Framtidens kardiologer

25-26 januari, 2024

Stockholm

Föreläsningar

SVENSKA KARDIOLOGFÖRENINGEN

Pfizer

AstraZeneca

PAH – vadå? En föreläsning från grunden

Göran Rådegran och Anna Werther Evaldsson

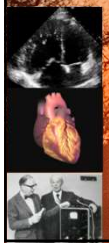
Torsdag 25 januari 2024, 09.30-11.30

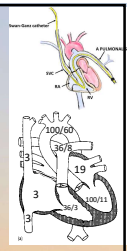
Stockholm 2024-01-25

- Pulmonell Hypertension & Oklar Andfåddhet -

Utredning & Behandling med fokus på Ekokardiografi & Hemodynamik

ANNA WERTHER EVALDSSON OCH GÖRAN RÅDEGRAN





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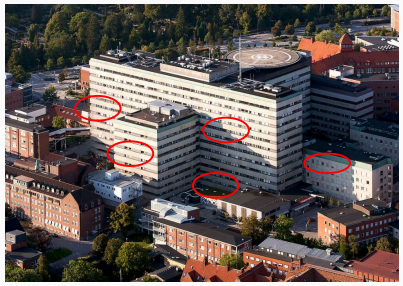
Göran Rådegran & Anna Werther Evaldsson

Head of the Hemodynamic Lab & PAH ward, Skåne University hospital, Lund, Sweden
Head & Secretary of the Swedish Association of Pulmonary Hypertension - SveFPH => SPAHR
Specialist BMA, PhD, board member in SHF echo group, VIC, Echocardiographic Lab, SUS, Lund



Disclosures:
- **Clinical trials PI for:** Acceleron, Actelion Pharmaceuticals, Bayer Health Care, GlaxoSmithKline, Janssen, Pfizer, United Therapeutics & Novartis.
- **Advisory boards for:** Acceleron, Actelion Pharmaceuticals, AOP Health / OrPHa Care, Bayer Health Care, Eli Lilly, GlaxoSmithKline, Janssen, MSD & Sanofi.
- **Research grants &/or lecture fees from:** Actelion Pharmaceuticals, AOP Health / OrPHa Care, Bayer Health Care, GlaxoSmithKline, Janssen, MSD & Nordic Infucare.

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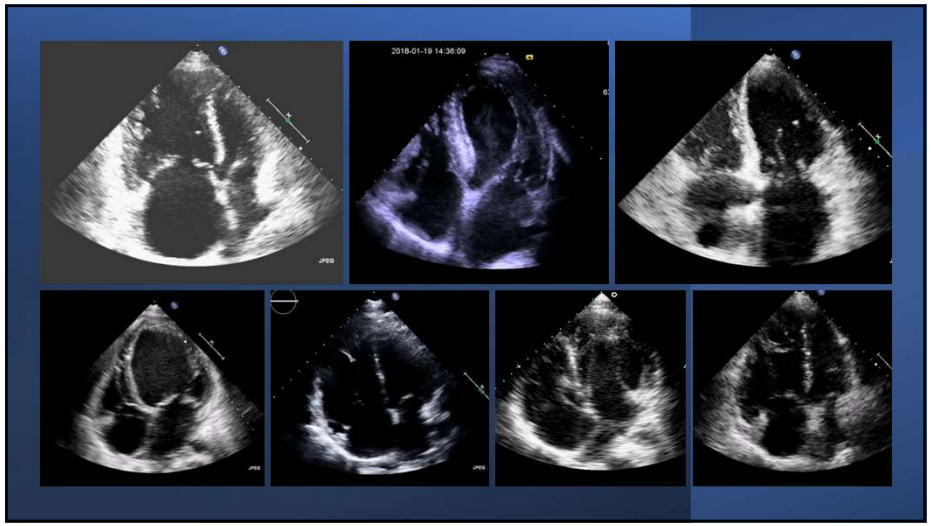

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Vad har dessa patienter gemensamt?

A: Klaffsjukdom

B: Snygga ekobilder

C: Medfött hjärtfel

D: Pulmonell hypertension

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Disposition - Pulmonell Hypertension

Del 1 - 45 min

- Inledning - PH - globalt problem
- Oklar dyspne´ - värdet av en strukturerad tidig utredning
- EKO & Hemodynamik vid differentiering av PH av olika genes - Patientfall 1-2
- Diskussion - Frågor

Paus - 30 min

Del 2 - 45 min

- EKO & Hemodynamik vid differentiering av PH av olika genes - Patientfall 3
- Behandling vid PAH - behandlingsalgoritmen
- Riskstratifiering vid PAH - Webb baserad - Patientfall 3
- Sammanfattning - Diskussion - Frågor

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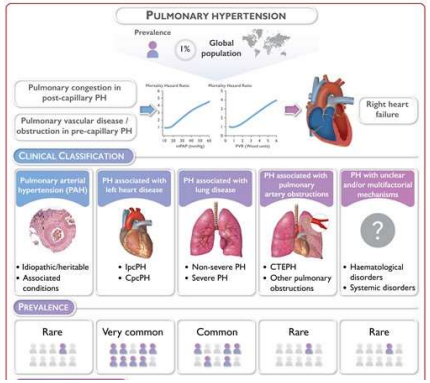
Pulmonell hypertension

Förhöjt tryck i lungkretsloppet

Pre- el postkapillär orsak

5 grupper av PH:

1. Pulmonell arteriell hypertension
2. Vänstersidig hjärtsjukdom
3. Associerad till lungsjukdom
4. Sekundärt till kronisk lungembolisering (CTEPH)
5. Multifaktorella/oklara orsaker



Figur 2

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Figure 1

Central illustration

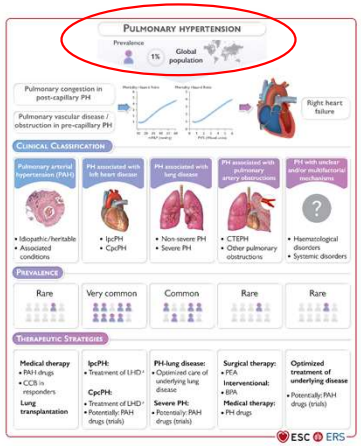

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Figure 1

Central illustration

Group 2 & 3
- The dominating causes of PH
- ~85-90 % of all PH cases

No available treatments for the PH component in Group 2-3.

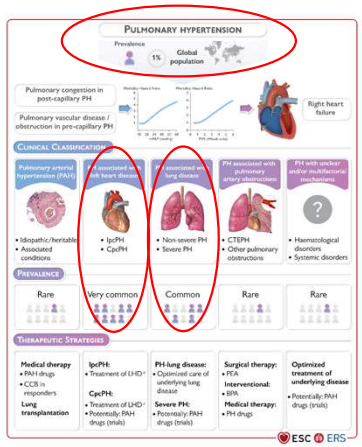

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Figure 11

Pathophysiology of pulmonary hypertension associated with left heart disease (group 2)

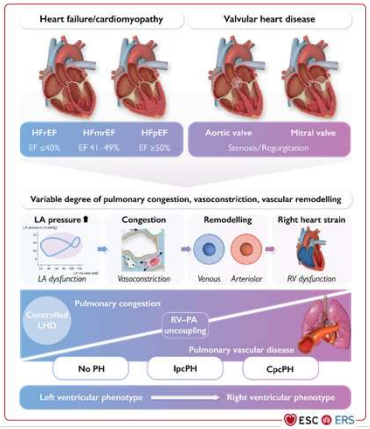

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Figure 12

Pathophysiology of pulmonary hypertension associated with lung disease (group 3)

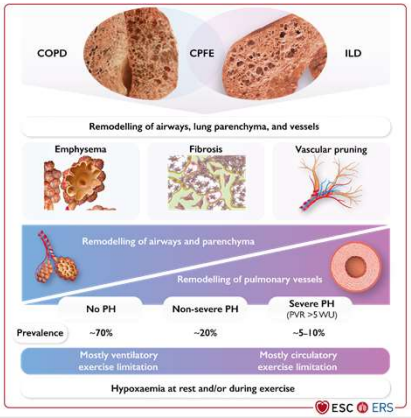

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Figure 1

Central illustration

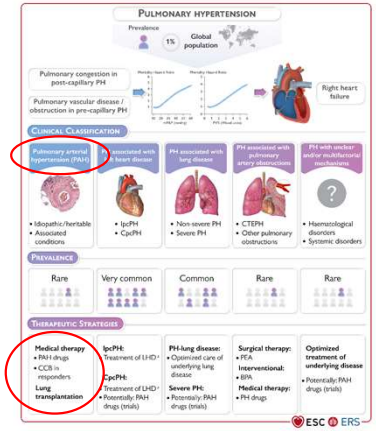

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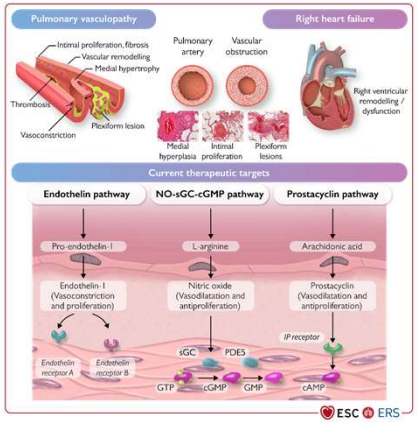
Figure 7

Pathophysiology and current therapeutic targets of pulmonary arterial hypertension (group 1)



PAH (Group 1) **in Sweden**

- Incidence - 8 cases / miljon / year
- Prevalence - 49 cases / miljon
- Totally ~ 500 cases

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Figure 1

Central illustration

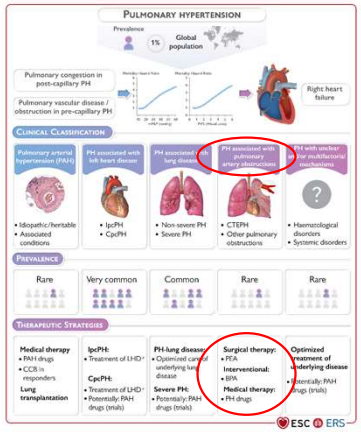

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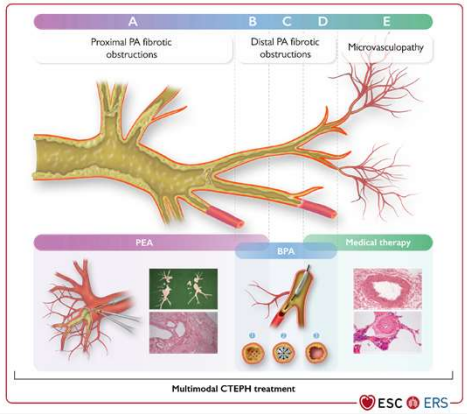
Figure 15

Overlap in treatments/multi-modality approach in chronic thrombo-embolic pulmonary hypertension



CTEPH (Group 4) **in Sweden**

- Incidence - 2 cases / miljon / year
- Prevalence - 19 cases / miljon
- Totally ~ 300 cases

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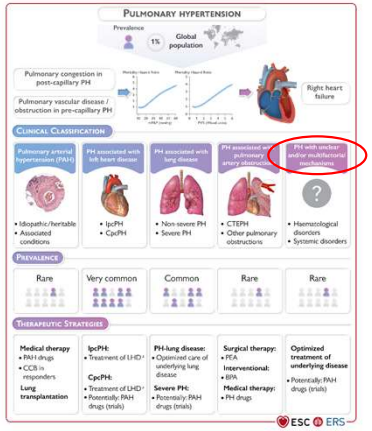
Figure 1

Central illustration



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Patient case - Anna

- Patient seeks primary care

- Unclear dyspnea
- Fatigue
- Dizines

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Patient case - Anna

- Patient seeks primary care

- Unclear dyspnea
- Fatigue
- Dizines

- Primary care dr interpretation

- Slight overweight
- Lack of training?
- Burned out?
- Resp. inf.?
- Asthma?

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Fallet Anna

A: Börja träna mer

B: Remiss till specialist

C: Kontakt med psykolog

D: Vidare utredning med labprover, spirometri, ekokardiografi mm

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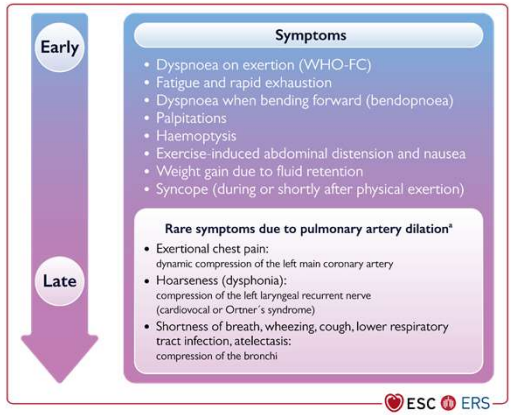
Figure 2

Symptoms in patients with pulmonary hypertension

- **Unspecific**

- **Unclear Dyspnea**



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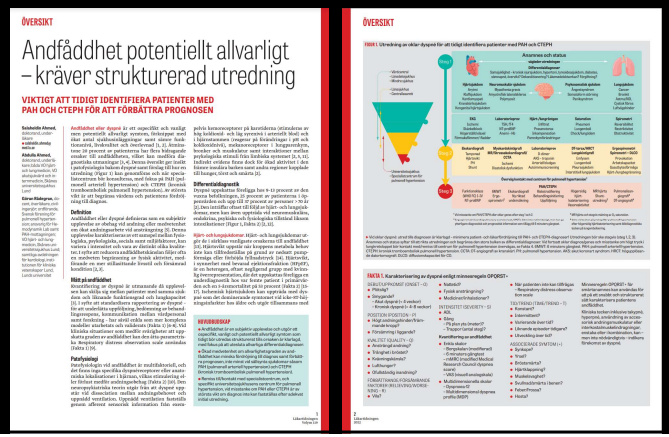
Dyspnea - potentially serious - demands a structurized work up


ÖVERSIKT

Andfåddhet potentiellt allvarligt – kräver strukturerad utredning

VIKTIGT ATT TIDIGT IDENTIFIERA PATIENTER MED PAH OCH CTEPH FÖR ATT FÖRBÄTTRA PROGNOSEN

ÖVERSIKT

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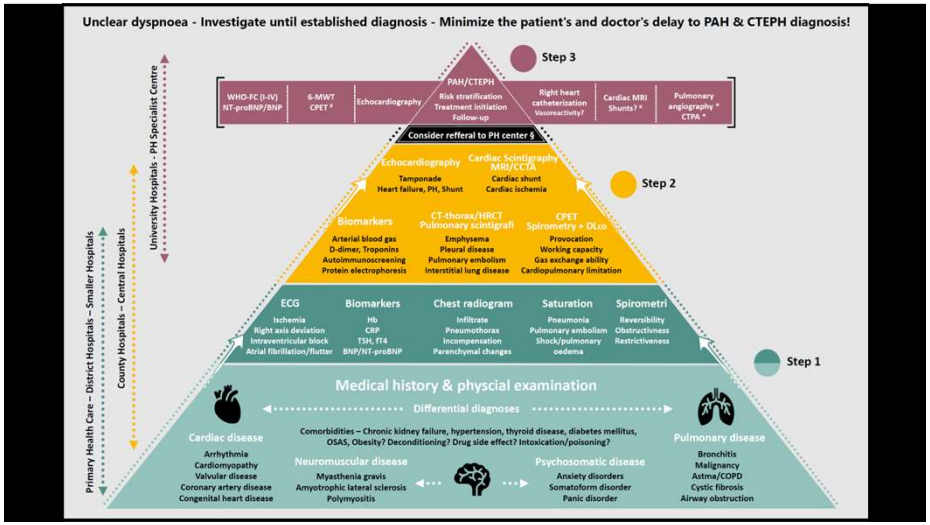

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Figure 6

Diagnostic algorithm of patients with unexplained dyspnoea and/or suspected pulmonary hypertension

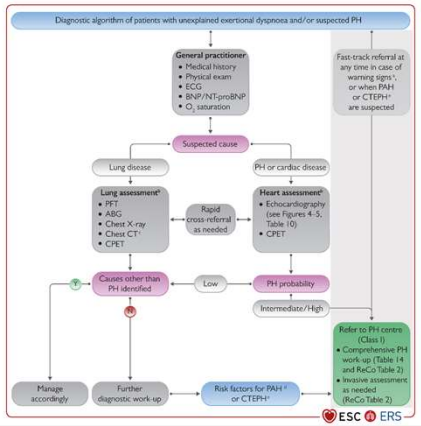

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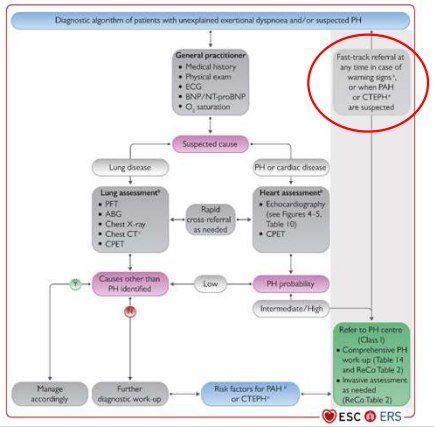
Figure 6

Diagnostic algorithm of patients with unexplained dyspnoea and/or suspected pulmonary hypertension



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Ekokardiografi

A: Utför själv

B: Skickar remiss till ett Ekolab/Klin Fys

C: Ingen erfarenhet alls

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Recommendations for diagnostic strategy (1)

Recommendations	Class	Level
Echocardiography		
Echocardiography is recommended as the first-line, non-invasive, diagnostic investigation in suspected PH	I	B
It is recommended to assign an echocardiographic probability of PH, based on an abnormal TRV and the presence of other echocardiographic signs suggestive of PH	I	B
It is recommended to maintain the current threshold for TRV (>2.8 m/s) for echocardiographic probability of PH according to the updated haemodynamic definition	I	C
Based on the probability of PH by echocardiography, further testing should be considered in the clinical context (i.e. symptoms and risk factors or associated conditions for PAH/CTEPH)	IIa	B
In symptomatic patients with intermediate echocardiographic probability of PH, CPET may be considered to further determine the likelihood of PH	IIb	C

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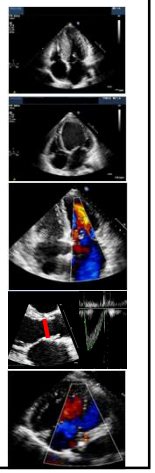
Ekokardiografi

- Hjärtats morfologi
- VK samt HK funktion
- Klaffvitier
- Non-invasiv hemodynamik
- Orsak till PH: LHD eller CHD
- Inte tillräckligt för att sätta diagnos – RHC behövs



HK = Höger kammare, VK = Vänster kammare
LHD= Left heart disease, CHD = Congentital heart disease
RHC = Right heart catheterization

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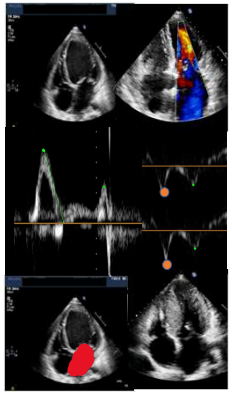
Differentiering från grupp 2 – PH sekundärt till vänstersidig hjärtsjukdom:

- Vänsterkammarens systoliska och diastoliska funktion (E/A samt E/é)
- Vänsterförmaksstorlek
- Klaffvitier
- Vänsterkammarhypertrofi



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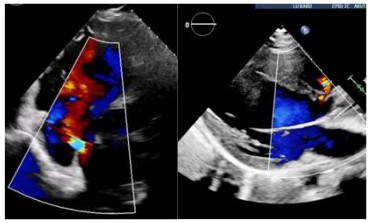
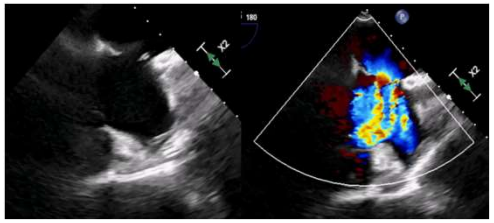
Differentiering från medfödda hjärtfel:

Färgdoppler



Misstanke om shunt - TEE



TEE= Transesofageal ekokardiografi

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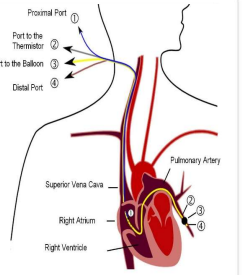
Hemodynamisk definition av pulmonell hypertension

Tabell 5

Definition	Haemodynamic characteristics
PH	mPAP >20 mmHg
Pre-capillary PH	mPAP >20 mmHg PAWP ≤15 mmHg PVR >2 WU
Isolated post-capillary PH	mPAP >20 mmHg PAWP >15 mmHg PVR ≤2 WU
Combined post- and pre-capillary PH	mPAP >20 mmHg PAWP >15 mmHg PVR >2 WU
Exercise PH	mPAP/CO slope between rest and exercise >3 mmHg/L/min



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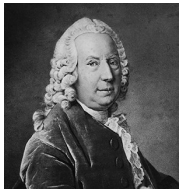
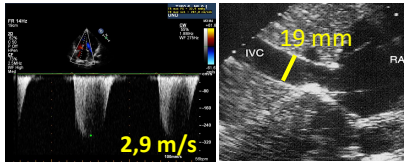
Beräkning av sPAP ekokardiografiskt



Daniel Bernoulli (1700-1782)

BERNOULLIS FÖRENKLADE EKVATION



$sPAP = (4xTRV_{max}^{2}) + CVP$

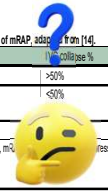


Table 1. Echocardiographic estimation of mRAP, adapted from [14].

