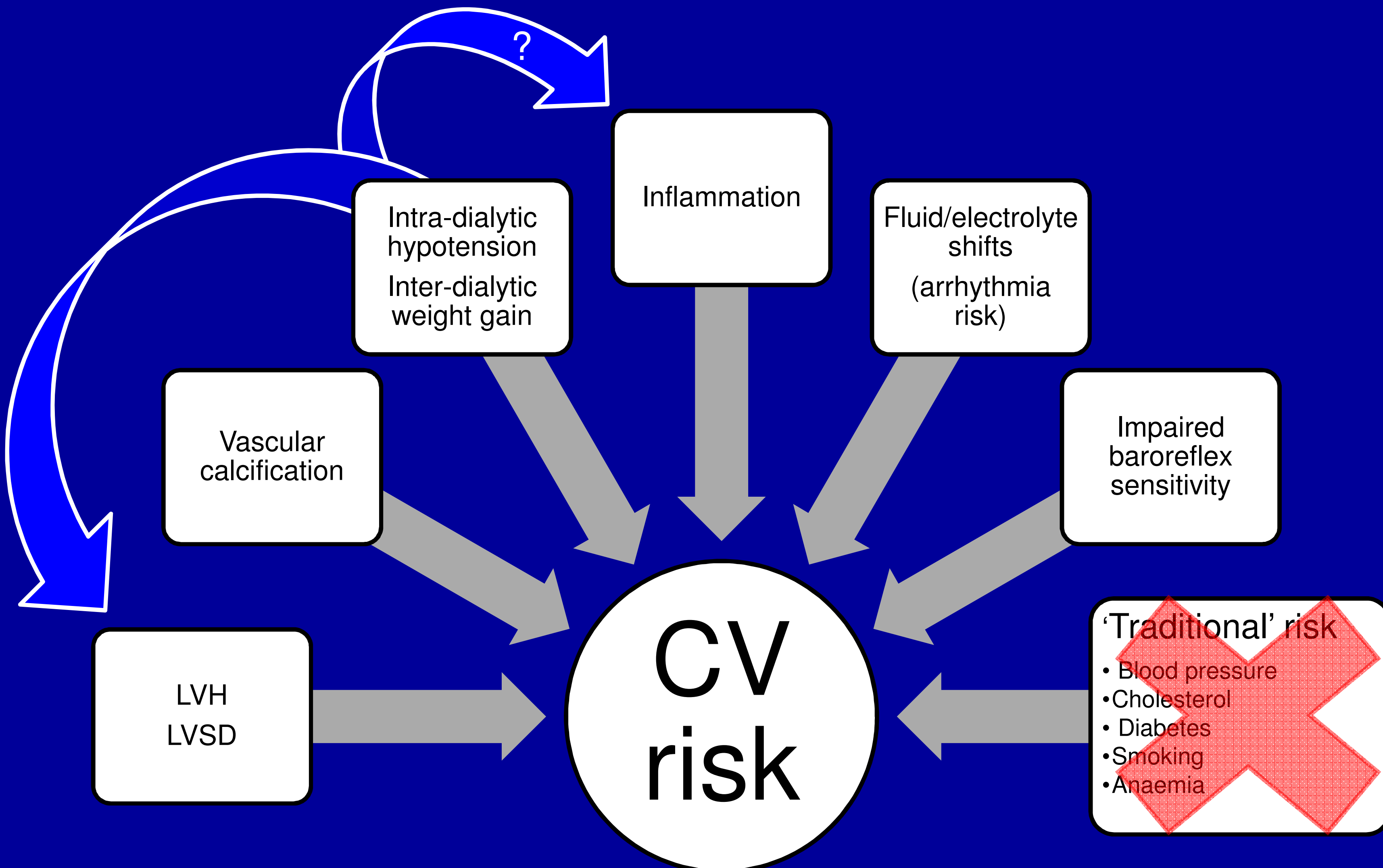
Cardiac risk factors in dialysis patients



Odudu A, McIntyre CW. J Ren Care 2010

Systemic circulatory stress in HD -Effects of HD on $ScVO_2$

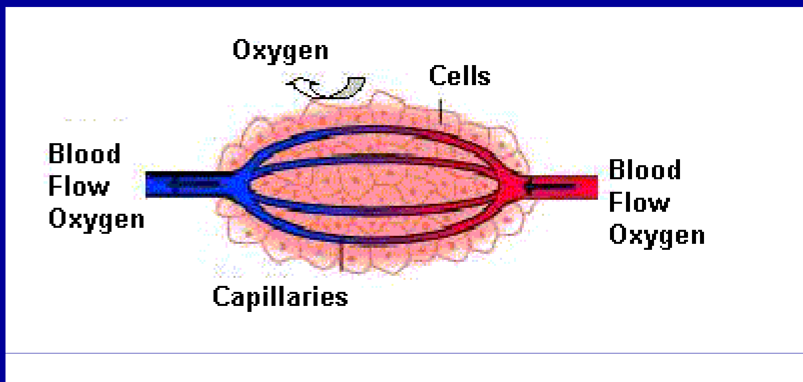
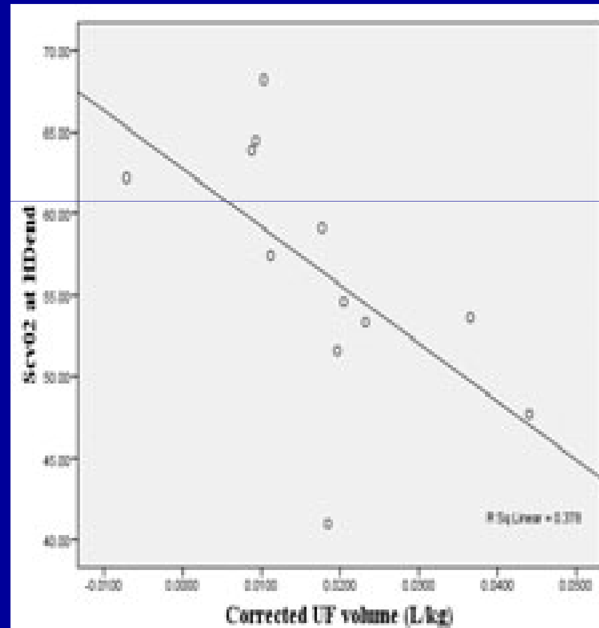


Table 1 Limits of mixed venous oxygen saturation

SvO_2 >75%	Normal extraction O_2 supply >O_2 demand
75% >SvO_2 >50%	Compensatory extraction Increasing O_2 demand or decreasing O_2 supply
50% >SvO_2 >30%	Exhaustion of extraction Beginning of lactic acidosis O_2 supply <O_2 demand
30% >SvO_2 >25%	Severe lactic acidosis
SvO_2 <25%	Cellular death

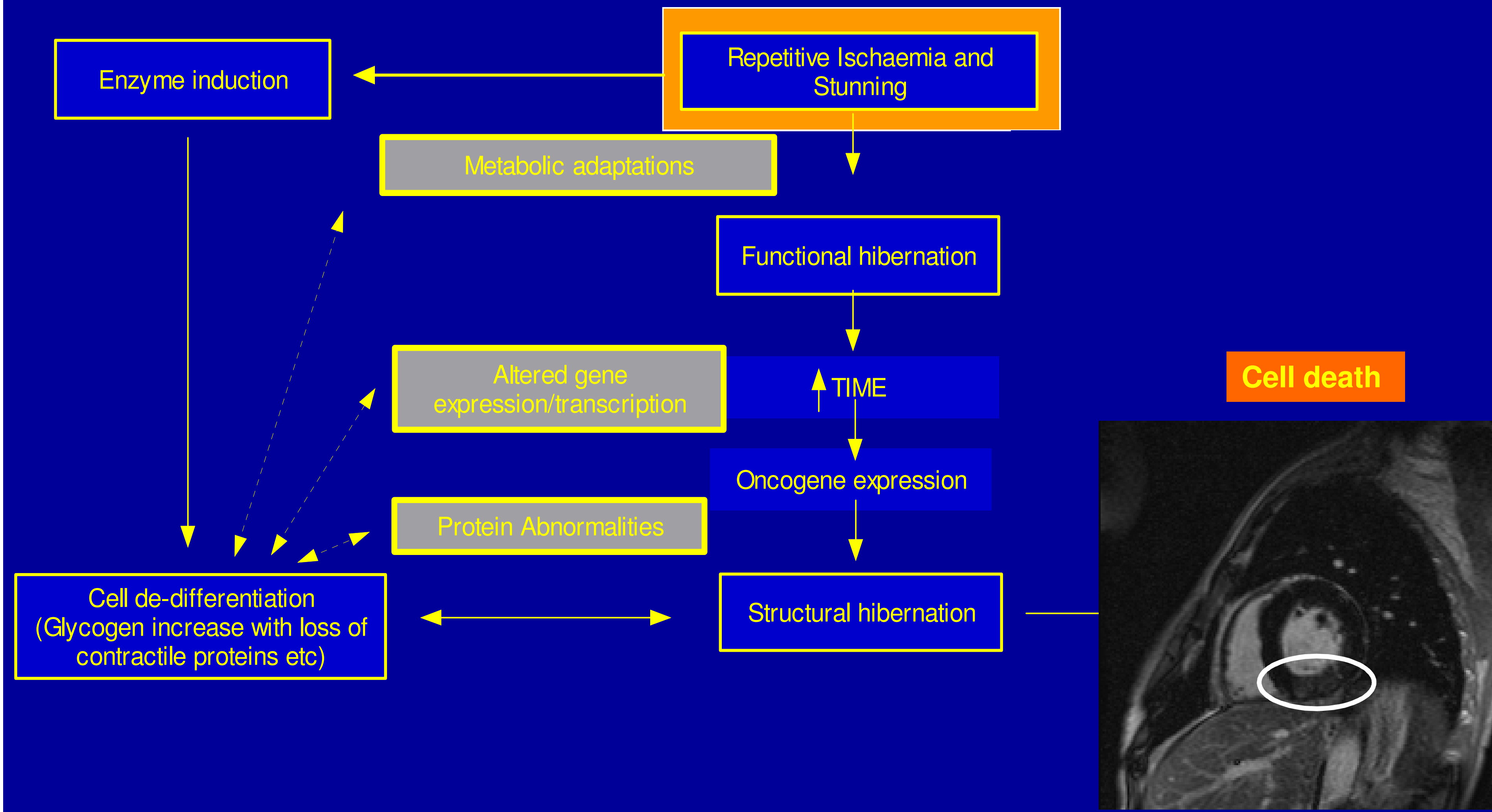
$ScVO_2$ Pre HD 63.5 ±1 3%, post HD 56.4 ± 8% (p=0.04)*



Scatter plot of ScvO2 at end of HD plotted against corrected ultrafiltration volume (UF volume / patient weight)

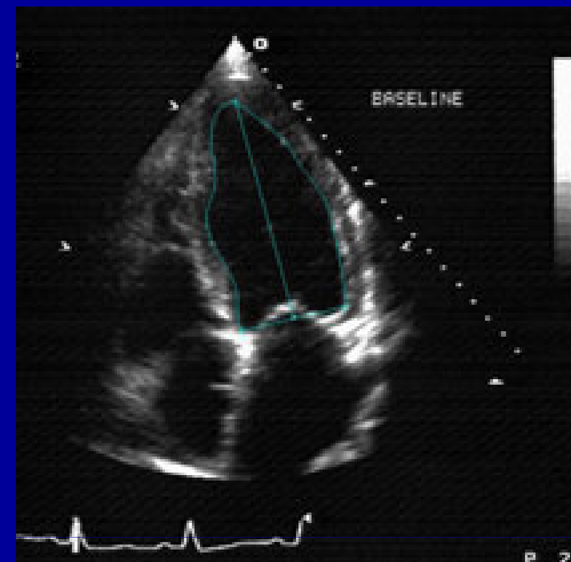
*Harrison L, Selby NM, McIntyre CW. BRS/RA 2010

