modern cardiology support for the acute oncology patient

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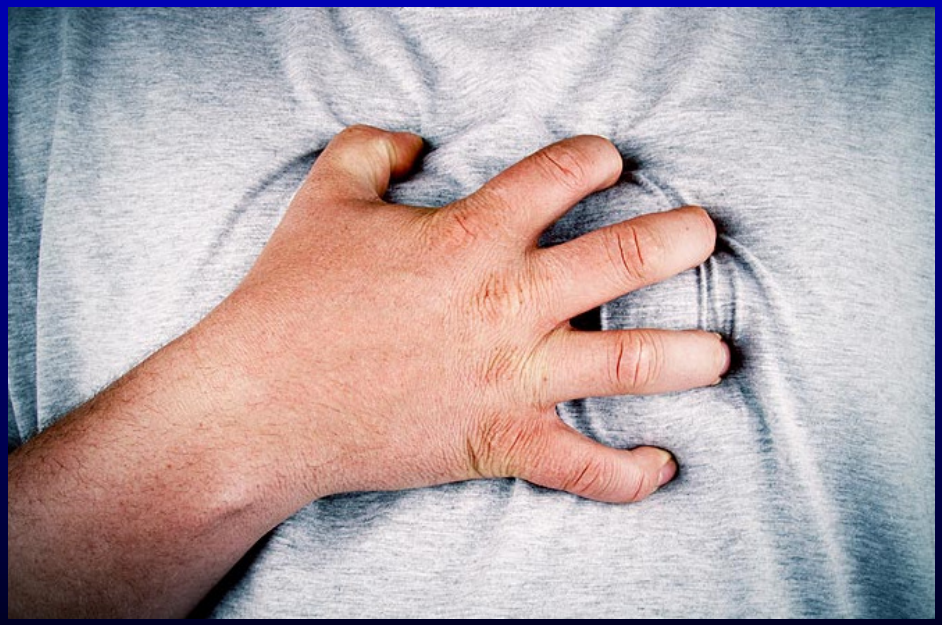
cardiology in acute oncology

what can go wrong ?

- acute coronary syndromes
  - 5FU
- arrhythmias
  - LQT
- heart failure
  - anthracyclines
  - trastuzumab
  - *et al.*

chest pain



acute coronary syndromes

Department of Health

Mending hearts and brains

Clinical case for change: Report by Professor Roger Boyle, National Director for Heart Disease and Stroke

2006 NHS

Department of Health

Treatment of Heart Attack National Guidance

Final Report of the National Infarct Angioplasty Project (NIAP)

British Cardiovascular Society 2008 NHS

ACS - organisation

ACS - complications

death

Method of treatment	30 days	1 year	18 months
PPCI	5.6	8.7	9.9
Thrombolysis	7.9	12.4	14.8

CTB Time	In-hospital	30 days	1 year
60–120 minutes	2.7	2.9	5.1
120–180 minutes	4.5	4.9	8.7
Greater than 180 minutes	11.4	12.2	15.9

Complications were low for patients receiving PPCI. The overall in-hospital stroke rate was 0.8% for PPCI patients and 1.3% for those receiving thrombolysis. The overall in-hospital rate of major bleeding was 3.5% in the PPCI group and 6.2% in those receiving thrombolysis.

ACS - ppci in oncology patients

anti-platelet agents

- ↑ bleeding risk if thrombocytopenic

heparin

- ↑ bleeding risk if liver dysfunction

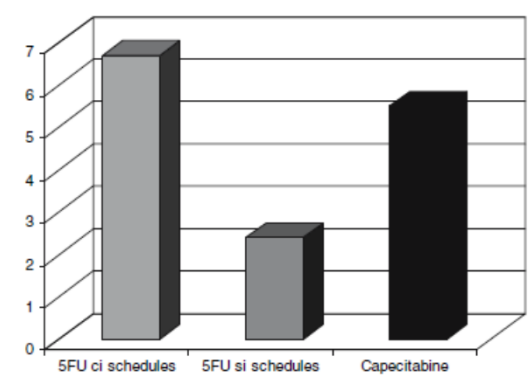
post-MI drugs

- aspirin, clopidogrel essential after stenting
- statin
- ACE inhibitor
- β-blocker.

chest pain 5-FU/capecitabine

risk

- case reports of chest pain, MI, death ≥ 1960s
- higher risk (x 4) in patients with CAD
- Kosmas *et al.* *J Cancer Res Clin Oncol* 2008;**134**:75-82
  n=644, no known CAD,
  26 developed symptoms & ECG changes:
  - $^{9}/_{381}$ = 2.4% si-5FU
  - $^{3}/_{54}$ = 5.6% capecitabine
  - $^{14}/_{209}$ = 6.7% ci-5FU (p=0.012).