	IVC size	IVC collapse %	RA pressure (mRAPecho)
Low	<2.1 cm	>50%	3 mmHg
Intermediate	<2.1 cm	≤50%	8 mmHg
	>2.1 cm		8 mmHg
High	>2.1 cm		15 mmHg

IVC (inferior vena cava), RA (right atrium), mRAP (mean right atrial pressure by echocardiography)

sPAP = systolic Pulmonary artery pressure
IVC = Inferior vena cava
TRV = Tricuspid regurgitation velocity
CVP= Central venous pressure

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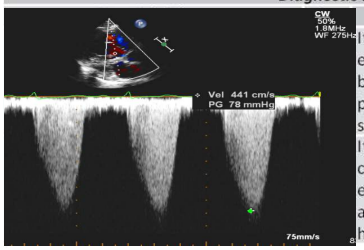
Diagnostic strategy



2022 Guidelines	Class
It is recommended to assign an echocardiographic probability of PH, based on an abnormal TRV and the presence of other echocardiographic signs suggestive of PH	I
It is recommended to maintain the current threshold for TRV (>2.8 m/s) for echocardiographic probability of PH according to the updated haemodynamic definition	I

- Sannolikhet för PH baserat på onormalt hög TRV samt förekomst av andra ekokardiografiska tecken till PH
- Rekommenderar bibehålla cut off för TRV_{max} >2.8 m/s

TRV = Tricuspid regurgitation velocity

2.8 m/s motsvarar 31 mmHg

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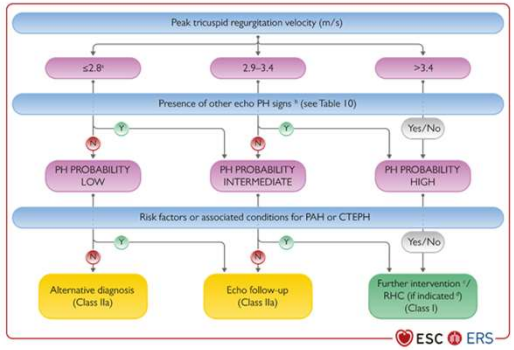
Ekokardiografisk sannolikhet för PH och rekommendation för vidare uppföljning

Figure 5

Echocardiographic probability of pulmonary hypertension and recommendations for further assessment



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Ytterligare ekokardiografiska parametrar för detektion av PH

Table 10 Additional echocardiographic signs suggestive of pulmonary hypertension

A: The ventricles	B: Pulmonary artery	C: Inferior vena cava and RA
RV/LV basal diameter/ area ratio >1.0	RVOT AT <105 ms and/or mid-systolic notching	IVC diameter >21 mm with decreased inspiratory collapse (<50% with a sniff or <20% with quiet inspiration)
Flattening of the interventricular septum (LVEI >1.1 in systole and/or diastole)	Early diastolic pulmonary regurgitation velocity >2.2 m/s	RA area (end-systole) >18 cm²
TAPSE/sPAP ratio <0.55 mm/mmHg	PA diameter >AR diameter PA diameter >25 mm	

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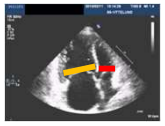
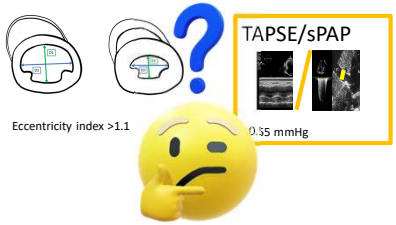


HK/VK >1.0

Avplaning av kammarseptum



Eccentricity index >1.1

0.55 mmHg

TAPSE = tricuspid annular plane systolic excursion
HK = höger kammare, VK = vänster kammare

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Ytterligare ekokardiografiska parametrar för detektion av PH

Table 10 Additional echocardiographic signs suggestive of pulmonary hypertension

A: The ventricles	B: Pulmonary artery	C: Inferior vena cava and RA
RV/LV basal diameter/ area ratio >1.0	RVOT AT <105 ms and/or mid-systolic notching	IVC diameter >21 mm with decreased inspiratory collapse (<50% with a sniff or <20% with quiet inspiration)
Flattening of the interventricular septum (LVEI >1.1 in systole and/or diastole)	Early diastolic pulmonary regurgitation velocity >2.2 m/s	RA area (end-systole) >18 cm²
TAPSE/sPAP ratio <0.55 mm/mmHg	PA diameter >AR diameter PA diameter >25 mm	

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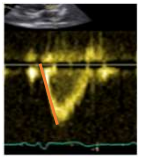
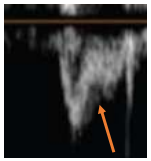
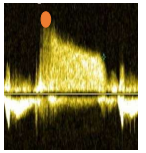


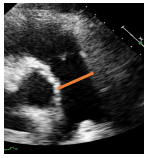
PAT <105 ms



Midsystolisk notch



EDPR vel >2.2 m/s



PA diameter >25 mm

PAT = pulmonary acceleration time
EDPR = early diastolic pulmonary regurgitation velocity
PA = Pulmonary artery

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Ytterligare ekokardiografiska parametrar för detektion av PH

Table 10 Additional echocardiographic signs suggestive of pulmonary hypertension

A: The ventricles	B: Pulmonary artery	C: Inferior vena cava and RA
RV/LV basal diameter/ area ratio >1.0	RVOT AT <105 ms and/or mid-systolic notching	IVC diameter >21 mm with decreased inspiratory collapse (<50% with a sniff or <20% with quiet inspiration)
Flattening of the interventricular septum (LVEI >1.1 in systole and/or diastole)	Early diastolic pulmonary regurgitation velocity >2.2 m/s	RA area (end-systole) >18 cm²
TAPSE/sPAP ratio <0.55 mm/mmHg	PA diameter >AR diameter PA diameter >25 mm	

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IVC > 21 mm,
Minskad/avsaknad andningsvariation

Högerförmaksarea >18 cm²

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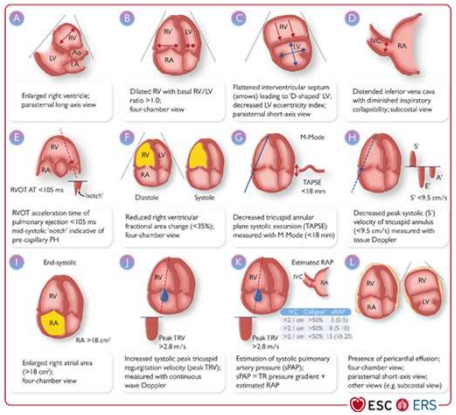
Ekokardiografiska parametrar vid bedömning av patienter med PH

Figure 4

Transthoracic echocardiographic parameters in the assessment of pulmonary hypertension



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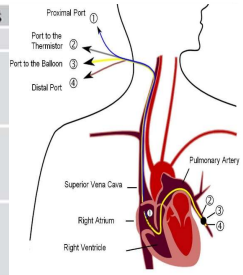
Hemodynamisk definition av pulmonell hypertension

Tabell 5

Definition	Haemodynamic characteristics
PH	mPAP >20 mmHg
Pre-capillary PH	mPAP >20 mmHg PAWP ≤15 mmHg PVR >2 WU
Isolated post-capillary PH	mPAP >20 mmHg PAWP >15 mmHg PVR ≤2 WU
Combined post- and pre-capillary PH	mPAP >20 mmHg PAWP >15 mmHg PVR >2 WU
Exercise PH	mPAP/CO slope between rest and exercise >3 mmHg/L/min



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2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension
(European Heart Journal, 2022 – doi: 10.1093/eurheartj/ehac237 and European Respiratory Journal, 2022 – doi: 10.1183/13993003.00879-2022)

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What's new in pulmonary hypertension diagnosis and phenotyping?

New Hemodynamic definition of PH - ESC:ERS's guidelines 2022

Humbert et al EHJ 2022

PA medel > 20 mmHg
Pulmonary hypertension (PH) at rest

PAWP ≤ 15 mmHg
PVR > 2 WU
Pre-capillary PH

1. PAH
3. Pulmonary disease, Hypoxia
4. CTEPH
5. Multifactorial, unclear

PVR > 2-3 WU *Treatment ?*
MPAP 20-24 mmHg *Treatment ?*

LHD - HFpEF
LHD phenotype, rest
Elderly, comorbid., PAWP 12-15
Exercise => PAWP > 25 mmHg
Vol load => PAWP ≥ 18 mmHg

Exercise PH
MPAP/CO slope
between rest & exercise
> 3 mmHg/l/min
Cardiax Ex. limitation
PAWP/CO slope > 2 mmHg/l/min

PAWP > 15 mmHg
Post-capillary PH

2. PH - Left Heart disease

Unclassified PH
PVR ≤ 2 WU

PVR ≤ 2 WU
Isolated post-capillary PH
IpcPH

PVR > 2 WU
Combined post- & pre-capillary PH
CpcPH

PAWP = Pulmonary Artery Wedge Pressure
CO = Cardiac Output

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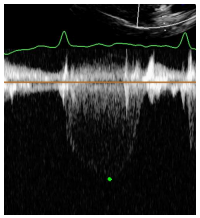
Fall 1

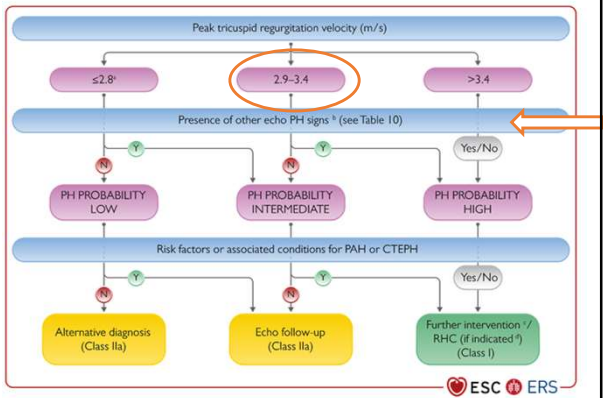
- Man, 81 år
- Övervikt
- Diabetes typ II
- Förmaksflimmer
- Ischemisk hjärtsjukdom samt tidigare infarkt
- OSAS (obstruktivt sömnapné syndrom)

41

Fall 1



Maxhastighet 3.4 m/s



CAD/MI = Coronary artery disease/Myocardial infarction
OSAS = Obstructive sleep apnea syndrome

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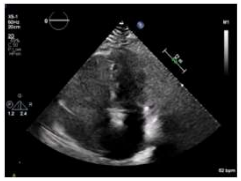
Fall 1 – Man 81 år, övervikt, DM typ 2, FF, CAD/MI, OSAS

HK dilatation

Normal septumrörlighet
Eccentricity index 0.9



HK/VK >1.0 ???

VK = vänster kammare
HK =höger kammare
CAD/MI = Coronary artery disease/Myocardial infarction
OSAS = Obstructive sleep apnea syndrome

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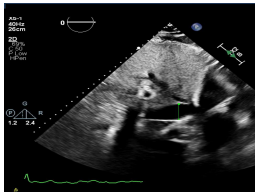
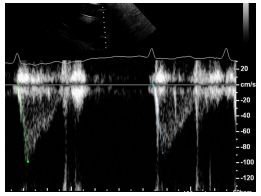
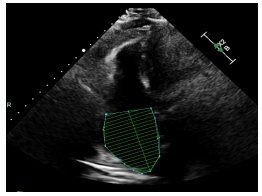
Fall 1 – Man 81 år, övervikt, DM typ 2, FF, CAD/MI, OSAS



IVC diameter 26 mm
Resp variabilitiet



PAT 80 ms
Ingen mid systolisk notch



RA area 28 cm²

IVC = inferior vena cava
PAT = pulmonary acceleration time
RA = right atrium (höger förmak)
CAD/MI = Coronary artery disease/Myocardial infarction
OSAS = Obstructive sleep apnea syndrome

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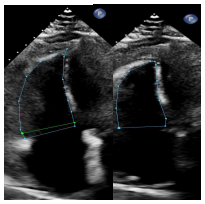
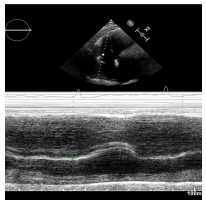
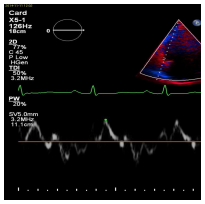
Fall 1 – Man 81 år, övervikt, DM typ 2, FF, CAD/MI, OSAS



RVFAC 37 %



TAPSE 24 mm



S´ 11 cm/s

FWS -29 %

RVFAC= right ventricular fractional area change
TAPSE = tricuspid annular plane systolic excursion
S´= systolisk maxhastighet basallateralt
FWS = free wall strain
CAD/MI = Coronary artery disease/Myocardial infarction
OSAS = Obstructive sleep apnea syndrome

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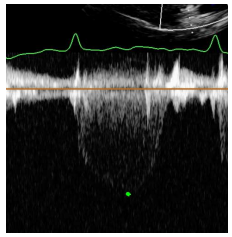
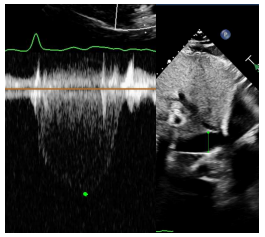
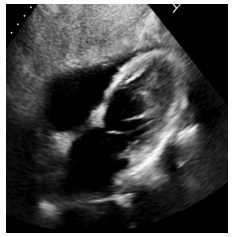
Fall 1 – Man 81 år, övervikt, DM typ 2, FF, CAD/MI, OSAS



TR maxgradient 46 mmHg



sPAP = 46 + 8 = 54 mmHg



Ingen perikardvätska

TR = tricuspid regurgitation
sPAP = systolic pulmonary arterial pressure
CAD/MI = Coronary artery disease/Myocardial infarction
OSAS = Obstructive sleep apnea syndrome

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Fall 1 – Man 81 år, övervikt, DM typ 2, FF, CAD/MI, OSAS

Table 10 Additional echocardiographic signs suggestive of pulmonary hypertension

A: The ventricles	B: Pulmonary artery	C: Inferior vena cava and RA
RV/LV basal diameter/ area ratio >1.0	RVOT AT <105 ms and/or mid-systolic notching	IVC diameter >21 mm with decreased inspiratory collapse (<50% with a sniff or <20% with quiet inspiration)
Flattening of the interventricular septum (LVEI >1.1 in systole and/or diastole)	Early diastolic pulmonary regurgitation velocity >2.2 m/s	RA area (end-systole) >18 cm²
TAPSE/sPAP ratio <0.55 mm/mmHg	PA diameter >AR diameter PA diameter >25 mm	

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A	B	C
??	80 ms NO Mid-systolic notch	26 mm Inspiratory collapse
No Flattening LVEI < 1.1	n.a	28 cm²
0.41	n.a	

CAD/MI = Coronary artery disease/Myocardial infarction
OSAS = Obstructive sleep apnea syndrome

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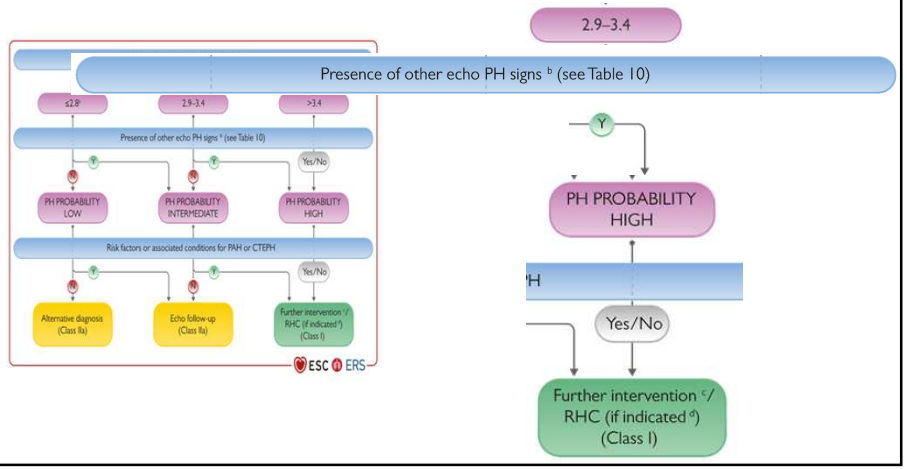
Fall 1 – Man 81 år, övervikt, DM typ 2, FF, CAD/MI, OSAS



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Fall 1 – Man 81 år, övervikt, DM typ 2, FF, CAD/MI, OSAS

- RHC – Hemodynamik – PH? PAH eller HFpEF?