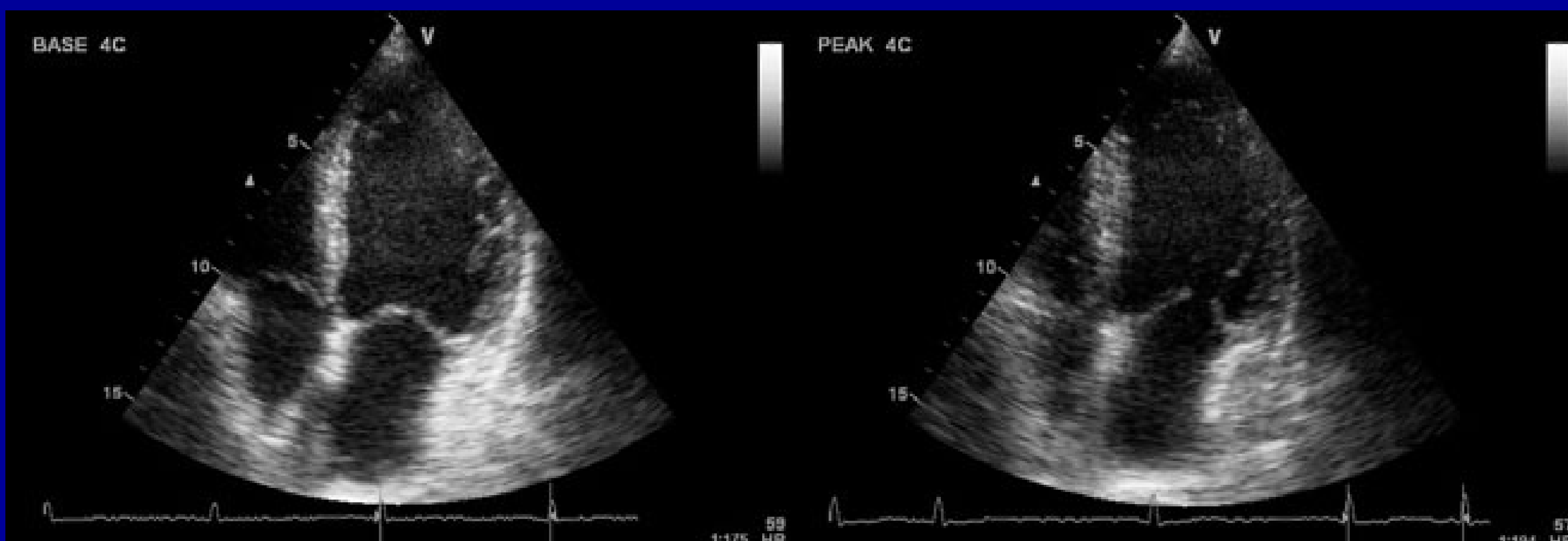
Repetitive cardiac injury-
Hibernation and heart failure



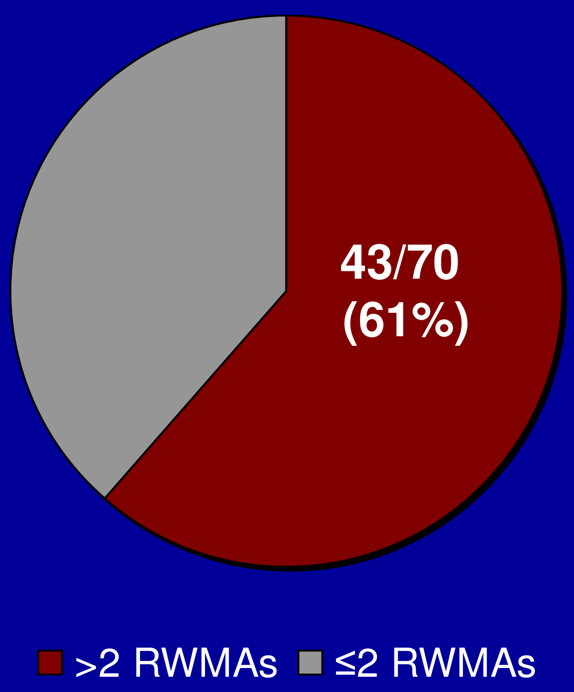
Assessing stress response to HD. Regional Wall Motion Analysis

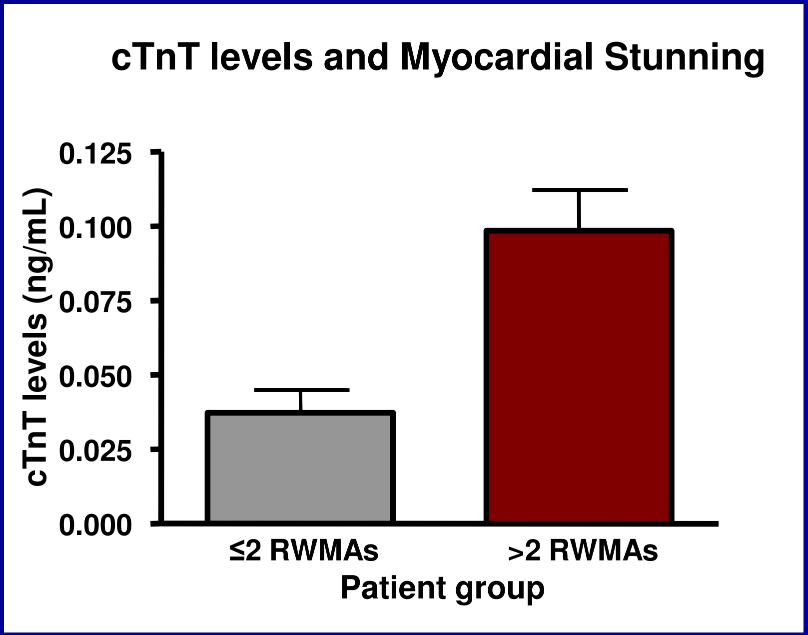
- Semi-automated software
- Wall motion is calculated over 10 regions and expressed as %SF
- RWMA is defined as reduction in SF of >20% between baseline and peak images
- More than 2 RWMAs are significant





HD induced RWMA – prevalence and cTnT levels

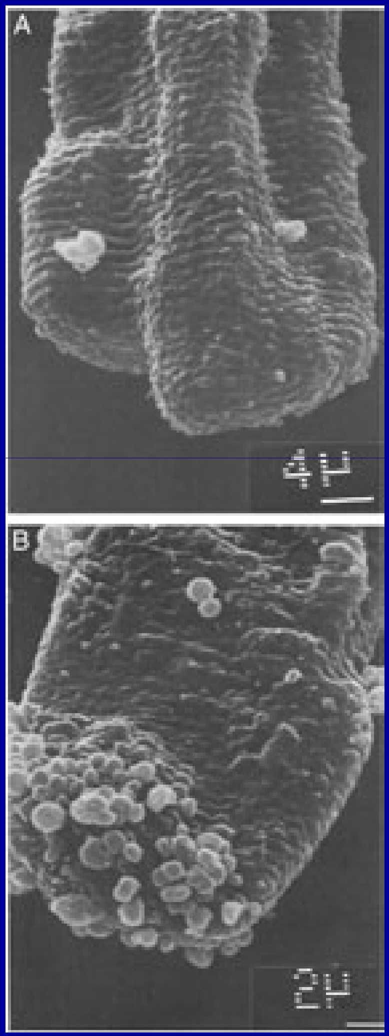




- The higher the cTnT, the greater the reduction in SF

Burton JO, Korsheed S, McIntyre CW. Clin J Am Soc Nephrol. 2009 May;4(5):914-20

Troponin release dose not require myocardial necrosis



•Blebs develop on myocyte surface

•Prolonged ischemia → bleb rupture, necrosis & prolonged troponin release

•Shorter periods of ischemia → bleb release without rupture, shorter period of troponin release

Hickman et al. *Clinica Chimica Acta* 2010

Factors associated with the presence of RWMAs

- Factors associated with development of >2 RWMAs (***r^2=0.602)***

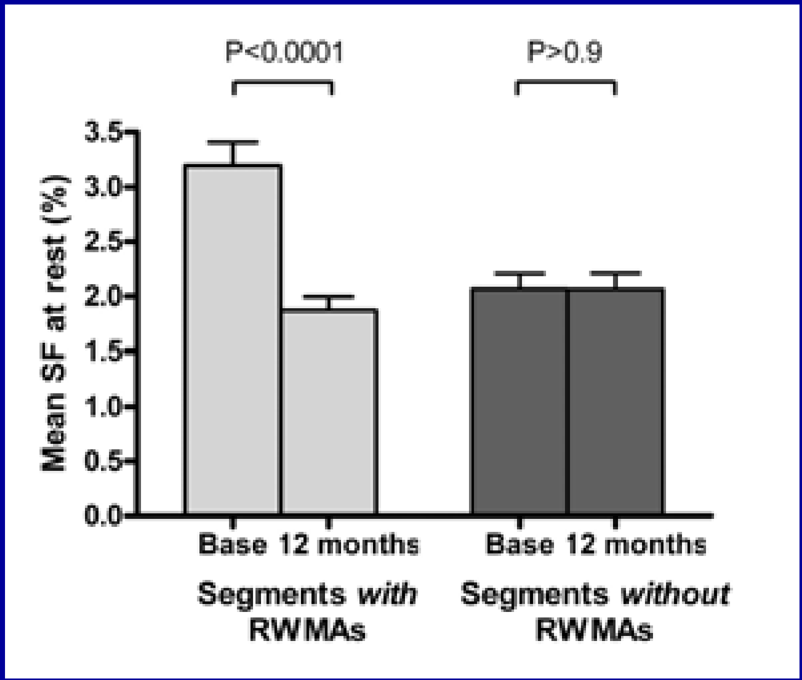
Factor associated with development of myocardial stunning	***OR***	***P value***
UF volume during HD of 1L	5.1	0.007
UF volume during HD of 1.5L	11.6	
UF volume during HD of 2L	26.2	
Max SBP reduction during HD of 10 mmHg	1.8	0.002
Max SBP reduction during HD of 20 mmHg	3.3	
Max SBP reduction during HD of 30 mmHg	6.0	

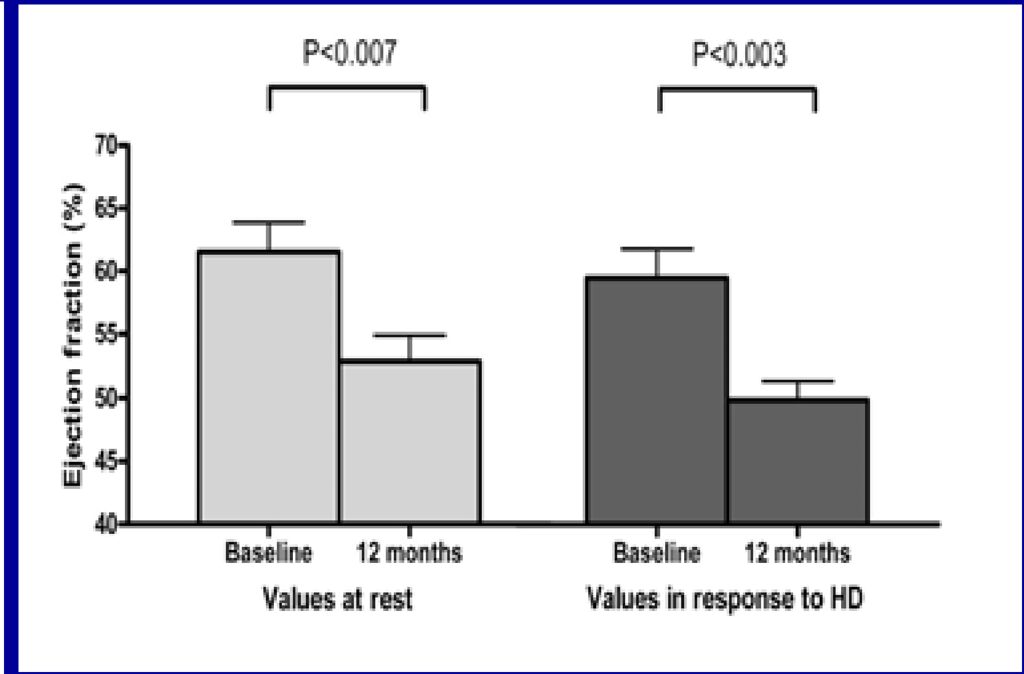
cTnT	1.26	1.04 – 1.54	0.004
Age	1.07	1.01 – 1.128	0.018

Burton JO, Korsheed S, McIntyre CW. Clin J Am Soc Nephrol. 2009 May;4(5):914-20

HD Induced Myocardial Stunning Lead to Myocardial Hibernation and Reduction in Overall Systolic Function

- **Hibernation of segments co-localised with stress induced RWMAs**
- **Reduction in LVEF ~ 10% (absolute)**
  - **At rest**
  - **At peak stress on HD**





