Case Studies in Cardiology
Testosterone in Cardiovascular Disease, Ischaemic Heart Disease (microvascular angina and coronary spasm), Hypertension and Sports Cardiology.

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- Testosterone in cardiovascular disease
- IHD
- Hypertension
- Sports Cardiology

Testosterone: a hormone preventing cardiovascular disease or a therapy increasing cardiovascular events?

European Heart Journal (2016) 37, 3569–3575

Testosterone and cardiovascular disease

Decreasing testosterone levels - older men
- decrease by 1–2% per year

- Low T
- Manopause
- Hypogonadism
- Andropause

Some of the symptoms of androgen deficiency include:

- breast development (gynaecomastia)
- reduced muscle mass and strength
- increased body fat, particularly around the abdomen
- weaker erections and orgasms
- reduced amount of ejaculate
- reduced bone mass, therefore increased risk of osteoporosis
- reduced sexual desire
- hot flushes and sweating
- lethargy and fatigue
- Depression
- loss of body hair

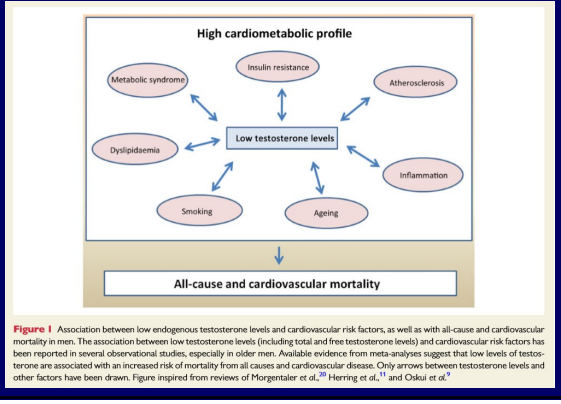

Figure 1 Association between low endogenous testosterone levels and cardiovascular risk factors, as well as with all-cause and cardiovascular mortality in men. The association between low testosterone levels (including total and free testosterone levels) and cardiovascular risk factors has been reported in several observational studies, especially in older men. Available evidence from meta-analyses suggest that low levels of testosterone are associated with an increased risk of mortality from all causes and cardiovascular disease. Only arrows between testosterone levels and other factors have been drawn. Figure inspired from reviews of Morgentaler *et al.*,[29] Herring *et al.*,[11] and Oskui *et al.*[9]

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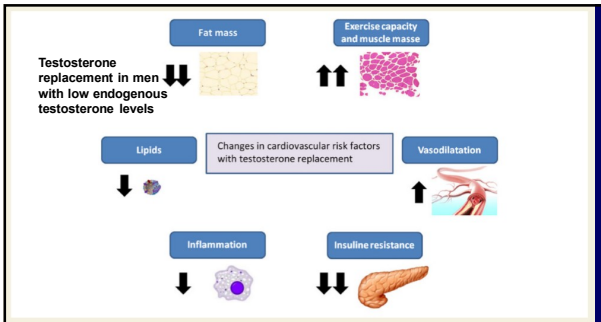

Figure 2 Changes in cardiovascular risk factors with testosterone replacement therapy in men with low endogenous testosterone levels. In men with low testosterone levels, testosterone therapy has been associated with a reduction in fat mass, total cholesterol, glucose concentration, serum concentrations of inflammatory markers and with an increase in time to onset of symptomatic angina with exercise (vasodilatation), muscle mass, and exercise capacity in men with symptomatic heart failure. Figure inspired from reviews of Morgentaler *et al.*,[29] Herring *et al.*,[11] and Oskui *et al.*[9]

Benefits were also demonstrated for sexual function, mood, and possibly other components of the metabolic syndrome

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Testosterone and cardiovascular disease

Table 3 Association between testosterone replacement therapy and cardiovascular outcomes

Years	Number of patients on testosterone	Country	Mean follow-up (years)	Mean age (years)	MACE	Results (users vs. non-users)
2010[17]	209	USA	0.5	74	MedRac cardiac events	OR 5.8 (95% CI 2.0–16.8)
2013[23]	1223	USA	2.3	60.6	Mortality, MI and Stroke	HR 1.29 (95% CI 1.04–1.58)
2013[24]	2994	Meta-analysis	NA	NA	CVD events (ICD classification)	OR 1.54 (95% CI 1.09–2.18)
2014[22]	55 593	USA	0.3	54.4	Non-fatal MI	RR 1.36 (95% CI 1.03–1.81)
2014[24]	6355	USA	NA	NA	MI	HR 0.84 (95% CI 0.69–1.02)

CI, confidence intervals; CVD, cardiovascular disease; HR, hazard ratios; ICD, international classification of disease; MACE, major adverse cardiovascular events; MI, myocardial infarction; NA, not available; OR, odds ratios; RR, relative risk; TRT, testosterone replacement therapy.

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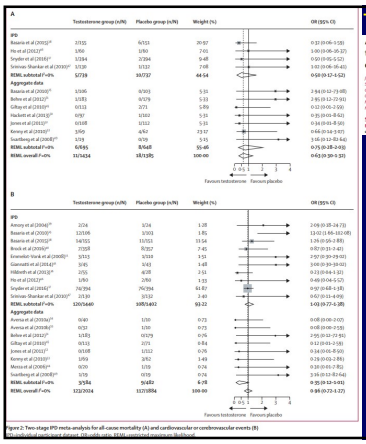

Figure 2: Two-stage IPD meta-analysis for all-cause mortality (A) and cardiovascular or cerebrovascular events (B)

Testosterone and cardiovascular disease

Adverse cardiovascular events and mortality in men during testosterone treatment: an individual patient and aggregate data meta-analysis

O.A

Summary

Background Testosterone is the standard treatment for male hypogonadism, but there is uncertainty about its cardiovascular safety due to inconsistent findings. We aimed to provide the most extensive individual patient

The NEW ENGLAND JOURNAL of MEDICINE

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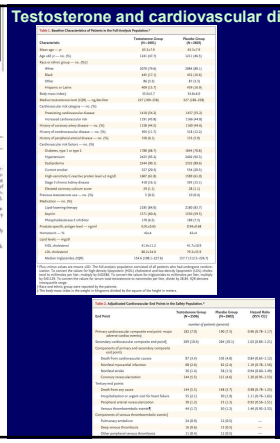
Cardiovascular Safety of Testosterone-Replacement Therapy

A.M. Lincoff, S. Bhasin, P. Flevaris, L.M. Mitchell, S. Basaria, W.E. Boden, G.R. Cunningham, C.B. Granger, M. Khera, I.M. Thompson, Jr., Q. Wang, K. Wolski, D. Davey, V. Kalahasti, N. Khan, M.G. Miller, M.C. Snabes, A. Chan, E. Dubiniere, X. Li, T. Yi, B. Huang, K.M. Pencina, T.G. Travison, and S.E. Nissen, for the TRAVERSE Study Investigators*

ABSTRACT



Testosterone and cardiovascular disease

Testosterone therapy

- In men with androgen deficiency with a diagnosis of hypogonadism resulting from an established medical disease of the testes, pituitary, or the hypothalamus
- Symptomatic
- Documented low testosterone levels
- Screening for androgen deficiency in the general population is not recommended.
- In older men with low testosterone levels, testosterone placement should be based on an individualized approach discussing the risks and benefits, as well as the uncertainty surrounding this therapy.

European Heart Journal (2016) 37, 3569–3575

Case 1

39 yr. old male admitted on the 20th July 2016 with a history of right-sided facial, arm and leg weakness, difficulties moving his lips and an expressive dysphasia. Two days earlier he complained of left-sided face and arm weakness that lasted 20 seconds. For the preceding three weeks he noticed that his vision was blurred.

An urgent CT – no significant findings.

ECG showed atrial fibrillation with a ventricular rate of 130 beats per minute.

He works as a personal trainer.
Previously lost 12-14 stone (76 -88 kg) over the preceding 3½ year period Using ephedrine, caffeine, anabolic androgenic steroids, thyroxine and caffeine.

PMx: nil.

FHx: mother died of a stroke at age 57 which may be related to a clot originating in her leg. He has a sister with three miscarriages.

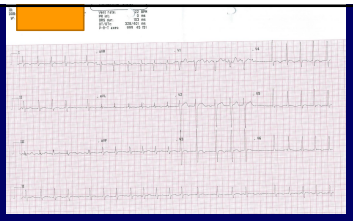
Case 1

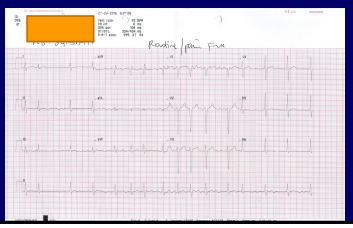
Non smoker. Drinks alcohol occasionally and denies using any recreational drugs.

HB mildly elevated at 171 gm/L with a normal MCV, CRP, ferritin, TFT's, haemoglobin A1c, beta-2 microglobulin, ANA and anti-cardiolipin antibody. Although lupus anticoagulant screen was done it could not be interpreted given that he was on Apixaban. Creatinine was mildly elevated at 135 mmol/L, with sodium of 138 mmol/L, potassium 4.9 mmol/L and an eGFR of 51 ml/min, LDH was mildly elevated at 353 IU/L. He was negative for factor V Leiden.

His ventricular rate was adequately controlled on bisoprolol 10 mg daily. He was also commenced on Ramipril and the dose was slowly titrated up to 5 mg bd, and Apixaban 5mg BD

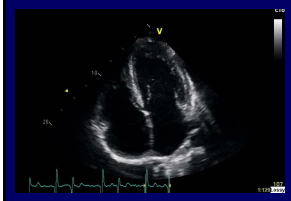
An inpatient echocardiogram demonstrated moderately dilated left ventricle (LVDD 6.5 cm, LVDS 4.97 cm) with significant LV systolic impairment. There was no significant valvular abnormalities. The right ventricular systolic pressure was 26 mmHg. Inferior vena-cava was dilated with poor inspiratory collapse.

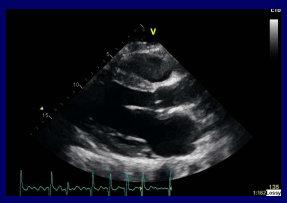


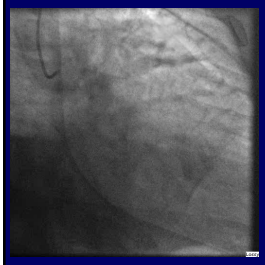


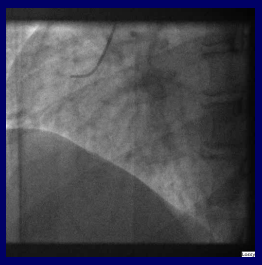
Case 1

Case 1









Case 1

Over a 3.5 years

Started with DNP (dinitrophenol)

Ephhedrine 30-90mg
Caffeine 200-400 mg,
Aspirin
} ECA stack. Daily. Occasionally omit stack 1-2 wks. up to 4 times over 3 years

T3 50mcg OD
Clembuterol 40-120 mcg OD
} Stack for 3 wks. Six times over 3 yrs.

Test 250 (fast and slow acting testosterone)
Decabolin
Winstrol
} Stack, twice wkly for 16 wks. Then stop for 3 months

Alternate

Test 300/400
Tren (trenbolone)
Anavar (oxandrolone)

Treatment

- Apixaban 5mg BD, Bisoprolol 10mg, Ramipril 10mg
- DC cardioverted – failed.
- Spironolactone 25mg added
- 15 months later LV size normal, preserved LV systolic function
- AF Ablation.
- 48 hours later reverted to AF
- Awaiting redo AF ablation
- Body dysmorphia
- Being considered for bariatric surgery

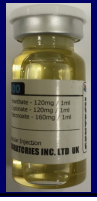
Case 2

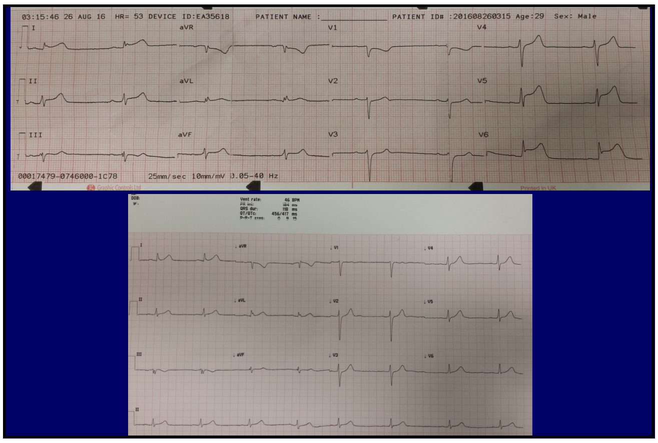
29 year male. Admitted in the early hours of the morning after awakening with acute onset heavy chest pain associated wit sweating.