	MAP mmHg	MPAP mmhg	TPG mmhg	PAWP mmhg	MRAP mmhg	HR min-1	CO l/min	CI l/min/m2	SVI ml/m2	a-vO2 ml/l	SaO2 %	SvO2 %	PVR WU	SVR WU
Vila	89	24	10	14	10	63	4,75	2,26	35,7	53,1	91,0	62,3	2,1	16,6
												2022		

HFpEF= Heart failure with preserved ejection fraction
mPAP = mean pulmonary arterial pressure
PAWP = Pulmonary arterial wedge pressure
PVR = Pulmonary vascular resistance
CAD/MI = Coronary artery disease/Myocardial infarction
OSAS = Obstructive sleep apnea syndrome

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Fall 1 – Man 81 år, övervikt, DM typ 2, FF, CAD/MI, OSAS

A: pre-kapillär PH

B: Post-kapillär PH

C: Kombinerad pre- och post-kapillär PH

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Fall 1 – Man 81 år, övervikt, DM typ 2, FF, CAD/MI, OSAS

- RHC – Hemodynamik – PH? PAH eller HFpEF?
- Beror på ESC/ERS guidelines 2015 vs. 2022 samt komorbiditetsbördan

	MAP mmHg	MPAP mmhg	TPG mmhg	PAWP mmhg	MRAP mmhg	HR min-1	CO l/min	CI l/min/m2	SVI ml/m2	a-vO2 ml/l	SaO2 %	SvO2 %	PVR WU	SVR WU
Vila	89	24	10	14	10	63	4,75	2,26	35,7	53,1	91,0	62,3	2,1	16,6

2015		2022
mPAP ≥ 25 mmHg **PAWP ≤ 15 mmHg** **PVR > 3WU**	Pre-capillary PH	mPAP >20 mmHg PAWP ≤15 mmHg PVR >2 WU
mPAP ≥ 25 mmHg **PAWP > 15 mmHg** **PVR ≤ 3WU**	Isolated post-capillary PH	mPAP >20 mmHg PAWP >15 mmHg PVR ≤2 WU

HFpEF= Heart failure
mPAP = mean pulmo
PAWP = Pulmonary a
PVR = Pulmonary vas
CAD/MI = Coronary a
OSAS = Obstructive sleep apnea syndrome

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Fall 1 – Man 81 år, övervikt, DM typ 2, FF, CAD/MI, OSAS

- Hemodynamik – Benlyft

	MAP mmHg	MPAP mmhg	TPG Mmhg	PAWP mmhg	MRAP mmhg	HR min-1	CO l/min	CI l/min/m2	SVI ml/m2	a-vO2 ml/l	SaO2 %	SvO2 %	PVR WU	SVR WU
Vila	89	24	10	14	10	63	4,75	2,26	35,7	53,1	91,0	62,3	2,1	16,6
Benlyft 10 sek				20										
Benlyft 2 min				22										

HFpEF= Heart failure with preserved ejection fraction
mPAP = mean pulmonary arterial pressure
PAWP = Pulmonary arterial wedge pressure
PVR = Pulmonary vascular resistance
CAD/MI = Coronary artery disease/Myocardial infarction
OSAS = Obstructive sleep apnea syndrome

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Sammanfattning

Fall 1

- Pulmonell hypertension
- PH grupp 2 - HFpEF – Benlyft
- Guidelines rekommenderar:
  Volyms- (500 ml iv, 5 min) eller
  arbetsbelastning vid PH och PAWP ~13-15 mmHg

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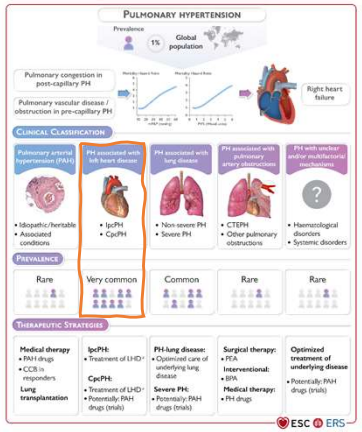
Figure 1

Central illustration



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(*European Heart Journal*; 2022 – doi: 10.1093/eurheartj/ehac237 and *European Respiratory Journal*; 2022 – doi: 10.1183/13993003.00879-2022)

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Fall 2

- Man 69 år
- Övervikt
- Hypertension
- Aortastenos
- LBBB
- Ischemisk hjärtsjukdom (CAD), STEMI, PCI

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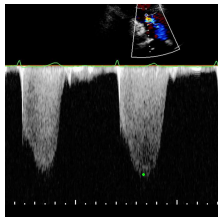
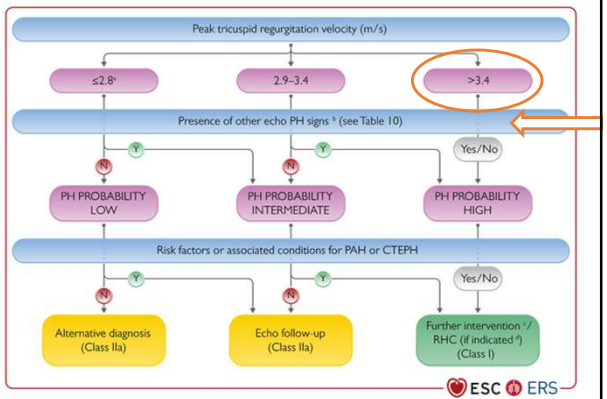
Fall 2

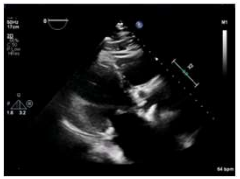


Maxhastighet 3.5 m/s

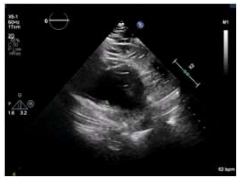


56

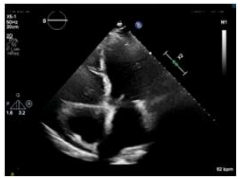
Fall 2 – Man 69 år, övervikt, hypertension, Aortastenos, LBBB, CAD/STEMI/PCI



HK dilatation



Normal septumrörlighet
Eccentricty index 0.6



HK/VK >1.0

VK = vänster kammare
HK =höger kammare

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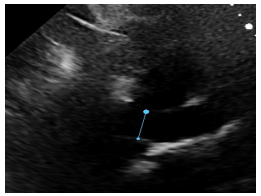
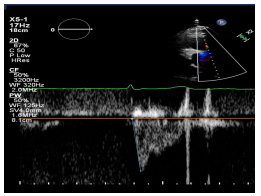
Fall 2 – Man 69 år, övervikt, hypertension, Aortastenos, LBBB, CAD/STEMI/PCI



IVC diameter 23 mm
Andningsvariabilitet



PAT 60 ms
Mid systolisk notch

RA area 22 cm²

IVC = inferior vena cava
PAT = pulmonary acceleration time
RA = right atrium (höger förmak)

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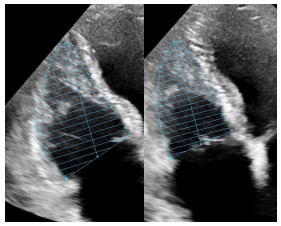
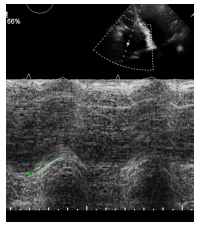
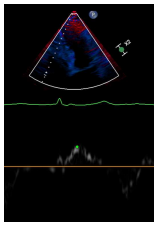
Fall 2 – Man 69 år, övervikt, hypertension, Aortastenos, LBBB, CAD/STEMI/PCI



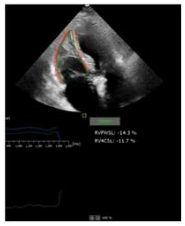
RVFAC 25 %



TAPSE 12 mm



S´6.5 cm/s



FWS -14 %

RVFAC= right ventricular fractional area change
TAPSE = tricuspid annular plane systolic excursion
S´= systolisk maxhastighet basallateralt
FWS = free wall strain

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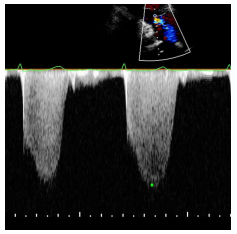
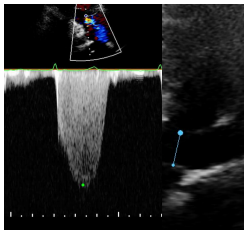
Fall 2 – Man 69 år, övervikt, hypertension, Aortastenos, LBBB, CAD/STEMI/PCI



TR maxgradient 66 mmHg



PASP = 66 + 8 = 74 mmHg

Perikardvätska

TR = tricuspid regurgitation
sPAP = systolic pulmonary arterial pressure
CAD/MI = Coronary artery disease/Myocardial infarction
OSAS = Obstructive sleep apnea syndrome

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Fall 2 – Man 69 år, övervikt, hypertension, Aortastenos, LBBB, CAD/STEMI/PCI

Table 10 Additional echocardiographic signs suggestive of pulmonary hypertension

A: The ventricles	B: Pulmonary artery	C: Inferior vena cava and RA
RV/LV basal diameter/ area ratio >1.0	RVOT AT <105 ms and/or mid-systolic notching	IVC diameter >21 mm with decreased inspiratory collapse (<50% with a sniff or <20% with quiet inspiration)
Flattening of the interventricular septum (LVEI >1.1 in systole and/or diastole)	Early diastolic pulmonary regurgitation velocity >2.2 m/s	RA area (end-systole) >18 cm²
TAPSE/sPAP ratio <0.55 mm/mmHg	PA diameter >AR diameter PA diameter >25 mm	

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A	B	C
>1.0	60 ms Mid-systolic notch	23 mm Inspiratory collapse
No Flattening LVEI < 1.1	2.5 m/s	22 cm²
0.16	31 mm	

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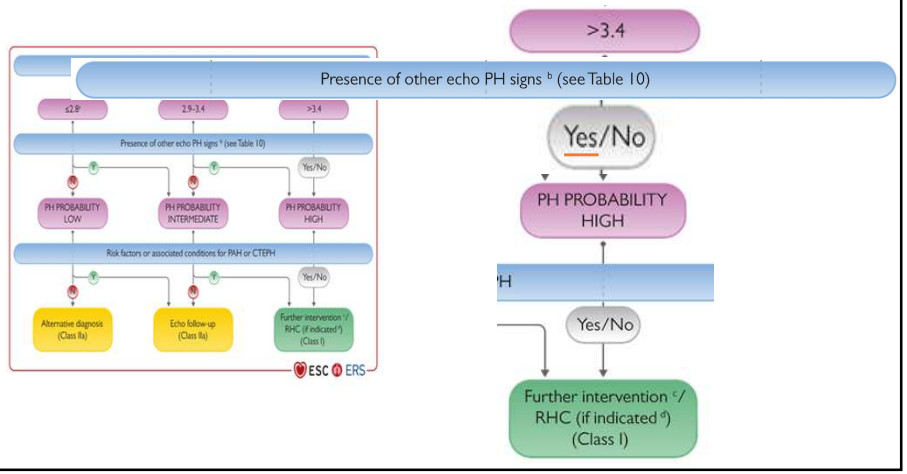
Fall 2 – Man 69 år, övervikt, hypertension, Aortastenos, LBBB, CAD/STEMI/PCI



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Fall 2
Hur ska vi utvärdera komorbiditeternas betydelse?

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Fall 2 – Man 69 år, övervikt, hypertension, Aortastenos, LBBB, CAD/STEMI/PCI

- RHC – Hemodynamik

	MAP mmHg	MPAP mmhg	TPG mmhg	PAWP mmhg	MRAP mmhg	HR min-1	CO l/min	CI l/min/m2	SVI ml/m2	a-vO2 ml/l	SaO2 %	SvO2 %	PVR WU	SVR WU
Vila	104	48	26	22	12	66	4,35	2,13	32,3	51,9	95,0	68,2	6,0	21,1

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Fall 2 – Man 69 år, övervikt, hypertension, Aortastenos, LBBB, CAD/STEMI/PCI

A: pre-kapillär PH

B: Post-kapillär PH

C: Kombinerad pre- och post-kapillär PH

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Fall 2 – Man 69 år, övervikt, hypertension, Aortastenos, LBBB, CAD/STEMI/PCI

- RHC – Hemodynamik - PH grupp 2 - HFrEF – kombinerad pre- och postkapillär PH
- Uppenbart redan i vila – annars volym- eller arbetsbelastning

	MAP mmHg	MPAP mmhg	TPG mmhg	PAWP mmhg	MRAP mmhg	HR min-1	CO l/min	CI l/min/m2	SVI ml/m2	a-vO2 ml/l	SaO2 %	SvO2 %	PVR WU	SVR WU
Vila	104	48	26	22	12	66	4,35	2,13	32,3	51,9	95,0	68,2	6,0	21,1

Combined post- and pre-capillary PH	mPAP >20 mmHg PAWP >15 mmHg PVR >2 WU

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Sammanfattning

Fall 2

- Pulmonell hypertension
- PH grupp 2 – Kombinerad pre- och postkapillär PH

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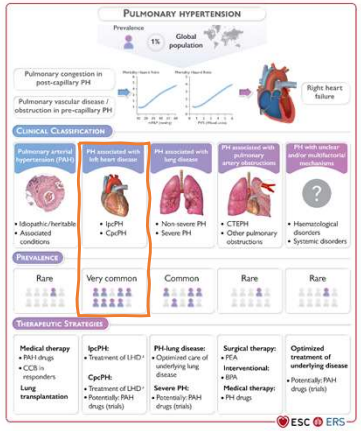
Figure 1

Central illustration



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2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension (*European Heart Journal*; 2022 – doi: 10.1093/eurheartj/ehac237 and *European Respiratory Journal*; 2022 – doi: 10.1183/13993003.00879-2022)

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Fall 3

- Kvinna 32 år gammal
- Upprepade synkoperingar
- Telefonkonsult från närliggande sjukhus

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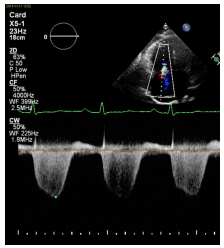
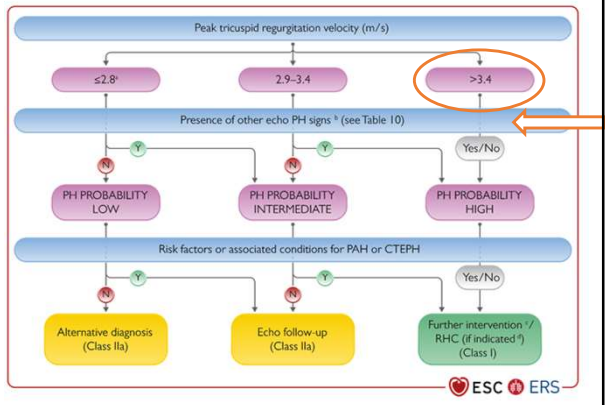
Fall 3



Maxhastighet 4.0 m/s



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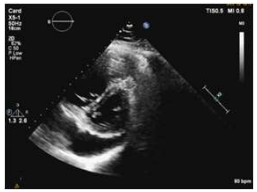
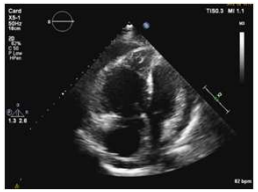
Fall 3 – Kvinna 32 år, upprepade synkoperingar

HK dilatation



D-formad VK
Eccentricity index >1.1



HK/VK >1.0

VK = vänster kammare
HK =höger kammare

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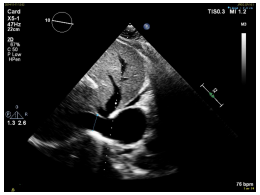
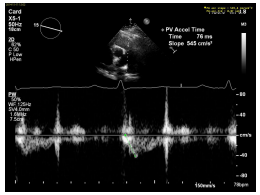
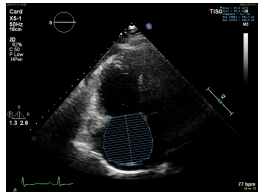
Fall 3 – Kvinna 32 år, upprepade synkoperingar



IVC diameter 24 mm
Ingen respirationsvariabilitet



PAT 70 ms
mid-systolisk notch



RA area 27 cm²

IVC = inferior vena cava
PAT = pulmonary acceleration time
RA = right atrium (höger förmak)

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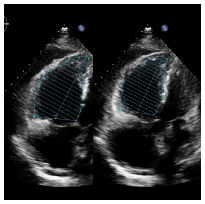
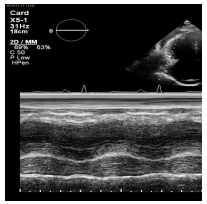
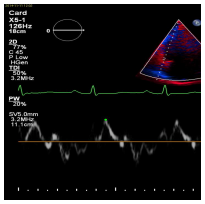
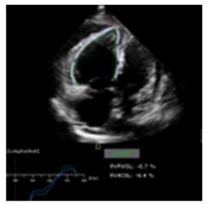
Fall 3 – Kvinna 32 år, upprepade synkoperingar


RVFAC 21 %


TAPSE 11 mm


S´ 11 cm/s


FWS -7 %

RVFAC= right ventricular fractional area change
TAPSE = tricuspid annular plane systolic excursion
S´= systolisk maxhastighet basallateralt
FWS = free wall strain

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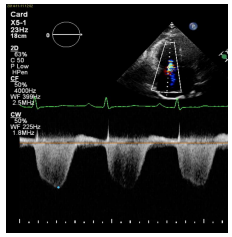
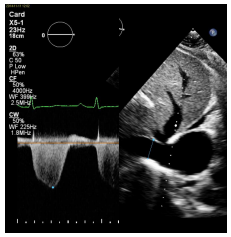
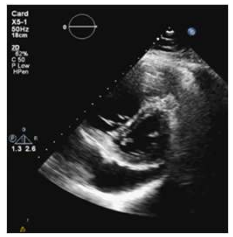
Fall 3 – Kvinna 32 år, upprepade synkoperingar


TR maxgradient 64 mmHg


sPAP = 64 + 15 = 79 mmHg


Perikardvätska

TR = tricuspid regurgitation
sPAP = systolic pulmonary arterial pressure

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Fall 3 – Kvinna 32 år, upprepade synkoperingar

Table 10 Additional echocardiographic signs suggestive of pulmonary hypertension

A: The ventricles	B: Pulmonary artery	C: Inferior vena cava and RA
RV/LV basal diameter/ area ratio >1.0	RVOT AT <105 ms and/or mid-systolic notching	IVC diameter >21 mm with decreased inspiratory collapse (<50% with a sniff or <20% with quiet inspiration)
Flattening of the interventricular septum (LVEI >1.1 in systole and/or diastole)	Early diastolic pulmonary regurgitation velocity >2.2 m/s	RA area (end-systole) >18 cm²
TAPSE/sPAP ratio <0.55 mm/mmHg	PA diameter >AR diameter PA diameter >25 mm	

© ESC/ERS 2022

A	B	C
>1.0	70 ms Mid-systolic notch	24 mm No inspiratory collapse
Flattening LVEI >1.1	2.7 m/s	27 cm²
0.13	36 mm	

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Fall 3 – Kvinna 32 år, upprepade synkoperingar

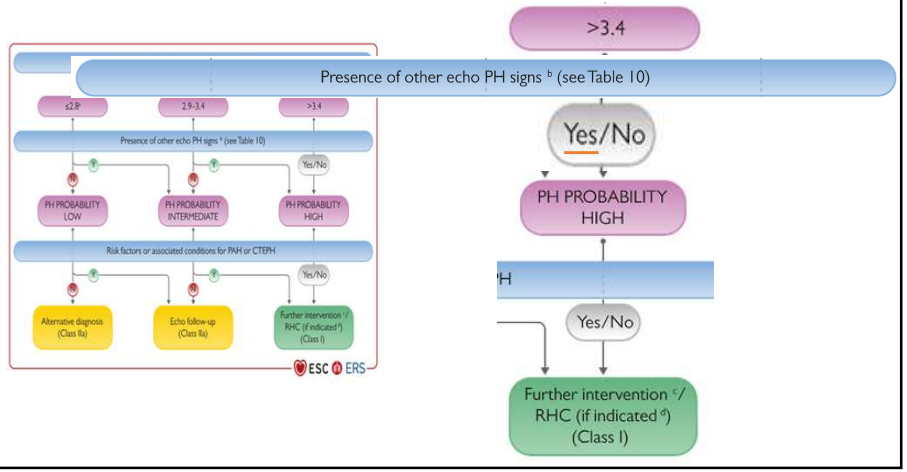

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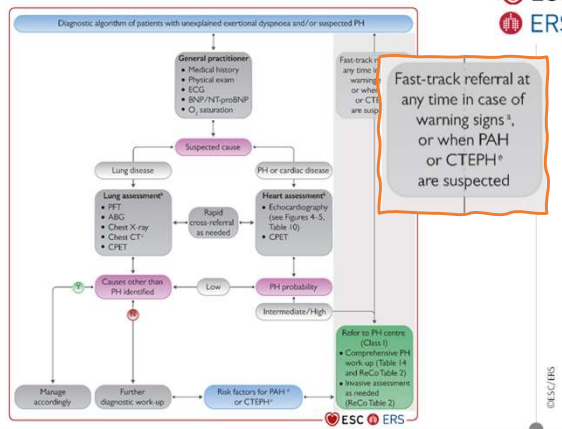
Figure 6