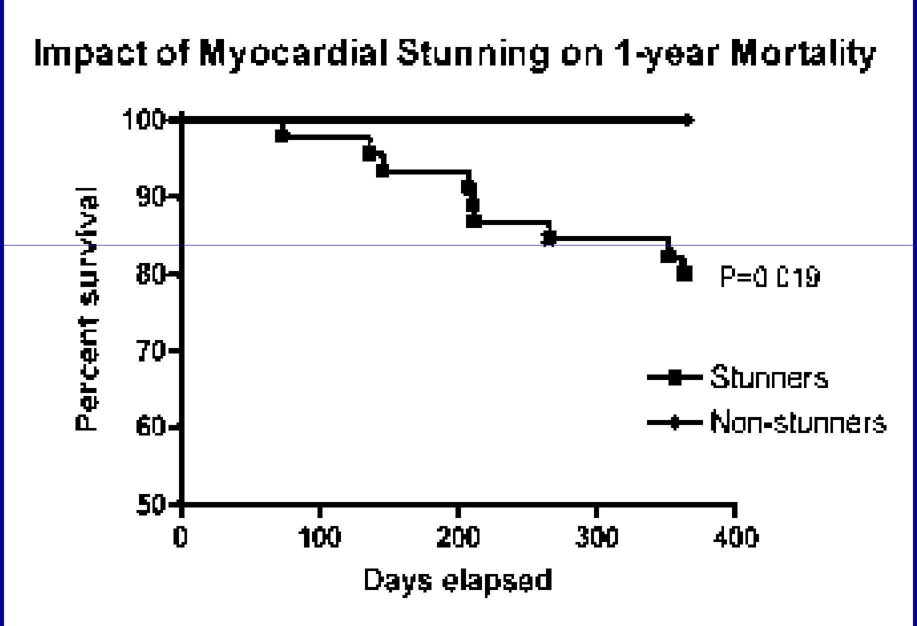
Burton JO, Korsheed S, McIntyre CW. Clin J Am Soc Nephrol. 2009 May;4(5):914-20
Burton JO, Jefferies HJ, *McIntyre CW* . Clin J Am Soc Nephrol. 2009 Dec;4(12):1925-31

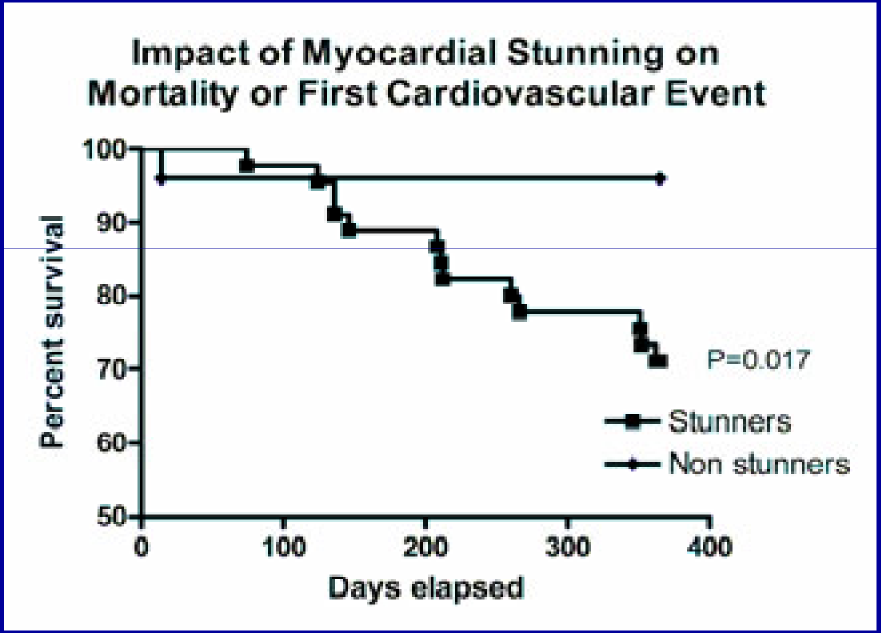
Other significant associations of Dialysis induced myocardial stunning

- **Inflammation***
  - **Increased levels of IL-6 and hs-CRP**
- **Markers of volume status****
  - **Increased TBW (deuterium based)**
  - **Increased levels of** NT-proBNP
- **Ventricular arrhythmias*****
  - 12 lead 24 hr Holter (intra and post dialytic monitoring)
  - complex ventricular arrhythmias (CVA) in 61% of patients
- **Elevated LAV******

*Jefferies HJ, McIntyre CW. EDTA 2008
**Jefferies HJ, McIntyre CW. RA/BRS 2008
***Burton JO, Korsheed S, McIntyre CW . Renal Failure 2008
****Haq I, Jefferies HJ, Burton JO, McIntyre CW.ASN 2009

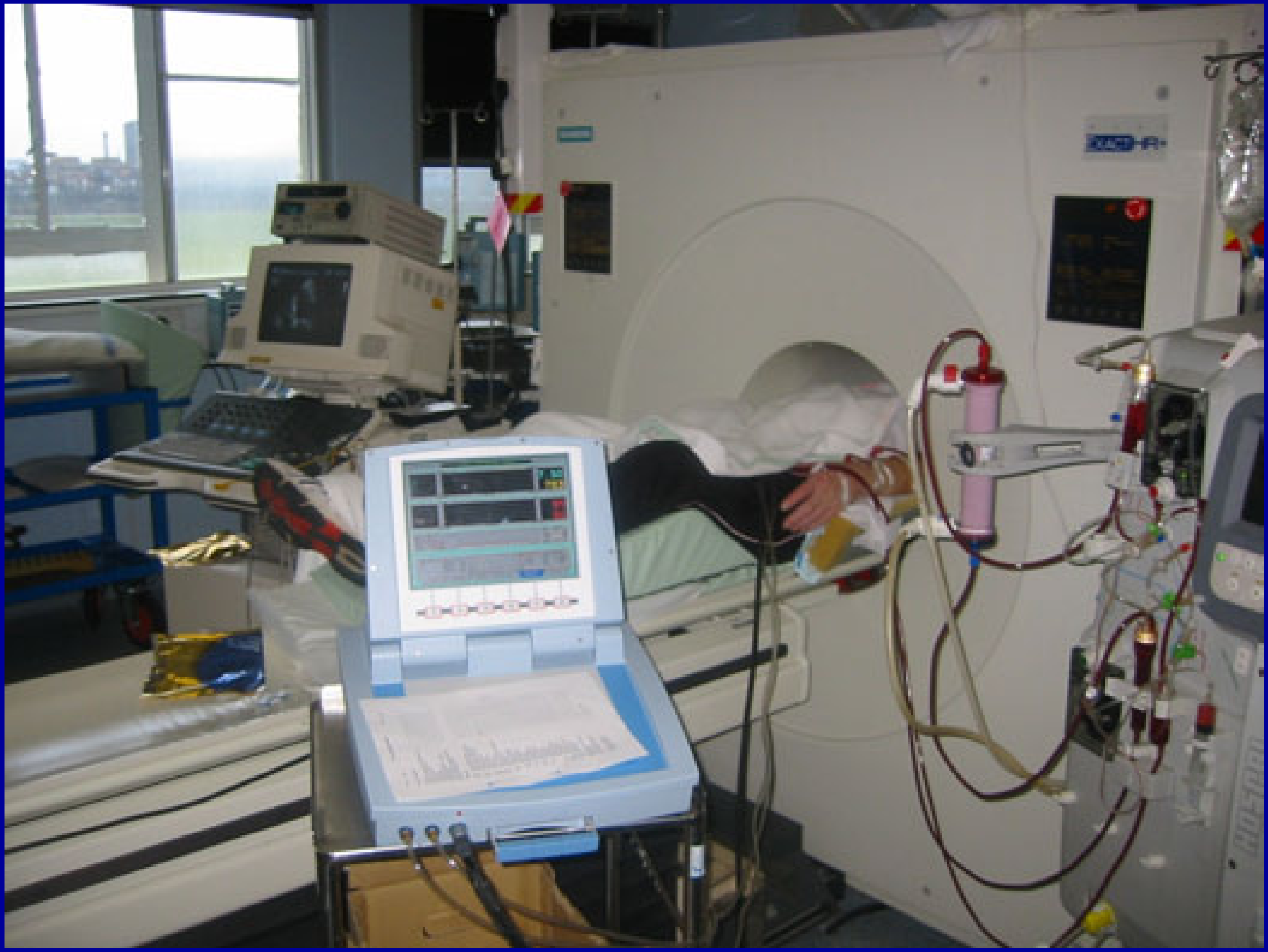
Mortality and time to CV event





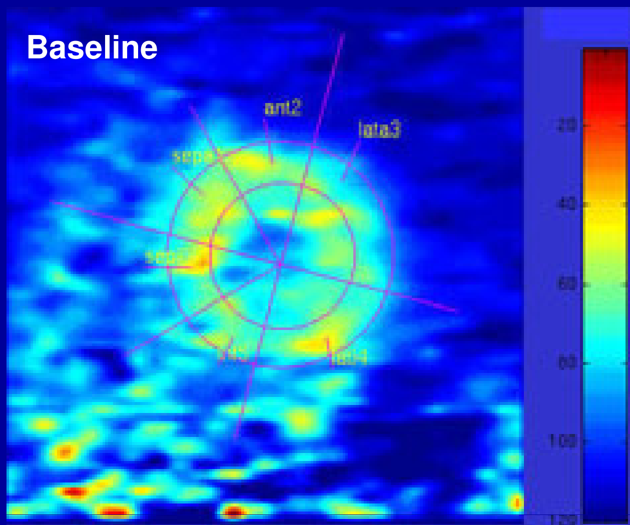
Burton JO, Korsheed S, McIntyre CW. Clin J Am Soc Nephrol. 2009 May;4(5):914-20

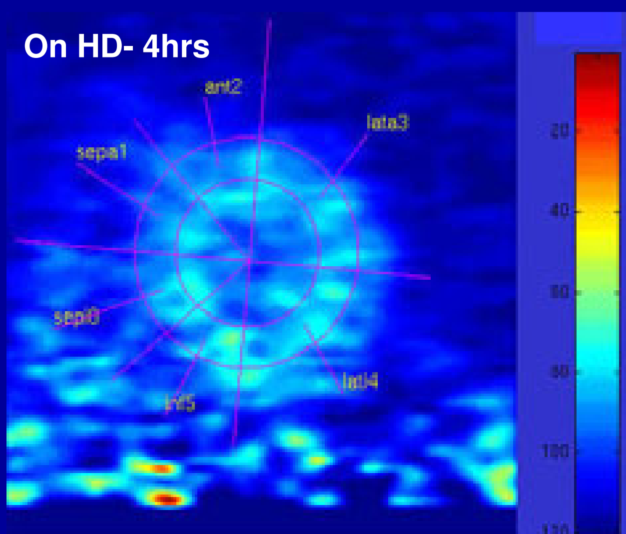
Intradialytic segmental myocardial perfusion- using cardiac water PET



McIntyre CW. Acute cardiac effects of haemodialysis. Kidney Int 2009

Effect of HD on global and segmental Myocardial Blood Flow





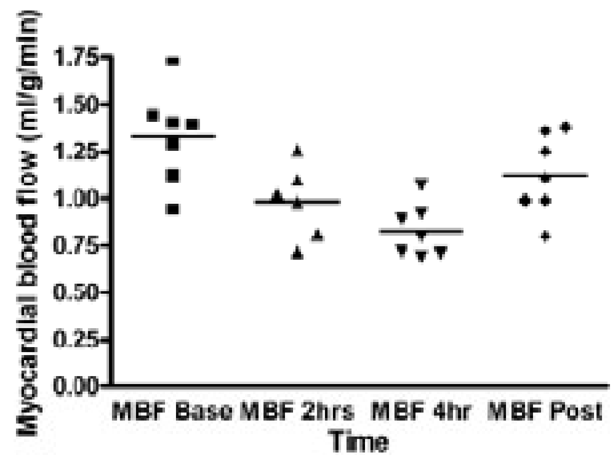


Figure 1. Mean global myocardial blood flow (MBF) reduced significantly during dialysis from baseline with partial restoration in the recovery period.