chest pain 5-FU/capecitabine

events

- all 26 had ECG ST ↑ or ↓
- $^{7}/_{26}$ (27%) ↑ CK-MB x 2 (MI)
- 17 S_x compatible with angina → 6 ↑ CK-MB
- 7 palpitations → 1 ↑ CK-MB, 2 AF, 1 AVB
- 2 syncope → 2 CHB (1 death).

chest pain 5-FU/capecitabine

mechanism

- unknown !
- in vitro evidence of coronary spasm relieved by nitrates
- no clinical data
- direct toxic effect on vascular endothelium
- acute myocarditis.

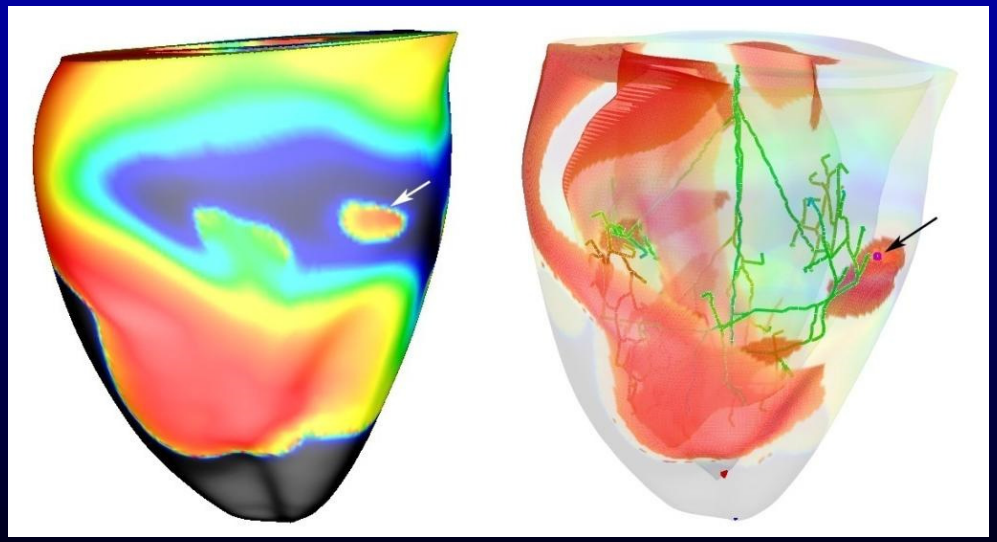
chest pain 5-FU/capecitabine

management

- symptoms → agent stopped
- ECG
- CK-MB (if ↑ x 2 → CCU 72h, no further 5FU)
- sublingual nitrates, cardiac monitoring
- patients without ↑ CK-MB, $^{3}/_{7}$ transdermal nitrates, continuous ECG monitoring, rechallenged at reduced dose → $^{3}/_{15}$ recurrent toxicity.

more data !