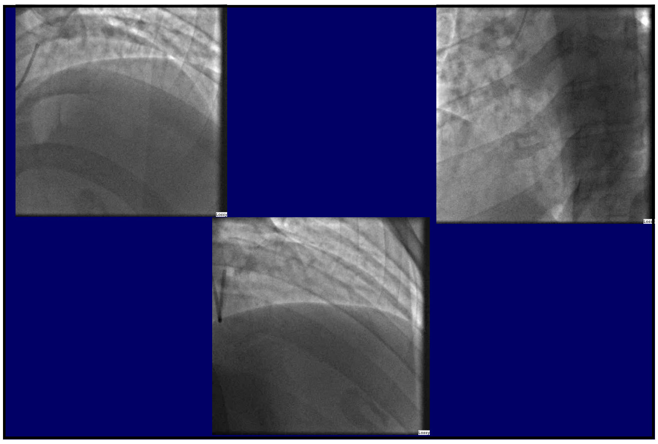
Smoker. Denied recreational drugs. No FHx of IHD. Cholesterol 4.2 mmol/l, HDL 0.49 mmol/l, TGL 0.89 mmol/l

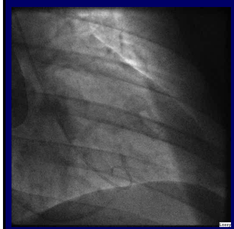
PMHx: Nil. Admits to using Test 400 and Stanvar (oxandrolone and stanozol) Winstrol)

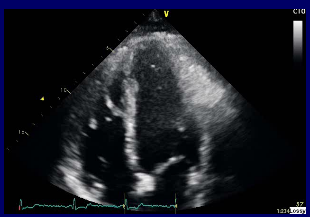
Paramedics ECG ST↑ I, AvI, V5, V6.











Case 3

49 year male. Active. High intensity interval training 3-4x/week

RF: pre-diabetic 2 yrs. on metformin. Choleterol 5.4 mmol/l, LDL 3.5 mmol/l, HDL 1.2 mmol/l, TGL 1.5 mmol/l. Ex-smoker 25 years.. No FHx.

PMx: low testosterone on a general health check, vitilgo, lumbar disc herniation

DHx (before MI): metformin 500mg BD and testosterone enanthate 210mg once weekly. No recreational drugs.

21/4/17: burning chest pain. Anterior MI. 2 stents to LAD

Reviewed 3rd May 2017

Diagnoses: **49 yr. old male**

1. Anterior wall myocardial infarction 21st April 2017 treated with two drug-eluting stents to the LAD at the Royal Free Hospital
2. Transthoracic echocardiogram showed significant LV impairment with an ejection fraction of 35%. Mild left atrial enlargement with normal RV size and function.
3. Vitiligo.
4. Fractured right elbow.
5. Lumbar disc herniation.
6. Testosterone replacement

I reviewed this gentleman today for the first time a cardiology opinion. On 21st April 2017, shortly after eating dinner he started developing burning/pressure-like chest pain which persisted throughout the night and in early hours of the morning. There was no radiation or associated symptoms. He was subsequently reviewed at [redacted] where he was diagnosed as having an anterior wall myocardial infarction and was sent to the [redacted] for primary angioplasty. He was discharged three days afterwards. Since discharge he has had no further chest pain or history of shortness of breath.

He recently developed a pruritic erythematous rash over his body, which is most likely an allergic reaction to one of his medication. This has improved following Piriton.

His risk factors include: a 2-year history of prediabetes, he is an ex-smoker for 25 years and his baseline cholesterol level in 2016 was 5.4 mmol/l, LDL 3.5 mmol/l, HDL 1.2 mmol/l, and triglycerides 1.5 mmol/l. He is also on testosterone enanthate injections once weekly (210 mg).

His current medication consist of metformin 500 mg BD, ticagrelor 90 mg BD, aspirin 75 mg daily, bisoprolol 2.5 mg daily, atorvastatin 80 mg daily, ramipril 2.5 mg daily, eplerenone 25 mg daily and testosterone replacement.

His father died at 78 years with progressive supranuclear palsy. His mother died at age 83 years with a history of Alzheimer's disease and a PE. He has an older sister with carpal tunnel syndrome.

He is married with three children: 9 years, 14 years and 16 years. He drinks up to two units of alcohol a week. He works in the banking sector.

On systemic enquiry he mentioned that he has sleep problems and can awake at 4 am at night and is unable to go back to sleep. He is a heavy snorer which has improved to some extent since he has lost weight. His wife mentioned that he has periods of apnoea at nights. He suffers with daytime lethargy.

Examination: weight 102 kg, height 1.86 meters and BMI 29.5. Pulse 68 beats per minute. JVP not elevated. Blood pressure 130/90 mmHg. Heart sounds S1 plus S2. His chest and abdomen were unremarkable.

His ECG today showed sinus rhythm with a normal axis and first degree AV block (PR interval 246 msec). There were biphasic T-waves in leads V2, V3 and T-wave inversion in leads V4, V5 and flattening in aVL.

In view of his significant LV impairment, I have suggested he increases his ramipril to 5 mg daily. After 72 hours if he remains stable and well I would suggest increasing his bisoprolol to 5 mg daily. The ramipril dose can be slowly increased up to 10 mg daily, monitoring his renal function and blood pressure. I will avoid increasing the bisoprolol to more than 5 mg., until next reviewed given his first-degree AV block.

It is difficult to be certain which drug is causing his rash. In my experience it could be the ticagrelor. As his rash has improved following Piriton, I would suggest monitoring this and if it worsens then I would suggest commencing clopidogrel. I have given a prescription for a loading dose of clopidogrel 300 mg (for one dose only) followed by 75 mg daily for 12 months, just in case his rash worsens.

Androgenic based steroids are associated with cardiovascular complications including myocardial infarctions and current guidelines do not recommend testosterone replacement following a myocardial infarction, unless clinically indicated in proven hypogonadism states with established medical disease of the testes, pituitary or hypothalamus. I have suggested discontinuing testosterone replacement, however Mr. [redacted] keen to continue it as it has made a significant impact to his quality of life.

I would suggest he sees Professor [redacted], Consultant Respiratory Physician to exclude sleep apnoea.

I would like to review him again in ~ three weeks' time with a repeat echocardiogram done just beforehand. I have also arranged for him to have a baseline blood test today as well as a lipid profile including Lipoprotein (a) level.

Yours Sincerely,

Dr Azad Ghuran MB ChB (Edin), MRCP, MD (Edin), FESC
Consultant Cardiologist

Dictated and verified by Doctor but not signed

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Re: **67 yr old male**

Diagnosis:

1. **Monomorphic ventricular ectopics with a burden of 4%**
2. **CTCA showed a calcium score of 18 Agatston units, with moderate calcified plaque disease in the proximal LAD and minor calcified plaque at the ostium of the left circumflex artery, and mild non-calcified plaque in the mid-course. Minor calcified plaque in the mid-course of the right coronary artery.**
3. **Normal perfusion CMR 2020**
4. **Pre-diabetes**
5. **Hypercholesterolaemia**
6. **Non-specific neurological symptoms, which have been previously investigated by neurologists with nerve conduction studies**
7. **Tongue leukoplakia**
8. **Persistent lymphocytosis – under Dr. Marcus, Consultant Haematologist**

Mr [redacted] made an appointment today for a cardiology review. He has no cardiorespiratory symptoms but wanted to discuss testosterone replacement. He also mentioned that his concentration and memory is more impaired and his libido is also reduced. Viagra has not helped. He is keen to try testosterone. He still continues to smoke ten cigarettes a day. He has reduced his alcohol intake to a quarter bottle of vodka a week or half a bottle of wine.

His current medication consists of rosuvastatin 20 mg daily, metformin SR 500 mg twice daily, omeprazole 20 mg daily, aspirin 75 mg daily and health supplements.

Examination today: Pulse 72 bpm and regular. JVP was not elevated, heart sounds S1 + S2. Blood pressure 131/68 mmHg.

His ECG showed normal sinus rhythm, with a ventricular rate of 73 bpm.

I reminded [redacted] that we had discussed, back in April 2022, testosterone and its association with cardiovascular disease, which remains controversial. He does have risk factors, with mild to moderate coronary artery disease on a CT coronary angiogram in 2020, and this will not be a contraindication to commencing testosterone replacement. If his symptoms are significant enough to outweigh the controversial risks of testosterone replacement, then there is no reason why he should not try it.

Interestingly, this week in the New England Journal of Medicine, the Traverse study was published. This was a randomized, placebo-controlled trial of transdermal testosterone in men 45-80 years of age, with reduced testosterone levels, and high risk for cardiovascular events. The principal finding was that testosterone replacement was noninferior to placebo with respect to major adverse cardiac events. I will therefore leave the final decision for Mr. [redacted] to make about whether he commences testosterone replacement, provided his levels are low. I also suggested speaking to an endocrinologist who has a lot of experience in prescribing testosterone, and I have suggested Dr [redacted].

For the time being, I have not arranged any further follow-up appointments, but I would be happy to see him again in clinic, should the need arise.

Yours sincerely,

Dr Azad Ghuran MB ChB (Edin), MRCP, MD (Edin), FESC
Consultant Cardiologist

Dictated and verified by Doctor but not signed to avoid delay

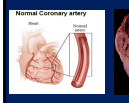
Copy: [redacted]

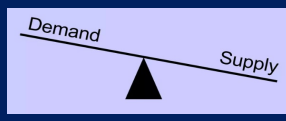
PS. His blood tests showed normal U&Es, B12, glucose, calcium, liver function, thyroid function and testosterone. His white cell count was mildly elevated (14) with a lymphocytosis, as previously noted. His HbA1c = 45 mmol/mol. The eGFR is 74 mL/min. Cholesterol 3.5 mmol/L, HDL 1.1 mmol/L, LDL 1.1 mmol/L and triglycerides X mmol/L.

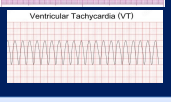
Ischaemic Heart Disease
Angina

Myocardial ischaemia

- The reduction in the supply of oxygen to less than the amount required by myocardial cells to maintain aerobic metabolism.
- Relative condition that depends on the balance among the coronary blood supply, the level of oxygenation of the blood, and the myocardial workload.