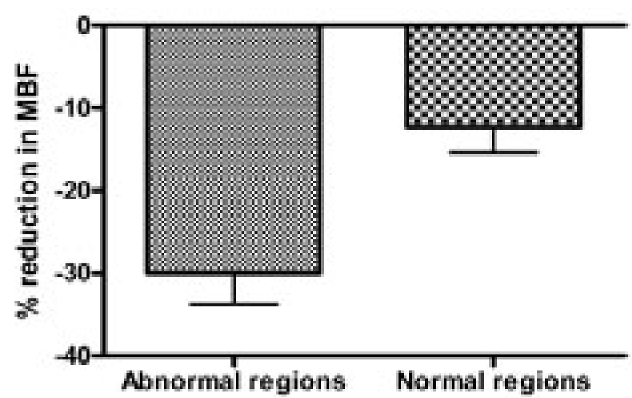
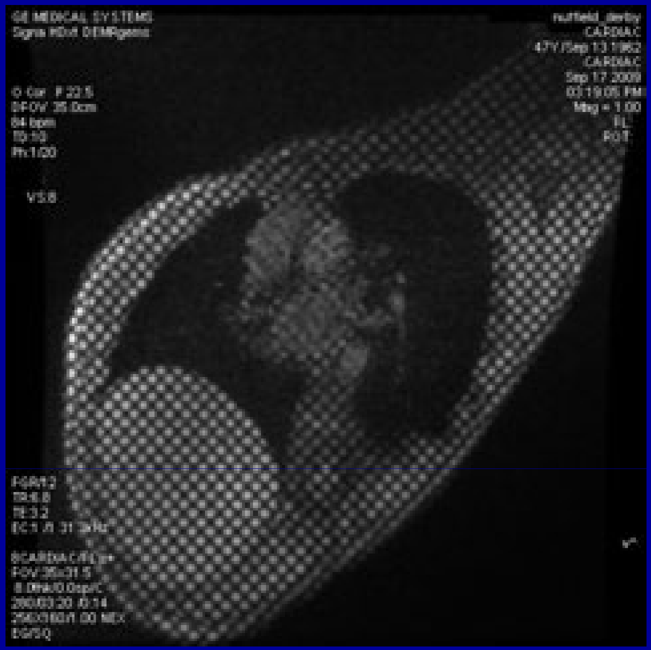
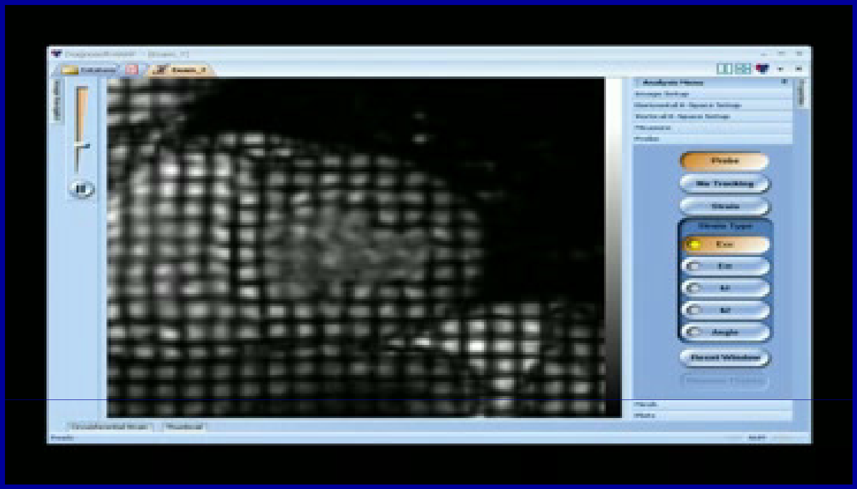


Figure 3. The development of regional ventricular dysfunction as measured by regional wall motion abnormalities (RWMA; abnormal regions) was associated with a greater reduction in MBF from baseline than areas that maintained normal movement (normal regions; $P = 0.001$).

McIntyre CW et al. Clin J Am Soc Nephrol. 2008 Jan;3(1):19-26

Uraemic effects on normal cardiac function

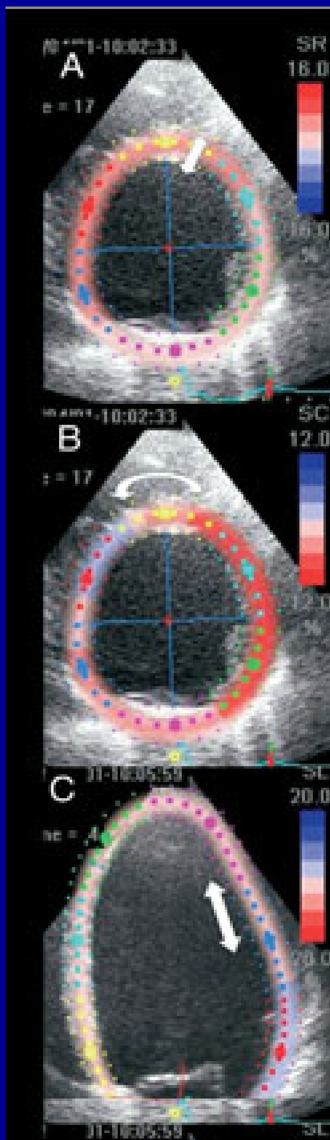


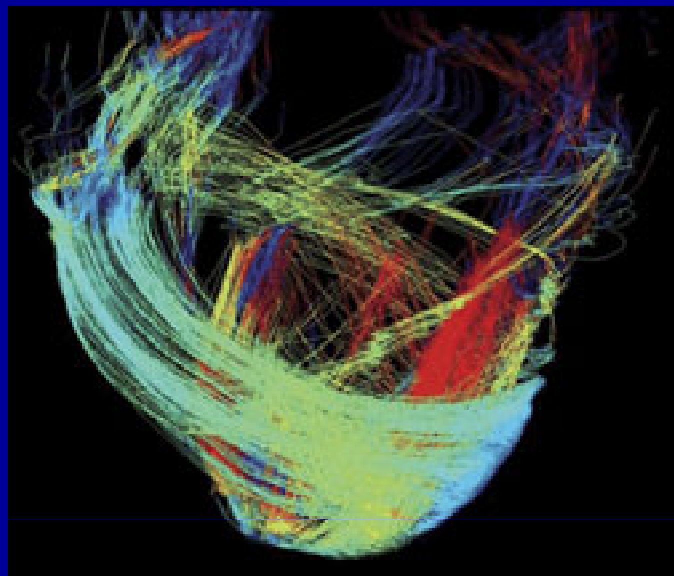


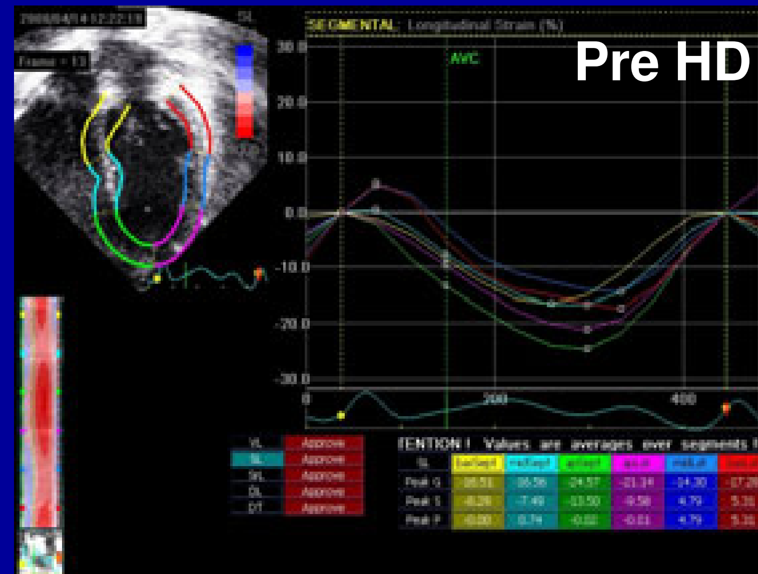
	Basal		Mid			Apical	
Segment	HD Pts	Controls	HD Pts	Controls	**Segment**	HD Pts	Controls
Anterior		-22±2		-23±2	**Anterior**		-27±2
Antero-septal		-19±2		-21±2	**Septal**		-24±2
Infero-septal		-18±1		-20±3	**Inferior**		-21±4
Inferior		-16±2		-18±2	**Lateral**		-25±3
Postero-Lateral		-21±2		-22±3			
Antero-Lateral		-21±2		-24±3			

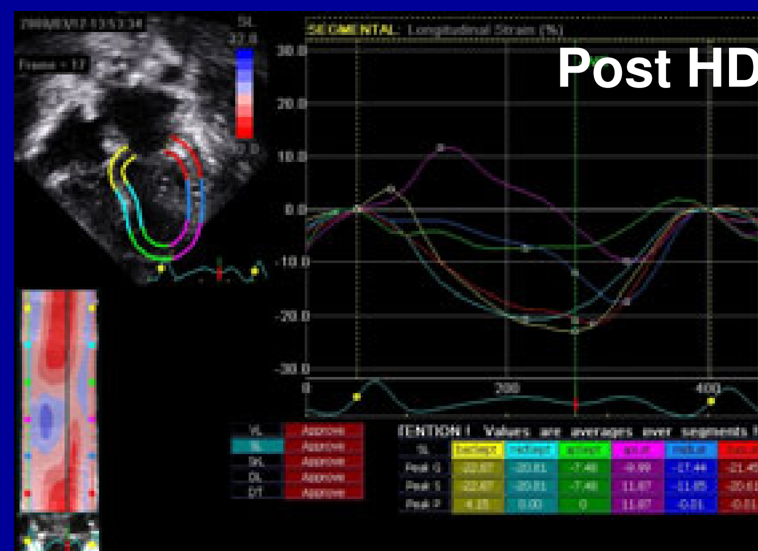
Odudu A, Eldehni MT, McIntyre CW. ISBP 2010

LV Strain studies- 2D Speckle tracing









- **predisposition to longitudinal axis dysfunction**

- **predisposition to LV mechanical asynchrony**

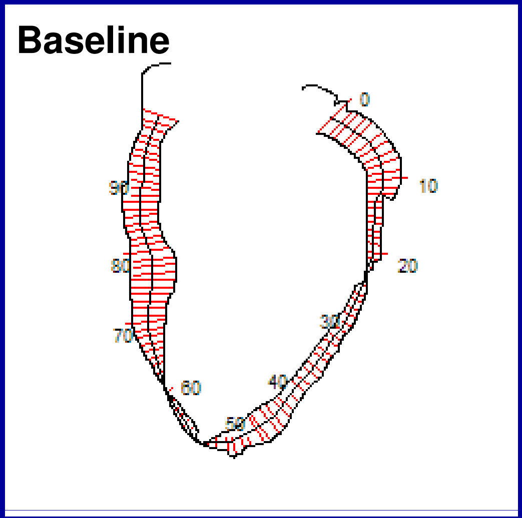
Hothi D, Rees L, McIntyre CW, Marek T. ASN 2009

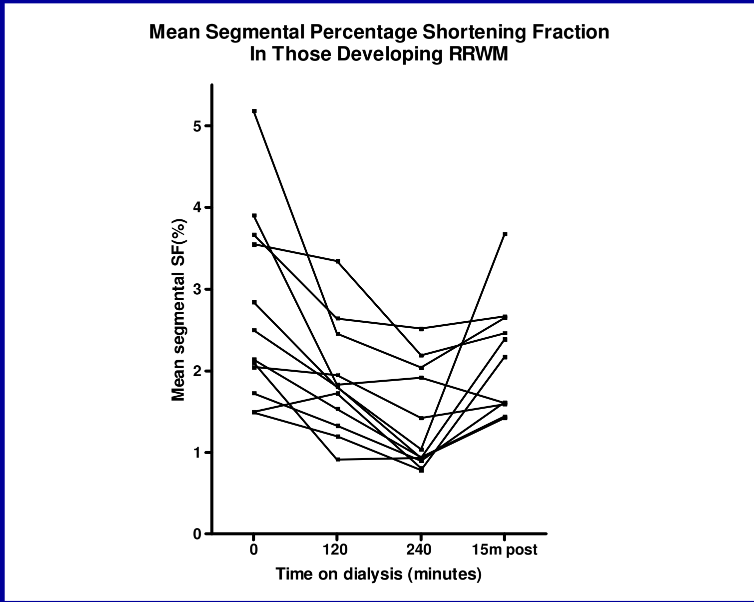
Children on dialysis-
uraemia without epicardial CAD

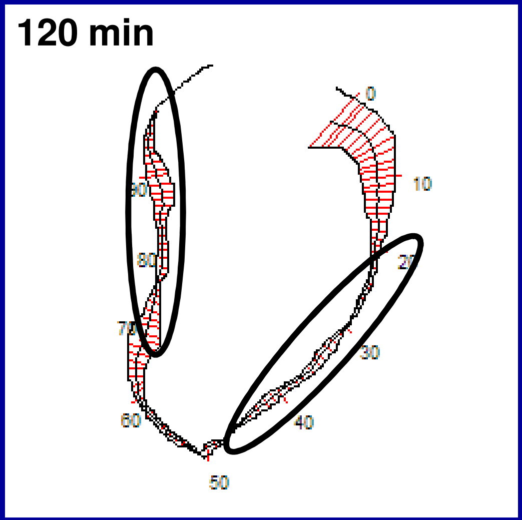
Patient	Age (yrs)	Months on Dialysis	Months on HD	Cause of ESRF	AV fistula	LV septum [Z-score]	LV Posterior wall [Z -score]
1	5.7	4	4	renal dysplasia	yes	1.3	1.7
2	17.1	130	89	cystinosis	yes	1.6	0.3
3	15.7	43	43	FSGS	yes	0.1	1.4
4	15.0	24	4	renal dysplasia	yes	0.3	0.2
5	15.7	32	32	FSGS	yes	2.6	1.9
6	13.8	7	4	renal dysplasia	no	5.9	6.3
7	11.2	41	35	renal dysplasia	yes	0.5	-0.6
8	13.6	15	15	FSGS	no	0.6	-1.1
9	2.2	7	7	glomerulocystic	no	1.5	1.7
10	17.0	12	12	bilateral VUR	yes	1.9	1.7
11	7.6	62	62	ARPKD	yes	1.0	0.3
12	14.6	23	6	cystic dysplasia	yes	2.6	1.2