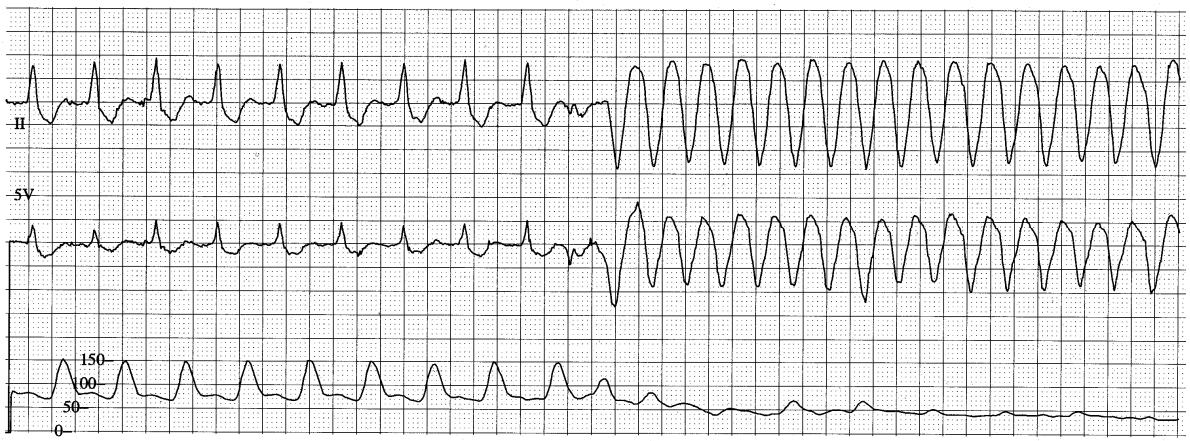
arrhythmias



arrhythmias

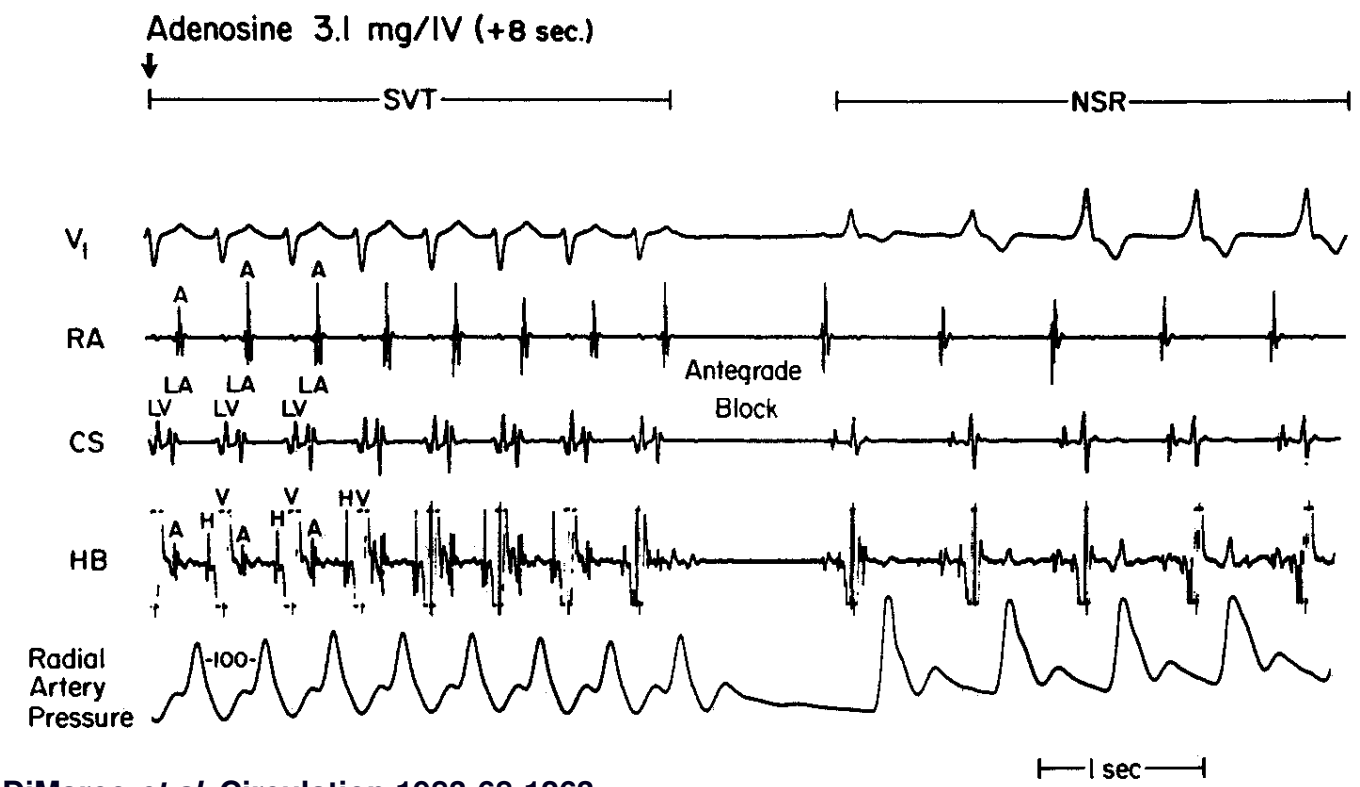
emergency treatment

- electricity!
  - pacing for bradycardia
  - cardioversion / defibrillation for unstable tachycardias.