Sepsis, operative stress, shock

Hypoxia

Chest Pain

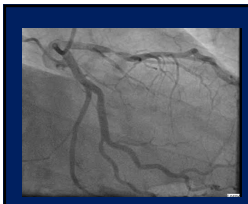
Diagnostic features of angina

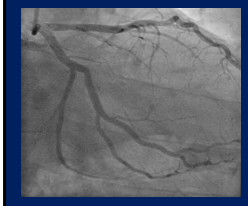
Aggravating factors:	predictable level of exercise, emotional stress, exercise plus heavy meal, cold weather
Relieving factors:	GTN, cessation of activity
Duration:	less than 15 minutes
Location:	retrosternal, infrequently epigastric or infrascapular
Radiation:	bilaterally across the chest, one or both arms, shoulders, back epigastrium, neck and lower jaw
Description:	heaviness, tightness, pressure, constriction, dull and deep, indigestion Ethnic groups/language barrier: sharp, burning, discomfort, "just pain", "like fire"

ACS – atypical chest pain presentations

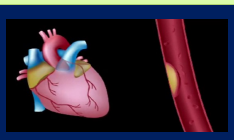
Females have atypical presentation

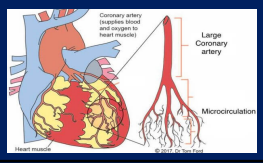
Mild dull pain
Isolated jaw pain
Isolated arm pain
Isolated interscapular pain
Bilateral wrist pain
Epigastric pain
Burning/sharp/tight chest pain associated with burping





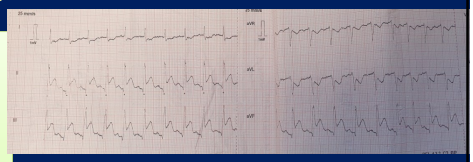
- 35-year-old man
- 3 episodes of exertional epigastric discomfort radiating into his abdomen and felt breathless. Lasted a few minutes and associated with bilateral arm ache.
- Symptoms improved 3 weeks later when seen in the RACPC. Positive ETT
- Chol. 6.6, HDL 1.20, LDL 5.05, TGL 0.78

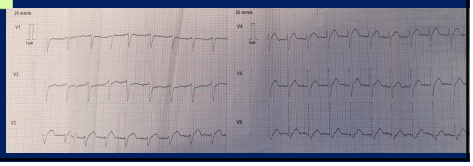


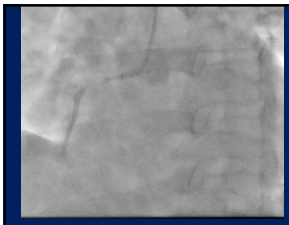


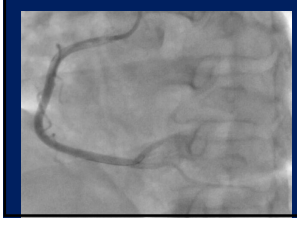
11th November 2023

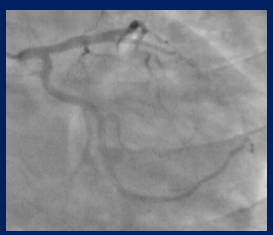
- 49 year old male
- Took 2 viagra tablets
- 3 hrs later, chest pain
- Paramedics – alert , ECG – inf MI
- Cardiac arrest. CPR, Lucas device
- Intubated and ventilated
- 70 minutes of CPR
- Adrenaline infusion
- BP 90 mmHg (systolic) – cath lab
- Coronary angiogram











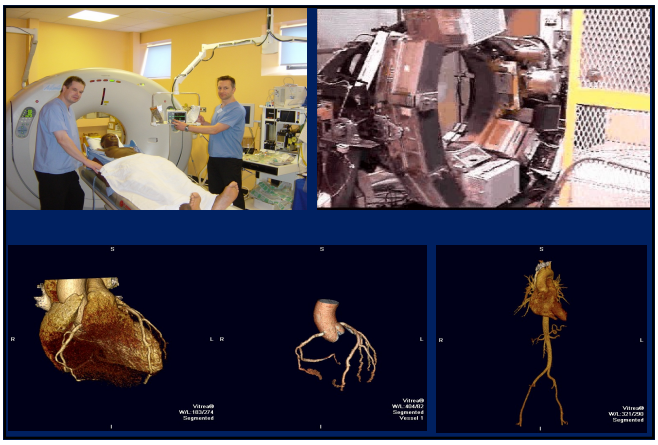
Primary Prevention

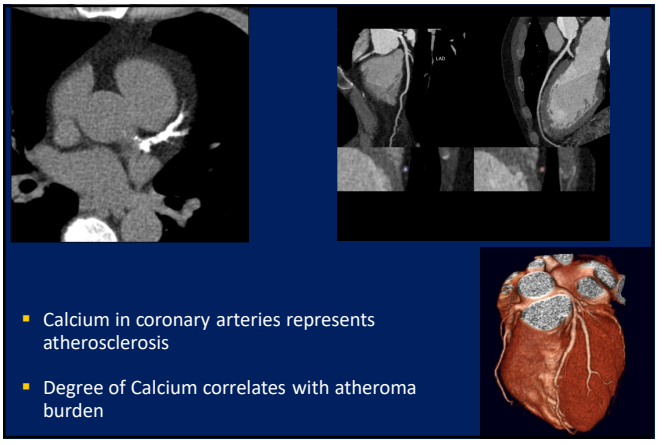
Risk Scores

- Framingham
- QRISK3
- JBS3
- ESC Heart Score
- Scottish ASSIGN

- FH (familial hypercholesterolaemia)
- Others

Q risk3 score	Goal
>20%	Very high risk, LDL < 1.4 mmol/l or at least a >50% reduction of LDL (non-HDl chol. < 2.1 mmol/l)
10-20%	High risk, LDL < 1.8 mmol/l (non-HDl chol < 2.5 mmol/l)
5-10%	Low-moderate risk, LDL < 2.5 mmo/L (non-HDl chol < 3 mmol/l)
1-5%	Low risk, LDL < 3 mol/L, (non-HDl chol < 3.5 mmol/l)
<1%	Very low risk





- Calcium in coronary arteries represents atherosclerosis
- Degree of Calcium correlates with atheroma burden

Coronary calcification in Asymptomatic

MESA (Multiethnic Study of Atherosclerosis)
NIH sponsored prospective study
6,814 Asymptomatic pts: 3.5 year follow-up

	Major Coronary Event		
CAC score	No. at risk	Hazard Ratio (95% CI)	P-value
0	8/3409	1.0	
1-100	25/1728	3.89 (2.72-8.79	<0.001
101-300	24/752	7.08 (3.05-16.47	<0.001
>300	32/833	6.84 (2.39-15.99)	<0.001

Detrano RC et al. N Engl J Med 2008;358:1336-5.

Comparative Effective Dose of Radiological Investigations

- PA/Lateral CXR 0.04-0.06 mSv
- Head CT 1-2 mSv
- Chest CT 5-7 mSv
- Abd/Pelvis CT 8-11 mSv
- Diagnostic Cor Angiogram 1-5 mSv
- MSCT angiography 0.6-4 mSv

Life time cancer risk
1mSv = 1:20,000 additional risk
10mSv = 1:2000 additional risk
20mSv = 1:1000 additional risk

Table 3. Estimated Risks of Fatal Malignancy or Death Resulting From Radiation Exposure and the Lifetime Odds of Dying as a Result of Selected Activities of Everyday Life

Exposure	Estimated Risk of Fatal Malignancy or Lifetime Odds of Dying (per 1000 Individuals)
Effective radiation dose	
1 mSv (calcium score/lung screen)	0.05
10 mSv (coronary CTA/abdomen CT, invasive coronary angiography, radionuclide myocardial perfusion study)[32]	0.5
50 mSv (yearly radiation worker allowance)	2.5
100 mSv (definition of low exposure)	5
Natural fatal cancer[39]	212
Passive smoking[33]	
Low exposure	4
High exposure, married to a smoker	10
Radon in home[34]	
US average	3
High exposure (1% to 3%)	21
Arsenic in drinking water[35,36]	
2.5 μg/L (US estimated average)	1
50 μg/L (acceptable limit before 2006)	13
Motor vehicle accident[37]	11.9
Pedestrian accident[37]	1.6
Drowning[37]	0.9
Bicycling[37]	0.2
Lightning strike[37]	0.013

CTA indicates CT angiogram.

National Safety Council estimates are based on data from National Center for Health Statistics and US Census Bureau. Deaths are classified on the basis of the Tenth Revision of the World Health Organization's *International Classification of Diseases*. Lifetime odds are approximated by dividing the 1-year odds by the life expectancy of a person born in 2005 (77.8 years).

AHA Science Advisory

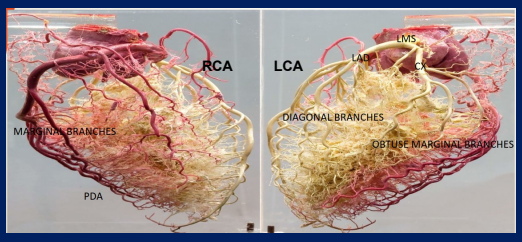
Ionizing Radiation in Cardiac Imaging
A Science Advisory From the American Heart Association Committee on Cardiac Imaging of the Council on Clinical Cardiology and Committee on Cardiovascular Imaging and Intervention of the Council on Cardiovascular Radiology and Intervention

TC Gerber et al. *Circulation.* 2009;119:1056-1965

INOCA

Ischaemia with non-obstructive coronary arteries

MINOCA – myocardial infarction with non-obstructive coronary arteries



European Heart Journal (2012) 33, 734–744
doi:10.1093/eurheartj/ehr211

CLINICAL RESEARCH
Coronary heart disease

Stable angina pectoris with no obstructive coronary artery disease is associated with increased risks of major adverse cardiovascular events

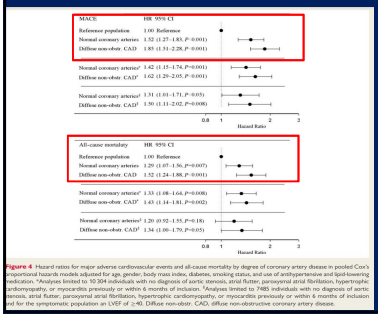
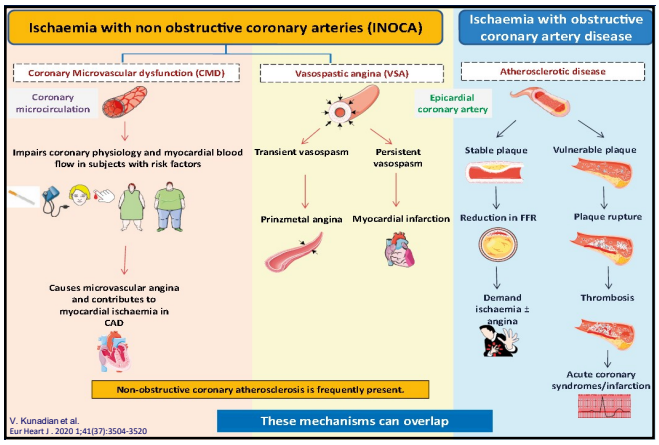


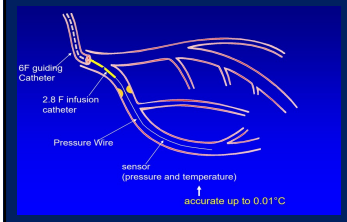
Figure 4 Hazard ratios for major adverse cardiovascular events and all-cause mortality by degree of coronary artery disease in pooled Cox's proportional hazards models adjusted for age, gender, body mass index, diabetes, smoking status, and use of antihypertensive and lipid-lowering medication. [a]Analyses limited to 10 304 individuals with no diagnosis of aortic stenosis, atrial flutter, paroxysmal atrial fibrillation, hypertrophic cardiomyopathy, or myocarditis previously or within 6 months of inclusion. [b]Analyses limited to 7485 individuals with no diagnosis of aortic stenosis, atrial flutter, paroxysmal atrial fibrillation, hypertrophic cardiomyopathy, or myocarditis previously or within 6 months of inclusion and for the symptomatic population an LVEF of ≥40. Diffuse non-obstr. CAD, diffuse non-obstructive coronary artery disease.

