# Stress-Induced (Tako-Tsubo) Cardiomyopathy

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# TTC: How much do we know?

- Epidemiology:

  Most common in ageing (?postmenopausal) women. Often after physical/emotional stress

- Clinical features:

  (1) Presentation with chest pain/(dyspnoea)

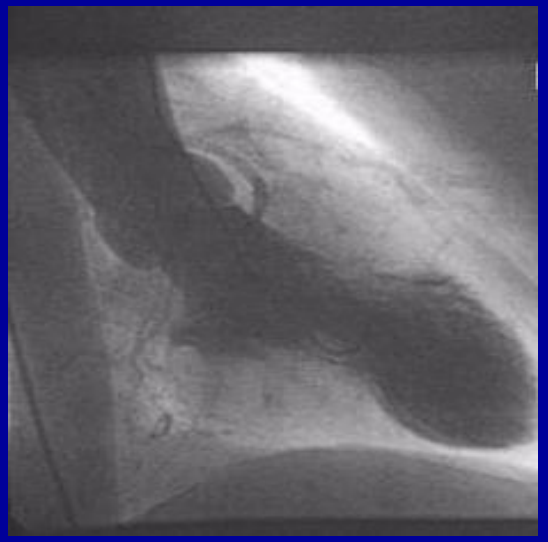
  (2) Often severely hypotensive (but clear lungs)

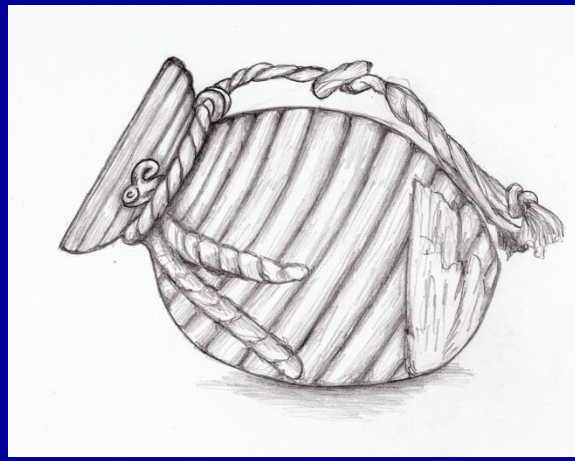
  (3) “Multi-regional” S-T elevation or T inversion

  (4) Regional wall motion anomalies, especially periapical

# Takotsubo: Background

- First described by Japanese in 1990
  - not widely investigated at the time
  - Plaque rupture/thrombosis theory relatively new
    - ? more interested in developing thrombolysis and PTCA
- Shape of Japanese octopus trap





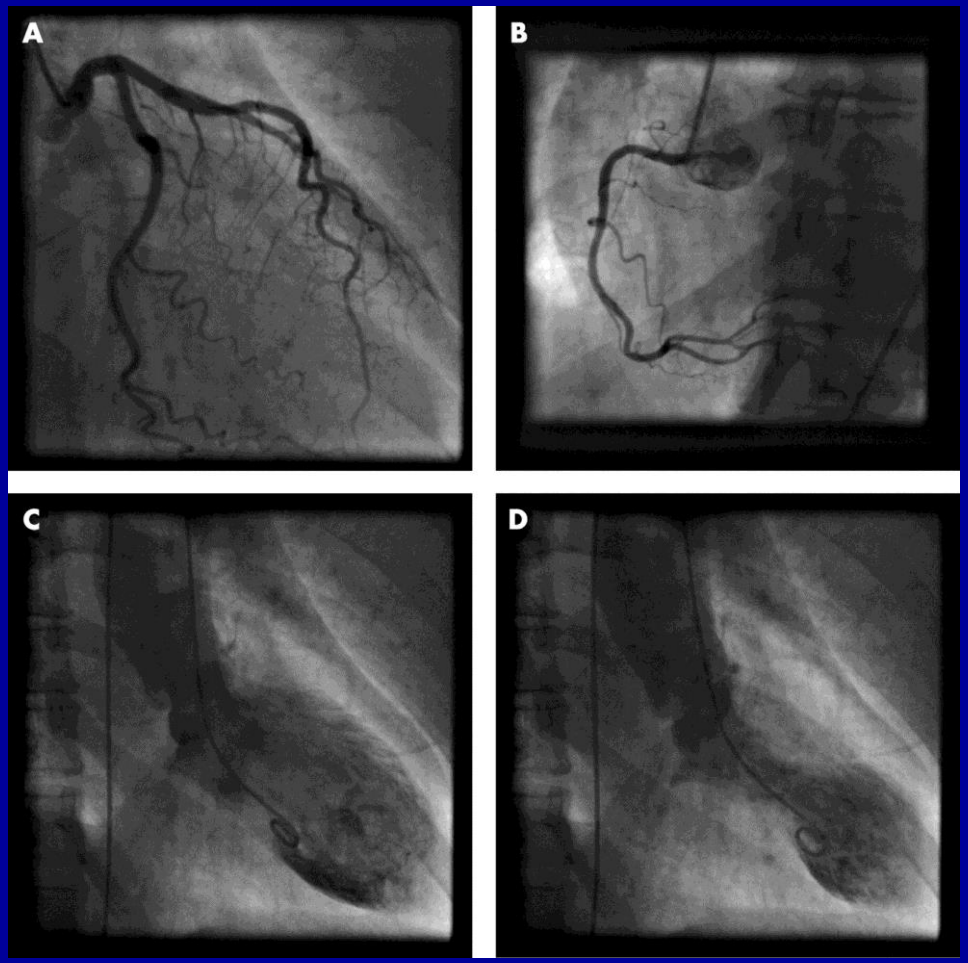
# SO: Can we make the diagnosis clinically?