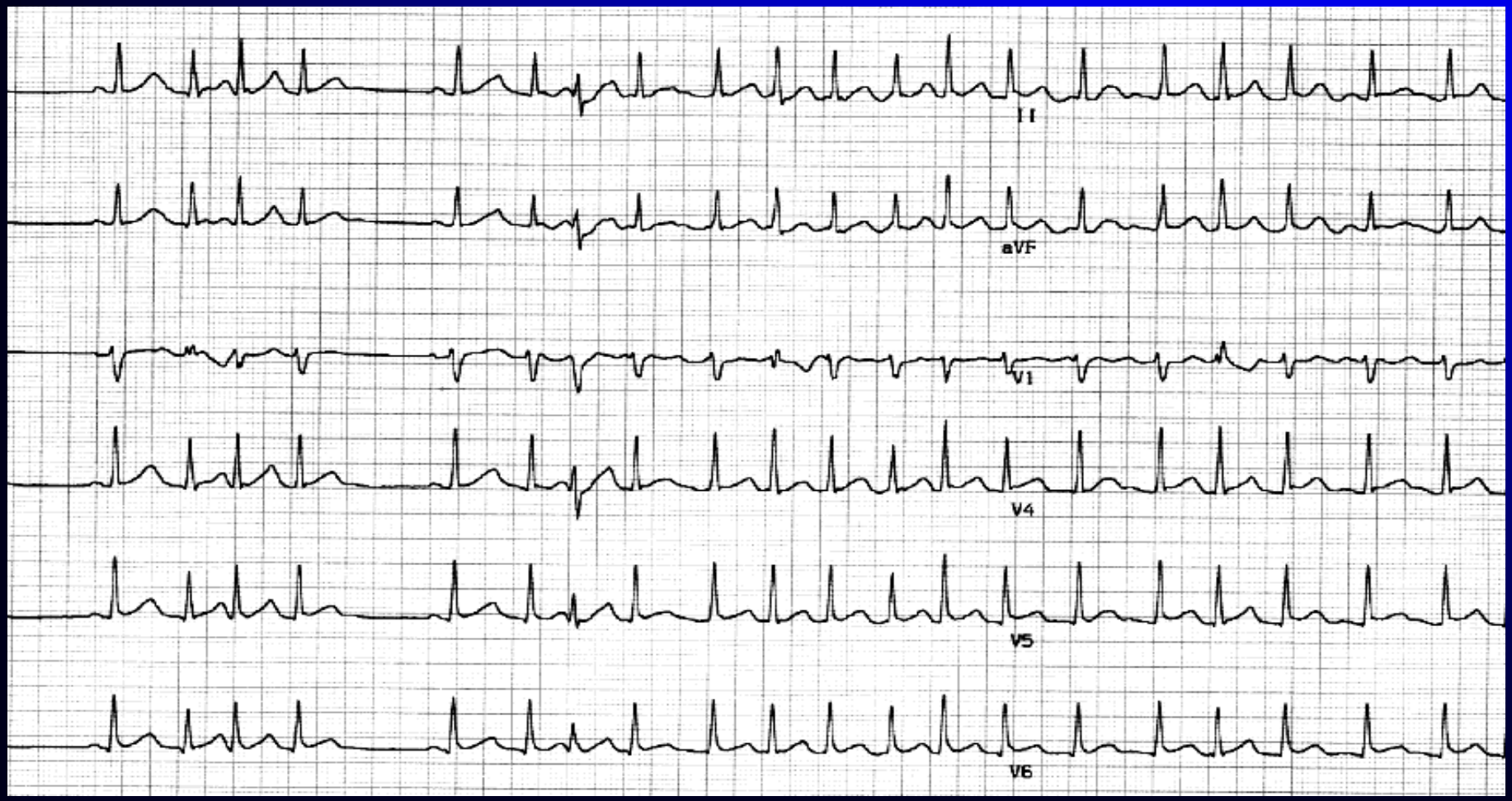
arrhythmias - SVT

acute management

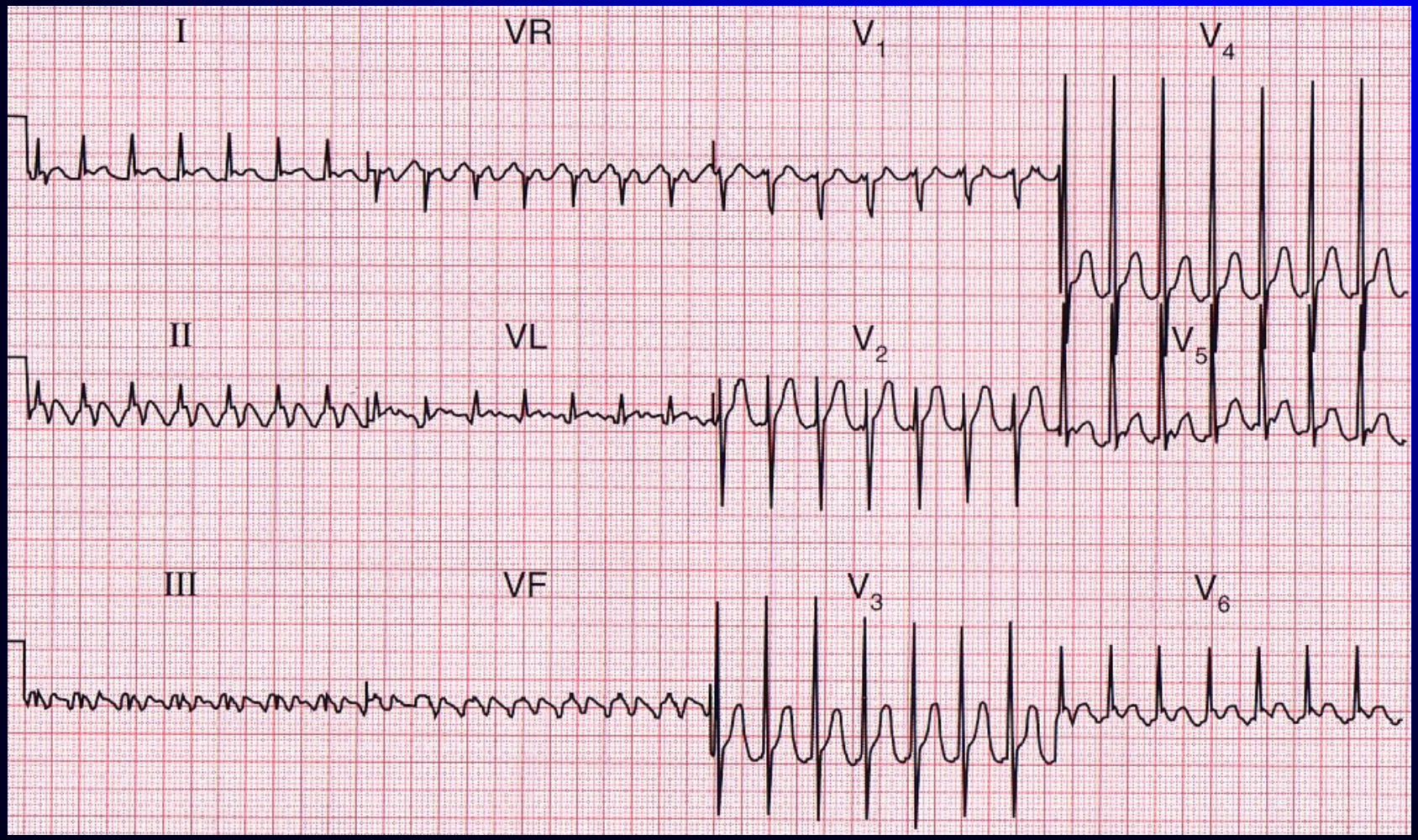


DiMarco *et al.* Circulation 1983;68:1263

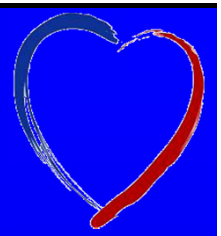
arrhythmias - atrial fibrillation



arrhythmias - atrial flutter



arrhythmias - AF and flutter



emergency treatment

- DC cardioversion under GA

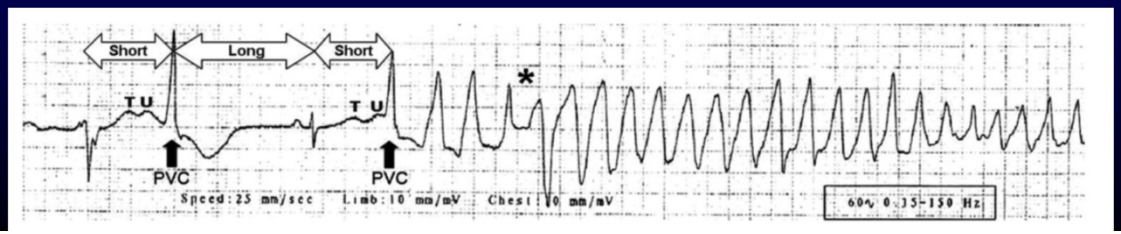
urgent treatment

- heart rate control
  - i.v. → p.o. β-blocker (or diltiazem)
- anticoagulation
  - for all if planning cardioversion
  - CHADS2 ≥ 2
  - heparin → warfarin INR 2.5
  - [dabigitran].