Prognosis of patients with INOCA is far from benign

- Impaired quality of life
- Higher risk of disability
- Increases mortality, morbidity
- Higher recurrence rates of hospital readmissions
- Higher rates of repeated coronary angiograms
- Higher healthcare costs



CMD Assessment



Non Invasive

- Cardiac MRI
- PET scan (nuclear)
- Echocardiogram

FFR, iFR, RFR
Coronary flow reserve (CFR)
Index of microcirculatory resistance (IMR)

INOCA

	INOCA endotypes	Pathophysiology	Diagnostic criteria
1	Microvascular angina[a]	CMD	Diagnostic guidewire and Adenosine test
			FFR >0.8
			CFR <2.0
			IMR ≥25[b]
			HMR ≥1.9[b]
			Vasoreactivity (acetylcholine test)
			No or <90% diameter reduction
			+angina
			+ischaemic ECG changes
2	Vasospastic angina	Epicardial spasm	Diagnostic guidewire and Adenosine test
			FFR >0.8
			CFR >2.0
			IMR <25
			HMR <1.9
			Vasoreactivity (acetylcholine test)
			≥90% diameter reduction
			+angina
			+ischaemic ECG changes
3	Both microvascular and vasospastic angina	Both CMD and epicardial spasm	Diagnostic guidewire and Adenosine test
			FFR >0.8
			CFR <2.0
			IMR ≥25
			HMR ≥1.9
			Vasoreactivity (acetylcholine test)
			No or <90% or ≥90% diameter reduction
			+angina
			+ischaemic ECG changes
4	Non-cardiac chest pain	None	Diagnostic guidewire and Adenosine test
			FFR >0.8
			CFR ≥2.0
			IMR <25
			HMR <1.9
			Vasoreactivity (acetylcholine test)
			No or <90% diameter reduction
			No angina
			No ischaemic ECG changes
5	Non-flow-limiting CAD[a]	Diffuse coronary artery atherosclerosis	Diagnostic guidewire and adenosine test
			FFR >0.8
			CFR ≥2.0
			IMR <25
			HMR <1.9
			Vasoreactivity (acetylcholine test)
			No or <90% diameter reduction
			No angina
			No ischaemic ECG changes

V. Kunadian et al. Eur Heart J . 2020 Oct 1;41(37):3504-3520

Table 2 Angina pharmacotherapy

Treatment	Angina type	Example	Investigation	Mechanism of action	Common side-effects
ß-blockers	MVA, CAD	Bisoprolol 1.25–10 mg	Reduced CFR and/or structural microvascular dysfunction (raised microvascular resistance)	Reduction in myocardial oxygen consumption	Fatigue, blurred vision, cold hands
Calcium channel antagonists	All	Dihydropyridine (amlodipine 2.5–10 mg daily) Non-dihydropyridine (verapamil 40–240 or diltiazem up to 500 mg; controlled release)	Propensity to coronary vasospasm (epicardial and/or microvascular)	↓ spontaneous and inducible coronary spasm via vascular smooth muscle relaxation and ↓ oxygen demand Vascular smooth muscle relaxation, reduction in myocardial oxygen consumption	Constipation, ankle swelling, flushing
Vasodilators					
Nitrates	CAD, VSA	Isosorbid mononitrate: 30–120 mg one time a day (controlled release)	Propensity to epicardial coronary vasospasm	↓ spontaneous and inducible coronary spasm via large epicardial vasodilation; ↓ oxygen demand. Lack of efficacy in microvascular angina with potential deleterious effect	Headaches, dizziness, flushing
Nicorandil	All	Nicorandil 5–30 mg two times a day	All	Potassium channel activator with ↓coronary microvascular dilatory effect	Dizziness, flushing, weakness, nausea
Rho kinase inhibitors	VSA, CMD	Fasudil: 5–20 mg, three times a day	Epicardial and/or microvascular vasospasm	Reduce calcium sensitization of vascular smooth muscle, maintains coronary vasodilation	Rashes, flushing, hypotension
Late Na+ Current Inhibitors	MVA, CAD	Ranolazine: 375–500 mg two times a day	Reduced CFR	Improves MPRI in patients with MVA and reduced CFR	Nausea, dizziness, headache
L-channel blockers	CAD, MVA	Ivabradine: 2.5–7.5mg two times a day	All	Ivabradine has shown anti-ischaemic and anti-anginal activity	Bradycardia, AF, headache
Partial fatty-acid oxidation inhibitors	CAD, MVA	Perhexeline: 50–400mg daily or Trimetazidine	Plasma concentration required for dose titration	Perhexeline inhibits carnitine O-palmitoyltransferase 1 and 2, which transfer free fatty acid from the cytosol into mitochondria	Dizziness, unsteady, nausea and vomiting
Improved endothelial function/pleiotropic					
ACE inhibitors	MVA, CAD	Ramipril: 2.5–10 mg daily	Hyper-reactivity to stimuli (eg, acetylcholine, exercise, stress)	Improve CFR, reduce workload, may improve small vessel remodelling, improves endothelial vasomotor dysfunction	Cough, renal impairment, hyperkalaemia
Statins	All	Atorvastatin: 10–80 mg daily Rosuvastatin: 5–40 mg daily	All	Improved coronary endothelial function reduced vascular inflammation	Myalgia, headache, cramps
Hormone replacement therapy*	MVA	Oestradiol: 1 mg daily	Angina in early menopause	Oestrogen therapy improves endothelial function short-term in CMD	↑ Risk of breast cancer, marginally ↑ risk of CVD
Tricyclic antidepressants (TCA)	MVA with abnormal pain processing	Amitriptyline: 5–10 mg nocte Imipramine: 10–200 mg daily	All	Counteracts enhanced nociception Thought to exert an analgesic effect on the visceral component associated with cardiac pain.	Blurred vision, dry mouth, drowsiness, impaired coordination
Non-pharmacological	All	Smoking cessation, Exercise, cardiac rehabilitation, Mediterranean diet, cognitive behavioural therapy, weight loss, Yoga	Metabolic syndrome, endothelial dysfunction, cardiovascular risk factors, anxiety/depression		Adjunctive non-pharmacological interventions

*May be helpful in some postmenopausal women. More information on experimentary pharmacotherapy in refractory angina can be found in review by Henry et al.[42]
CAD, angina with obstructive coronary artery disease; MPRI, myocardial perfusion reserve index; MVA, microvascular angina; VSA, vasospastic angina.

Pharmacologic Treatment

- Aspirin
- PDE-5 inhibitors
- L-arginine
- Aminophylline
- Endothelin receptor blockers

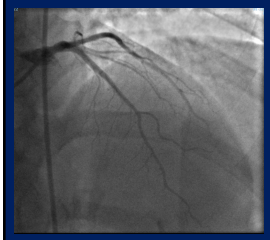
Non-Pharmacologic Treatment

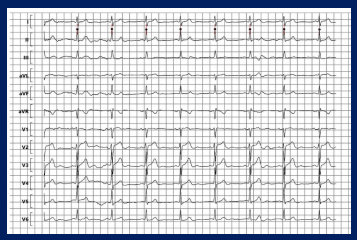
- Exercise
- Cognitive behavioural therapy
- TENS

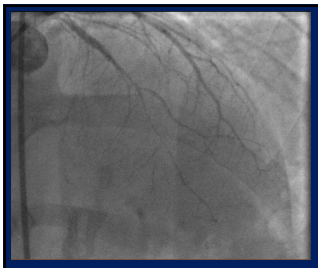
T Ford, Colin Berry. Heart 2020;106:387-398
C. Noel Bairey Mertz et al. Circulation. 2017;135:1075

Mr. DK – 37 yr.
Recurrent chest tightness – exertion and rest.
Awoke at 3 am, chest tightness "someone was sitting on chest". Radiated to his neck and associated with sweating. Eased after 30 minutes.
A&E. Normal ECG, chest x-ray, and blood tests (FBC, CRP, D-dimer, clotting, liver function test, U&Es and troponin). Advised Gaviscon. Already on Omeprazole 20 mg daily.

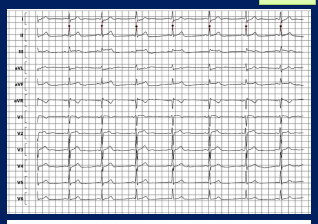
PMHx: Raynaud's disease. Previous CTCA: no obstructive disease.

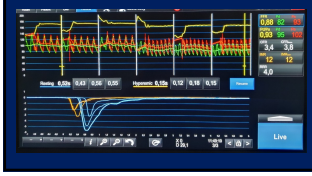


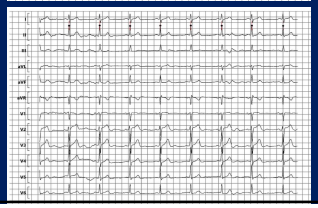




Mr. DK







HT

Clinical History :

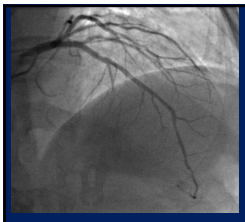
73 yr. old Asian male
Crescendo angina
Angio 2019 moderate RCA disease
Possible significant LAD disease.
Awaiting knee surgery turned down due to anginal symptoms. If possible within 1 month

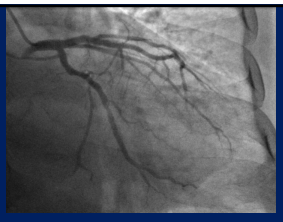
Coronary angiogram. RRA. 6F

LMS: unobstructed
LAD: mild disease in proximal and mid course. Mild-moderate disease in distal LAD at apex
Cx: 40% hazy lesion in mid course
RCA: mild disease in proximal and mid course. Diffuse moderate disease in distal PDA with slow flow.

XB3 Guide.
Pressure wire X in Cx. RFR/FFR = 1.
Coronary flow reserve: 1.8
Index of myocardial resistance: 40

Diagnosis: coronary microvascular disease. Stop ISMN (which can sometimes paradoxically worsen anginal symptoms, and start Ranolazine 375mg BD. Can be listed for orthopaedic surgery from a cardiac perspective.





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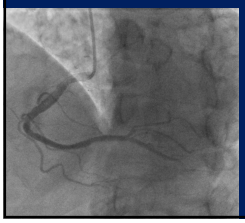
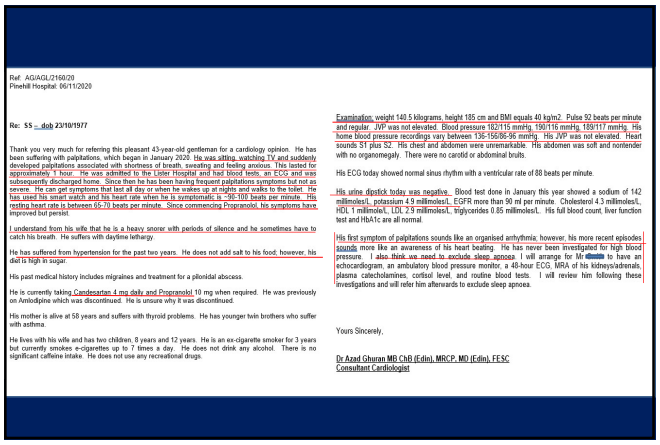


Conclusion

- INOCA is a major health problem with significant morbidity and mortality
- Under-diagnosed and under-treated
- Prompt assessment with validated methodology will allow early diagnosis and treatment

Hypertension



Ref: AG/AGL/2160/20
Pinehill Hospital: 06/11/2020

Re: SS – dob 23/10/1977

Thank you very much for referring this pleasant 43-year-old gentleman for a cardiology opinion. He has been suffering with palpitations, which began in January 2020. He was sitting, watching TV and suddenly developed palpitations associated with shortness of breath, sweating and feeling anxious. This lasted for approximately 1 hour. He was admitted to the Lister Hospital and had blood tests, an ECG and was subsequently discharged home. Since then he has been having frequent palpitations symptoms but not as severe. He can get symptoms that last all day or when he wakes up at nights and walks to the toilet. He has used his smart watch and his heart rate when he is symptomatic is ~90-100 beats per minute. His resting heart rate is between 65-70 beats per minute. Since commencing Propranolol, his symptoms have improved but persist.

I understand from his wife that he is a heavy snorer with periods of silence and he sometimes have to catch his breath. He suffers with daytime lethargy.

He has suffered from hypertension for the past two years. He does not add salt to his food; however, his diet is high in sugar.

His past medical history includes migraines and treatment for a pilonidal abscess.

He is currently taking Candesartan 4 mg daily and Propranolol 10 mg when required. He was previously on Amlodipine which was discontinued. He is unsure why it was discontinued.

His mother is alive at 58 years and suffers with thyroid problems. He has younger twin brothers who suffer with asthma.

He lives with his wife and has two children, 8 years and 12 years. He is an ex-cigarette smoker for 3 years but currently smokes e-cigarettes up to 7 times a day. He does not drink any alcohol. There is no significant caffeine intake. He does not use any recreational drugs.

Examination: weight 140.5 kilograms, height 185 cm and BMI equals 40 kg/m2. Pulse 92 beats per minute and regular. JVP was not elevated. Blood pressure 162/115 mmHg, 190/116 mmHg, 189/117 mmHg. His home blood pressure recordings vary between 136-156/86-95 mmHg. His JVP was not elevated. Heart sounds S1 plus S2. His chest and abdomen were unremarkable. His abdomen was soft and nontender with no organomegaly. There were no carotid or abdominal bruits.