Hothi D, Rees L, McIntyre CW. Clin J Am Soc Nephrol. 2009 Apr;4(4):790-7

Recurrent HD induced myocardial stunning in children



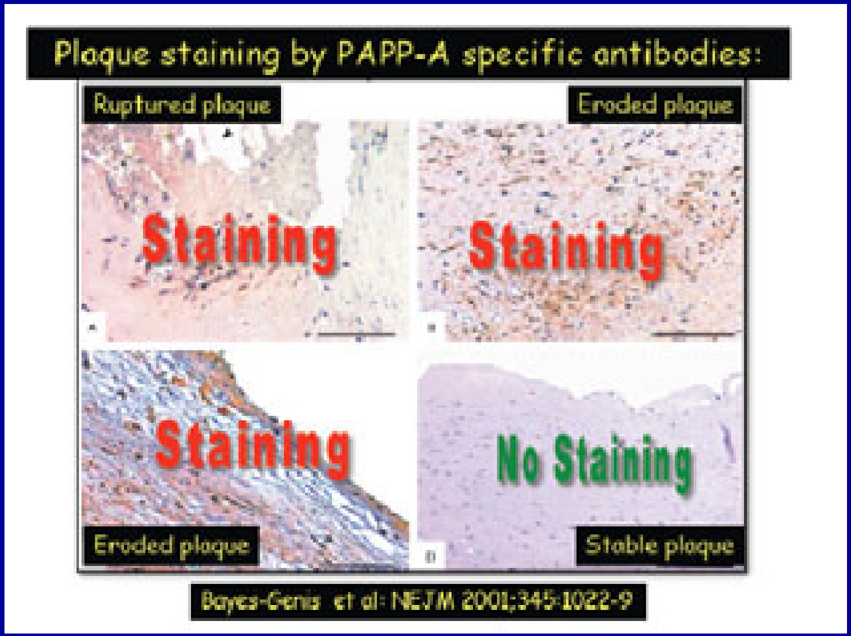




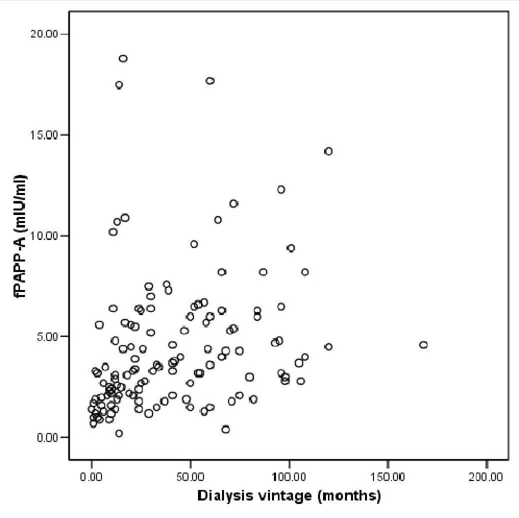
Proportion stunning	11/12
Age (years)	12.4(2-17)
UF volume(L)	1.2±079
Delta BP (mmHg)	25.5± 9
Pre HD LVEF (%)	55± 8.3
Post HD LVEF (%)	54.6± 7.5

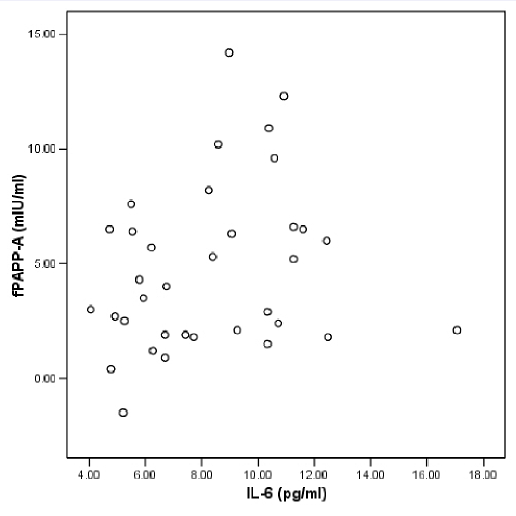
Hothi D, Rees L, McIntyre CW. Clin J Am Soc Nephrol. 2009 Apr;4(4):790-7

PAPP-A in HD patients
Combined study with Finland



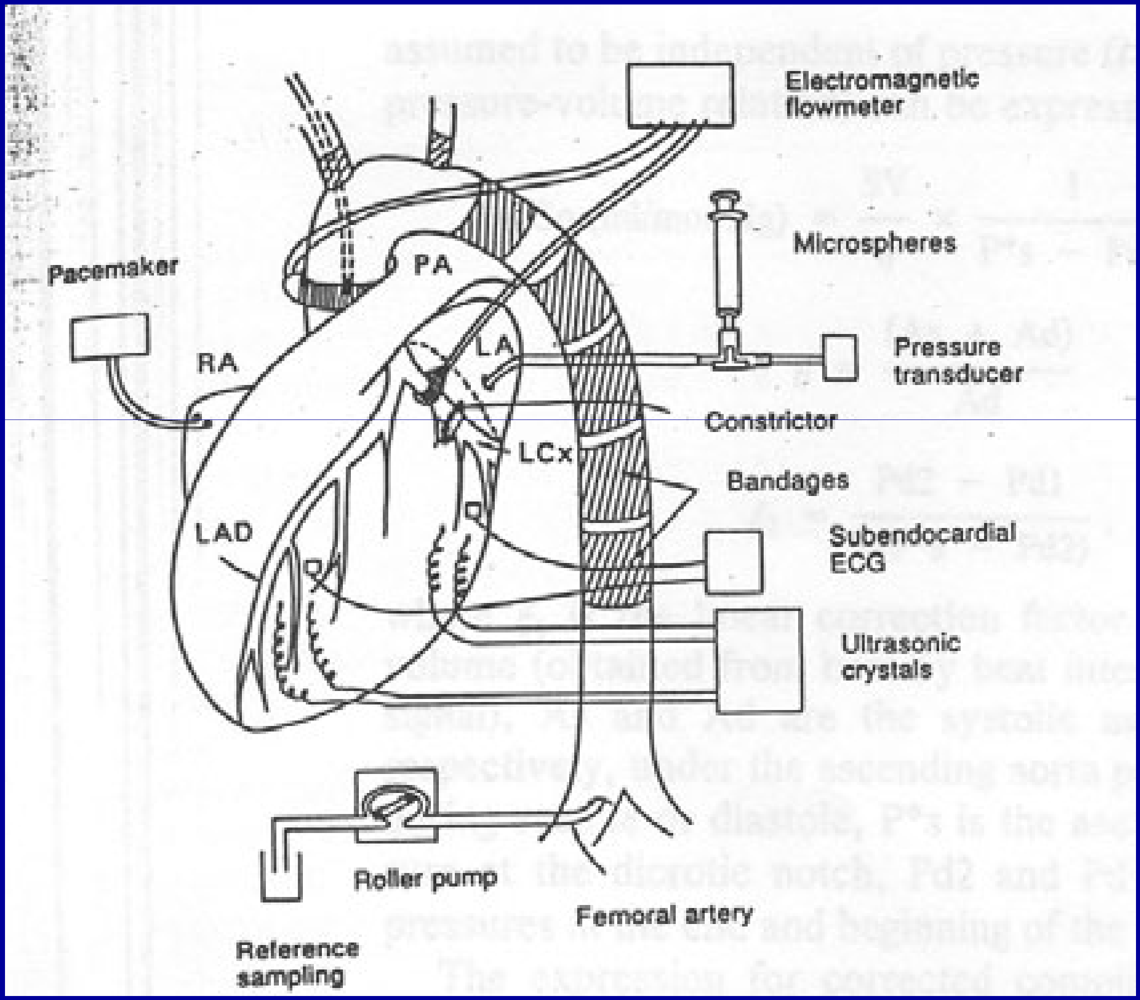
- Strongly associated with ACS and outcomes*
- NO ASSOCIATION WITH HD INDUCED ACUTE CARDIAC INJURY**





*Risto T. Clin Chemistry 2009
**Jefferies HJ, Risto T, Whitforth S, McIntyre CW. ASN 2009

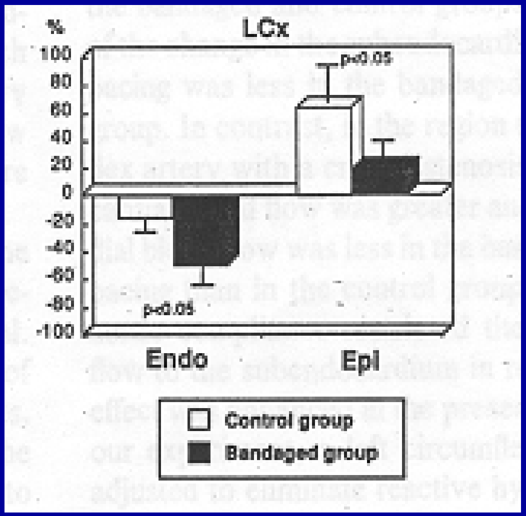
How can aortic compliance induce myocardial ischaemia ?



ECG changes

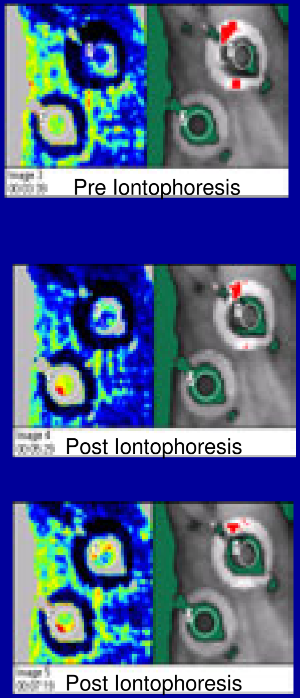
- 3-4 mm ST depression
- at rest and stressed