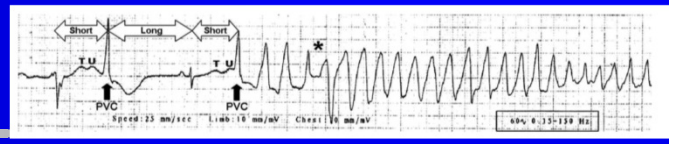
arrhythmias -TdP

characteristics

- LQTs (multiple)
- drug-induced LQT (multiple - http://www.qtdrugs.org)
  - short – long – short
  - twisting of the points → syncope / pre-syncope
  - warm up / down
  - spontaneous termination
  - degeneration to VF → death.



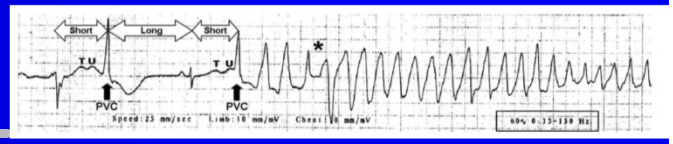
arrhythmias -TdP



risk factors

- ↑ QT (QTc > 500ms → x 2-3 risk) – check !
- drugs
- bradycardia, pauses
- ↓ K^+, Mg^{2+}, Ca^{2+}
- PVCs
- age
- female sex
- structural heart disease.

arrhythmias -TdP



management

- ♥ continuous ECG monitoring
- ♥ stop drug(s)
- ♥ magnesium sulphate i.v.
- ♥ replace K^+ to 4.5 – 5.0mM
- ♥ pacing for bradycardia.

Drew *et al. JACC* 2010;**55**:934-947

heart failure

cardiac toxicity – the problem

cytotoxics
(anthracycline)

pathway block
(HER2)