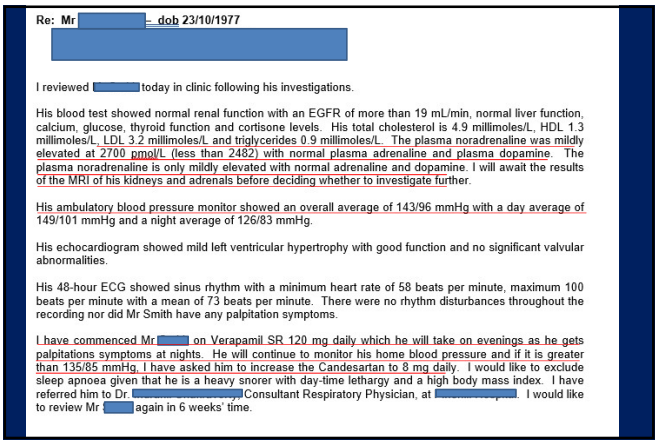
His ECG today showed normal sinus rhythm with a ventricular rate of 88 beats per minute.

His urine dipstick today was negative. Blood test done in January this year showed a sodium of 142 millimoles/L, potassium 4.9 millimoles/L, EGFR more than 90 ml per minute. Cholesterol 4.3 millimoles/L, HDL 1 millimole/L, LDL 2.9 millimoles/L, Triglycerides 0.85 millimoles/L. His full blood count, liver function test and HbA1c are all normal.

His first symptom of palpitations sounds like an organised arrhythmia; however, his more recent episodes sounds more like an awareness of his heart beating. He has never been investigated for high blood pressure. I also think we need to exclude sleep apnoea. I will arrange for Mr [redacted] to have an echocardiogram, an ambulatory blood pressure monitor, a 48-hour ECG, MRA of his kidneys/adrenals, plasma catecholamines, cortisol level, and routine blood tests. I will review him following these investigations and will refer him afterwards to exclude sleep apnoea.

Yours Sincerely,

Dr Azad Ghuran MB ChB (Edin), MRCP, MD (Edin), FESC
Consultant Cardiologist



Re: Mr [redacted] – dob 23/10/1977

I reviewed [redacted] today in clinic following his investigations.

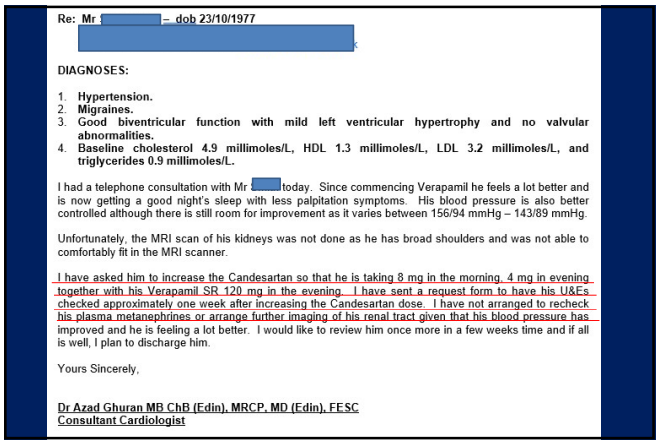
His blood test showed normal renal function with an EGFR of more than 19 mL/min, normal liver function, calcium, glucose, thyroid function and cortisone levels. His total cholesterol is 4.9 millimoles/L, HDL 1.3 millimoles/L, LDL 3.2 millimoles/L and triglycerides 0.9 millimoles/L. The plasma noradrenaline was mildly elevated at 2700 pmol/L (less than 2482) with normal plasma adrenaline and plasma dopamine. The plasma noradrenaline is only mildly elevated with normal adrenaline and dopamine. I will await the results of the MRI of his kidneys and adrenals before deciding whether to investigate further.

His ambulatory blood pressure monitor showed an overall average of 143/96 mmHg with a day average of 149/101 mmHg and a night average of 126/83 mmHg.

His echocardiogram showed mild left ventricular hypertrophy with good function and no significant valvular abnormalities.

His 48-hour ECG showed sinus rhythm with a minimum heart rate of 58 beats per minute, maximum 100 beats per minute with a mean of 73 beats per minute. There were no rhythm disturbances throughout the recording nor did Mr Smith have any palpitation symptoms.

I have commenced Mr [redacted] on Verapamil SR 120 mg daily which he will take on evenings as he gets palpitations symptoms at nights. He will continue to monitor his home blood pressure and if it is greater than 135/85 mmHg, I have asked him to increase the Candesartan to 8 mg daily. I would like to exclude sleep apnoea given that he is a heavy snorer with day-time lethargy and a high body mass index. I have referred him to Dr [redacted] Consultant Respiratory Physician, at [redacted]. I would like to review Mr [redacted] again in 6 weeks' time.



Re: Mr [redacted] – dob 23/10/1977

DIAGNOSES:

1. **Hypertension.**
2. **Migraines.**
3. **Good biventricular function with mild left ventricular hypertrophy and no valvular abnormalities.**
4. **Baseline cholesterol 4.9 millimoles/L, HDL 1.3 millimoles/L, LDL 3.2 millimoles/L, and triglycerides 0.9 millimoles/L.**

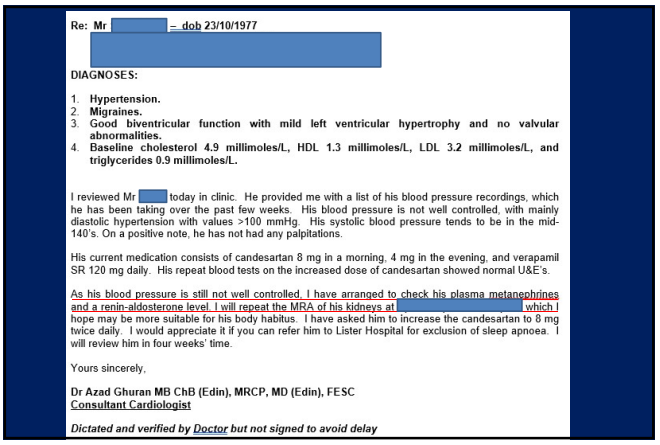
I had a telephone consultation with Mr [redacted] today. Since commencing Verapamil he feels a lot better and is now getting a good night's sleep with less palpitation symptoms. His blood pressure is also better controlled although there is still room for improvement as it varies between 156/94 mmHg – 143/89 mmHg.

Unfortunately, the MRI scan of his kidneys was not done as he has broad shoulders and was not able to comfortably fit in the MRI scanner.

I have asked him to increase the Candesartan so that he is taking 8 mg in the morning, 4 mg in evening together with his Verapamil SR 120 mg in the evening. I have sent a request form to have his U&Es checked approximately one week after increasing the Candesartan dose. I have not arranged to recheck his plasma metanephrines or arrange further imaging of his renal tract given that his blood pressure has improved and he is feeling a lot better. I would like to review him once more in a few weeks time and if all is well, I plan to discharge him.

Yours Sincerely,

Dr Azad Ghuran MB ChB (Edin), MRCP, MD (Edin), FESC
Consultant Cardiologist



Re: Mr [redacted] – dob 23/10/1977

DIAGNOSES:

1. **Hypertension.**
2. **Migraines.**
3. **Good biventricular function with mild left ventricular hypertrophy and no valvular abnormalities.**
4. **Baseline cholesterol 4.9 millimoles/L, HDL 1.3 millimoles/L, LDL 3.2 millimoles/L, and triglycerides 0.9 millimoles/L.**

I reviewed Mr [redacted] today in clinic. He provided me with a list of his blood pressure recordings, which he has been taking over the past few weeks. His blood pressure is not well controlled, with mainly diastolic hypertension with values >100 mmHg. His systolic blood pressure tends to be in the mid-140's. On a positive note, he has not had any palpitations.

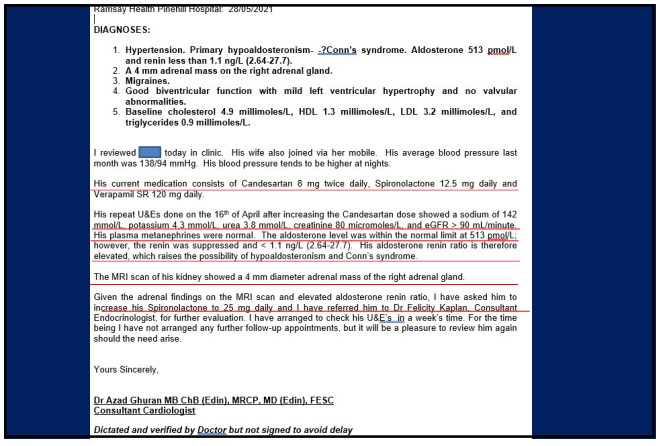
His current medication consists of candesartan 8 mg in a morning, 4 mg in the evening, and verapamil SR 120 mg daily. His repeat blood tests on the increased dose of candesartan showed normal U&E's.

As his blood pressure is still not well controlled, I have arranged to check his plasma metanephrines and a renin-aldosterone level. I will repeat the MRA of his kidneys at [redacted] which I hope may be more suitable for his body habitus. I have asked him to increase the candesartan to 8 mg twice daily. I would appreciate it if you can refer him to Lister Hospital for exclusion of sleep apnoea. I will review him in four weeks' time.

Yours sincerely,

Dr Azad Ghuran MB ChB (Edin), MRCP, MD (Edin), FESC
Consultant Cardiologist

Dictated and verified by Doctor but not signed to avoid delay



Ramsay Health Pinehill Hospital: 28/05/2021

DIAGNOSES:

1. **Hypertension. Primary hypoaldosteronism- -?Conn's syndrome. Aldosterone 513 pmol/L and renin less than 1.1 ng/L (2.64-27.7).**
2. **A 4 mm adrenal mass on the right adrenal gland.**
3. **Migraines.**
4. **Good biventricular function with mild left ventricular hypertrophy and no valvular abnormalities.**
5. **Baseline cholesterol 4.9 millimoles/L, HDL 1.3 millimoles/L, LDL 3.2 millimoles/L, and triglycerides 0.9 millimoles/L.**

I reviewed [redacted] today in clinic. His wife also joined via her mobile. His average blood pressure last month was 138/94 mmHg. His blood pressure tends to be higher at nights.

His current medication consists of Candesartan 8 mg twice daily, Spironolactone 12.5 mg daily and Verapamil SR 120 mg daily.

His repeat U&Es done on the 16th of April after increasing the Candesartan dose showed a sodium of 142 mmol/L, potassium 4.3 mmol/L, urea 3.8 mmol/L, creatinine 80 micromoles/L, and eGFR > 90 mL/minute. His plasma metanephrines were normal. The aldosterone level was within the normal limit at 513 pmol/L, however, the renin was suppressed and < 1.1 ng/L (2.64-27.7). His aldosterone renin ratio is therefore elevated, which raises the possibility of hypoaldosteronism and Conn's syndrome.

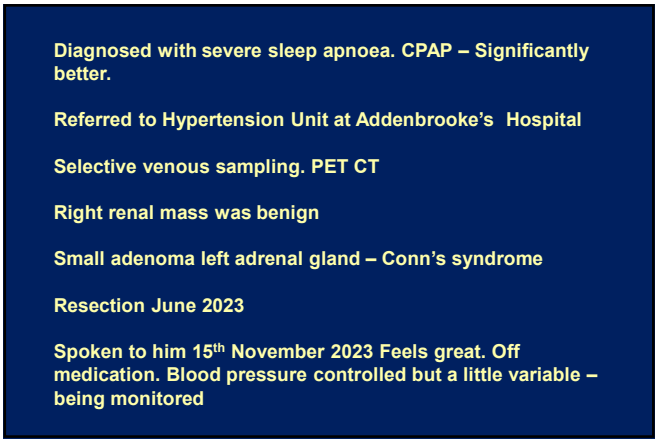
The MRI scan of his kidney showed a 4 mm diameter adrenal mass of the right adrenal gland.