Diagnostic algorithm of patients with unexplained dyspnoea and/or suspected pulmonary hypertension



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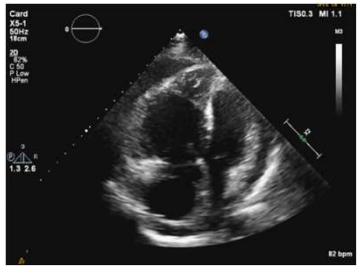
Fall 3 – Kvinna 32 år, upprepade synkoperingar

Resultat från PH utredning:



WHO FC	III
Pre-Syncope	x 5
6MWD	220 m
NT-proBNP	8081
Hemodynamik	Ingen vasoresponder
mPAP	50 mmHg
PAWP	6 mmHg
mRAP	11 mmHg
PVR	14.9 WU
CO	3.0 l/min
Ekokardiografi	TRV >3.4 m/s Ekokardiografiska tecken till PH
Lungscint	Inga tecken till Lungemboli
Spirometri	Måttligt nedsatt diffusions kapacitet
HRCT	Inga tecken till fibros eller emfysem. PVOD?

mPAP = mean pulmonary arterial pressure
PAWP = pulmonary arterial wedge pressure
mRAP = mean right atrial pressure
PVR = pulmonary vascular resistance
CO = cardiac output

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Fall 3 – Kvinna 32 år, upprepade synkoperingar

A: pre-kapillär PH

B: Post-kapillär PH

C: Kombinerad pre- och post-kapillär PH

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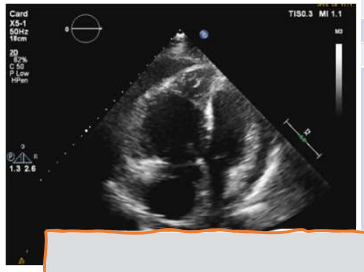
Fall 3 – Kvinna 32 år, upprepade synkoperingar

Resultat från PH utredning:



WHO FC	III
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Hemodynamik	Ingen vasoresponder
mPAP	50 mmHg
PAWP	6 mmHg
mRAP	11 mmHg
PVR	14.9 WU
CO	3.0 l/min
Pre-capillary PH	mPAP >20 mmHg PAWP ≤15 mmHg PVR >2 WU
HRCT	Inga tecken till fibros eller emfysem. PVOD?

CO = cardiac output

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Clinical classification of pulmonary hypertension (1)

ESC ERS

GROUP 1 Pulmonary arterial hypertension (PAH)
1.1 Idiopathic
1.1.1 Non-responders at vasoreactivity testing
1.1.2 Acute responders at vasoreactivity testing
1.2 Heritable
1.3 Associated with drugs and toxins
1.4 Associated with:
1.4.1 Connective tissue disease
1.4.2 HIV infection
1.4.3 Portal hypertension
1.4.4 Congenital heart disease
1.4.5 Schistosomiasis
1.5 PAH with features of venous/capillary (PVOD/PCH) involvement
1.6 Persistent PH of the newborn

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2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension
(*European Heart Journal*; 2022 – doi: 10.1093/eurheartj/ehac237 and *European Respiratory Journal*; 2022 – doi: 10.1183/13993003.00879-2022)

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Sammanfattning

Fall 3

- Pre-kapillär PH
- PAH
- Insattes på PAH behandling …

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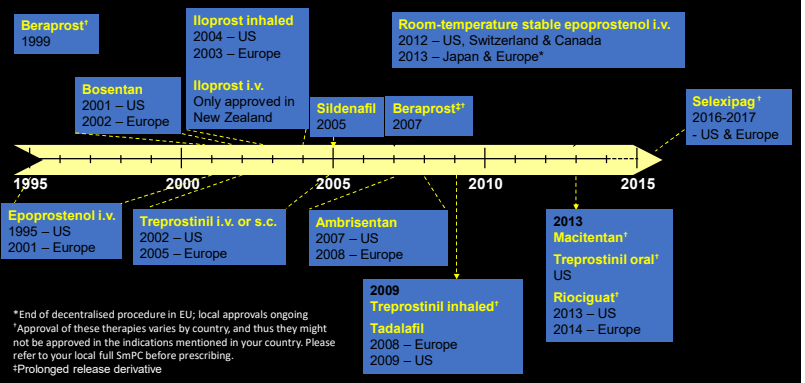
History of Approval of Vasoactive PAH therapies



*End of decentralised procedure in EU; local approvals ongoing
†Approval of these therapies varies by country, and thus they might not be approved in the indications mentioned in your country. Please refer to your local full SmPC before prescribing.
‡Prolonged release derivative

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PAH - Treatment alternatives in relation to individual Decisions

Oral therapies	
ERA	**Dual** Bosentan, Macitentan **Single** Ambrisentan
PDE5i or sGC stimulators	Sildenafil, Tadalafil Riociguat
Prostacyclin analogues or receptor agonists	Treprostinil, Selexipag
I.V, S.c and inhalation therapies	
Prostacyclin analogues	Epoprostenol, Treprostinil

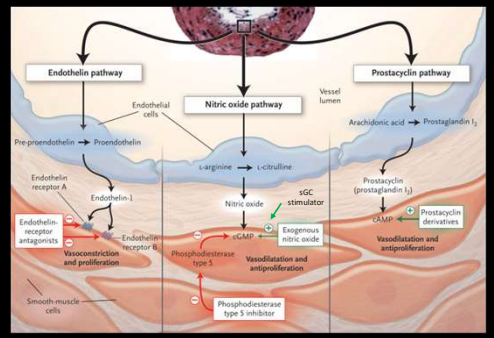

Image adapted from Humbert M, *et al. New Engl J Med* 2004; 351:1425-36.

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Behandlingsalgoritm vid I/H/D-PAH eller APAH-CTD

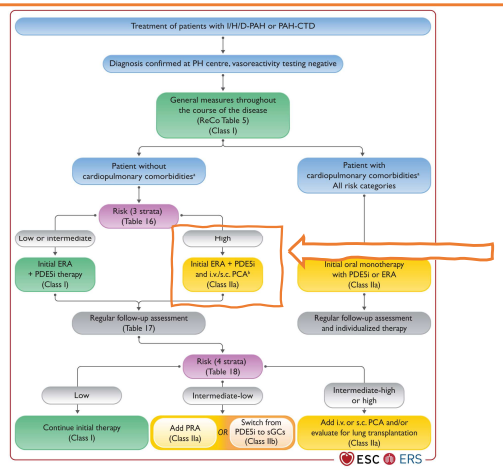

Figure 9

Eur Heart J, Volume 43, Issue 38, 7 October 2022, Pages 3618–3731, https://doi.org/10.1093/eurheartj/ehac237

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The New ESC/ERS 2022 PH guidelines - Risk stratification in PAH

- The expanded 3-strata model at baseline

Determinants of prognosis (estimated 1-year mortality)	Low risk (<5%)	Intermediate risk (5–20%)	High risk (>20%)
Clinical observations and modifiable variables			
Signs of right HF	Absent	Absent	Present
Progression of symptoms and clinical manifestations	No	Slow	Rapid
Syncope	No	Occasional syncope[a]	Repeated syncope[b]
WHO-FC	I, II	III	IV
6MWD[c]	>440 m	165–440 m	<165 m
CPET	Peak VO_2 >15 mL/min/kg (>65% pred.) VE/VCO_2 slope <36	Peak VO_2 11–15 mL/min/kg (35–65% pred.) VE/VCO_2 slope 36–44	Peak VO_2 <11 mL/min/kg (<35% pred.) VE/VCO_2 slope >44
Biomarkers: BNP or NT-proBNP[d]	BNP <50 ng/L NT-proBNP <300 ng/L	BNP 50–800 ng/L NT-proBNP 300–1100 ng/L	BNP >800 ng/L NT-proBNP >1100 ng/L
Echocardiography	RA area <18 cm^2 TAPSE/sPAP >0.32 mm/mmHg No pericardial effusion	RA area 18–26 cm^2 TAPSE/sPAP 0.19–0.32 mm/mmHg Minimal pericardial effusion	RA area >26 cm^2 TAPSE/sPAP <0.19 mm/mmHg Moderate or large pericardial effusion
cMRI[e]	RVEF >54% SVI >40 mL/m^2 RVESVI <42 mL/m^2	RVEF 37–54% SVI 26–40 mL/m^2 RVESVI 42–54 mL/m^2	RVEF <37% SVI <26 mL/m^2 RVESVI >54 mL/m^2
Haemodynamics	RAP <8 mmHg CI ≥2.5 L/min/m^2 SVI >38 mL/m^2 SvO_2 >65%	RAP 8–14 mmHg CI 2.0–2.4 L/min/m^2 SVI 31–38 mL/m^2 SvO_2 60–65%	RAP >14 mmHg CI <2.0 L/min/m^2 SVI <31 mL/m^2 SvO_2 <60%

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Fall 3 – Kvinna 32 år, upprepade synkoperingar - Insatt på trippelbehandling

Datum	RA area (cm^2) PEX	mPAP mmHg (PAWP, mmHg)	mRAP mmHg (SvO2, %)	CO l/min (CI) l/min/m^2	PVR WU	FC/6MWT NTproBNP	ERA mg	PDE5i mg	PC ng/kg/min
Baseline	27 +++	50 (6)	11 (44.4)	3.0 (1.4)	14.9	3 / 220 8031	-	-	-
							Upprepade synkoperingar		
2.5 veckor	25 +++	51 (14)	22 (61.9)	5.7 (2.7)	6.5	3 / 240 577	3. Bosentan => Macitentan 10x1	2. Sildenafil => Tadalafil 40x1	1. Flolan => Treprostinil 20
2.5 mån	23 +	34 (5)	4 (70.0)	5.9 (2.9)	4.9	1 / 375 140	Macitentan 10 x 1	Tadalafil 40 x 1	Treprostinil 27.5
9 mån	18 -	23 (3)	3 (64.2)	6.0 (2.9)	3.4	1 / 430 178	Macitentan 10 x 1	Tadalafil 40 x 1	Treprostinil 35
18 mån	18 -	-	-	-	-	1 / 455 158	Macitentan 10 x 1	Tadalafil 40 x 1	Treprostinil 35
22 mån	17 -	29 (5)	2 (71.6)	6.4 (3.0)	3.7	1 / 475 < 50	Macitentan 10 x 1	Tadalafil 40 x 1	Treprostinil 35

RA = right atrium
mPAP = mean pulmonary arterial pressure
PAWP = pulmonary arterial wedge pressure
mRAP = mean right atrial pressure
CO = cardiac output
PVR = pulmonary vascular resistance
FC = Functional Class
6 MWT = 6 minutes walking test
ERA = Endotelin receptor antagonist
PDE5i = PDE5 inhibitors
PC = Prostacyclins

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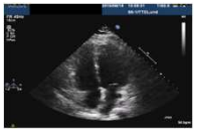
Fall 3 – Kvinna 32 år, upprepade synkoperingar

Baseline
HK – Uttalat dilaterad
HK – Uttalat nedsatt funktion
HK/HF - 66 mmHg
PASP - 85 mmHg
TAPSE/PASP - 0.13
PEX - Uttalat

2.5 veckor
HK - Uttalat dilaterad
HK – Uttalat nedsatt funktion
HK/HF - 61 mmHg
PASP - 76 mmHg
TAPSE/PASP - 0.18
PEX- 20-30 mm

2.5 månader
HK – Mätttligt dilaterad
RV – Mätttligt nedsatt funktion
HK/HF - 51 mmHg
PASP 54 mmHg
TAPSE/PASP - 0.37
PEX- Inget



9 månader
HK – Lindrigt dilaterad
RV – Lindrigt nedsatt funktion
HK/HF - 50 mmHg
PASP 53 mmHg
TAPSE/PASP - 0.36
Peric. exudate - Inget

18 månader
HK – Lindrigt dilaterad
RV – Normal funktion
HK/HF - 36 mmHg
PASP – 39 mmHg
TAPSE/PASP - 0.53
PEX - Inget

22 månader
HK – Lindrigt dilaterad
RV – Normal funktion
HK/HF - 32 mmHg
PASP – 35 mmHg
TAPSE/PASP - 0.71
PEX - Inget

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Key Message - Launch of a new tool for Riskstratification

- Riskstratification - www.svefph.se


ESC European Heart Journal Open (2021) 1, 1–9 https://doi.org/10.1093/ehjopen/oeab012

ORIGINAL ARTICLE
Vascular medicine

Evaluation of the European Society of Cardiology/European Respiratory Society derived three- and four-strata risk stratification models in pulmonary arterial hypertension: introducing an internet-based risk stratification calculator

Abdulla Ahmed [1,2]*, Salahaldin Ahmed [1,2], Daniel Kempe [3,4], and Göran Rådegran [1,2]


Pulmonary Circulation

LETTER TO THE EDITOR

Risk assessment in pulmonary arterial hypertension: A step towards clinical implementation based on the 2022 ESC/ERS pulmonary hypertension guidelines

Dear Editor,


RAPPORT

Prognostisk riskstratifiering vid pulmonell arteriell hypertension

IMPLEMENTERING AV KALKYLATOR FÖR VÅGLEDNING VID BEHANDLING

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Summary

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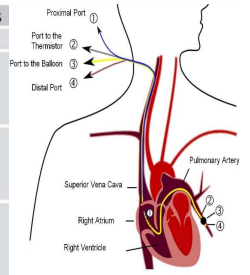
Hemodynamisk definition av pulmonell hypertension

Tabell 5

Definition	Haemodynamic characteristics
PH	mPAP >20 mmHg
Pre-capillary PH	mPAP >20 mmHg PAWP ≤15 mmHg PVR >2 WU
Isolated post-capillary PH	mPAP >20 mmHg PAWP >15 mmHg PVR ≤2 WU
Combined post- and pre-capillary PH	mPAP >20 mmHg PAWP >15 mmHg PVR >2 WU
Exercise PH	mPAP/CO slope between rest and exercise >3 mmHg/L/min



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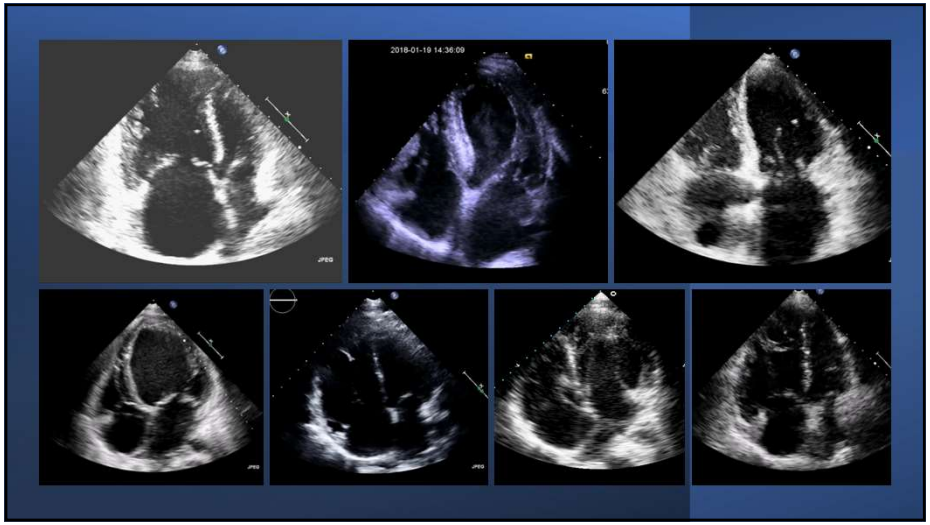

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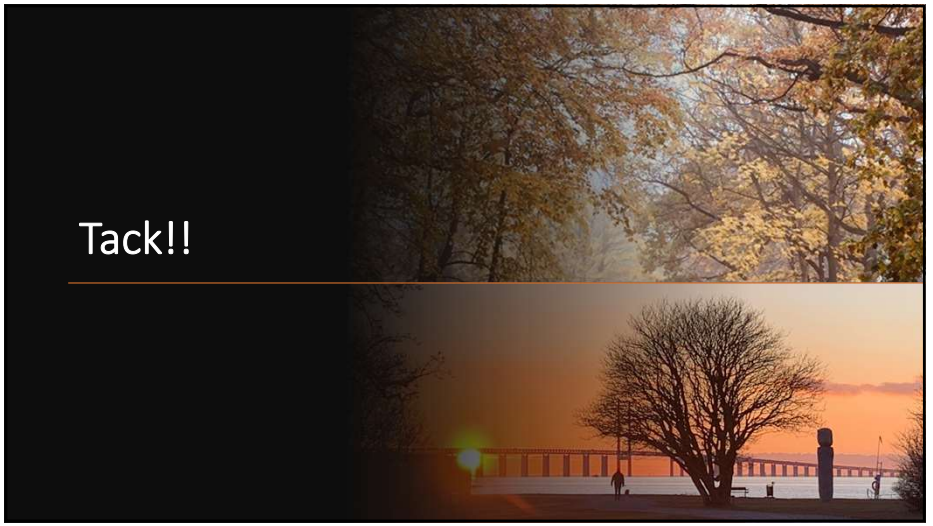
SAMMANFATTNING

- Utredning av oklar dyspné
- Ekokardiografi rekommenderas som första linjens modalitet vid misstänkt PH
- Sannolikheten för PH baseras på TI vmax (>2.8 m/s) + andra ekokardiografiska tecken till PH
- Vid hög klinisk misstanke om PH, med misstanke om PAH eller CTEPH, bör RHC utföras för att säkerställa diagnos
- Vid PAH/CTEPH finns riktade behandlingar
- Ny hemodynamisk definition av PH
  - mPAP > 20 mmHg vid RHC
- För differentiering mellan pre- och post-kapillär PH hemodynamiskt → volym- eller arbetsbelastning för att demaskera förhöjda fyllnadstryck

TI (tricuspidalisinsufficens)
RHC (Högersidig hjärtkat)

93

Tack!!