~~myocardium~~ + ~~function~~ → symptoms

~~little mitosis~~
0.45 to 1% / year

~~requirement for adaptation~~

↓

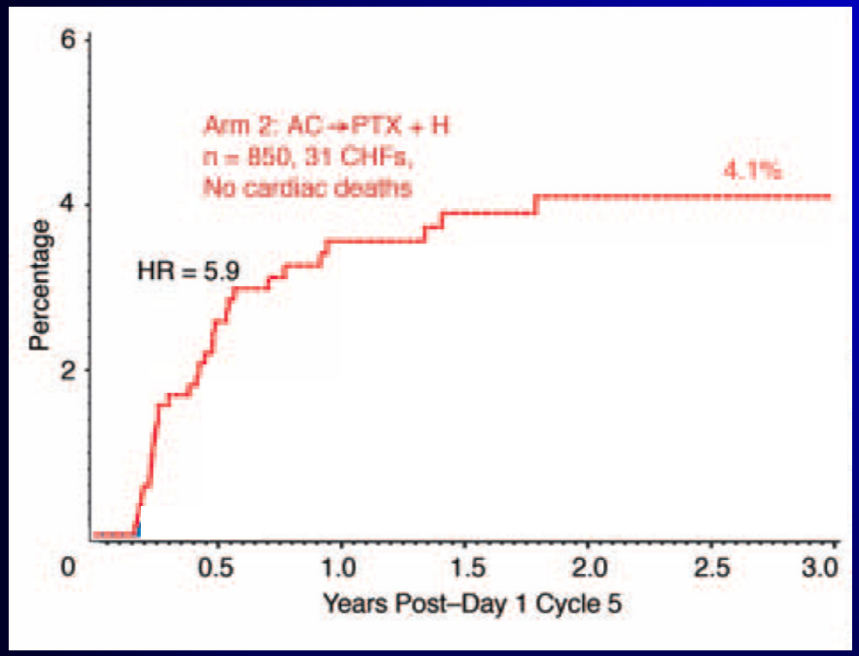
heart failure

trastuzumab

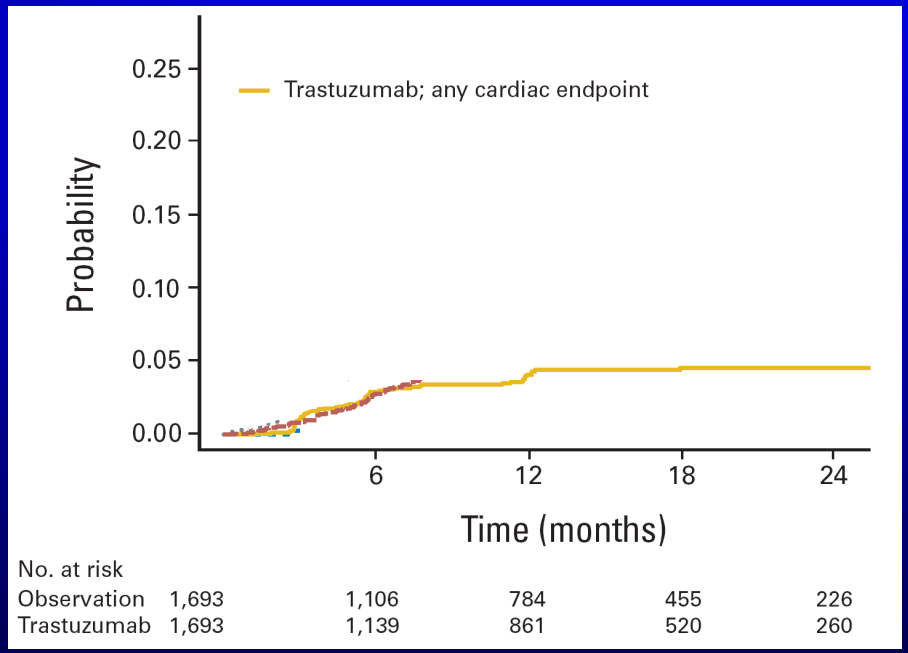
	FinHer	pivotal metastatic	NOAH	NSABP B-31	BCIRG 006	HERA
timing of trastuzumab	before	concurrent	concurrent	after mean 21 days	after mean 21 days	after mean 89 days
LVEF ↓ ≥ 10%	6.8%	28%	23%	14%	18%	7%
NYHA III/IV	0.9%	16%	2%	4%	2%	0.6%
substantial recovery reported	N/A	N/A	Yes	Yes	N/A	Yes