Given the adrenal findings on the MRI scan and elevated aldosterone renin ratio, I have asked him to increase his Spironolactone to 25 mg daily, and I have referred him to Dr Felicity Kaplan, Consultant Endocrinologist, for further evaluation. I have arranged to check his U&E's in a week's time. For the time being I have not arranged any further follow-up appointments, but it will be a pleasure to review him again should the need arise.

Yours Sincerely,

Dr Azad Ghuran MB ChB (Edin), MRCP, MD (Edin), FESC
Consultant Cardiologist

Dictated and verified by Doctor but not signed to avoid delay



Diagnosed with severe sleep apnoea. CPAP – Significantly better.

Referred to Hypertension Unit at Addenbrooke's Hospital

Selective venous sampling. PET CT

Right renal mass was benign

Small adenoma left adrenal gland – Conn's syndrome

Resection June 2023

Spoken to him 15th November 2023 Feels great. Off medication. Blood pressure controlled but a little variable – being monitored

Hypertension

Investigation of patients with hypertension - baseline investigations

Blood tests - FBC, U&E, CREATININE, URIC ACID, LFT, gamma GT, Ca& P04, fasting GLUCOSE, fasting LIPIDS, TFT

ECG Presence of left ventricular hypertrophy

Urine tests Dip stick to test for CELLS, PROTEIN, BLOOD AND GLUCOSE

Ambulatory BP monitor / validated home BP monitor

Echocardiogram (open access) - Presence of left ventricular hypertrophy

Hypertension

Patients requiring further investigation to exclude secondary causes

- Young age < 30 - 40yrs (particularly if end organ damage, CVD, renal disease of DM) and no risk factors
- Moderate/severe hypertension
- Presentation with hypertensive emergency
- Raised creatinine
- Blood, protein or cells in urine
- Low plasma K
- Variable hypertension
- Resistant hypertension - failure to respond to multiple antihypertensive drugs
- Large postural drop in blood pressure
- Sudden loss of BP control and non-dipping or reverse dipping on ABPM

Factors that can increase Blood Pressure

Medications
- NSAIDS
- Recreational drugs - Cocaine, Amphetamines
- Over the counter "cold" medication - phenylephrine
- Anabolic Steroids
- Oral Contraceptives

Excessive EtOH (>3-4 drinks/day)
High Salt Diet
Obesity
Sleep apnoea

Hypertension

Criteria for requesting 24 hour urinary catecholamines excretion
- Clinical suspicion of phaeochromocytoma (headaches, palpitations and sweating)
- Moderate/severe hypertension
- Variable hypertension/postural hypotension
- Failure to respond to drug treatment

Criteria for renal investigations
- Clinical suspicion of renal disease
- Severe hypertension
- Young age <40yrs
- Raised creatinine
- Blood, protein or cells in urine
- Failure to respond to drug treatment

Which renal investigation?
- Renal U.S. if underlying renal disease suspected
- Renal CT angiogram, magnetic resonance angiography or invasive renal angiogram if renal artery stenosis is suspected.

Criteria for requesting plasma renin and aldosterone measurements

- clinical suspicion of 1° Hyperaldosteronism

Hypertension

Symptoms	Possible cause
Low Potassium (excluding diuretic induced hypokalaemia) 50% of patients with Conn's do not have hypokalaemia. Low potassium brought on by a small dose of diuretic may be a clue.	Primary Hyperaldosteronism (Including Conn's) Secondary Hyperaldosteronism (e.g. Renal Artery Stenosis, renal artery fibromuscular dysplasia)
Cushingoid appearance, oligomenorrhorea, easy bruising	Cushing's Glucocorticoid treatment
Palpitations, sweats, postural hypotension, anxiety pale skin (pallor), blurred vision, weight loss, increased thirst and urination, constipation, abdominal pain, elevated glucose, red and white blood cells, psychiatric disturbances, and cardiomyopathy.	Phaeochromocytoma
Cardiac murmur without previous investigation Radiofemoral delay	Aortic coarctation
Resistant hypertension	Sleep apnoea, non-compliance

For Urinary and Plasma Catecholamine Assessment

For Catecholamine assessment
Avoid 48 hours before:

- Chocolate
- Cocoa
- Bananas
- Citrus fruits
- Vanilla
- Alcohol
- Tea/coffee

For 5HIAA
Avoid 48 hours before:

- Banana
- Chocolate
- Dried fruits
- Citrus fruits
- Avocado
- Tomato
- Plum
- Kiwi
- Pineapple
- Mollush

For Urinary and Plasma Catecholamine Assessment

Medications associated with false-positive screening tests

Class	Name
Antihypertensive	Beta-blocker (labetalol, sotalol) Alpha-2 agonist (alpha-methyldopa) Alpha-2 antagonist (phenoxybenzamine) Alpha, beta-1, beta-2 agonist (ephedrine) Calcium channel blocker (dihydropyridines)
Stimulant	Caffeine Nicotine Amphetamine Cocaine
Anxiolytic	Buspirinone
Analgesic	Acetaminophen
Anti-inflammatory	Sulfasalazine
Antidepressant	Tricyclic antidepressants Monoamine oxidase inhibitors
Dopamine agonist	Levodopa

CASE 1

I should be most grateful for your help in the unusual situation with this twenty year old healthy asymptomatic young woman who checked her blood pressure yesterday because her father was checking his and found that it was very high at 172/116 and on repeated measurements up to 183/126. This morning she rechecked it for me again and again it was very similar with the diastolic blood pressure consistently over 120. We brought her to the surgery and checked it here and on repeated readings her diastolic blood pressure was 120 and systolic 160. [redacted] has no symptoms at all, in particular no chest pain, no palpitations, no headache and no visual symptoms and no sweating. She is not known to have had any blood pressure problems before. It was checked at the Practice in April 2019 when it was 130/70 and in January 2019 it was 110/70. She is on no regular medication. Her father has raised blood pressure but there is no family history of premature heart disease or stroke.

At surgery her pulse was 96 and regular. Her weight is 67.4kg which makes her BMI 21.5. Her urine dipstick was clear. I sent her for baseline bloods and started her on Amlodipine 5mg which we increased to 10 mg after a few days as her diastolic BP remained at >100. I organised for her to have an ECG, and sought advice from an endocrinologist via advice and guidance. This included further blood test to check pituitary function, US of liver (raised ALT) and kidneys, and referrals for review. We do not have access to 24 hr BP monitoring.

I enclose the ECG, and her blood results to date are available on ICE- so far nothing highly significant.

Thank you for your assessment of her and further help.

20 year old female

[redacted] DOB 06/04/2000

Thank you for referring this lady for a Cardiology opinion. She was incidentally found to have significantly elevated home blood pressure recordings using her father's blood pressure monitor. She was referred to the Endocrinology Team. Between your referral and my telephone consultation today she has had a number of blood tests which has demonstrated elevated urinary catecholamine levels. [redacted] Consultant Endocrinologist is currently investigating her. I understand an MIBG scan has been arranged at UCL Hospital. Her blood pressure was also better controlled. She is currently taking Amlodipine 10mg daily and Doxazosin 1mg daily.

It is interesting that she is minimally symptomatic with occasional headaches and the odd palpitation symptoms.

As she is currently being investigated I have not got too involved apart from arranging an echocardiogram as a baseline. I will write and let you know the results. I have not arranged any further follow-up appointments.

Yours sincerely,

Dictated and verified by Doctor but not signed

Dr Azad Ghuran MB ChB, MRCP, MD, FESC
Consultant Cardiologist

Sample BS-20218E0827 (TYPE UNSPECIFIED) Collected 05 Aug 2020 15:52 Received 05 Aug 2020 15:52

PLASMA METANEPHRINES

PLASMA NORMETADRENALINE	13782	pmol/L	

Interpretation:

Below 1000 pmol/l - catecholamine secreting tumour unlikely

Between 1000 and 2500 pmol/l - equivocal

Neither rules in nor rules out diagnosis of catecholamine secreting tumour

Above 2500 - high likelihood of catecholamine secreting tumour

PLASMA METADRENALINE	207	pmol/L	

Interpretation:

Below 600 pmol/l - catecholamine secreting tumour unlikely

Between 600 and 900 pmol/l - equivocal

Neither rules in nor rules out diagnosis of catecholamine secreting tumour

Above 900 - high likelihood of catecholamine secreting tumour.

hypertension in her 20s. Previously raised plasma mets, requesting repeat and al

Sample 0020L655500 (Blood) Collected 29 Jul 2020 09:07 Received 03 Aug 2020 14:24

24HR URINE METADRENALINES

Dates of collection		29/07/20-30/07/20		
24hr Urine Volume		2.83	Litre	
Urine Normetadrenaline	*	38.18	umol/24hr	0 - 3.3
Urine Metadrenaline		0.59	umol/24hr	0 - 1.2
Urine Methoxytyramine	*	12.11	umol/d	0 - 2.5

Raised level(s) highly suggestive of a

neuroendocrine tumour.

As reported by St Helier Hospital

Chemical Pathology Department.

I had a telephone consultation with [redacted] today. This telephone consultation was an administrative error as I had discharged her when I last spoke to her given that she was being reviewed by the Endocrinology Team - Dr [redacted]. Nevertheless it was facinating to catch up with [redacted]

Her echocardiogram from October 2021 showed a structurally normal heart with normal left ventricular wall thickness.

Helena consistently had elevated urinary and plasma metadrenalines. She was referred for an MIBG scan to UCL in London. This showed no significant catecholamine activity. Because of the persistently elevated metanephrines she was referred to Dr [redacted], Consultant Endocrinologist at Addeenbrook's Hospital. An abdominal CT scan showed a paraganglioma in the bladder which was confirmed on an MRI and subsequently a PET scan. She has now had this resected by a Urologist at Addenbrooke's Hospital. She says she is feeling a lot better and is now having bladder retraining exercises. She is also off her Doxazosin 12mg which she was taking pre-operatively.

[redacted] history is quite fascinating as she had minimal symptoms apart from a serendipitous pickup of an elevated blood pressure whilst using her father's blood pressure machine. She had minimal palpitation symptoms and her occasional headaches settled after increasing her hydration.

As she is currently doing well no further cardiology input is required, I have again discharged her. I wish her all the best for the future.

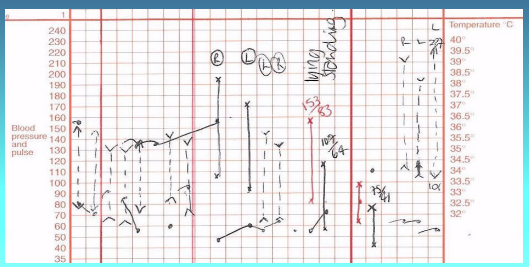
Yours sincerely,

Dictated and verified by Doctor but not signed

Dr Azad Ghuran MB ChB, MRCP, MD, FESC
Consultant Cardiologist

Phaeochromocytoma

52 yr. old female with episodic severe headache, photophobia, N&V, agitation, confusion, and aggression

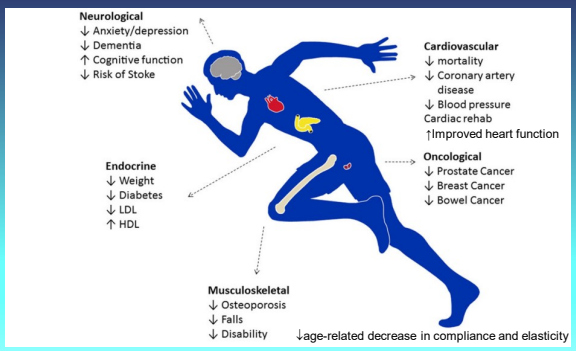


Causes of Pseudo-Resistant Hypertension

1. **Poor patient adherence : up to 50-60%!**
   - Side effects of medication
   - Complicated dosing schedules
   - Poor relations between doctor and patient
   - Inadequate patient education
   - Memory or psychiatric problems or poor cognition (elderly)
   - Costs of medication
2. **Related to antihypertensive medication**
   - Inadequate doses : **50% of the prescriptions!**
   - Inappropriate combinations
3. **Physician inertia**
   - failure to change or increase dose regimens when not at goal

Sports Cardiology

Engaging in sports and regular physical activity has a myriad of positive impacts on cardiovascular health.