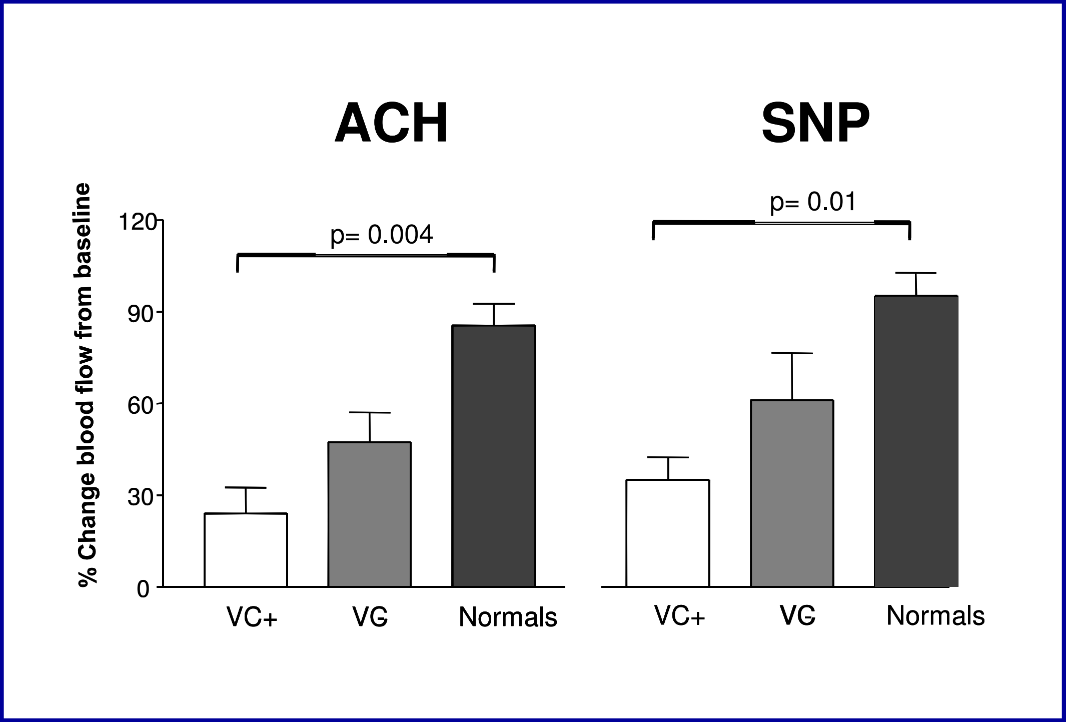
Myocardial perfusion



Watanabe et al. J Am Coll Cardiol 1993;21:1497-1506

Microcirculatory disturbance in HD and vascular calcification





Sigrist MK, McIntyre CW. Nephron Clin Pract. 2008;108(2):c121-6

Myographic ex-vivo arterial assessment

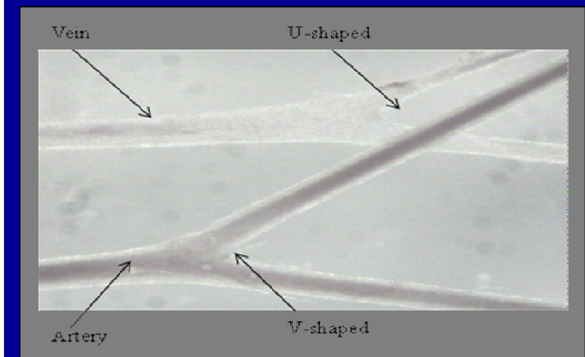
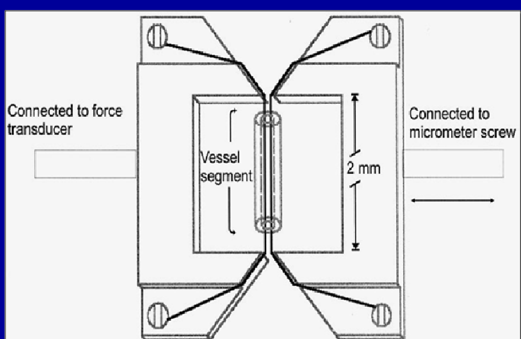
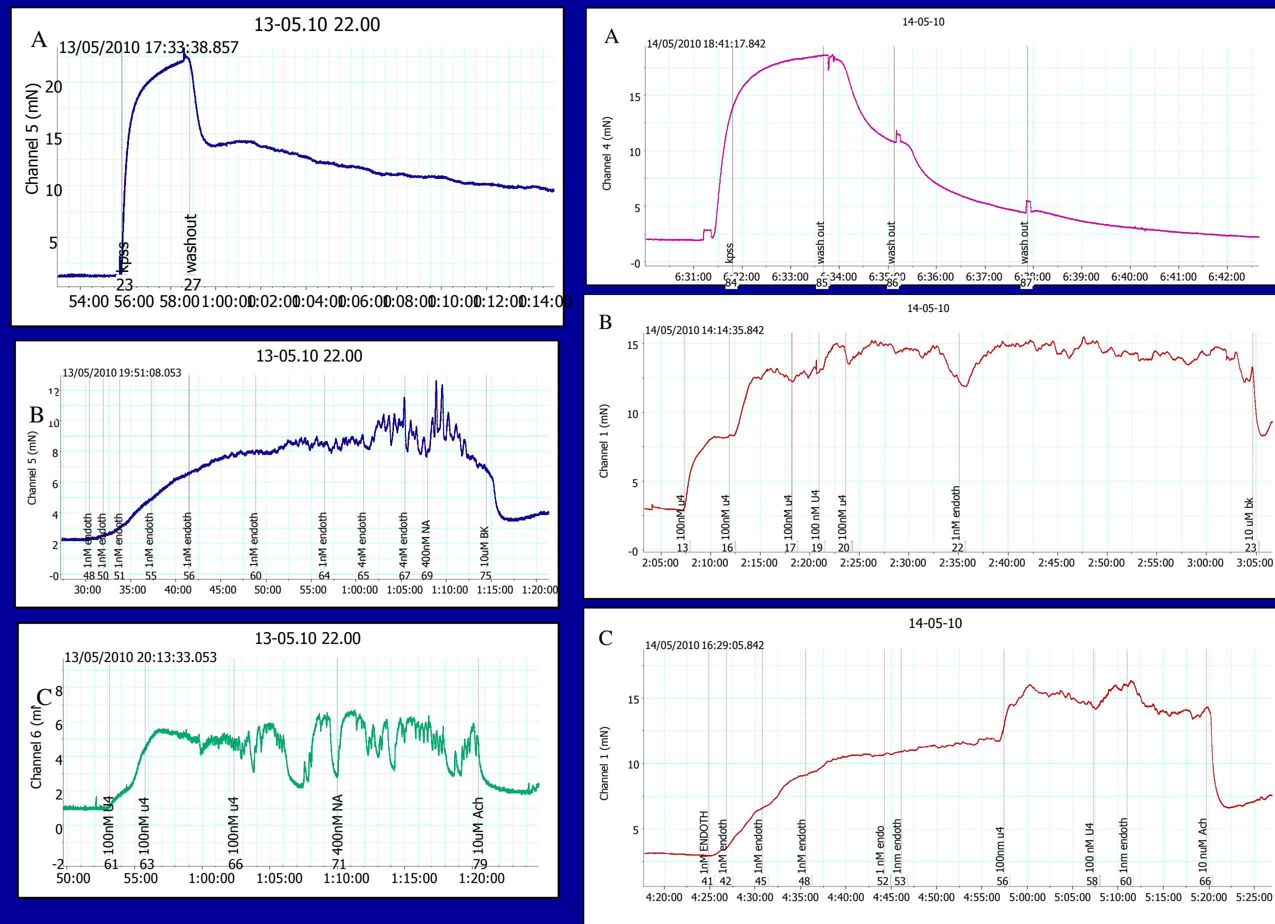


Figure 14. Differences between artery and vein.



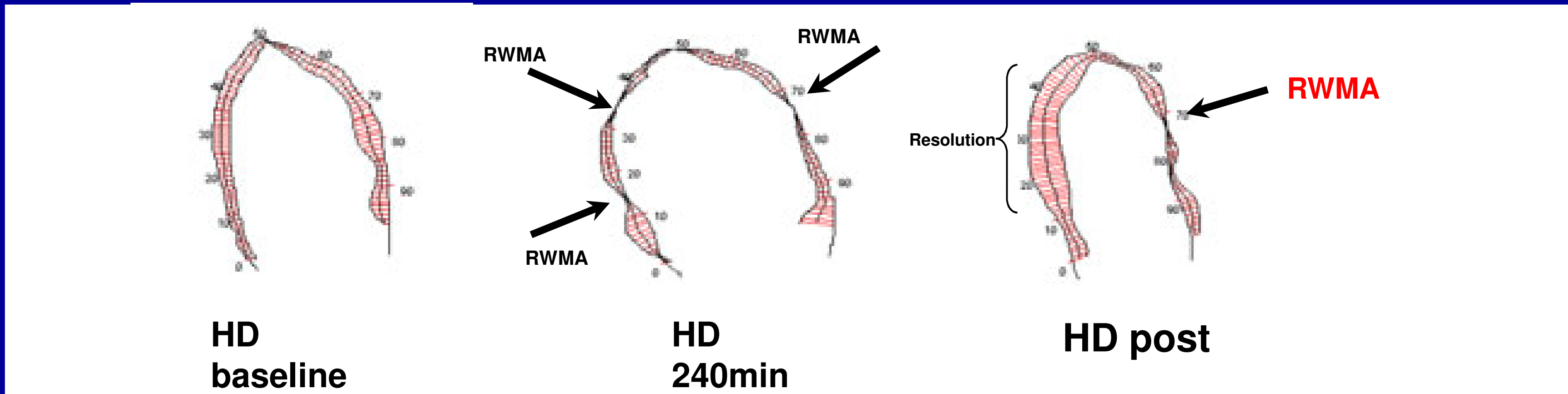
NON CKD **HAEMODIALYSIS**

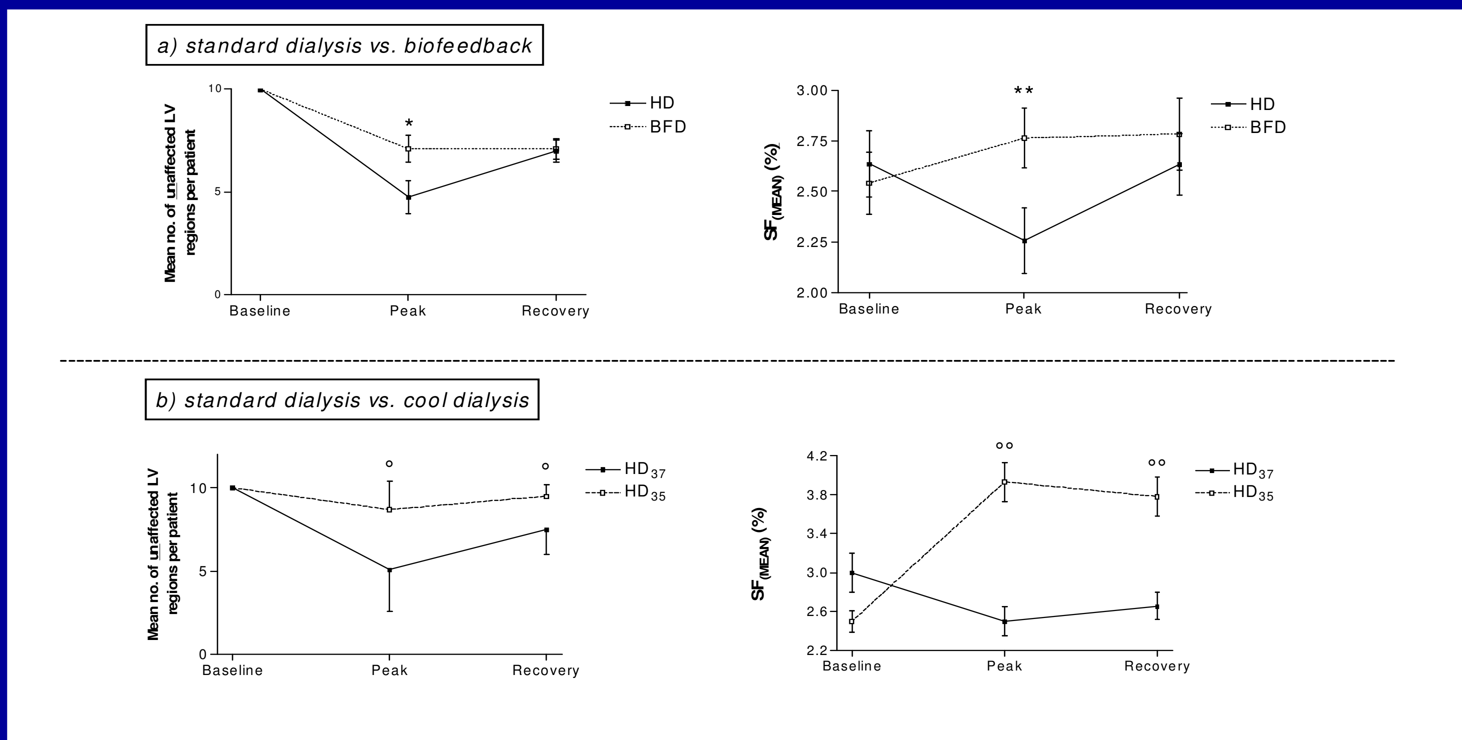


Responses of resistance arteries to (A) KPSS, (B) BK and (C)

Bushroffa A, Odudu A, Ehehni MT, O'Sullivan S, McIntyre CW. Unpublished data

Reduction in HD induced circulatory stress ameliorates myocardial stunning

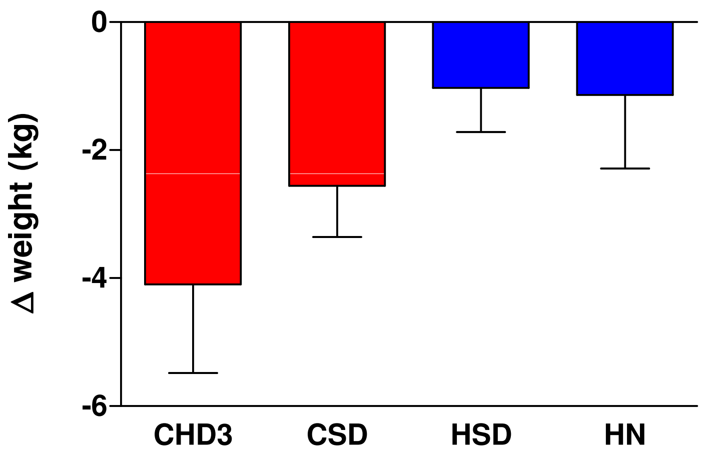




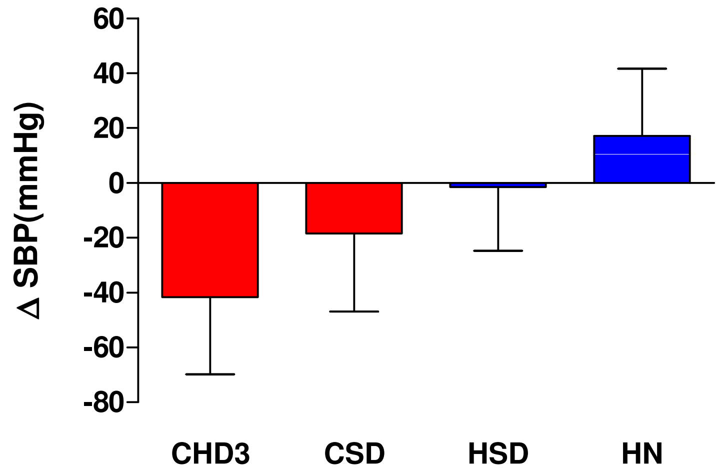
N Selby, S Lambie, C Baker, P Camici, C McIntyre. AJKD 2006
Selby NJ, Burton JO, McIntyre CW. Clin J Am Soc Nephrol 2006