- 63-year old woman comes home to find her husband dead
- Develops severe chest pain
- Hospital admission: anterior S-T elevation
- Thrombolysis: S-T resolution
- Subsequent cardiac catheterisation: normal coronaries: periapical hypokinesis

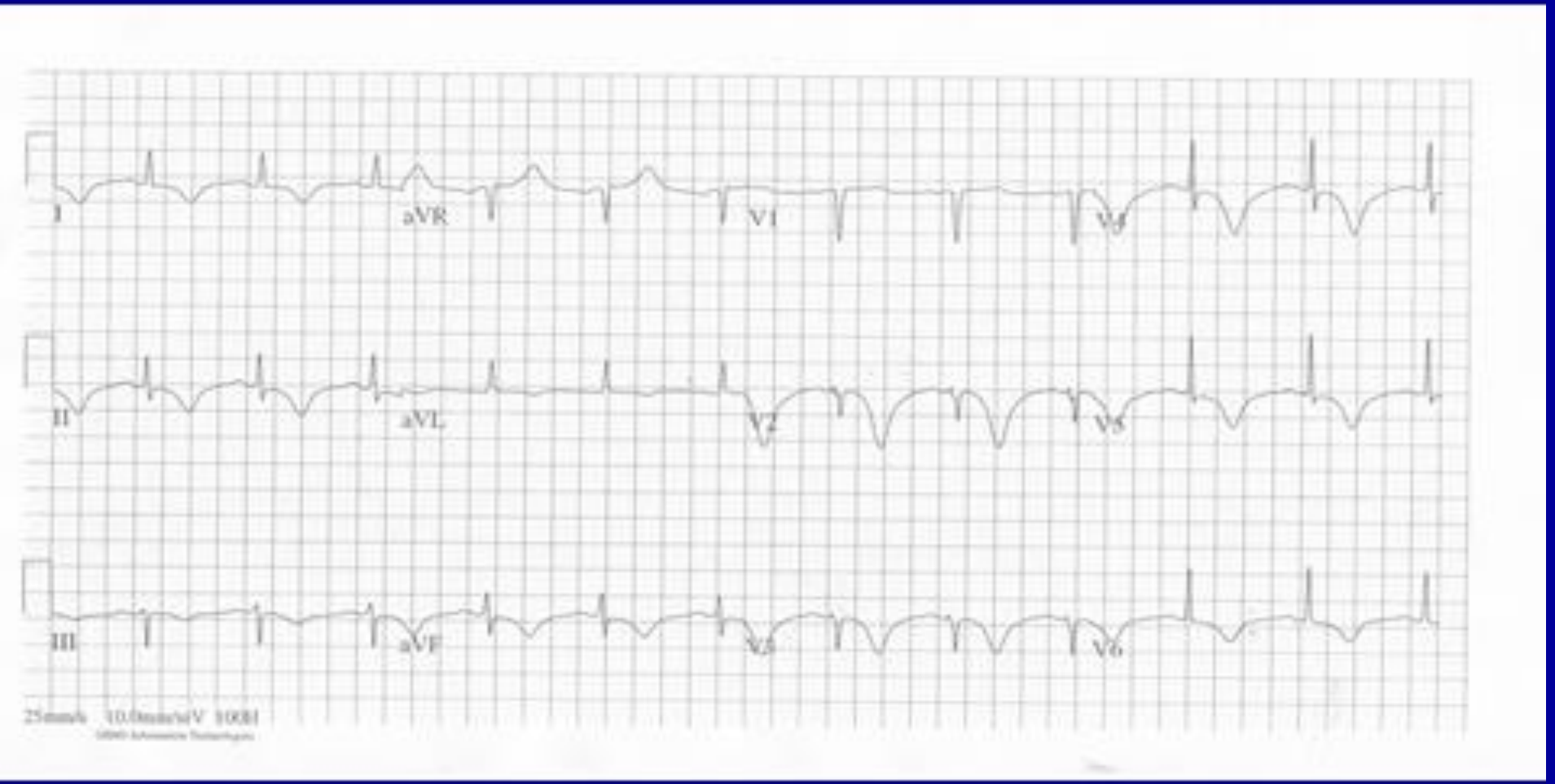
# Shock/Arrhythmias early in TTC

- Approximately 20% severely hypotensive at admission: best treatment uncertain
- Outflow tract obstruction and mitral regurgitation MAY contribute, but probably multifactorial
- Pre-hospital arrhythmia rate uncertain, but about 5% develop torsades post admission

# TTC: the catheteriser's view



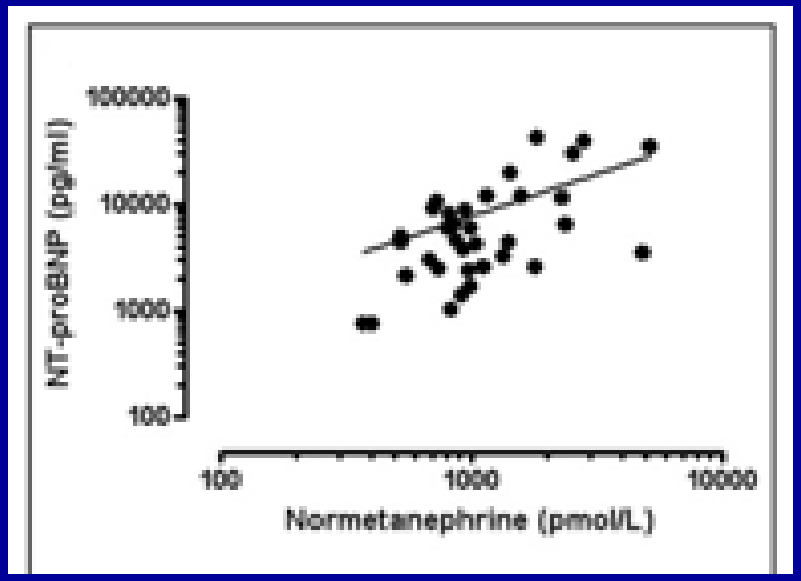
# Diagnosing TTC : “Multiregional” changes