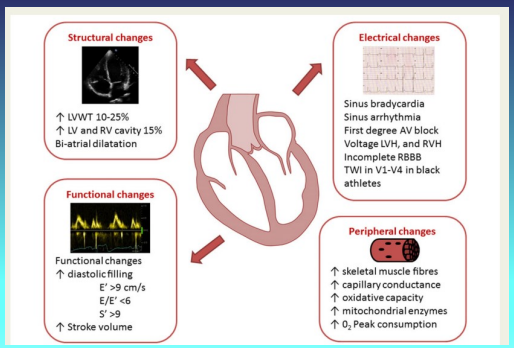
The UK Chief Medical Officers' Guidelines recommend each week adults do:

- At least 150 minutes moderate intensity activity, 75 minutes' vigorous activity, or a mixture of both
- Strengthening activities on two days
- Reducing extended periods of sitting

Four Types of Exercise Can Improve Your Health and Physical Ability in Elderly patients

- Endurance
- Strength
- Balance
- Flexibility

Cardiovascular and peripheral adaptation to exercise in athletes



AV, atrioventricular; LV, left ventricular; LVH, left ventricular hypertrophy; LVWT, left ventricular wall thickness; RV, right ventricle; RVH, right ventricular hypertrophy; TWI, T-wave inversion

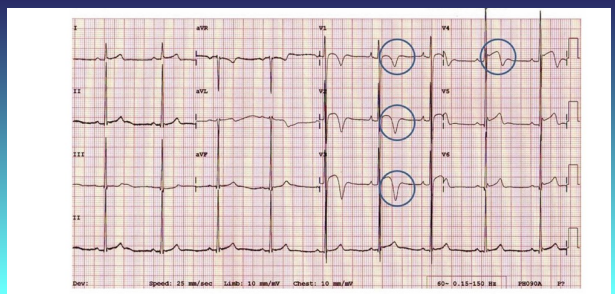


Figure 5 ECG from a black athlete demonstrating voltage criteria for LVH, J-point elevation and convex ('domed') ST segment elevation followed by TWI in V1-V4 (circles). This is a normal repolarisation pattern in black athletes. LVH, left ventricular hypertrophy; TWI, T wave inversion.

Drezner JA, *et al*. *Br J Sports Med* 2017;**51**:704–731. doi:10.1136/bjsports-2016-097331

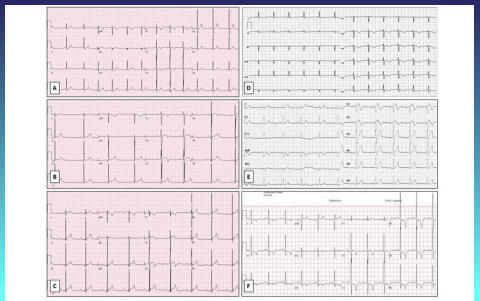
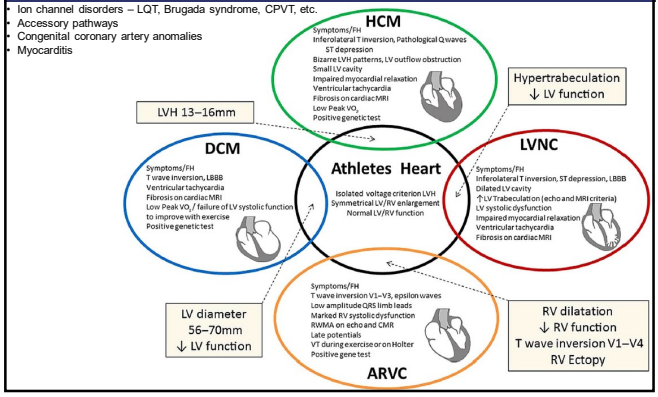


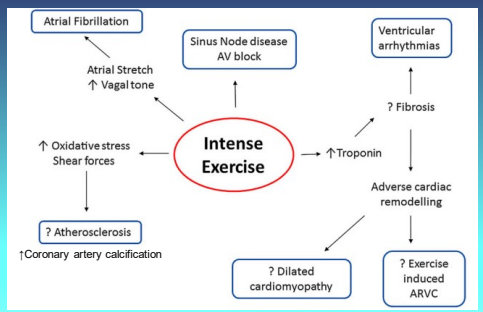
Figure 6 Normal and abnormal patterns of TWI. (A) Anterior TWI in V1-V3 in a 12-year-old asymptomatic athlete without a family history of SCD considered a normal 'juvenile' pattern. (B) TWI in V1-V4 in a 17-year-old asymptomatic mixed race (Middle-Eastern/black) athlete without a family history of SCD. This is a normal repolarisation pattern in black athletes. (C) Biphasic TWI in V3 in a 31-year-old asymptomatic black athlete without a family history of SCD. Anterior biphasic T waves are considered normal in adolescents <16 years old and in adults when found in a single lead, most commonly V3. (D) Abnormal TWI in V1-V6 in an adult symptomatic former soccer player with genetically confirmed ARVC and a positive family history of SCD (brother died at 26 years of age). (E) An ECG demonstrating the type 1 Brugada pattern with high take-off ST elevation ≥2 mm with downsloping ST segment elevation followed by a negative symmetric T wave in V1-V2. (F) Inferolateral TWI in leads I, II, III, aVF, V2-V6 and ST segment depression in leads II, aVF, V4-V6 in a 31-year-old asymptomatic professional soccer referee. These markedly abnormal findings require a comprehensive evaluation to exclude cardiomyopathy. ARVC, arrhythmogenic right ventricular cardiomyopathy; SCD, sudden cardiac death; TWI, T wave inversion.

Sudden cardiac death in sport

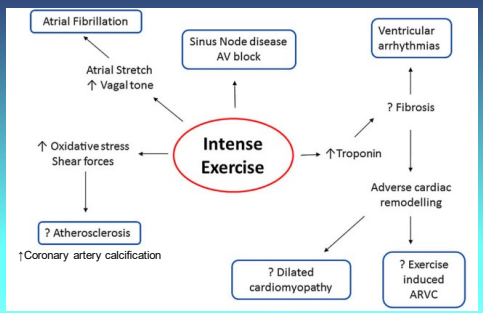
- Ion channel disorders – LQT, Brugada syndrome, CPVT, etc.
- Accessory pathways
- Congenital coronary artery anomalies
- Myocarditis



Can exercise damage a previously normal heart?



Can exercise damage a previously normal heart?



Consultant Respiratory Physician
[redacted]

56 year old male runner

Dear Tim

Re: [redacted]

Thank you very much for referring this pleasant 56-year old gentleman for a cardiology opinion. You recently reviewed him for increasing shortness of breath on exertion earlier this year. This can sometimes be associated with a feeling of tightness across his chest, but his predominant symptom is shortness of breath. Since changing his inhalers, he has felt a lot better and has restarted exercising frequently, running shorter distances and a slower pace. Whilst you were examining him in clinic, you noted a transient tachycardia whilst auscultating his heart, which precipitated this cardiology referral.

Mr [redacted] has no convincing history of palpitation symptoms, apart from that episode whilst in clinic. There is no history of diabetes or hypertension. He had a BUPA medical yesterday, and it was noted that his blood pressure was initially high and after the third attempt, it came down to 140/81 mmHg. He was advised to have his blood pressure further investigated.

You investigated him with an HRCT, which showed no significant abnormality, with a possible pancreatic lesion. He subsequently had a CT of his abdomen, which excluded any abnormalities.

His past medical history includes eczema, a left inguinal hernia repair, and repair of a perforated right eardrum.

His current medication consists of Fostair inhaler and Ventolin inhaler, and Elocon cream.

His father died at 78-years and had a history of bladder cancer and atrial fibrillation.

He lives with his wife and has two children, 20-years and 22-years. He does not smoke. He drinks twelve units of alcohol a week. He works as an insurance manager.

Examination: pulse 54 bpm and regular. JVP was not elevated. Blood pressure 150/90 mmHg, 150/90 mmHg and 146/90 mmHg. Heart sounds S1 + S2. His chest and abdomen were unremarkable.

His ECG showed normal sinus rhythm, with a ventricular rate of 54 bpm.

His blood tests at his medical showed an Hb of 136 g/L, HbA1c 31 mmol/mol, cholesterol 5.64 mmol/L, LDL 3.6 mmol/L, HDL 1.3 mmol/L and triglycerides 1.68 mmol/L. Height 176.5 cm, weight 84.2 kg, and BMI = 27 kg/m².

I have arranged for Mr [redacted] to have an echocardiogram, 24-hour blood pressure monitor and a 48-hour ECG. He had a thyroid function test done yesterday at his medical and he will chase the result. I will also arrange an exercise tolerance test for completeness, given his history of chest tightness on exertion, although this sounds more asthma / chest related. I will review him after his investigations.

Yours sincerely,

Dr Azad Ghuran MB ChB (Edin), MRCP, MD (Edin), FESC
Consultant Cardiologist

I reviewed Mr [redacted] today in clinic following his investigations.

His echocardiogram showed normal biventricular cavity size with normal left ventricular wall thickness and good biventricular function. There were no valvular abnormalities.

His ambulatory blood pressure monitor showed an overall average of 136/81 mmHg, a day average of 137/83 mmHg and a night average of 135/75 mmHg. His nocturnal blood pressure is therefore high and he did not have any significant sleep disturbance with the blood pressure monitor.

His 48-hour ECG showed sinus rhythm. There were two short runs of an atrial tachycardia up to 16 beats which were asymptomatic. This is what you probably felt when you were examining Mr Poole. The overall supraventricular ectopic burden was less than 1%.

He underwent an exercise tolerance test today using the Bruce protocol. He exercised for 10 minutes 21 seconds reaching stage 4. He achieved 100% of his target heart rate and a workload of 13.40 METS. There was a mild non-specific upsloping ST changes. This test was discontinued because of fatigue. There was an exaggerated blood pressure response reaching 216/72 mmHg in stage 2 and 234/76 mmHg in stage 3, shortly before stopping.

Based on his 24-hour ambulatory blood pressure monitor and exaggerated blood pressure response on exercise, he will need to commence anti-hypertensive medication. I have therefore commenced him on Telmisartan 40 mg daily as well as Atorvastatin 20 mg daily in view of his mildly elevated cholesterol level. I have opted for using Telmisartan as it has a half-life of 24 hours and will therefore reduce the peaks and troughs variation of blood pressure control. I have also showed Mr [redacted] how to obtain a validated blood pressure monitor on the internet and he will start recording his home blood pressure.

I would like to review him again in 6-8 weeks' time to see how he is getting on.

Yours Sincerely,

Dr Azad Ghuran MB ChB (Edin), MRCP, MD (Edin), FESC
Consultant Cardiologist

EXERCISE STRESS TEST REPORT

Patient Name: Poole, Jonathan
Patient ID: X3471598
Height:
Weight:
[redacted]
Study Date: 22.09.2022
Test Type: --
Protocol: BRUCE

DOB: 09.07.1966
Age: 56yrs
Gender: Male
Race:

Referring Physician: --
Attending Physician: --
Technician: --

Medications:
--

Medical History:
--

Reason for Exercise Test:
--

Exercise Test Summary

Phase	Name	Stage Name	Time in Stage	Speed (mph)	Grade (%)	HR (bpm)	BP (mmHg)	Comment
PRETEST		SUPINE	00:02	0.00	0.00	71		
MANUAL		STAGE 1	00:02	0.00	0.00	89		
EXERCISE		STAGE 1	03:00	1.70	10.00	113		
		STAGE 2	03:00	2.50	12.00	113	216/72	
		STAGE 3	03:00	3.40	14.00	144	234/76	
		STAGE 4	01:20	4.20	16.00	164		
		STAGE 5	00:01	4.20	16.00	164		
RECOVERY			00:01	0.00	0.00	164	240/68	
MANUAL		STAGE 3	00:49	0.00	0.00	102		
		STAGE 5	00:08	0.00	0.00	101		
		STAGE 4	00:03	0.00	0.00	102		
		STAGE 5	00:02	0.00	0.00	102		
		STAGE 7	00:01	0.00	0.00	102		
		STAGE 9	00:01	0.00	0.00	102		
		STAGE 11	00:01	0.00	0.00	102		
		STAGE 13	00:01	0.00	0.00	103		
		STAGE 15	00:01	0.00	0.00	102		
		STAGE 16	00:01	0.00	0.00	102		
		STAGE 17	00:01	0.00	0.00	102		
		STAGE 20	00:05	0.00	0.00	102		
		STAGE 21	00:01	0.00	0.00	104		
		STAGE 23	01:36	0.00	0.00	94	187/90	

The patient exercised according to the BRUCE for 10:21 min:s, achieving a work level of Max. METS: 13.40. The resting heart rate of 69 bpm rose to a maximal heart rate of 164 bpm. This value represents 100 % of the maximal, age-predicted heart rate. The resting blood pressure of --/-- mmHg , rose to a maximum blood pressure of 240/68 mmHg. The exercise test was stopped due to Fatigue.