Daily dialysis impact on UF and BP

Weight change Pre-dialysis to Peak stress



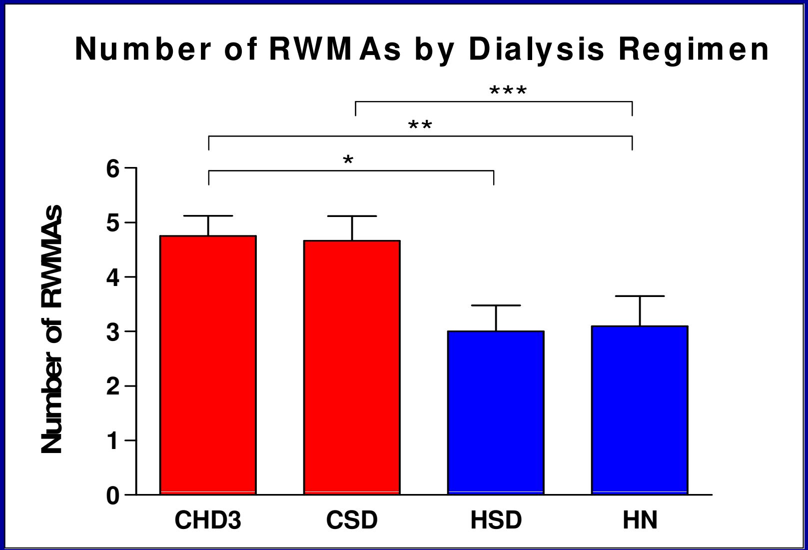
Change in Systolic BP, Pre-dialysis to Peak stress

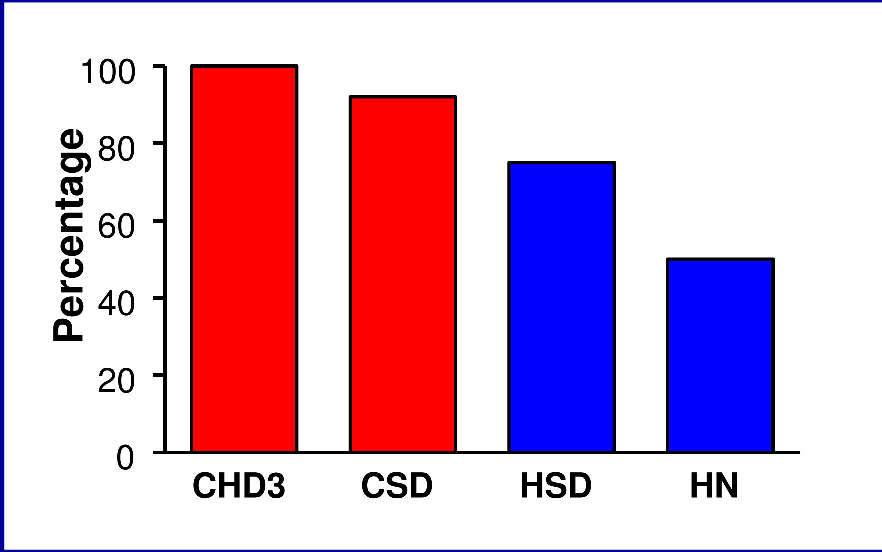


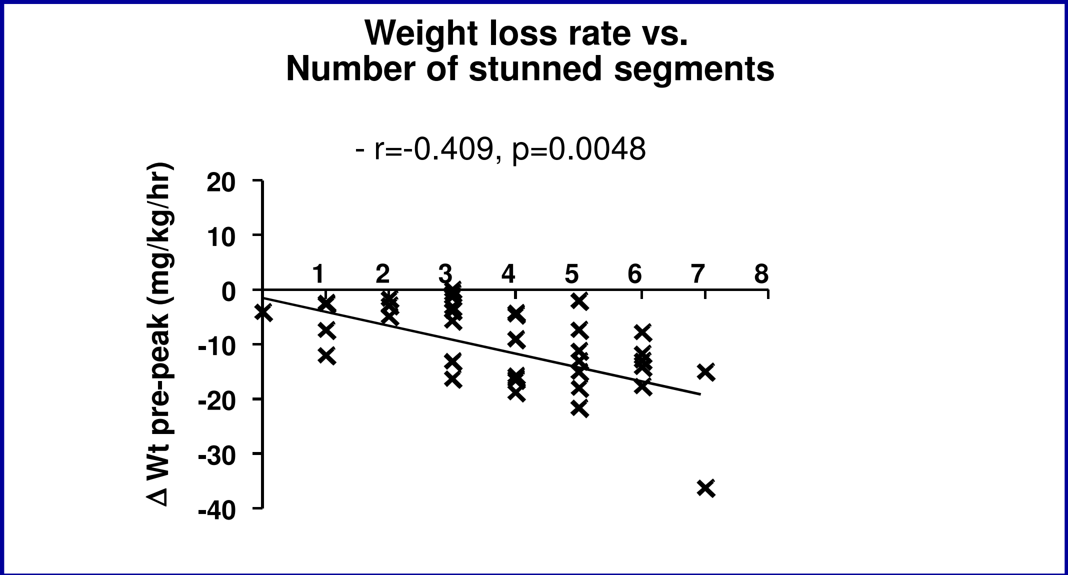
Patients fully matched for age, sex, history of IHD and dialysis vintage

Jefferies HJ, Schiller B, Moran J, McIntyre CW. Accepted for publication CJASN 2010

Impact of dialysis schedule-
Intradialytic cardiac stunning

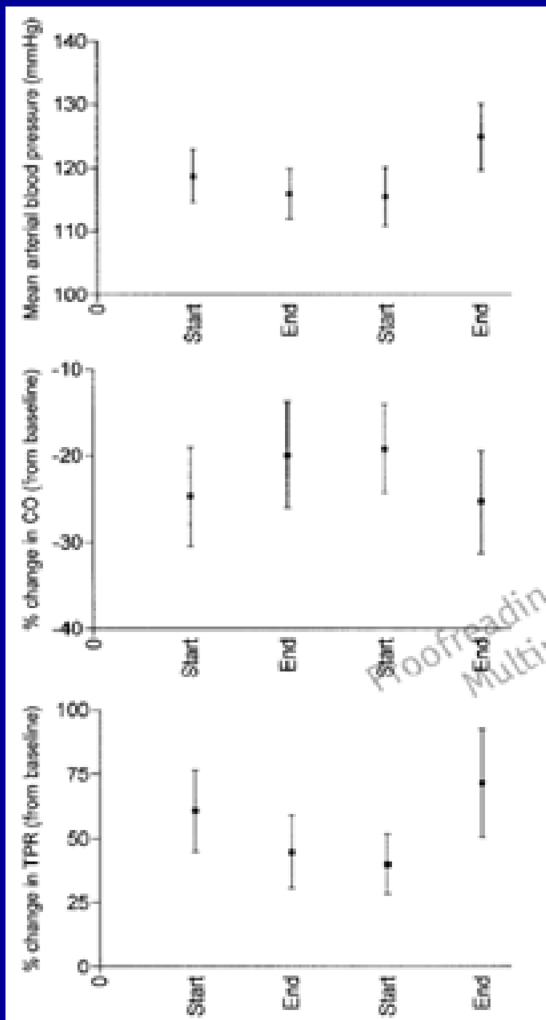


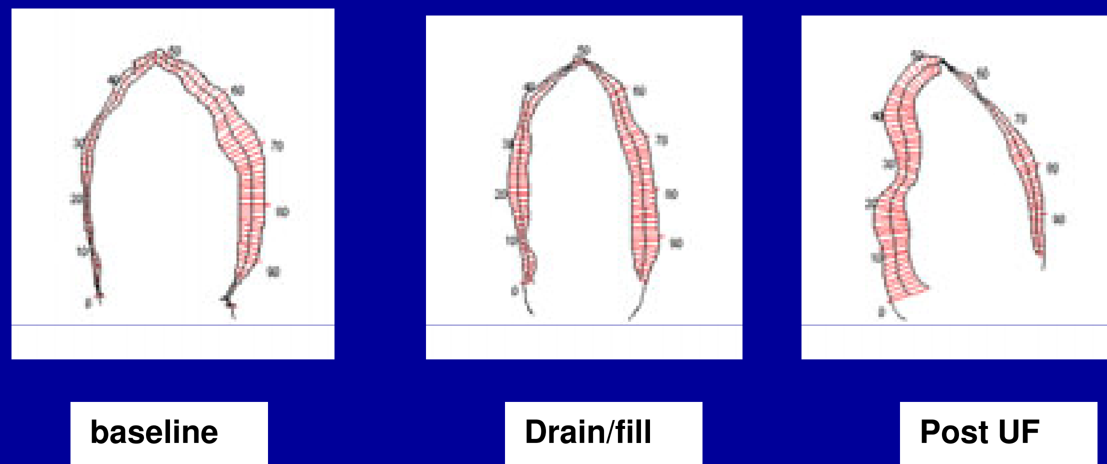




Jefferies HJ, Schiller B, Moran J, McIntyre CW. Accepted for publication CJASN 2010

Peritoneal dialysis is not associated with myocardial stunning





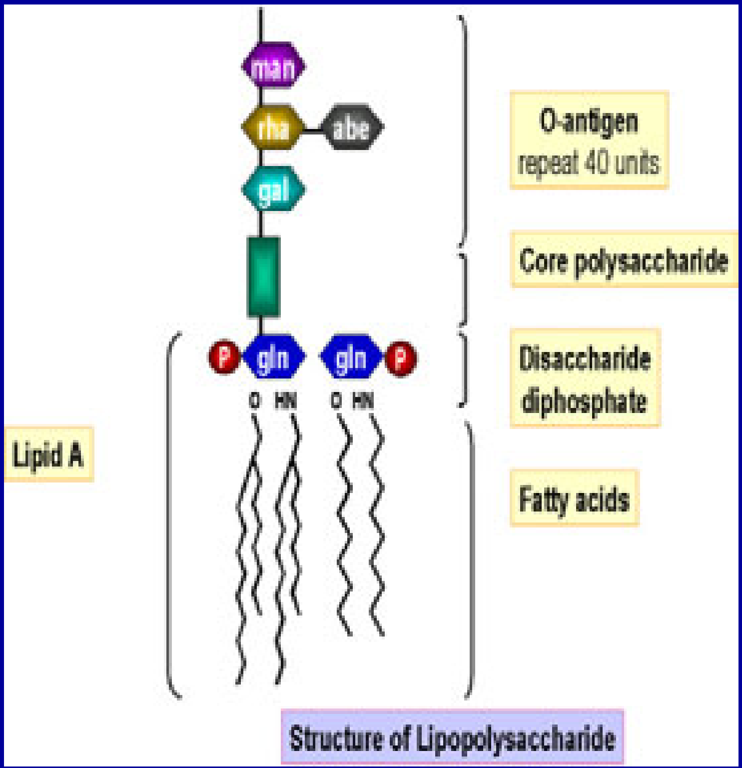
Limited evidence (<5% of segments during drain/fill cycle)

Studied during drain/fill and at peak ultrafiltration
Patients studied had little structural cardiac disease