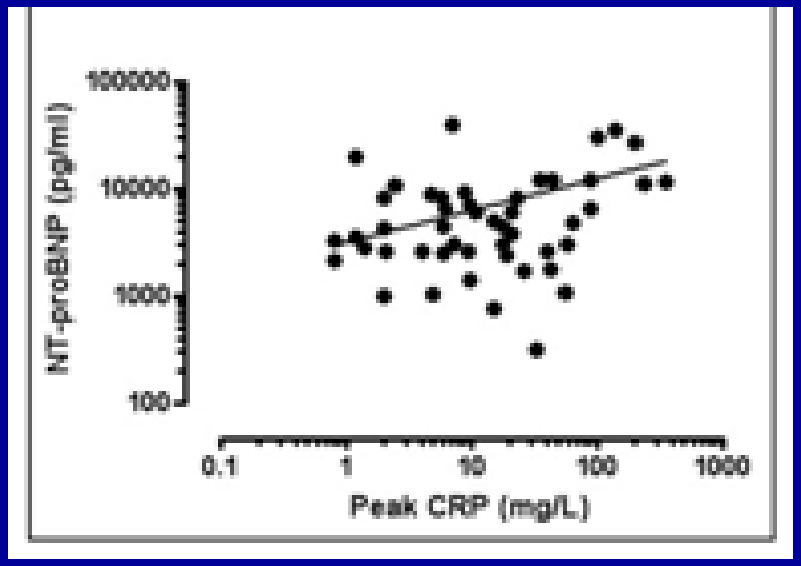


# Are there useful biomarkers?

- Troponin/CK elevation usually minor
- Moderate elevation of CRP
- Dramatic elevation of BNP/NT-proBNP at 24 hours
- Marked elevation of catecholamines