94

DT-kranskärl

Kari Feldt

Torsdag 25 januari 2024, 12.35-14.30

DT kranskärl – diagnostik för framtidens kardiologer

Sv. Kard. Föreningen 2024/01

1. Bakgrund – Riktlinjer & CCTA i Sverige.
2. Lite om DT fysik & premedicinering
3. CCTA – Hur gör vi? + Kliniska case
4. Pivotala studier
5. Sammanfattning

Kari Feldt, Bitr. Överläkare, Kardiolog
PO Kranskärl/Klaff /DT Hjärtlab
ME Kardiologi & ME Radiologi
Karolinska Universitetssjukhuset

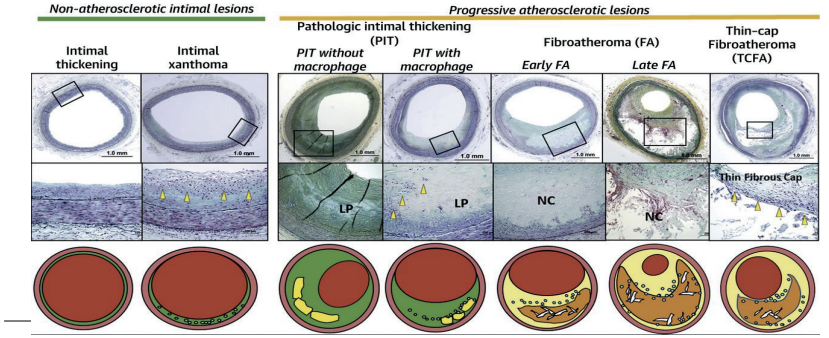
Epikardiell kransartärsjukdom (CAD)

Icke-obstruktiv CAD

Plack, <50% stenos
FFR >0.8 (föga flödesbegränsning)
Koronar dysfunktion kan finnas

Obstruktiv CAD

Plack, >50% stenos
FFR ≤0.8 (signifikant stenos)
Stenos > ischemi > angina



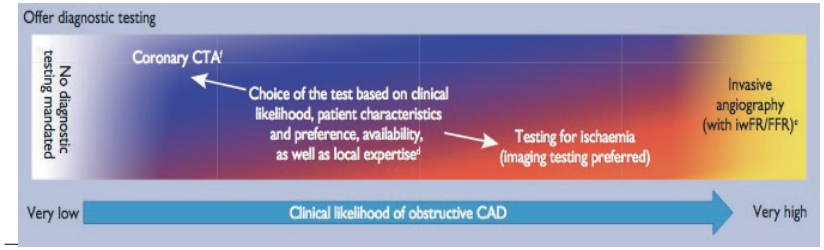
Abdelrahman KM, JACC 2020

ESC European Society of Cardiology
European Heart Journal (2020) **41**, 407–477
doi:10.1093/eurheartj/ehz425

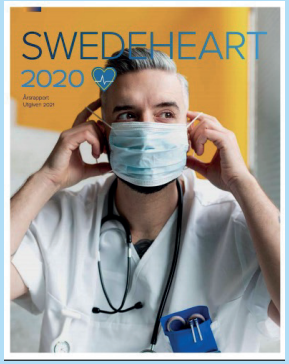
ESC GUIDELINES

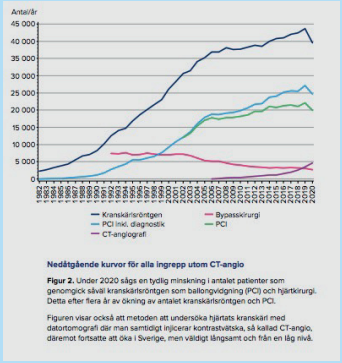
2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes

The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC)



Nationellt: CCTA ökade trots pandemi





Swedeheart Årsrapport 2020

CT-angio fortfarande underutnyttjad undersökningsmetod

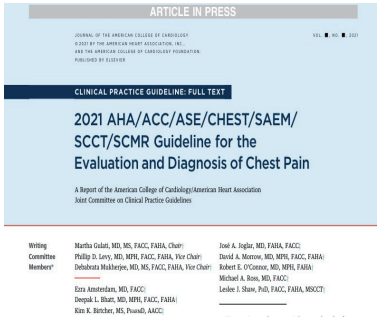
Undersökning av hjärtats kranskärl med datortomografi där man samtidigt injicerar kontrastvätska, så kallad CT-angio, ökar i Sverige, men väldigt långsamt och från en låg nivå (Figur 2).

Metoden är mycket träffsäker när det gäller att utesluta förträngningar i kranskärlen och har flera fördelar framför kranskärlsröntgen. Patienten behöver inte genomgå onödiga undersökningar och onödiga resurser tas inte från vården. Först om metoden visar någon form av förträngning kan man behöva gå vidare med kranskärlsröntgen.

Vid de CT-angio som gjordes i Sverige under 2020 visade 80 procent inga förträngningar eller icke-signifikanta förträngningar (Figur 8). En 1-årsuppföljning av de CT-angio som gjordes 2019 verkar bekräfta CT-angios pålitlighet – i 80 procent av fallen behövdes ingen form av intervention (Figur 9).

SWEDEHEART anser att användningen av CT-angio bör öka i Sverige.

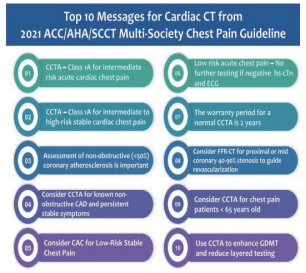
Nordamerikanska riktlinjer 2021-


ARTICLE IN PRESS

CLINICAL PRACTICE GUIDELINE: FULL TEXT

2021 AHA/ACC/ASE/CHEST/SAEM/ SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain

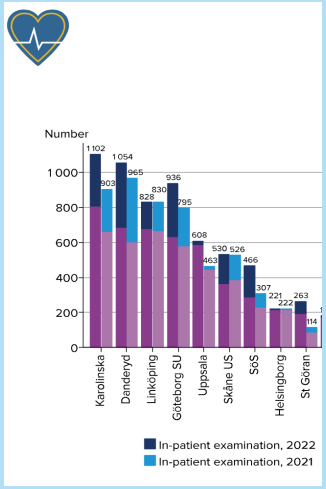
A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines



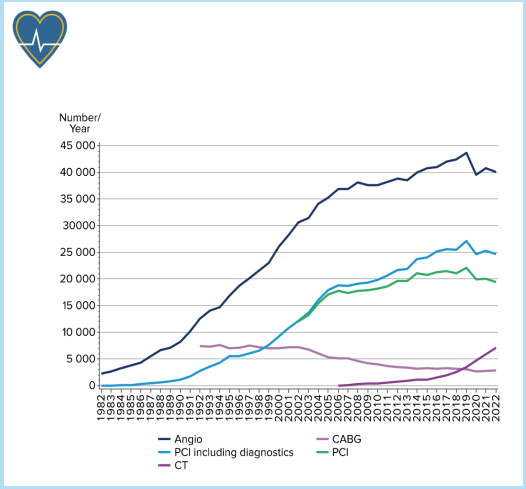
JCCT Editorial, Oct 2021

Patient <65/70 år med oklar bröstsmärta ska i första hand utredas med DT kranskärl
Patient >65/70 år med känd kranskärlssjukdom (mm.) kan utredas med fysiologiskt test
Även svårvärderad AKUT bröstsmärta (intermediär risk) kan utredas med DT kranskärl

CCTA och Cor-ai i Sverige (SWEDEHEART 2022)



CCTA i Sverige. Ca. 80 mL kontrast och 2mSV stråldos



Trend: cor-ai (överst) och CCTA (nederst) i Sverige sedan 1982

Årlig genomsnittlig bakgrundstrålning är 2.4 mSv för icke rökare I Sverige

SCCT 2023…

KAROLINSKA UNIVERSITETSSJUKHUSET

Styrande lokalt dokument 1 (7)

Oklar bröstsmärta – Utredning av kroniska koronarsyndrom, Patientflöde Kranskärl, ME Kardiologi

- Steg 1: Klassificera bröstsmärtan
- Steg 2: Värdera PTP (Pre-Test Probability) för obstr.CAD
- Steg 3: Välj lämplig diagnostisk undersökning
- Steg 4: Behandla påvisad CAD (prognos, symptom)

K. Feldt, ME Kardiologi & Radiologi. Lena Forsberg, ME KlinFys, Dimitrios Venetsanos, Angio/PCI, Liyew Desta, Angio/PCI m.fl..

1

Patients with angina and/or dyspnoea and suspected coronary artery disease

ESC European Society of Cardiology

Clinical classification of suspected angina

Typical angina	Meets the following three characteristics: 1. Constricting discomfort in the front of the chest or in the neck, jaw, shoulder, or arm; 2. Precipitated by physical exertion; 3. Relieved by rest or nitrates within 5 min.
Atypical angina	Meets two of these characteristics.
Non-anginal chest pain	Meets only one or none of these characteristics.

©ESC

www.escardio.org/guidelines

ESC Guidelines on the diagnosis and management of chronic coronary syndromes (European Heart Journal 2019; 10.1093/eurheartj/ehz425)

2- ESC

Pre-test sannolikhet för obstruktiv CAD vid angina eller dyspné

Table 5 Pre-test probabilities of obstructive coronary artery disease in 15 815 symptomatic patients according to age, sex, and the nature of symptoms in a pooled analysis[64] of contemporary data[7,8,62]

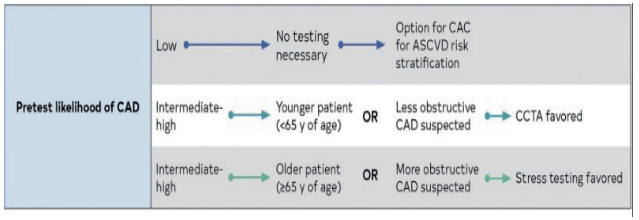
	Typical		Atypical		Non-anginal		Dyspnoea[a]	
Age	Men	Women	Men	Women	Men	Women	Men	Women
30–39	3%	5%	4%	3%	1%	1%	0%	3%
40–49	22%	10%	10%	6%	3%	2%	12%	3%
50–59	32%	13%	17%	6%	11%	3%	20%	9%
60–69	44%	16%	26%	11%	22%	6%	27%	14%
70+	52%	27%	34%	19%	24%	10%	32%	12%

©ESC 2019

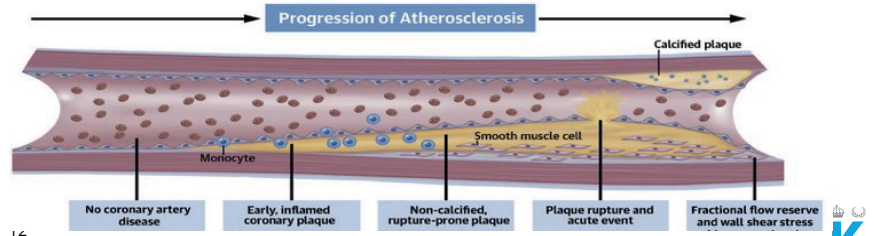
CAD = coronary artery disease; PTP = pre-test probability.

Knuuti J, et al. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes

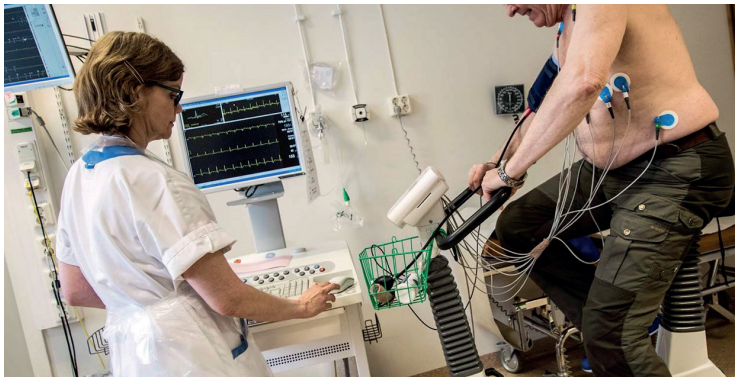
3 – Beroende på PTP: Välj diagnostisk undersökning, eller avstå?



JACC 2021, October 28. AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain



Abdelrahman, K.M. JACC 2020



Use of exercise electrocardiogram in the initial diagnostic management of patients with suspected coronary artery disease

Recommendations	Class[a]	Level[b]
Exercise ECG is recommended for the assessment of exercise tolerance, symptoms, arrhythmias, BP response, and event risk in selected patients.[c]	I	C
Exercise ECG may be considered as an alternative test to rule-in and rule-out CAD when non-invasive imaging is not available.[73,83]	IIb	B

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Karolinska Universitetssjukhuset

Computed Tomography (CT) history

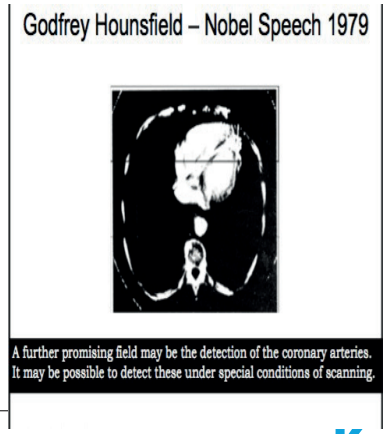
Godfrey Hounsfield, inventor of clinical CT in 1971

Nobel prize, 1979 (Medicine and Physiology)

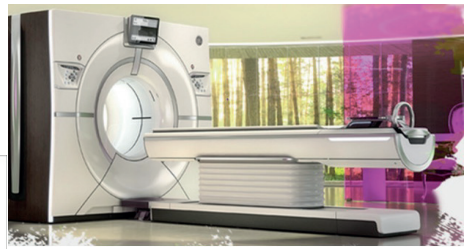
Shared with Allan Cormack (SA)

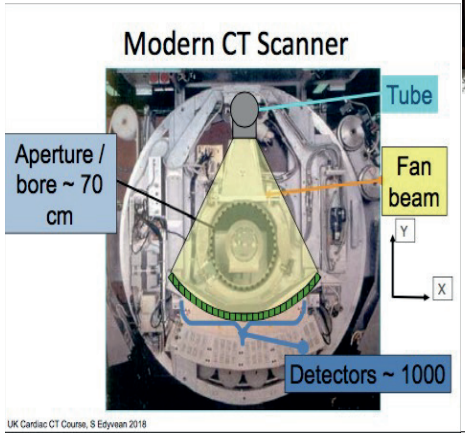
1st October 1971; 1st patient s

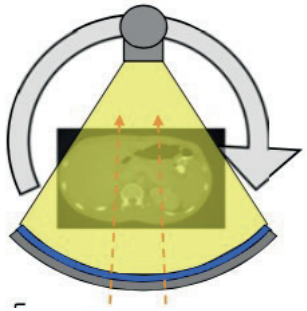
1919 – 2004



How does CT work

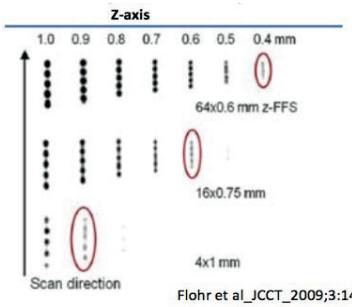






Spatial Resolution

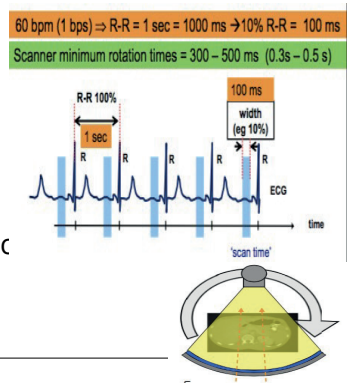
Ability to resolve two adjacent structures separately
= the ability to view small objects



Imaging Modality	Spatial resolution (mm)
Cardiac CT Angiography	0.3 – 0.6
Catheter angiography	0.15 – 0.2
IVUS	0.10-0.15
Cardiac MRI	1.0 – 7.0
SPECT	4.0 – 15.0
Echocardiography	0.5 – 2.0

Temporal Resolution

Good temporal resolution achieved by **"freezing"** the heart motion with ECG gating:
Image acquired during phase of least cardiac motion: **mid diastole** or end-systole.



Poor time resolution blurs the effec
of good physical/spatial resolution

Pre-treatment: Beta-blockers & Nitroglycerin + "Maximize" temporal and spatial resolution

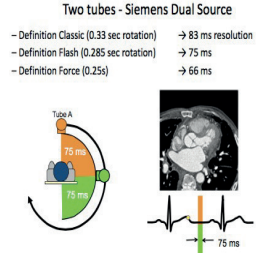
Slow and regular heart rate

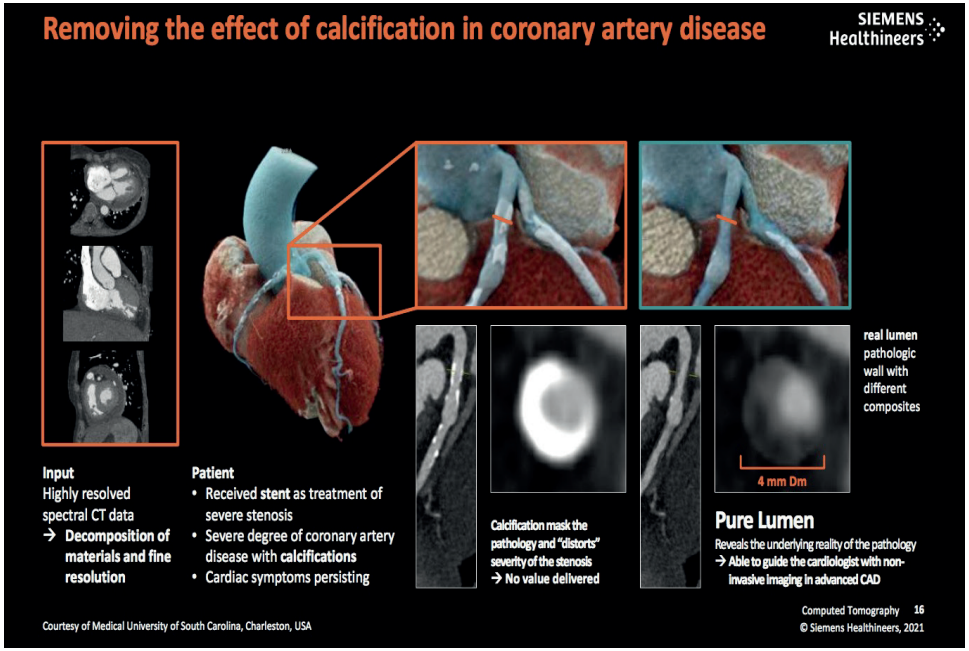
Dilated coronary arteries

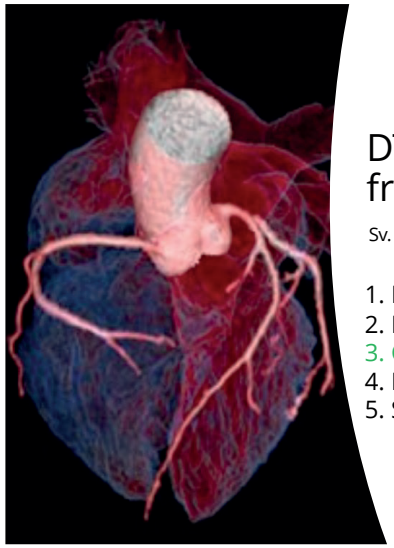
Fast rotation (270 ms/ rotation)

Multi-sector reconstruction

Two tubes (Siemens) for simultaneous 2 sector scanning







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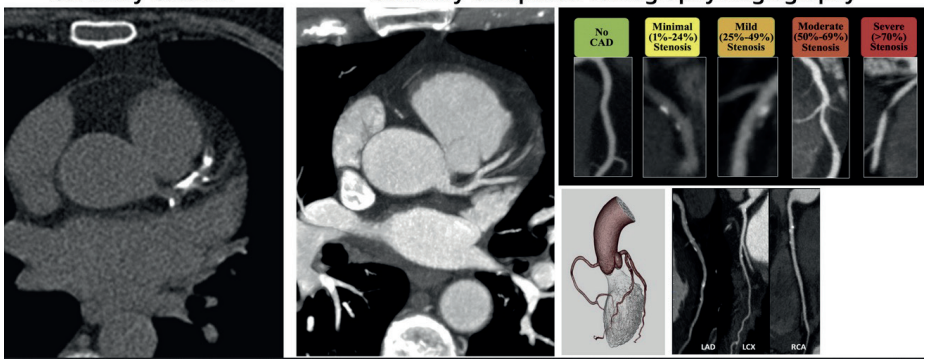
DT Hjärta-Kranskärl (Cardiac CT), avbildar:

1) Aterosklerosbörda (kärlvägg)
2) Stenosgrad (lumen)
3) Placktyp (icke förkalkad, förkalkad, blandad) +/- högrisk karakteristika

Coronary Calcium | Coronary Computed Tomography Angiography



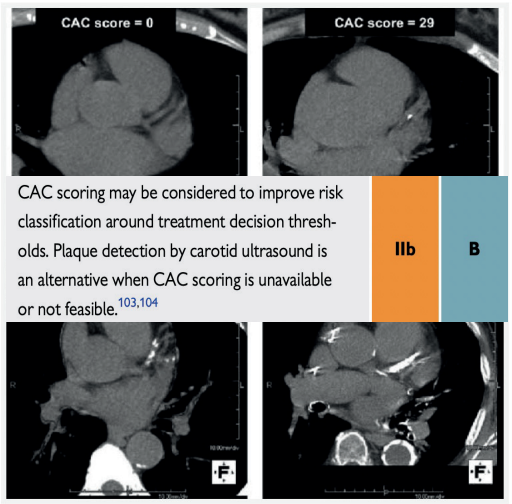
Journal of Cardiovascular Computed Tomography 2021 1593-109DOI:
(10.1016/j.jcct.2020.11.002)

Kalk i kranskärl: kvantifierbart (**calcium score**), men kan även orsaka artefakter som försvårar angiografisk bedömning

Stort förkalkat plack I prox. LAD – stenosgrad ej bedömbar.