Selby NM, McIntyre CW. PDI 2010

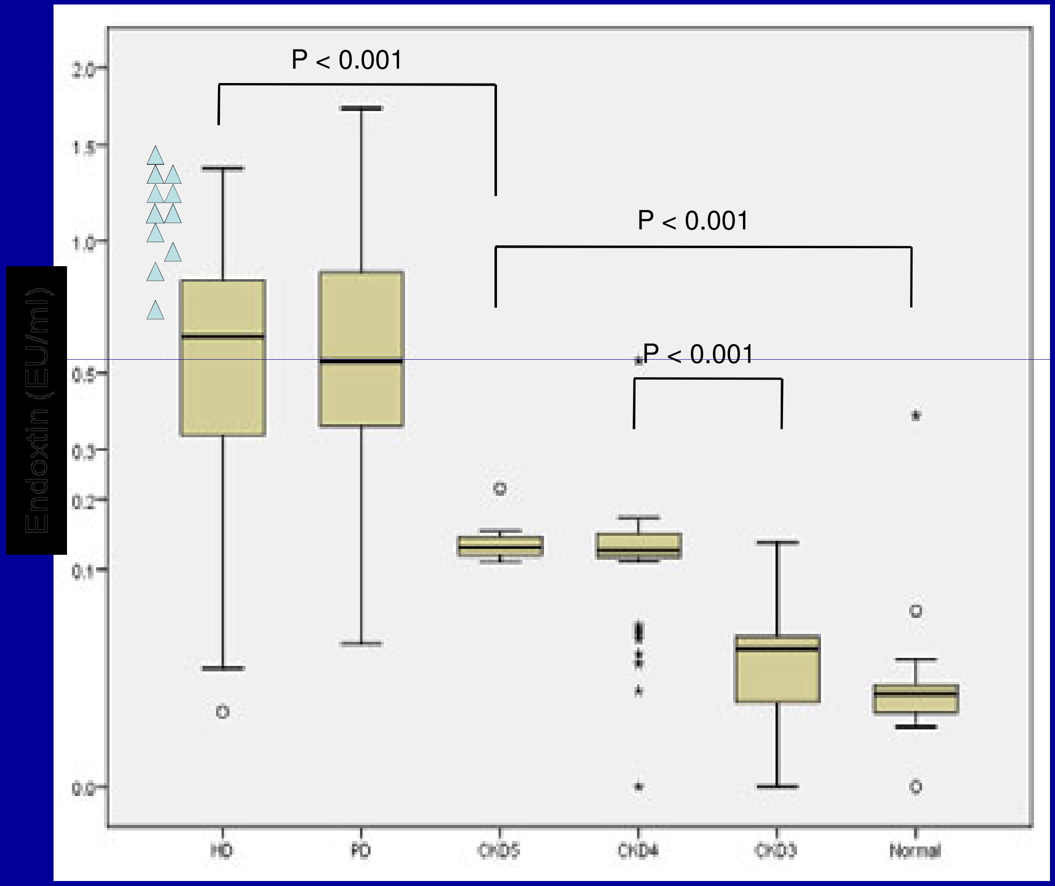
Endotoxin and heart failure

- Bacterial endotoxin is a lipopolysaccharide (LPS) comprising over 70% of the total bacteria in the **human gut**
- Stimulus for immune activation in the pro-**inflammatory** state of congestive heart failure (CHF)*
- ET enters the circulation via bacterial translocation from the gut
  - bowel **oedema**
  - **hypoperfusion**
- Endotoxinaemia reduces with
  - Reduction in **venous congestion**
  - Selective **gut detoxification**



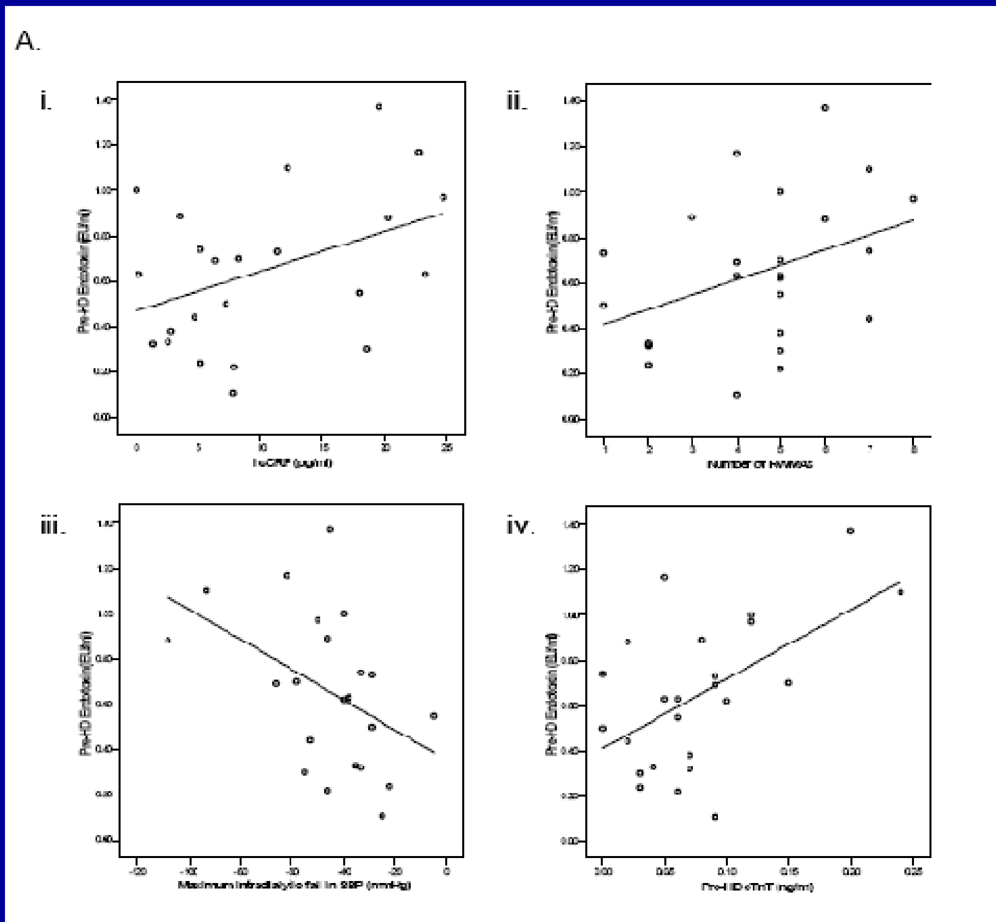
*Anker, S.D., et al. Am J Cardiol, 1997

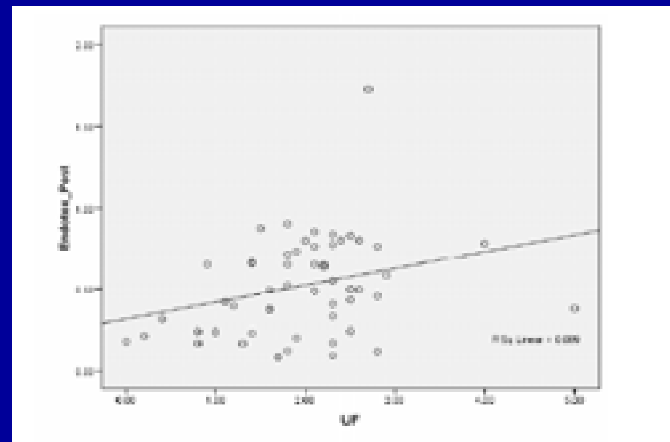
Endotoxaemia in CKD 3- 5D

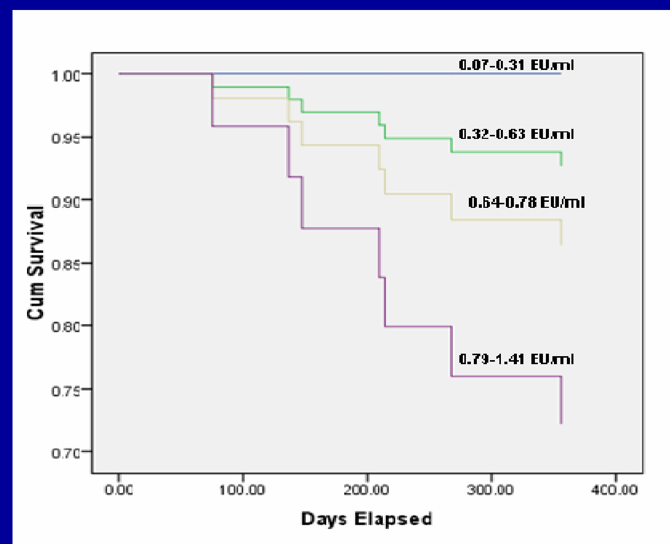


McIntyre CW et al. Clin J Am Soc Nephrol 2010

Effect of haemodialysis related factors on Endotoxaemia

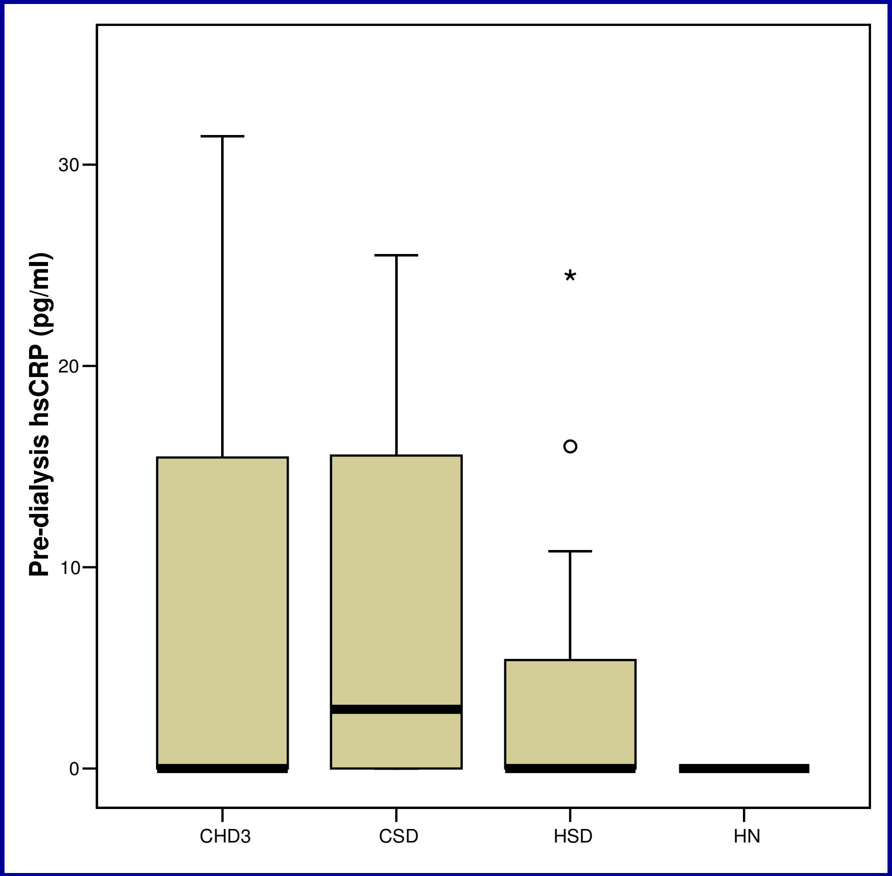


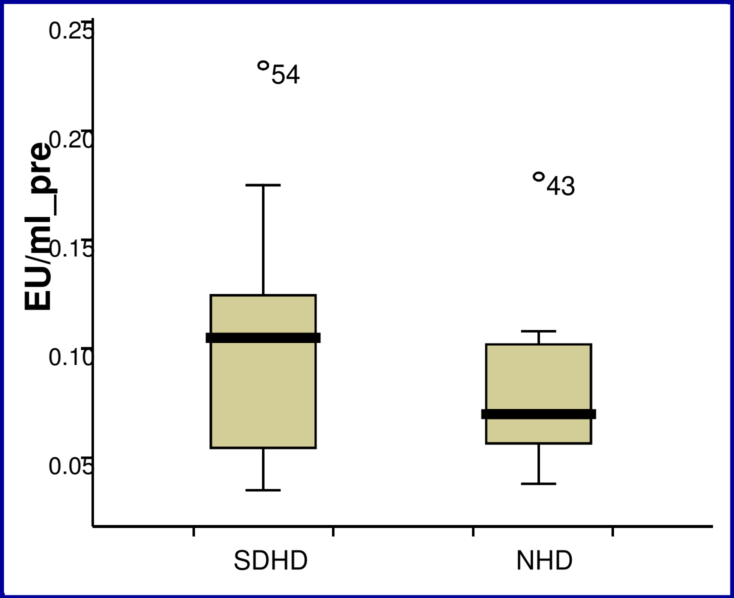




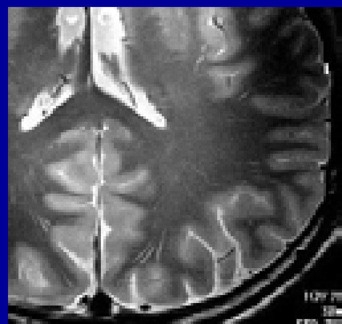
McIntyre CW et al. Clin J Am Soc Nephrol 2010

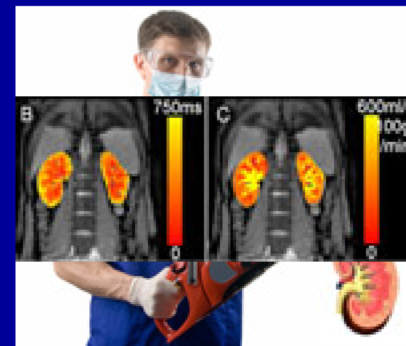
Endotoxinaemia and inflammation in daily dialysis patients

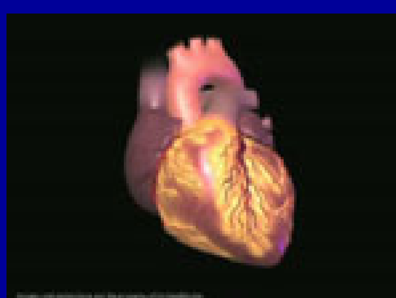




Dialysis hurts hearts- and a whole lot more besides







ENDOTOXIN

Interventional studies are great…..but make sure you're testing the right one