# Catecholamines and systemic inflammation in TTC




Nguyen et al, Am J Cardiol, 2011

# Takotsubo Cardiomyopathy presenting as S-T elevation myocardial infarction

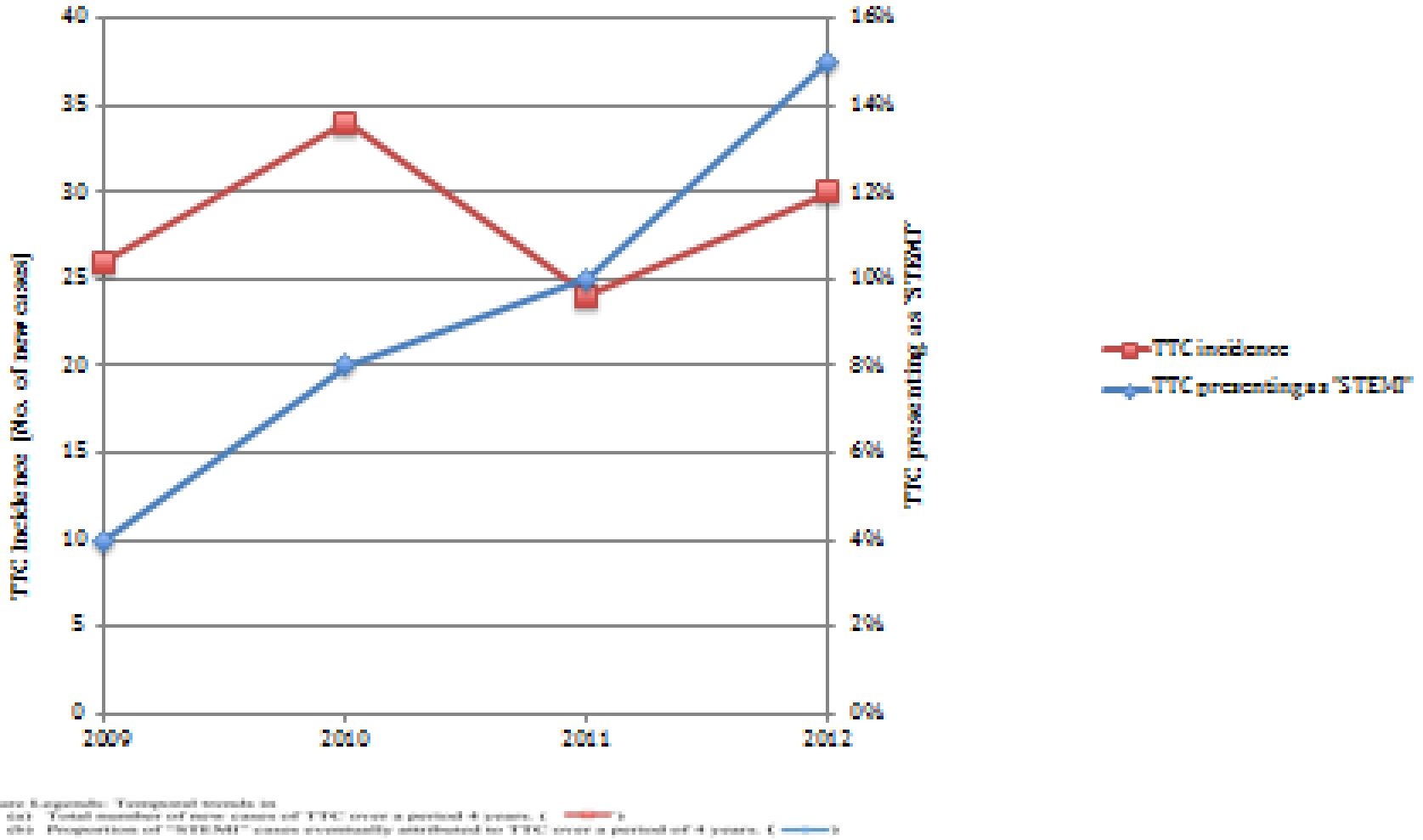
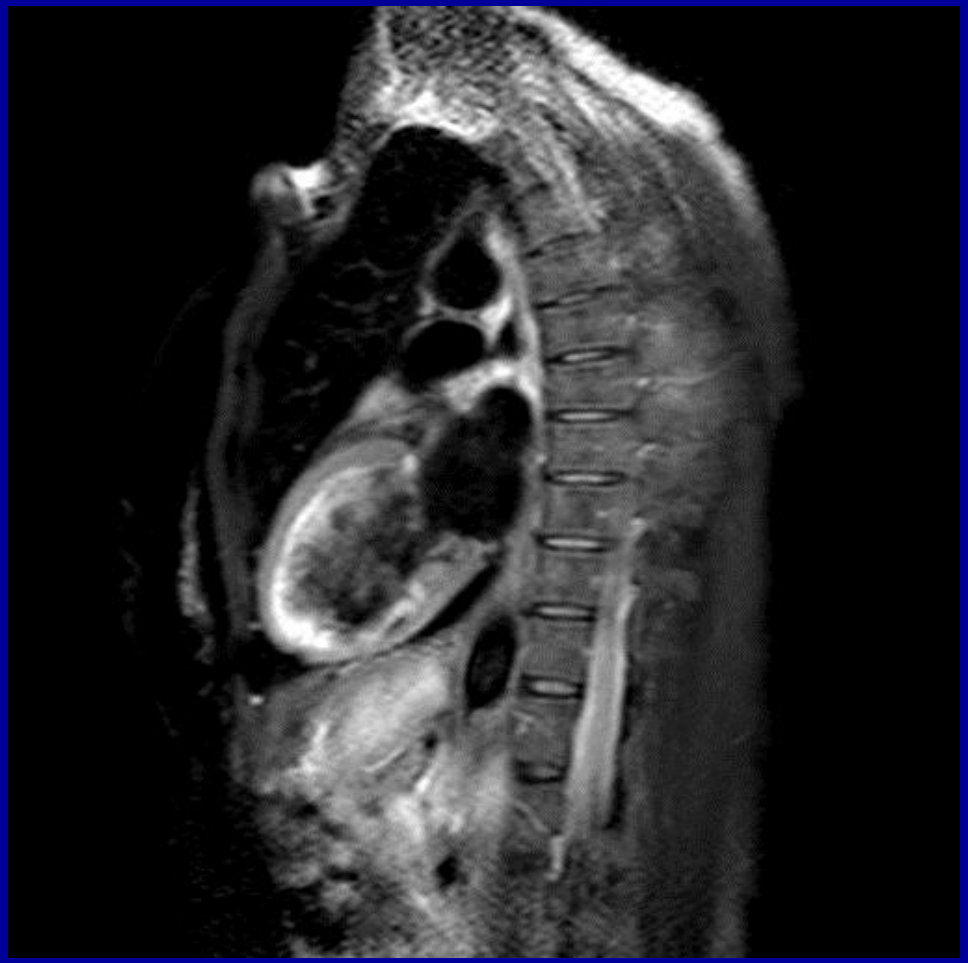