Feldt, K. 2023

Coronary Artery Calcium Score (CAC) – bildserie utan kontrast



CAC scoring may be considered to improve risk classification around treatment decision thresholds. Plaque detection by carotid ultrasound is an alternative when CAC scoring is unavailable or not feasible.[103,104]

IIb | B

Non-contrast CT scans showing different scores from a calcium score test.

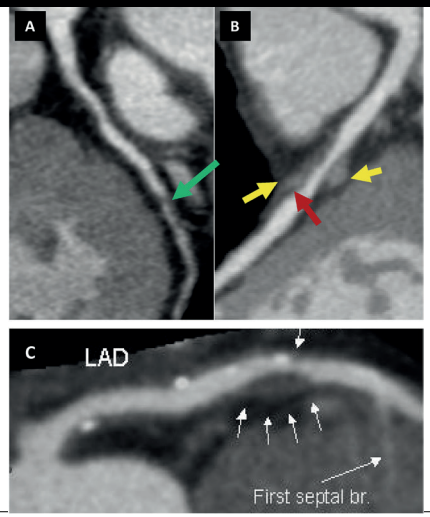
+ kvantifierar åder**förkalkning**
+ oberoende riskmarkör för kardiovask. händelse (utöver kliniska riskfaktorer)

- **avbildar inte åderförfettning** (”mjuka”, icke-förkalkade plack förbises)
- avbildar inte stenoser
- bör **relateras till ålder, kön** (t.ex. MESA calcium calculator ger normalvärden för åldrarna **45-83**)

Overall amount of coronary plaque	CAC
Mild	1-100
Moderate	101–300
Severe	301–999
Extensive	>1000

Frank L J Visseren et al. 2021 ESC Guidelines on cardiovascular disease prevention. *European Heart Journal*, Volume 42, Issue 34, 7 September 2021
Cury RC, Leipsic J, CAD-RADS2 Consensus Document (SCCT), Radiol Cardiothorac Imaging. 2022 Sep

DT kranskärl (CCTA) – avbildar både kärlvägg (plack) OCH lumen (stenos)



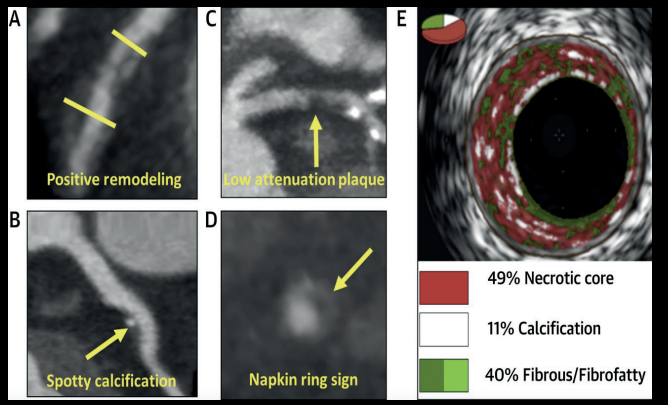
A: Icke förkalkat plack med >90% stenos
(hos pat med stabil angina).

B: Icke förkalkat plack, 70-90% stenos och två högrisk-karakteristika
(pat med plackruptur, NSTEMI)
- lågattenuerande plack (röd)
- positiv remodellerering (gul)

C: "Vulnerabelt" plack, 40-60% stenos i prox LAD. Tre högriskarakteristika.
(lågattenuerande plack, pos. remodellering av kärlväggen, fläckvis förkalkning)

Journal of Cardiovascular Computed Tomography 2021 1593-109DOI: (10.1016/j.jcct.2020.11.002)

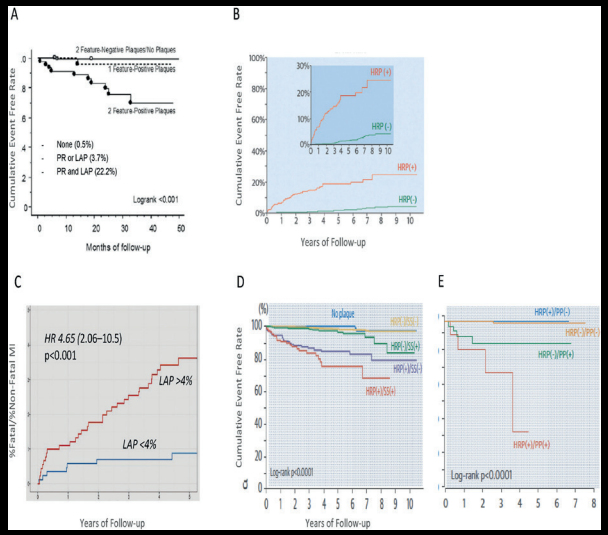
High Risk Plaque (HRP) features - CCTA and IVUS (intravascular ultrasound of arterial wall)



If 1 or more adverse plaque feature -> **x3** risk of CHD death or MI
If both >70% stenosis and adverse plaque -> **x10** risk

Williams, M et al JACC Jan. 2019, vol 73 (SCOT-HEART trial data)

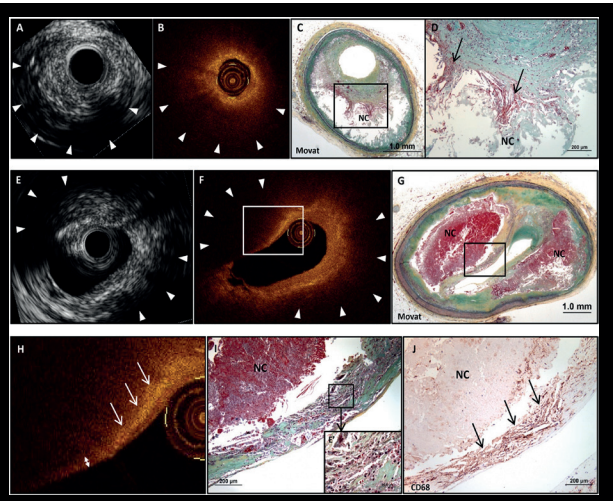
Fig. 5



- **A. 2-feature positive** (+/+) plaques have 45-fold higher likelihood of cardiac events as compared to -/- plaques.
- B. ...and 9-fold higher event rate up to 10 y. of follow-up.
- C. The extent of necrotic core (**LAP volume** >4%)
- **D. HRP and added luminal stenosis** (red) increase discriminatory value
- E. as does **HRP and added plaque progression** in serial CTCTA.

Shaw et al. Journal of Cardiovascular Computed Tomography
Volume 15 Issue 2 Pages 93-109 (March 2021)
DOI: 10.1016/j.jcct.2020.11.002

Journal of Cardiovascular Computed Tomography 2021 1593-109DOI: (10.1016/j.jcct.2020.11.002)



Stabilt plack
=fibroaterom med tjock fibrös "kappa"

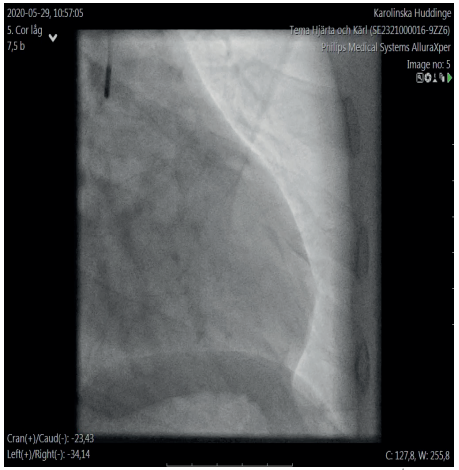
Högriskplack
- tunn fibrös kappa
- Stor plackvolym
- Nekrotisk kärna
- Positiv remodellering

CCTA avbildning av aterosclerotiska plack:

1. Hög grad av korrelation mellan CCTA, Cor-ai med IVUS/OCT, och PAD (histopatologi).
2. Observationsstudier tyder på hög precision för detektion av pat. med ökad risk för CV events
3. **Plackbörda på CCTA associerad m. framtida koronara händelser även hos FH-pat.**

(1-2) Journal of Cardiovascular Computed Tomography 2021 1593-109DOI: (10.1016/j.jcct.2020.11.002)
(3) Tada H, Kawashiri MA, Okada H, et al. Assessment of coronary atherosclerosis in patients with familial hypercholesterolemia by coronary computed tomography angiography. *Am J Cardiol* 2015;115:724-29.

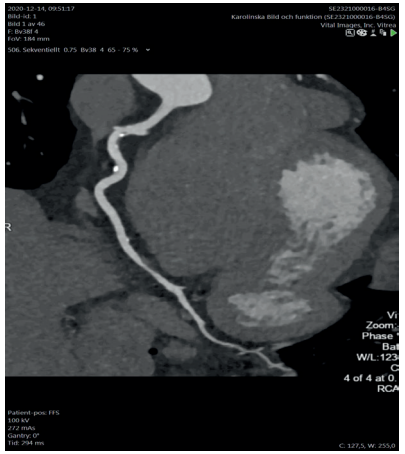
Kvinna <50 år med typiska bröstsmärtor och högt LDL (PTP 10%).

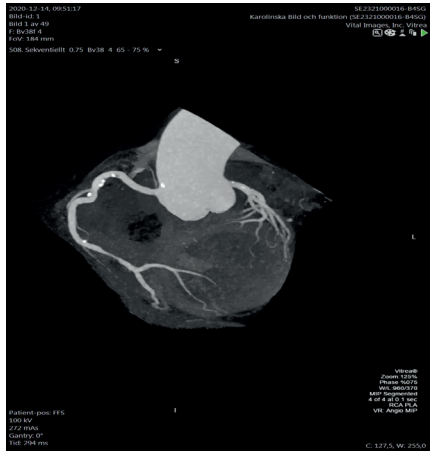


Feldt,K & Damlin A. 2023

65 y/o man med låggradiga CBS sedan månader.

Arbetsprov: 170W (89%), inga CBS, arb-EKG i gråzon (ST-sänkningar med snabb regress)





Distala RCA: icke-förkalkat plack, 50-70% stenos, två högrisk-karakteristika (lågattenuerande, pos. remodellering av kärlväggen). Feldt,K & Damlin A. 2023

CCTA: Pivotala studier att känna till

Sv. Kard Föreningen 2024-01-25

- PROMISE
- SCOT-HEART (5 årsdata)
- DISCHARGE
- RAPID-CTCA

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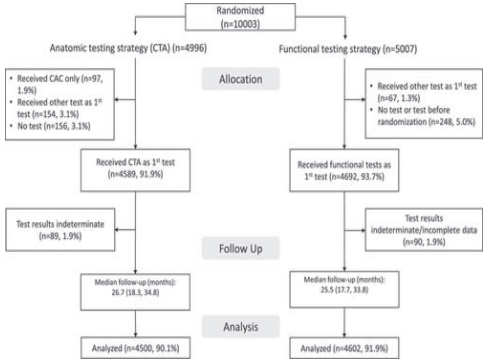
PROMISE- Comparing CCTA & Functional testing



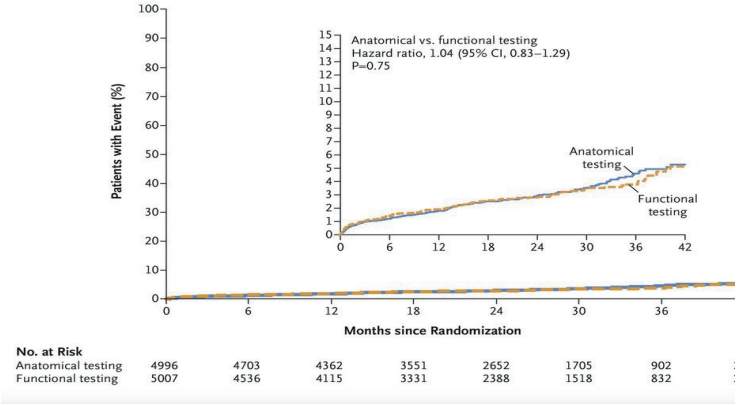
10 000 patients with stable chest pain of intermediate risk (mean age 61, 2.4 risk factors, mean PTP 53%)

Randomized to CTCA or Functional Testing

Follow up: 26 months

Udo Hoffmann. Circulation. Prognostic Value of Noninvasive Cardiovascular Testing in Patients With Stable Chest Pain, Volume: 135, Issue: 24, Pages: 2320-2332, DOI: (10.1161/CIRCULATIONAHA.116.024360)

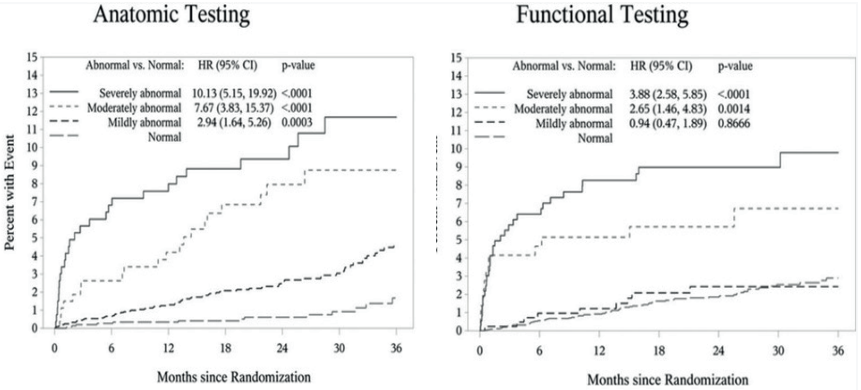
PROMISE



Unadjusted Kaplan–Meier estimates of the primary **composite end point** (death from any cause, nonfatal myocardial infarction, hospitalization for unstable angina, or major procedural complication).
The adjusted **hazard ratio** for a CTA strategy, as compared with a usual-care strategy of functional testing, was **1.04 (95% CI, 0.83 to 1.29)**

Douglas PS et al, N Engl J Med 2015; 372:1291-1300
DOI: 10.1056/NEJMoa1415516

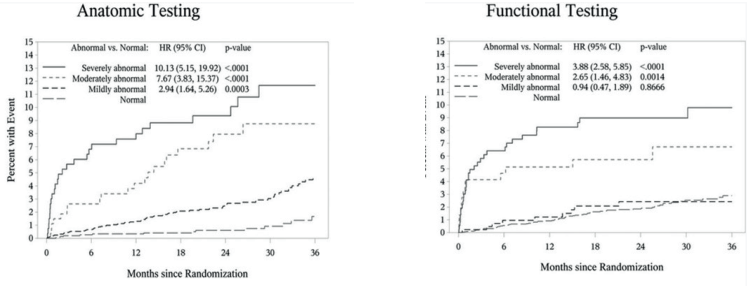
PROMISE- Comparing CCTA & Functional testing



The discriminatory ability of CTA in predicting events was significantly better than functional testing (c-index, 0.72; 95% CI, 0.68–0.76 versus 0.64; 95% CI, 0.59–0.69; *P*=0.04).
= Normal CCTA -> Nearly excludes CV events (<1% over 2 years)
= Stenosis 1-69% on CCTA ("non stenotic", but abnormal) -> Most CV events occurred in this group

Udo Hoffmann. Circulation. Prognostic Value of Noninvasive Cardiovascular Testing in Patients With Stable Chest Pain, Volume: 135, Issue: 24, Pages: 2320-2332,)

PROMISE- (RCT) DT kranskärl vs. Fysiologisk ischemidiagnostik



Udo Hoffmann. Circulation. Volume: 135, Issue: 24, Pages: 2320-2332,)

Anatomic Testing

1. Clinical trials report a higher diagnostic sensitivity for CCTA compared with stress testing for detecting obstructive CAD on ICA (2, 3, 4,37,38,88). CCTA without stenosis or plaque has a low CAD event rate. From the PROMISE trial, the 3-year CAD event rate for negative test findings was 0.9% for CCTA versus 2.1% for stress testing (17). **= 2 års garantitid vid normal/negativ DT kranskärl**

JACC 2021, October 28. AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain.