Interpretation

Summary: Resting ECG: normal.
Functional Capacity: normal.
HR Response to Exercise: appropriate.

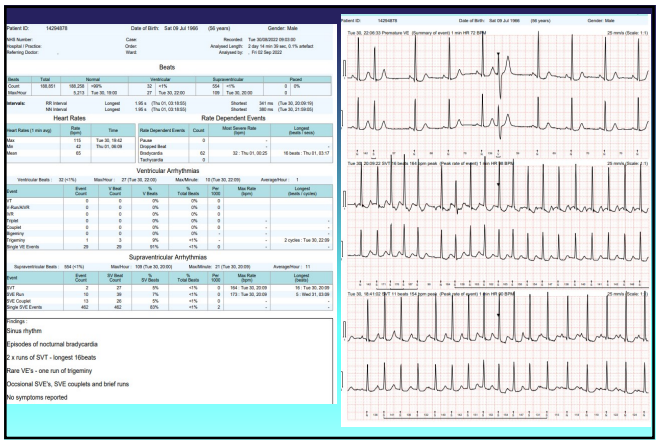
Date of birth:	09/07/1966 (56 Years)	Gender:	Male		
Height:		Weight:			
BMI:		BSA:			
Physician:	DR GHURAN	Ward/Dept:			

Recording information

Start:	01/09/2022 10:17:00	Ambulatory Arterial Stiffness Index (AASI):	0.33
End:	02/09/2022 10:56:00	Morning Surge Index (MSI):	3.31
Duration:	1.00:39:00	Comfort mode max. pressure:	170
Successful readings:	32 (88.09%)	Child mode:	Disabled
Systolic = limits:	59.38%	Serial number:	90227-004186
Diastolic = limits:	46.88%		

Summary of entire recording - Successful: 68.09% (32 of 47), Avg.: 136/81 mmHg

	Hourly avg.	Std. dev.	Min.	Max.	Dipping
Overall summary - Successful: 68.09% (32 of 47), Avg: 136/81 mmHg					
Systolic above limits: 59.38%, Diastolic above limits: 46.88%					
Systolic (mmHg)	136	13.80	110 (06:24 Fri)	164 (15:58 Thu)	4.18%
Diastolic (mmHg)	81	12.60	56 (06:24 Fri)	114 (12:24 Thu)	12.19%
MAP (mmHg)	100	12.03	73 (06:24 Fri)	130 (12:24 Thu)	6.66%
Pulse pressure (mmHg)	55	9.79	36 (20:24 Thu)	77 (18:24 Thu)	
Heart rate (BPM)	63	4.79	51 (06:24 Fri)	72 (15:58 Thu)	
Wake periods summary - Successful: 64.10% (25 of 39), Avg: 137/83 mmHg					
Systolic > 135 mmHg: 59.09%, Diastolic > 85 mmHg: 44.06%					
Systolic (mmHg)	137	14.40	110 (06:24 Fri)	164 (15:58 Thu)	
Diastolic (mmHg)	83	12.21	56 (06:24 Fri)	114 (12:24 Thu)	
MAP (mmHg)	102	12.24	73 (06:24 Fri)	130 (12:24 Thu)	
Pulse pressure (mmHg)	54	9.97	36 (20:24 Thu)	77 (18:24 Thu)	
Heart rate (BPM)	62	4.77	51 (06:24 Fri)	72 (15:58 Thu)	
Sleep periods summary - Successful: 87.80% (7 of 8), Avg: 133/78 mmHg					
Systolic > 120 mmHg: 71.43%, Diastolic > 75 mmHg: 57.14%					
Systolic (mmHg)	133	11.16	117 (01:24 Fri)	149 (03:24 Fri)	
Diastolic (mmHg)	78	11.27	61 (02:24 Fri)	92 (23:24 Thu)	
MAP (mmHg)	96	10.27	84 (02:24 Fri)	114 (23:24 Thu)	
Pulse pressure (mmHg)	56	8.87	48 (01:24 Fri)	72 (03:24 Fri)	
Heart rate (BPM)	64	4.69	58 (05:24 Fri)	71 (23:24 Thu)	



I reviewed Mr [redacted] today in clinic following his CT coronary angiogram. This showed a calcium score of 0 with normal unobstructed coronary arteries.

He recently returned from a 20 km run in Spain during a hot day. He completed the Marathon without any problems. He is now running up to 15 miles a week. His blood pressure is also better controlled based on his morning and evening blood pressure.

I have reassured Mr [redacted] that there is no cardiac pathology of concern, and he should continue his normal activities. As he gets older, he will lose some of his physiological reserves and he has to bear this in mind.

For the time being, I have not arranged any further follow-up appointments, but I would be happy to see him again in clinic should the need arise.

Yours Sincerely,

Dr Azad Ghuran MB ChB (Edin), MRCP, MD (Edin), FESC

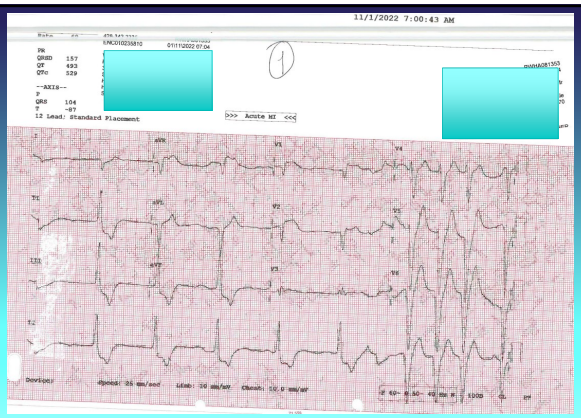
Consultant Cardiologist

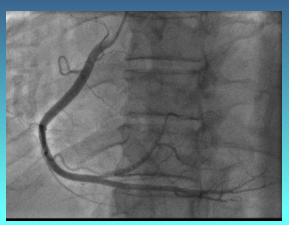
53 yr old male marathon runner
Runs ~ 80 miles/week
2nd best for his age group in the UK

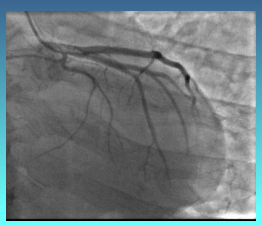
PMHx: asthma, GORD

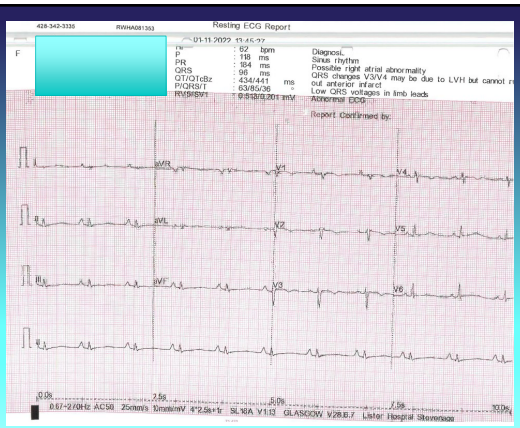
Wife witnessed collapsed ~0600. Ran 11 miles the day before.
CPR commenced
Paramedics/ air ambulance – multiple shocks, amiodarone,
Down time~1 hour. Intubated and ventilated

ECG showed frequent VE's

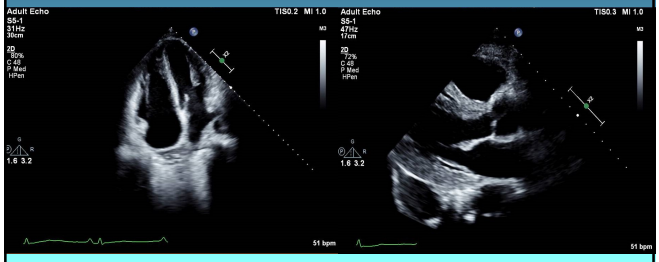








TTE : 1/11
Technically difficult study patient intubated and lying flat on his back
1 - Dilated RV with severely impaired systolic function (radial + longitudinal). Impression of akinetic mid-to-apical
free wall segments. Increased trabeculations also seen on the RV free wall - ?meaning. Septal flattening seen during
diastole and systole, consistent with RV volume and pressure overload.
2 - Normal sized LV with at least mild LVH and overall moderate-to-severely impaired systolic function in presence of
sinus brady (?stunned endocardium post-arrest). Visual EF 30-35%.
3 - Moderately dilated RA.
4 - Mild TR. Estimated RVSP 20mmHg + RAP. In context of dilated and impaired RV and dilated RA, there is likely a



Conclusion

1. Mildly dilated LV and preserved ejection fraction. No LVH.
2. Severely dilated RV with regional wall motion abnormalities and moderately reduced ejection fraction.
3. Myocardial fibrosis in the RVOT and RV inferior to inferolateral free walls.
4. No LV inflammation, fibrosis or infarction.
5. Moderate bilateral pleural effusions.

This study suggests an arrhtymogenic cardiomyopathy.

- Miraculous recovery
- Fully recovered – physically and cognitively
- ICD
- Wants to restart marathon running.

ESC European Heart Journal (2021) 42, 17–96 doi:10.1093/eurheartj/ehaa605

ESC GUIDELINES

2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease

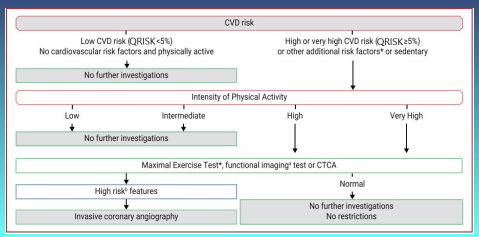
The Task Force on sports cardiology and exercise in patients with cardiovascular disease of the European Society of Cardiology (ESC)

Recommendations for exercise and sports participation in individuals with arrhythmogenic cardiomyopathy

Recommendations	Class[a]	Level[b]
Exercise recommendations		
Participation in 150 min of low-intensity exercise per week should be considered for all individuals.	IIa	C
Participation in low- to moderate-intensity recreational exercise/sports, if desired, may be considered for individuals with no history of cardiac arrest/VA, unexplained syncope, minimal structural cardiac abnormalities, <500 PVCs/24 h and no evidence of exercise-induced complex VAs.	IIb	C
Participation in high-intensity recreational exercise/sports or any competitive sports is not recommended in individuals with ACM, including those who are gene positive but phenotype negative.[Ref.386]	III	B
Follow-up and further considerations relating to risk		
Annual follow-up is recommended for individuals who exercise on a regular basis.	I	C
Six-monthly follow-up should be considered in adolescent individuals and young adults who are more vulnerable to exercise-related SCD.	IIa	C
Annual assessment should be considered for genotype-positive/phenotype-negative individuals for phenotypic features and risk stratification purposes.	IIa	C
Six-monthly follow-up should also be considered in individuals with high arrhythmic risk genotypes such as DSP, TMEM43, and carriers of multiple pathogenic variants.	IIa	C

ACM = arrhythmogenic cardiomyopathy; PVC = premature ventricular contraction; SCD = sudden cardiac death; VA = ventricular arrhythmia.
[a]Class of recommendation.
[b]Level of evidence.
Refer to Table 4 for different indices of exercise intensity and training zones.

Proposed Pre-Participation Cardiovascular Screening Evaluation for the over 40's Prior to Engaging in Sports.



Adapted from A. Pelliccia et al. ESC guidelines on Sports Cardiology

Pelliccia A, Sharma S, Gati S, etal. 2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease. European Heart Journal (2021);42:17-96

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