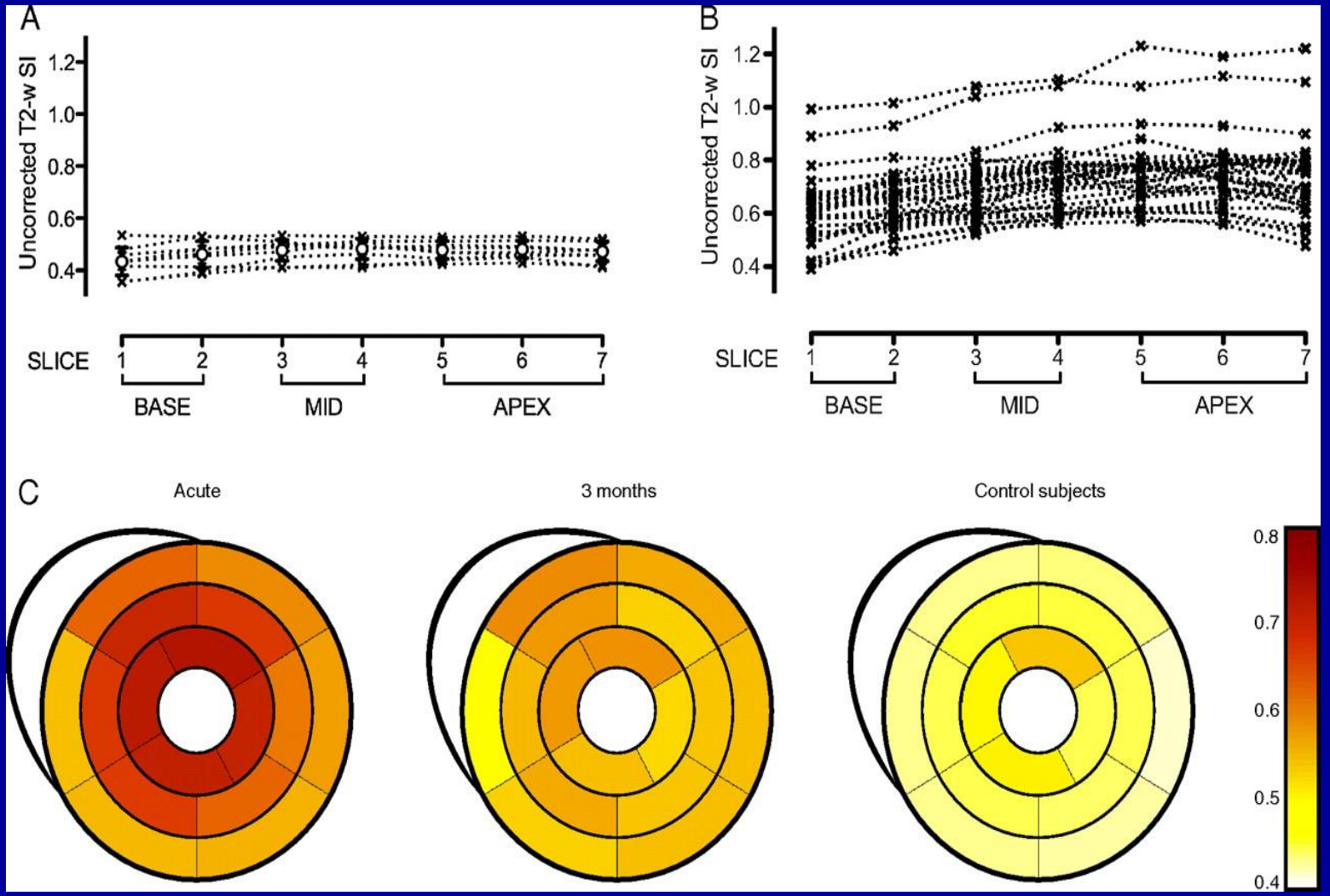

Figure 1 legends: Temporal trends in
(a): Total number of new cases of TTC over a period 4 years. (——)
(b): Proportion of "STEMI" cases eventually attributed to TTC over a period of 4 years. (——)