PROMISE

Low prevalence of myocardial ischemia and obstructive CAD in contemporary stable chest pain populations. Of those randomized:
12.6% (n=582/4602) had a positive functional test
11.9% (n=534/4500) had >70% coronary stenosis (or >50% in LM)

CTCA adds the detection of nonobstructive CAD = identification of additional at risk patients


The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 APRIL 2, 2015 VOL. 372 NO. 14
Outcomes of Anatomical versus Functional Testing for Coronary Artery Disease
Pamela S. Douglas, M.D., Udo Hoffmann, M.D., M.P.H., Manesh R. Patel, M.D., Daniel B. Mark, M.D., M.P.H., Hussein R. Al-Khalidi, Ph.D., Brendan Cavanaugh, M.D., Jason Cole, M.D., Rowena J. Dolor, M.D., Christopher B. Fordyce, M.D., Megan Huang, Ph.D., Muhammad Akram Khan, M.D., Andrzej S. Kosinski, Ph.D., Mitchell W. Krucoff, M.D., Vinay Malhotra, M.D., Michael H. Picard, M.D., James E. Udelson, M.D., Eric J. Velazquez, M.D., Eric Yow, M.S., Lawton S. Cooper, M.D., M.P.H., and Kerry L. Lee, Ph.D., for the PROMISE Investigators*

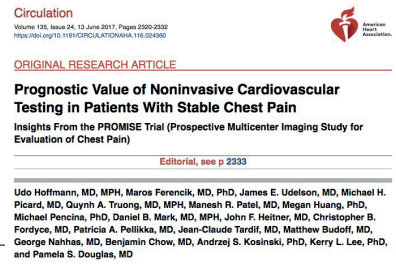
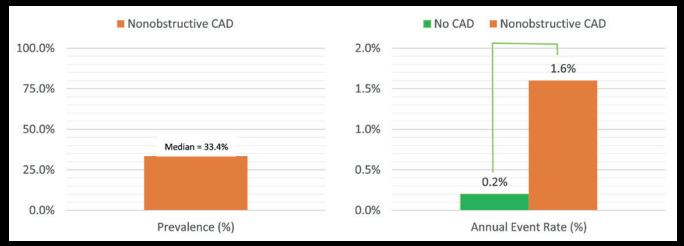

Circulation
Volume 135, Issue 24, 13 June 2017, Pages 2320-2332
https://doi.org/10.1161/CIRCULATIONAHA.116.024360
ORIGINAL RESEARCH ARTICLE
Prognostic Value of Noninvasive Cardiovascular Testing in Patients With Stable Chest Pain
Insights From the PROMISE Trial (Prospective Multicenter Imaging Study for Evaluation of Chest Pain)
Editorial, see p 2333
Udo Hoffmann, MD, MPH, Maros Ferencik, MD, PhD, James E. Udelson, MD, Michael H. Picard, MD, Quynh A. Truong, MD, MPH, Manesh R. Patel, MD, Megan Huang, PhD, Michael Pencina, PhD, Daniel B. Mark, MD, MPH, John F. Heitner, MD, Christopher B. Fordyce, MD, Patricia A. Pellikka, MD, Jean-Claude Tardif, MD, Matthew Budoff, MD, George Nahhas, MD, Benjamin Chow, MD, Andrzej S. Kosinski, PhD, Kerry L. Lee, PhD, and Pamela S. Douglas, MD

Fig. 1

PREVALENS & ÅRLIG ADVERSE EVENT RATE HOS PATIENTER MED ICKE OBSTRUKTIV CAD (1-49% stenos)



- Meta-analys från 17 publicerade studier (N=49 957)
- Pat som söker för misstänkt angina
- Median uppföljning 2.5 år
- Blandade events: mortalitet (all-cause/CAD), AKS, koronar revaskularisering

Journal of Cardiovascular Computed Tomography 2021 1593-109DOI: (10.1016/j.jcct.2020.11.002)

Original Article

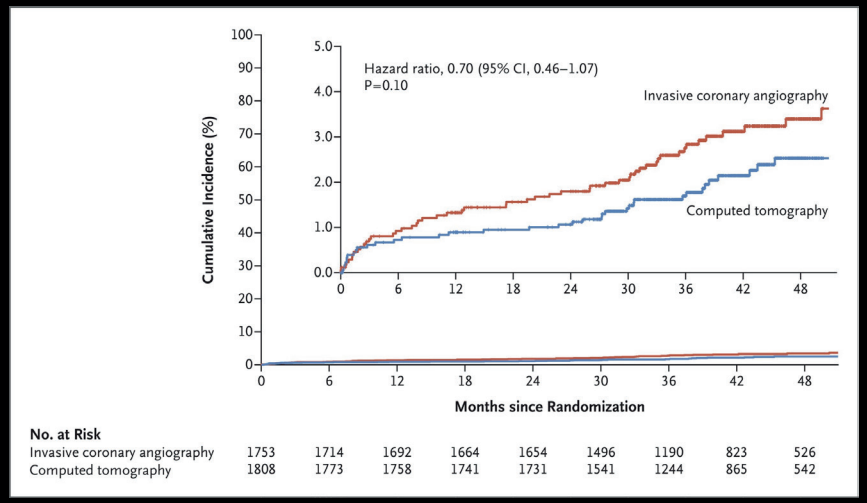
CT or Invasive Coronary Angiography in Stable Chest Pain

N Engl J Med
Volume 386(17):1591-1602
April 28, 2022

The DISCHARGE Trial Group

- Multicenter RCT with 3561 patients.
- Stable chest pain, intermediate risk for obstructive coronary artery disease, were randomly assigned to CCTA or invasive coronary angiography.
- Primary outcome: major adverse cardiovasc. events (MACE)
- Secondary outcome: procedural complications

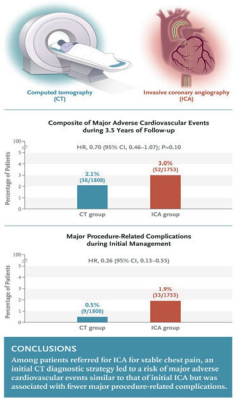
Time-to-Event Curves for the Primary Composite Outcome.



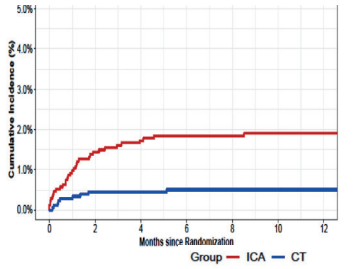
The DISCHARGE Trial Group. N Engl J Med2022;386:1591-1602

CT or Invasive Coronary Angiography in Stable Chest Pain

The DISCHARGE Trial Group



S5. Cumulative Incidence Curves for Major Procedure-Related Complications



1.9% (n=33)

0.5% (n=9)

HR_{kompl} 0.26 (0.13-0.55) till fördel för CCTA vs. Cor-ai

Pga. 1.9% komplikationer vid cor-ai med/utan PCI
-Procedurrel. infarkt 0.6%;
-VT/VF 0.3%
-blödning/mjukdelar mm. 0.6%
Jämnt fördelat mellan ICA med resp. utan PCI (se tabell S8).

The DISCHARGE Trial Group. N Engl J Med2022;386:1591-1602

Overview/Conclusions

- Over 3.5 years of follow-up, there was no significant between-group difference in the risk of major adverse cardiovascular events.
- Major procedure-related complications were **less common** with CT.

Outcome	Computed Tomography (N=1808)	Invasive Coronary Angiography (N=1753)	Effect Size (95% CI)†
Expanded major adverse cardiovascular events — no. (%)‡			
Cardiovascular death, myocardial infarction, stroke, transient ischemic attack, or major procedure-related complication	50 (2.8)	80 (4.6)	0.60 (0.42 to 0.85)
Secondary outcomes			
Major procedure-related complications during initial management — no. (%)‡¶	9 (0.5)	33 (1.9)	0.26 (0.13 to 0.55)
Nonfatal myocardial infarction	3 (0.2)	10 (0.6)	
Nonfatal stroke	0	1 (0.1)	
Cardiac arrhythmia: ventricular tachycardia or fibrillation	0	6 (0.3)	
Complication prolonging hospitalization by ≥24 hr	4 (0.2)	11 (0.6)	
Dissection of coronary artery or aorta	2 (0.1)	2 (0.1)	
Cardiac arrest	0	2 (0.1)	
Cardiac tamponade	0	1 (0.1)	

Annals of Internal Medicine
Ann Intern Med. 2023; 176(4):433-442. doi:10.7326/M22-3027

From: Subclinical Coronary Atherosclerosis and Risk for Myocardial Infarction in a Danish Cohort [A Prospective Observational Cohort Study]

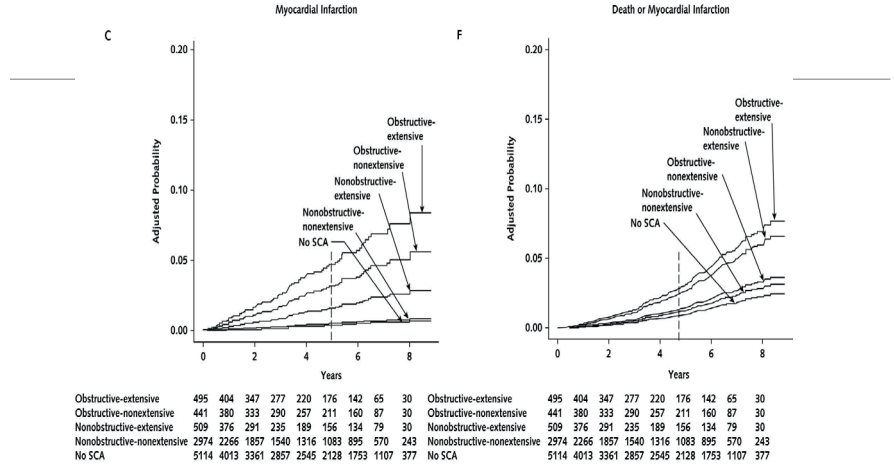


Figure Legend:

Annals of Internal Medicine
Ann Intern Med. 2023; 176(4):433-442. doi:10.7326/M22-3027

From: Subclinical Coronary Atherosclerosis and Risk for Myocardial Infarction in a Danish Cohort [A Prospective Observational Cohort Study] - COPENHAGEN GENERAL POPULATION STUDY (N=9533)

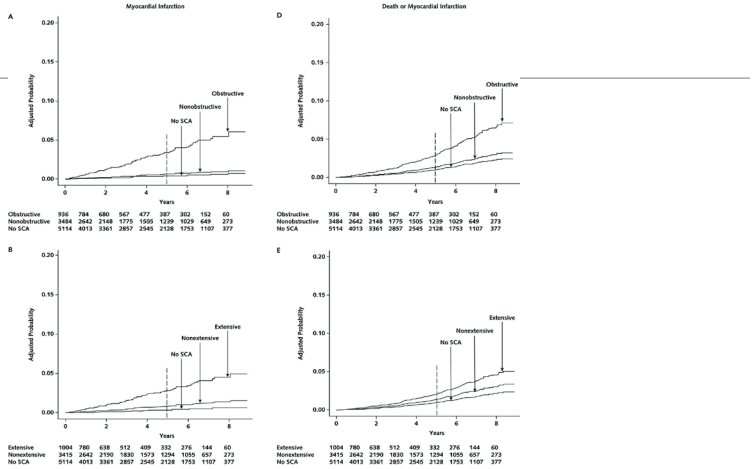


Figure Legend:

Time to event curves show adjusted probabilities for primary end point of myocardial infarction and secondary composite end point of death or myocardial infarction stratified by CTA findings of SCA. The dotted line indicates 5-y probabilities. Analyses were adjusted for sex, age, arterial hypertension, hypercholesterolemia, current smoking, overweight or obesity, diabetes, aspirin, statin, education level, and income class. CTA = computed tomography angiography; SCA = subclinical coronary atherosclerosis. A and D: Nonobstructive and obstructive. B and E: Nonextensive and extensive. C and F: Combined groups of SCA. For combined groups, plots show increased incidence of myocardial infarction in case of either obstructive-nonextensive or obstructive-extensive SCA (*C*), and increased incidence of either death or myocardial infarction in case of nonobstructive-extensive and obstructive-extensive SCA (*F*).

Annals of Internal Medicine
Ann Intern Med. 2023; 176(4):433-442. doi:10.7326/M22-3027

From: Subclinical Coronary Atherosclerosis and Risk for Myocardial Infarction in a Danish Cohort [A Prospective Observational Cohort Study]

CTA Findings	Mean Adjusted 5-Year Probabilities (95% CI)	Mean Risk Difference, %	Mean Relative Risk (95% CI)
No subclinical coronary atherosclerosis	0.36 (0.16–0.76)	– (Reference)	1.00 (Reference)
Any subclinical coronary atherosclerosis	1.02 (0.55–1.89)	0.67	2.95 (1.54–5.64)
Obstructive subclinical coronary atherosclerosis			
Nonobstructive	0.59 (0.30–1.17)	0.23	1.59 (0.76–3.33)
Obstructive	3.40 (1.68–6.89)	3.04	9.19 (4.49–18.82)
LAD obstructive (1VD)	3.07 (1.47–6.43)	2.71	8.36 (3.86–18.11)
Cx obstructive (1VD)	3.75 (0.84–16.63)	3.39	10.19 (2.76–37.60)
RCA obstructive (1VD)	3.17 (0.94–10.72)	2.81	8.62 (2.63–28.28)
Multi-VD/LM-obstructive	4.26 (1.86–9.78)	3.90	11.60 (4.78–28.14)
Extent of subclinical coronary atherosclerosis			
Nonextensive	0.84 (0.44–1.62)	0.49	2.28 (1.14–4.56)
Extensive	2.83 (1.33–5.98)	2.48	7.65 (3.53–16.57)
Combined groups of subclinical coronary atherosclerosis			
Nonobstructive-nonextensive	0.49 (0.22–1.08)	0.13	1.29 (0.58–2.90)
Nonobstructive-extensive	1.60 (0.64–4.00)	1.24	4.22 (1.55–11.54)
Obstructive-nonextensive	3.13 (1.47–6.67)	2.77	8.28 (3.75–18.32)
Obstructive-extensive	4.71 (2.11–10.53)	4.35	12.48 (5.50–28.12)

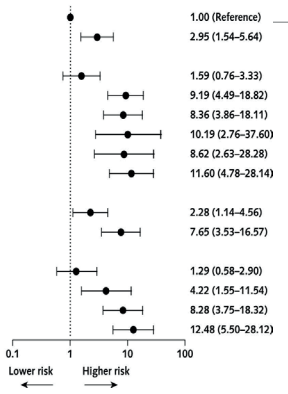


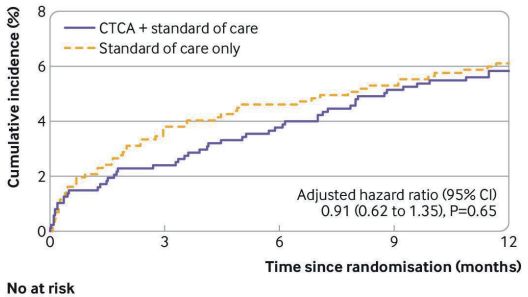
Figure Legend:

Analyses were adjusted for sex, age, arterial hypertension, hypercholesterolemia, current smoking, overweight or obesity, diabetes, aspirin, statin, education level, and income class. 1VD = single vessel disease; CTA = computed tomography angiography; Cx = circumflex artery; LAD = left anterior descending artery; LM = left main artery; RCA = right coronary artery; VD = vessel disease.

RAPID-CTCA

Cumulative incidence of primary endpoint of one year all cause death or non-fatal myocardial infarction (type 1 or 4b).

Ingen skillnad i antal terapeutiska koronara interventioner eller 1-års utfall av död eller hjärtinfarkt



No at risk

CTCA + standard of care	877	854	842	830	814
Standard of care only	871	836	828	822	802

Alasdair J Gray et al. BMJ 2021;374:bmj.n2106

DT kranskärl – modaliteten för framtidens kardiologer

Sv. Kard. Föreningen 2024/01

1. Bakgrund – Riktlinjer & CCTA i Sverige.
2. Lite om DT fysik & premedicinering
3. CCTA – Hur gör vi? + Kliniska case
4. Pivotala studier
5. Sammanfattning

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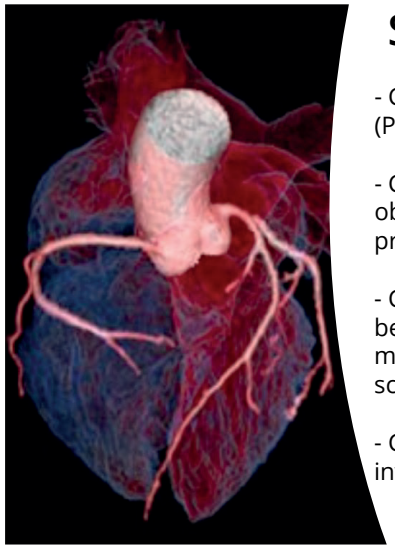


Sammanfattning (1)

- CCTA (vs. scint) är en patientsäker metod (PROMISE).

- CCTA ökar diagnostisk precision (hittar icke-obstruktiv koronar-sjd) och har högt negativt prediktivt värde (PROMISE)

- CCTA kan leda till ökad sekundärprev. behandling (statin, aspirin mfl.) + bättre timing med inv. angio/PCI jmf. arbetsprov och/eller scint (SCOT-HEART)

- CCTA är förenad med färre komplikationer än invasiv angio med/utan PCI (DISCHARGE)

Sammanfattning (2)

- CCTA stratifierar risk för CV event även hos asymtomatiska individer baserat på aterosklerosbörda + stenosgrad (bl.a. Copenhagen Gen. Pop.), samt förekomst av HRP/vulnerabla plack-karakteristika.

- CCTA kan användas vid akut/oklar bröstsmärta med intermediär risk, **men** ev. nyttan jmf. "usual care" är oklar (RAPID-CCTA)
–>svensk-nordisk multi-center RCT pågår (**FAST-CCTA**)

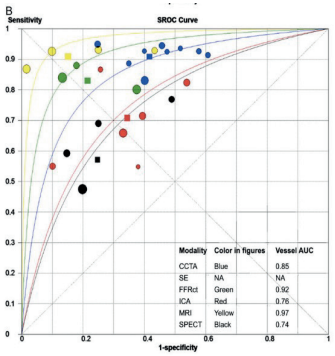
European Heart Journal (2017) 38, 991–998
doi:10.1093/eurheartj/ehw095

META-ANALYSIS
Imaging

Diagnostic performance of cardiac imaging methods to diagnose ischaemia-causing coronary artery disease when directly compared with fractional flow reserve as a reference standard: a meta-analysis

Ibrahim Danad[1,2], Jackie Szymonifka[1,2], Jos W.R. Twisk[3], Bjarne L. Norgaard[4], Christopher K. Zarins[5,6], Paul Knaapen[7], and James K. Min[1,2]*

Vessel based analysis	Sensitivity	Specificity
CCTA	0.91 (0.88-0.92)	0.58 (0.55-0.61)
FFR-CT	0.83 (0.78-0.87)	0.78 (0.78-0.81)
Invasiv Angio	0.71 (0.69-0.74)	0.66 (0.64-0.68)
MR	0.91 (0.84-0.95)	0.85 (0.79-0.89)
MPS (scint)	0.57 (0.49-0.64)	0.75 (0.69-0.80)
Stress-eko (patient baserad analys)	0.77 (0.61-0.88)	0.75 (0.63-0.85)



3 - DT kranskärl eller fysiologisk ischemidiagnostik? – beror på tillgänglighet, lokal expertis, och klinisk frågeställning…

Vägledning vid remittering till DT kranskärl

DT kranskärl är förstahandsmetod för diagnostik av kranskärlsanatomin inkl. anomala avgångar/förlopp, graden av ateroscleros och förekomsten av högrisk-kranskärlsplack ("adverse plaque", vulnerabla plack). DT kranskärl möjliggör drämed tidig upptäckt av icke-obstruktiv CAD (1–49% stenos). Samtidigt har <50% diameterstenos på DT högt negativt prediktivt värde avseende flödesbegränsande stenos – d vs talar emot "signifkant stenos". Strålduen är i median ca 2.5 mSv, kontrastdosen ca 80 mL (Karolinska, 2019). Remiss skrivs till FO Thoraxradiologi Solna el. Huddinge.

Följande faktorer *försvårar* teknisk bedömbarhet vid DT kranskärl:
- Oregelbunden takykardi med vilopuls >90/min *trots behandling*. (Förmaksflimmer eller extraslag i sig utgör inte kontraindikation).
- BMI> 34
- Betydande kranskärlsförkalkningar (vanligare hos män >70 år; kan ibland bedömas utifrån tidigare utförd DT thorax).
- Kranskärlsstent med <3 mm stentdiameter, komplexa stentade kärlavsnitt (bifurkationer, stent-i-stent, stent i kalk). I regel är funktionellt ischemitest att föredra i dessa fall.
- GFR <20 mL/min, *el.* 20–29 mL/min och ej lämplig för uppvätskning före/efter DT.

Vägledning i valet av funktionellt ischemitest

Dobutaminstresseko (DSE): Utförs på ME Kardiologi H, ME Klinisk fysiologi H. Ger samtidig information om kammar- och klafffunktion. Patienten bör klara av dobutamin-infusion och förväntas ha acceptabla transmissionsförhållanden för ekokardiografi (med kontrast).

Övervåg annat test än DSE om: pacemakerberoende rytm, svår obesitas, förmaksflimmer, LBBB, ischemisk kardiomyopati med omfattande regionalitet, dilaterad kardiomyopati.

Myokardperfusionsscintigram (MPS): Utförs på ME Klinisk fysiologi S och H med cykelbelastning eller farmakologisk belastning (adenosin, regadenoson). MPS är lämpligt även vid pacemaker, förmaksflimmer, obesitas, LBBB.