trastuzumab - time course

B-31



HERA

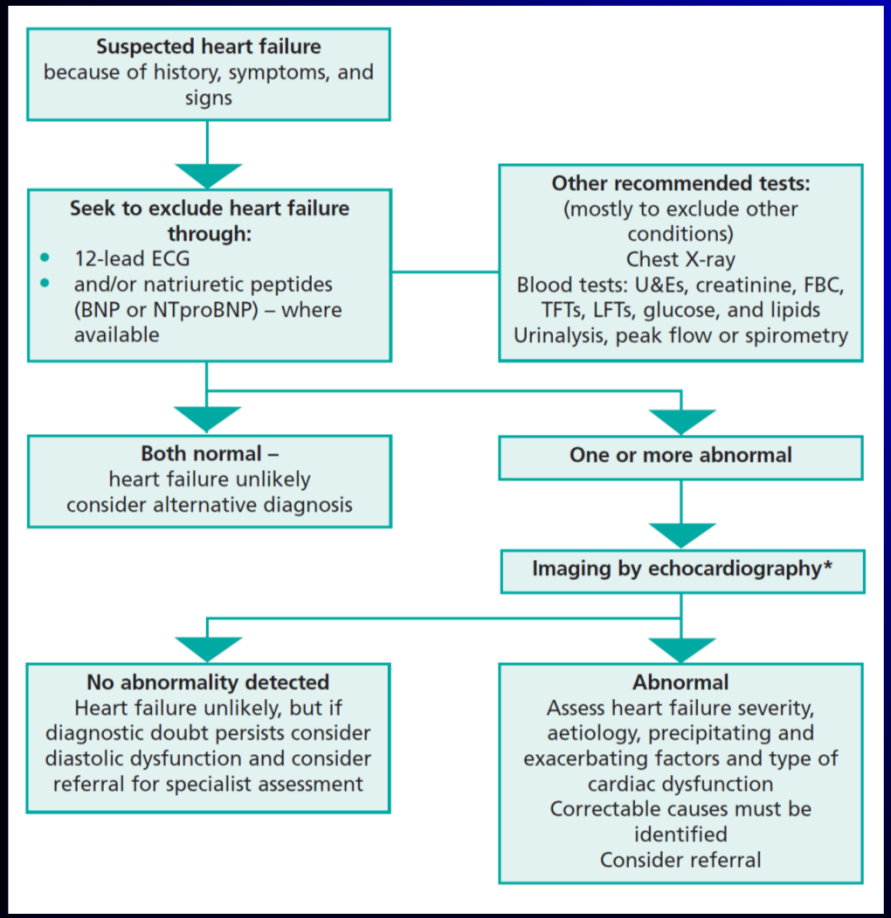


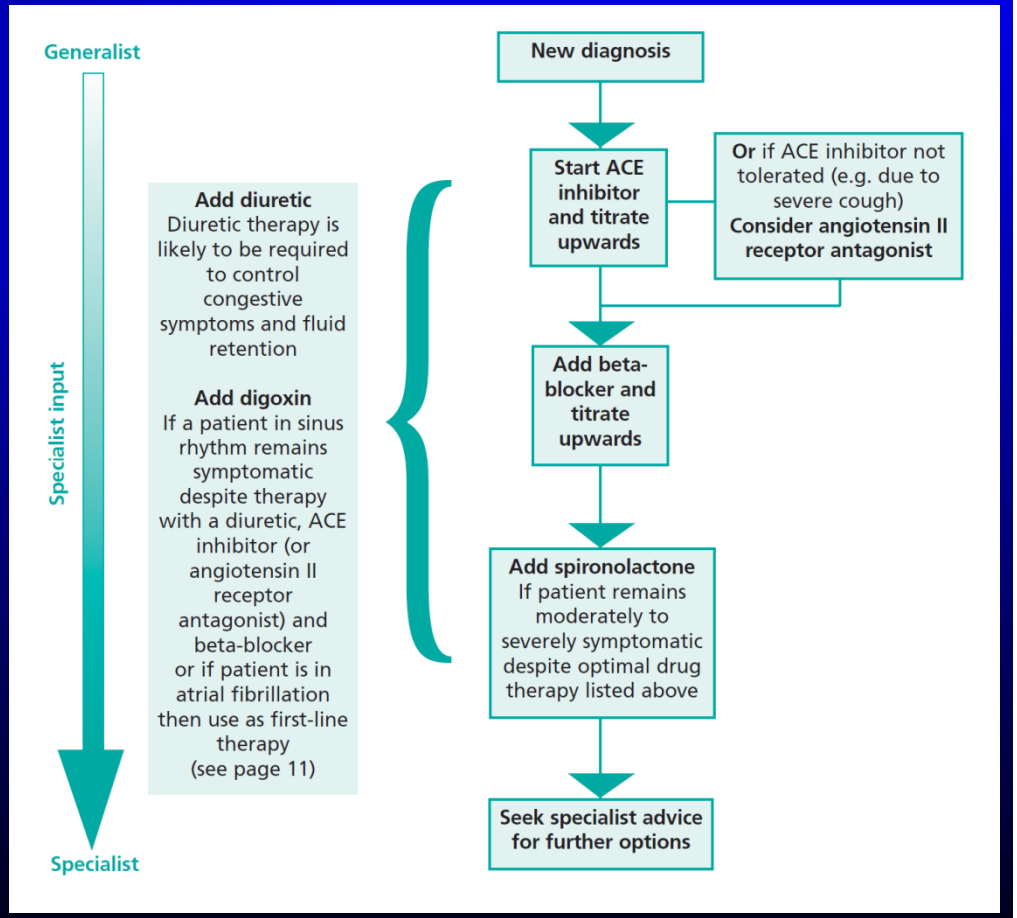
trastuzumab - reversibility

- CREC – 79% symptomatic pts improved on R_x
  - recovery: trastuzumab + Pac ($^5/_5$) >> trastuzumab + AC ($^{14}/_{21}$)
- B-31, n=31 NYHA III/IV
  - 1 had S_x at $^6/_{12}$
  - 29% complete recovery of EF
  - 75% had EF >50%
- HERA (Suter *et al. JCO* 2007;**25**:3859-3865)

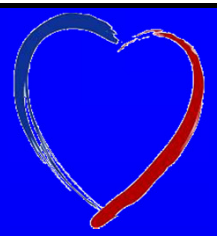
	n	asymptomatic	recovery (EF >55%)
↓ EF + asymptomatic	25	25 (100%)	17 (68%)
↓ EF + NYHA II	36	36 (100%)	24 (67%)
↓ EF + NYHA III-IV	10	8 (80%)	6 (60%)

management – NICE 2006





treatment - ACEi ± β-blocker



ACE*i*

- e.g. perindopril 2mg od
- c.i. known renal artery stenosis, (renal failure)
- GP will check C&Es and titrate to 4mg od

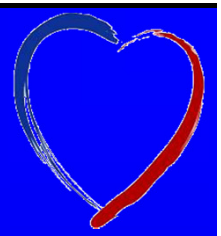
β-blocker

- e.g. bisoprolol 1.25mg od
- c.i. symptomatic bradycardia, severe asthma
- GP check HR/symptoms and titrate to 10mg od

continue unless there is a reason to stop.

conclusions

oncology ⇆ cardiology



- increasing interaction
  - new drugs
  - increasing awareness of the risks of old drugs
- new management for MI (acute & chronic)
- capecitabine > si 5-FU
- watch QT (don't believe the ECG machine!)
- heart failure
  - acute
  - chronic - ↑ ACEi, β-blockers, aldosterone antagonists, devices
- need more good trial data.