# Apical ballooning in TTC

# TTC as Pan-carditis



# Regional T2 quantitation (Neil et al,2012)



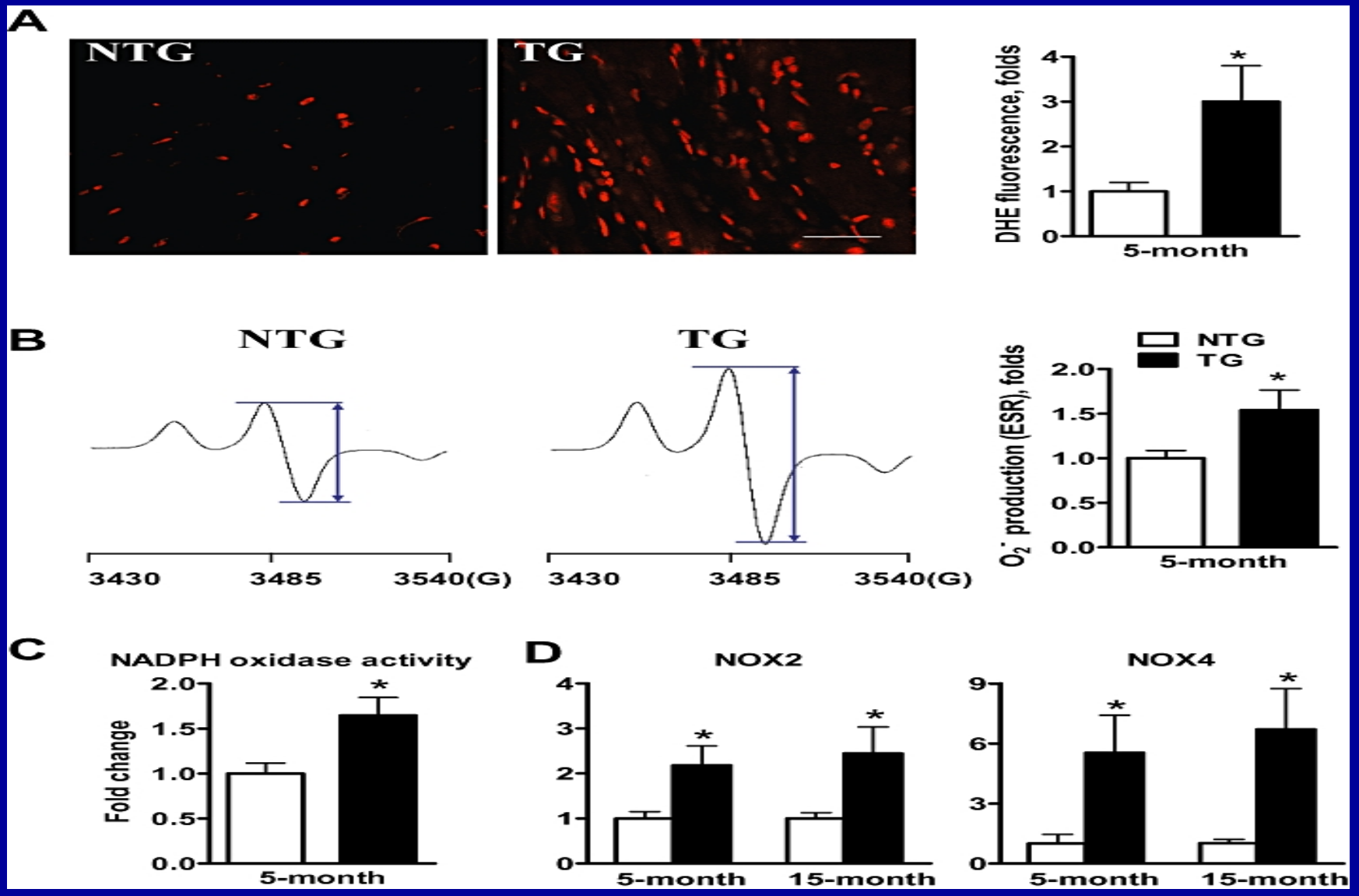
# Catecholamine surges:- Pivotal to onset of TTC?

- Documented in phaeochromocytoma, dobutamine stress imaging, treatment of anaphylaxis
- Catecholamine levels usually but not always markedly elevated
- Probable association with tricyclic and SNRA antidepressant therapy

# Beta-2 adrenoceptors and TTC

- In rats, adrenaline induced TTC-like changes via beta-2 stimulation
- This is both negatively inotropic and cardioprotective in long term
- Levosimendan appears to “rescue” hearts
- Beta-2 stimulation also increases ROS production, via NAD(P)H oxidase

# Beta-2 adrenoceptors and ROS



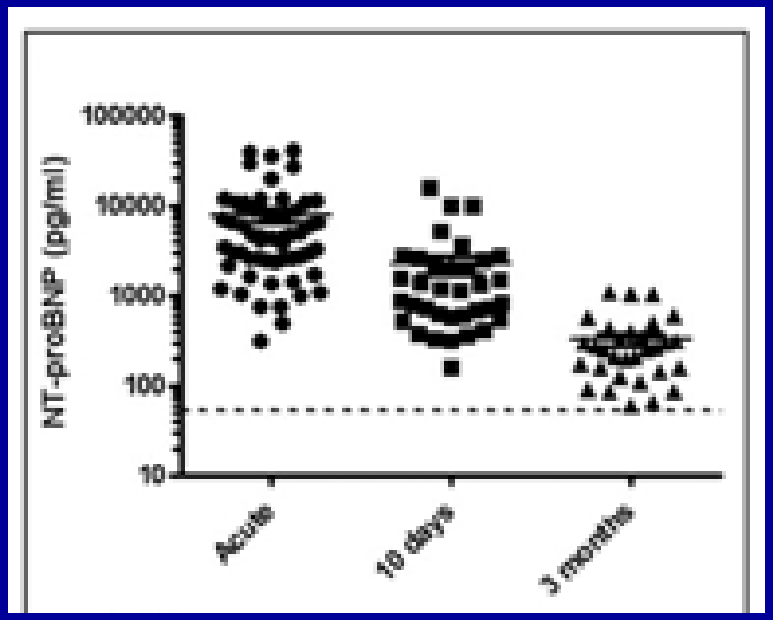
# Recovery from TTC

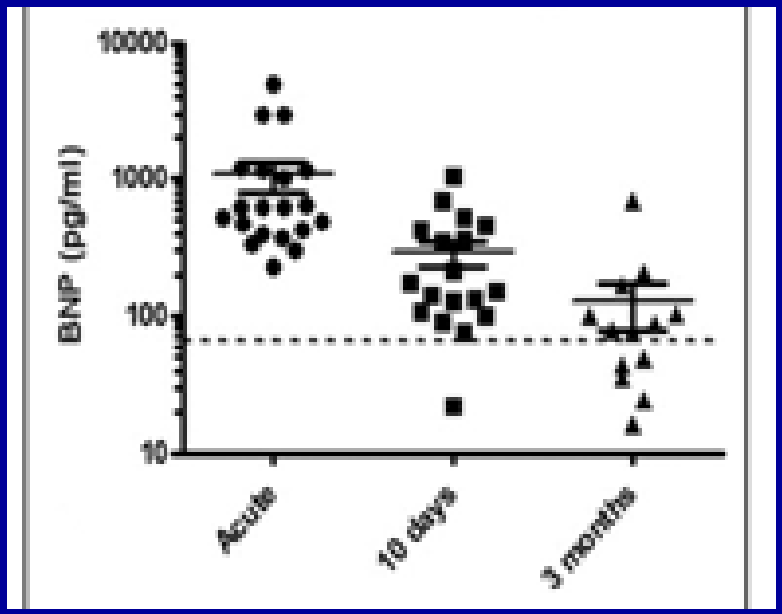
- LVEF is usually normal within 2 weeks
- However, most patients remain symptomatic for at least 3 months
- This reflects slow resolution of myocardial inflammation (and perhaps some permanent fibrosis)
- Recurrence rate approximately 3% per annum

# Evidence for slow resolution of TTC myocarditis

- On CMR,T2 score remains abnormal
- Global longitudinal strain remains depressed (about 10%)
- Persistent elevation of BNP and CRP

# BNP/NT-proBNPpro BNP elevation in TTC




Nguyen et al, Am J Cardiol, 2011

# New directions: mechanisms

- Female rats develop TTC-like changes 24 hours after isoprenaline injection
- Addressing:-

(a)Post-receptor signal transduction, given that beta-2 receptors are coupled to NOS

(b)Inflammasome activation: role of TxNIP

(c) Energetics deficiency: P-MRS studies

# Current Therapeutics

- Try to avoid catecholamine administration, even if patient shocked: ?levosimendan
  ?IABP
- Beta-blockers seem to be ineffective

- Theoretical case for at least 3 months' ACE inhibitor therapy

# Longer term issues

- Avoid tricyclic antidepressants and venlafaxine
- Explain to patient that condition is relatively benign, but patient should be aware of recurrence risk
- Expect lassitude/dyspnoea for 3 months
- If recurrent, ? phaeochromocytoma

# Potential future therapy

- Avoidance of nitrosative stress and its consequences:-

  (a) peroxynitrite decomposition

  (b) PARP inhibitors

- TxNIP suppression: ACE inhibitors, metformin

# Who did the work?

## Adelaide

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