Favors use of CCTA	Favors use of stress imaging
• Rule out obstructive CAD • Detect nonobstructive CAD	• Ischemia-guided management
• High-quality imaging and expert interpretation routinely available	• High-quality imaging and expert interpretation routinely available
• Age <65 y	• Age ≥65 y
• Prior functional study inconclusive	• Prior CCTA inconclusive
• Anomalous coronary arteries • Require evaluation of aorta or pulmonary arteries	• Suspect scar (especially if PET or stress CMR available) • Suspect coronary microvascular dysfunction (when PET or CMR available)

JACC 2021, October 28.
AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain

3 – Vilken diagnostisk undersökning?

Diagnostik i regel inte nödvändig

DT kranskärl

Ischemi-Diagnostik?

Table 5 Pre-test probabilities of obstructive coronary artery disease in 15 815 symptomatic patients according to age, sex, and the nature of symptoms in a pooled analysis[64] of contemporary data[7,8,62]

	Typical		Atypical		Non-anginal		Dyspnoea[a]	
Age	Men	Women	Men	Women	Men	Women	Men	Women
30–39	3%	5%	4%	3%	1%	1%	0%	3%
40–49	22%	10%	10%	6%	3%	2%	12%	3%
50–59	32%	13%	17%	6%	11%	3%	20%	9%
60–69	44%	16%	26%	11%	22%	6%	27%	14%
70+	52%	27%	34%	19%	24%	10%	32%	12%

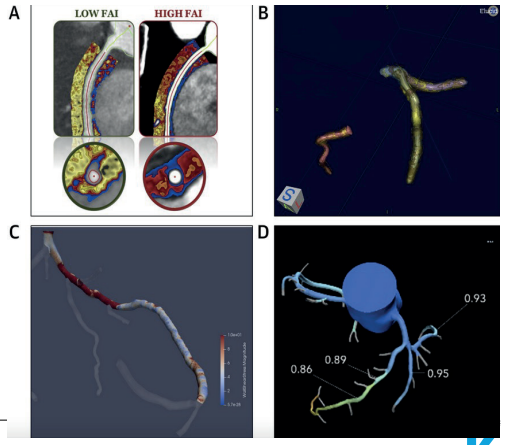
©ESC 2019

CAD = coronary artery disease; PTP = pre-test probability.

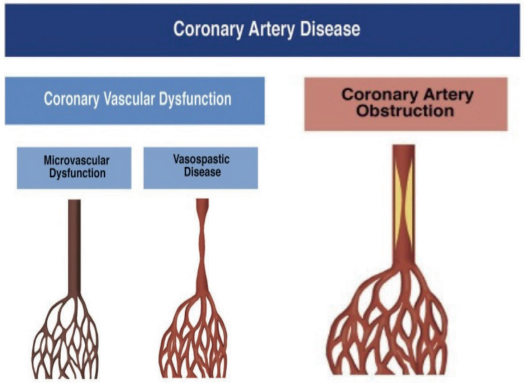
Knuuti J, et al. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes

Imaging Atherosclerosis and Beyond - Emerging Technologies

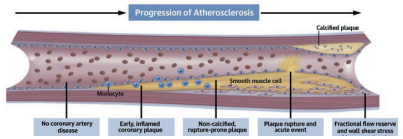
- **Perivascular fat attenuation index (FAI)**, detects phenotypic changes in adipocytes in perivascular fat as a response to vascular inflammation
- **Plaque quantification** and characterization (vascuCAP, Elucid Bioimaging, Boston, MA)
- **Wall shear stress** profile
- **FFR-CT** calculations (HeartFLow, Redwood City, CA)

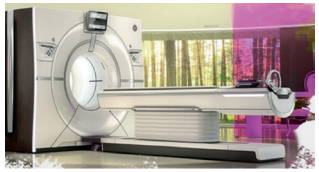


Summa summarum



Adapterad från: Jansen, T.P.J. et al. J Am Coll Cardiol. 2021;78 (14):1471-1479.





DT kranskärl – 1’ metod för koronar anatomi

- avbildar ateroskleros fr. tidigt stadium
- graderar stenos
- >50% stenos betraktas som obstruktiv
- kan avbilda vulnerabla plack
- färre komplikationer jmf. Inv. Angio.
- endast 2 mSv stårlning/80mL IVK

)

Biokemi för kardiologer

Ola Hammarsten

Torsdag 25 januari 2024, 15.00-17.00

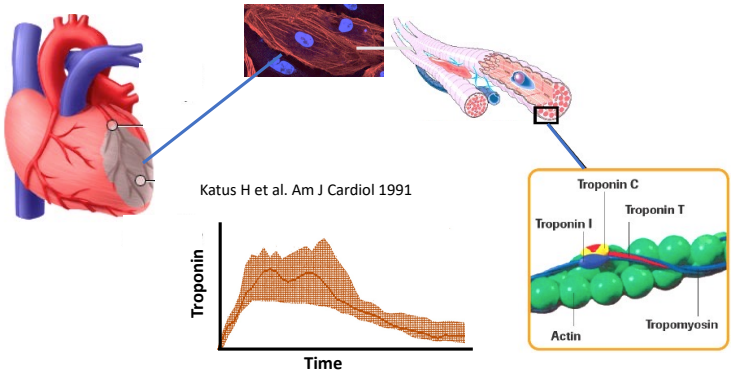
GÖTEBORGS UNIVERSITET

Latest news on cardiac tropnin

Ola Hammarsten
Professor and Senior
Physician at Sahlgren's
University Hospital
Sweden

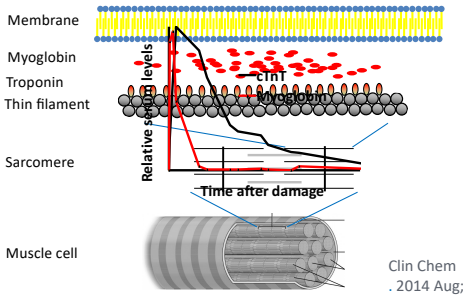
Sahlgrenska akademin

What is cardiac troponin?



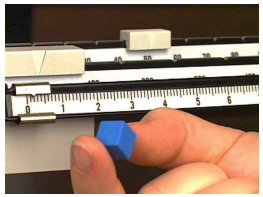
Katus H et al. Am J Cardiol 1991

Kinetics of troponins



Clin Chem
. 2014 Aug;60(8):1098-104.
doi: 10.1373/clinchem.2013.217943.

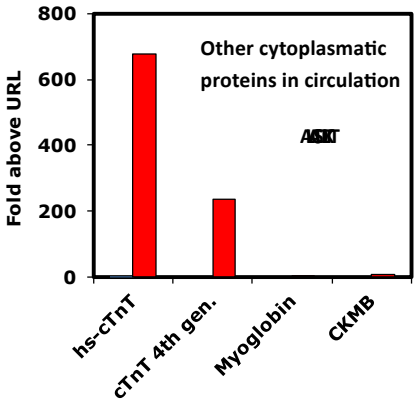
Expected elevations from 1cm³ damaged human cardiac tissue



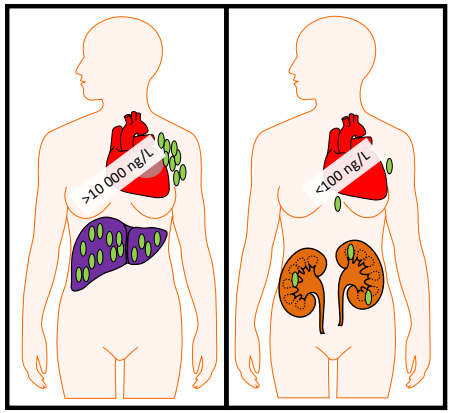
Troponin T 9486 ng/L

Myoglobin 520 ug/L

CKMB 46 ug/L

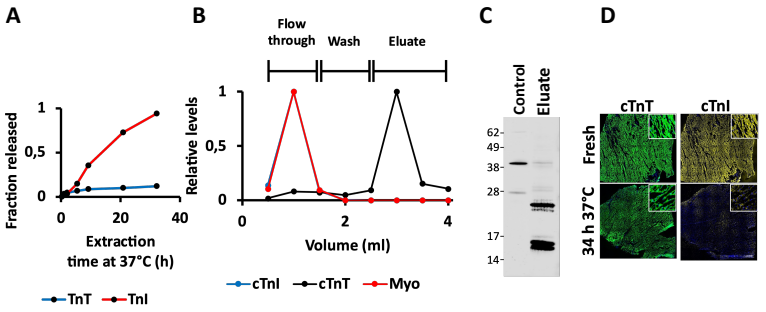


Clearance of troponins

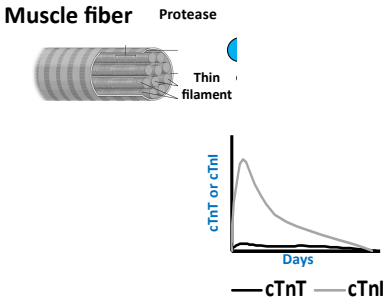


Sci Rep 2020 Apr 22;10(1):6791. doi: 10.1038/s41598-020-63744-8
Clin Biochem. 2017 Jun;50(9):468-474. doi: 10.1016/j.clinbiochem.2017.02.007.
Clin Chem. 2020 Feb 1;66(2):333-341. doi: 10.1093/clinchem/hvz003.

cTnT is retained in necrotic cardiac tissue



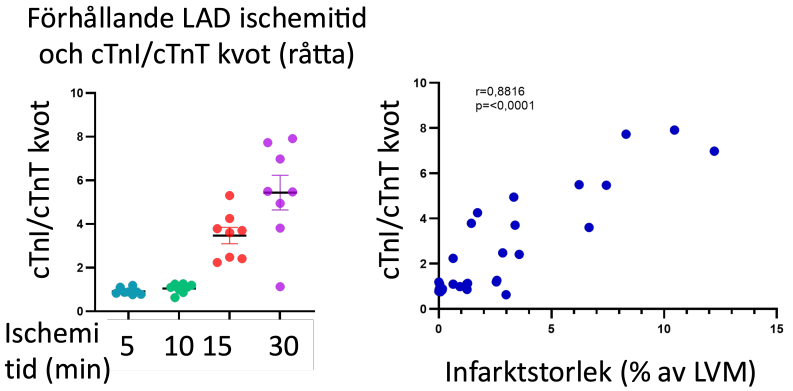
Kinetics of troponin I and troponin T



Clin Chem. 2020 Feb 1;66(2):333-341.doi: 10.1093/clinchem/hvz003.

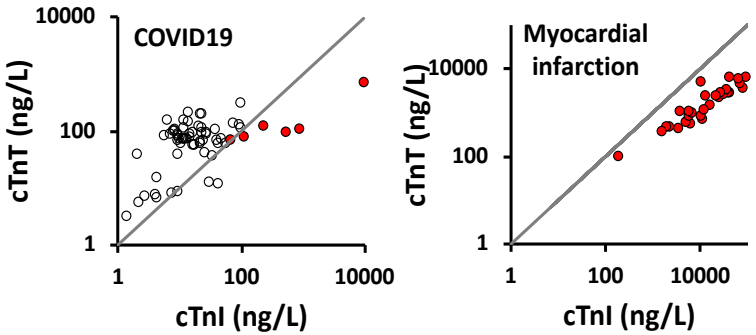
Eur Heart J Acute Cardiovasc Care . 2016 Aug;5(4):354-63. doi: 10.1177/2048872615585518. Epub 2015 May 5.

A high cTnI/cTnT ratio may indicate necrosis



Eur Heart J Acute Cardiovasc Care . 2023 Jun 2;12(6):355-363. doi: 10.1093/ehjacc/zuad017

A high cTnI/cTnT ratio may indicate necrosis



Clin Chim Acta
. 2022 Feb 15;527:33-37.
doi: 10.1016/j.cca.2021.12.030.

nature medicine

Perspective

https://doi.org/10.1038/s41591-023-02513-2

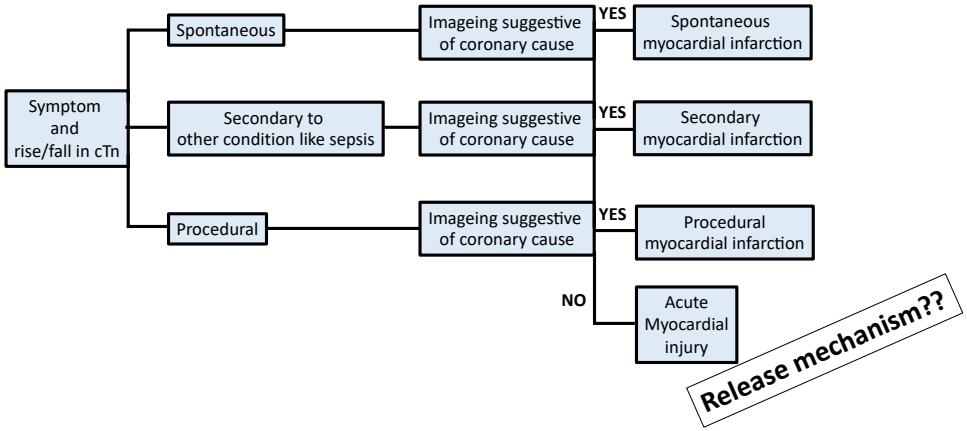
A new clinical classification of acute myocardial infarction

Received: 19 May 2023

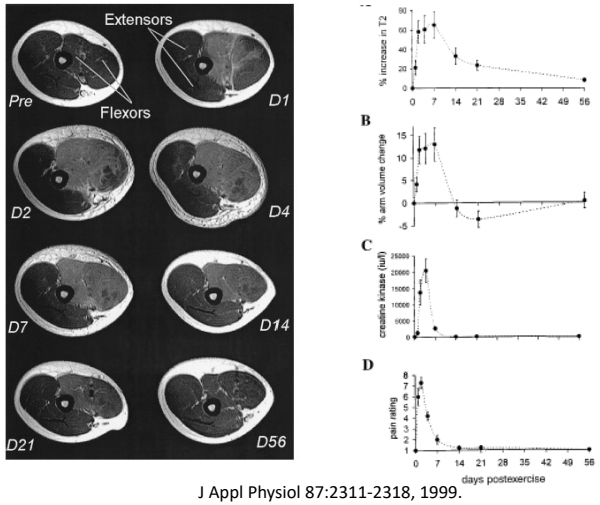
Accepted: 26 July 2023

Bertil Lindahl [1,2] & Nicholas L. Mills [2,3]

Retirement of type 2 myocardial infarction?



CK is released after, not during exercise



J Appl Physiol 87:2311-2318, 1999.

Myoglobin frisättning kommer inte under utan efter ansträngning

Int. J. Sports Med. 7 (1986) 259–263

Muscle Cell Leakage of Myoglobin After Long-Term Exercise and Relation to the Individual Performances

L.-E. Roxin[1], G. Hedin[2], and P. Venge[1]

Department of Clinical Chemistry[1] and Infectious Diseases[2], University Hospital, Uppsala, Sweden

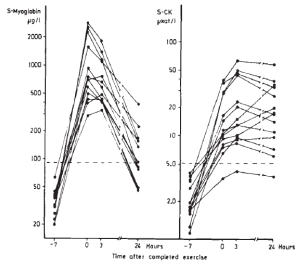


Fig. 1 Myoglobin and creatinine kinase (CK) in serum before and after an 89-km ski race. The dotted lines indicate the means + 2 SD for the age-matched reference group.

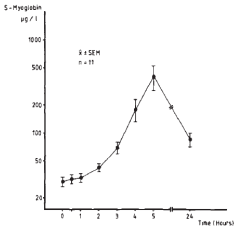
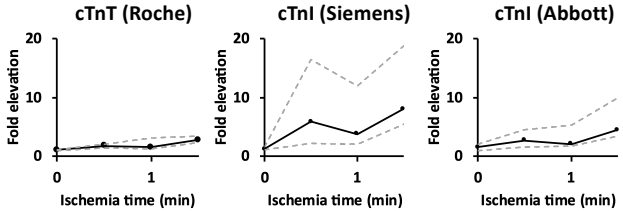


Fig. 6 The alterations of S-myoglobin during 5 h of bicycle exercise in a group of 11 men (mean ± SEM).

Apparent non-necrotic release after short ballon-ischemia



Circulation. 2021;143:1095–1104.

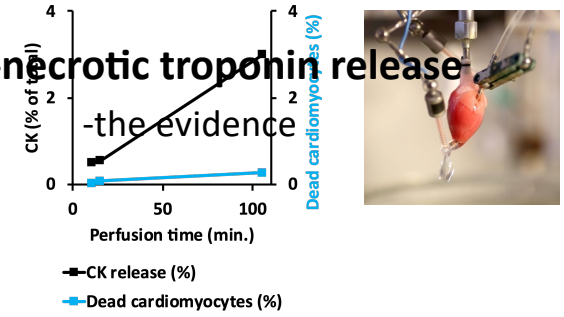
Circulation

ORIGINAL RESEARCH ARTICLE

Temporal Release of High-Sensitivity Cardiac Troponin T and I and Copeptin After Brief Induced Coronary Artery Balloon Occlusion in Humans

Over tenfold more CK than dead cardiomyocytes

Non-necrotic troponin release -the evidence



Life Sci. 1996;58(7):545-50.doi: 10.1016/0024-3205(95)02262-7.

Troponin release from turnover of troponin?

300mg troponin per heart

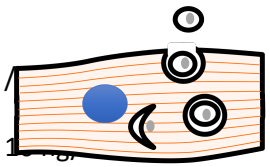
1% turnover per day

3mg troponin mobilized /

Median troponin T level 1

10/40 000 = 0.025%

Secretory autophagy



J Cell Biol . 2022 Jun 6;221(6):e202110151.doi: 10.1083/jcb.202110151.
Cell. 2020 Oct 1;183(1):94-109.e23. doi: 10.1016/j.cell.2020.08.031.

<0.025% of mobilized troponin ever in circulation

Circulation

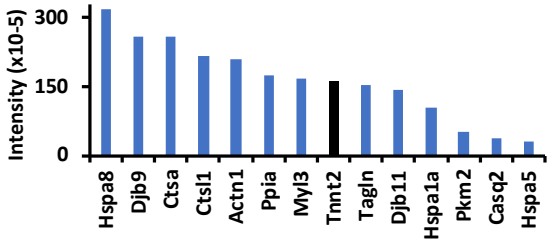
ORIGINAL RESEARCH ARTICLE

Secretome Analysis of Cardiomyocytes Identifies PCSK6 (Proprotein Convertase Subtilisin/Kexin Type 6) as a Novel Player in Cardiac Remodeling After Myocardial Infarction

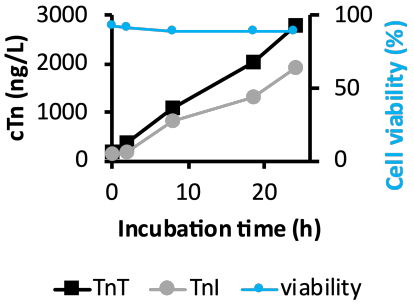
Editorial, see p 1645

Tim Christian Kuhn, MD
Johannes Knobel

Top 100, cytoplasmic proteins secreted by NRVCMs 0-12h

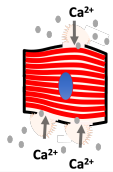
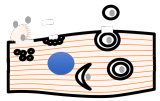


Apparent non-necrotic release from cardiac cell cultures



Aida Muslimovic (unpublished)

Possible troponin release mechanisms

Mechanism	Kinetics
Necrosis 	Rise and fall
Cell wounds and/or exocytosis 	Rise and fall or stable

Secretory autophagy

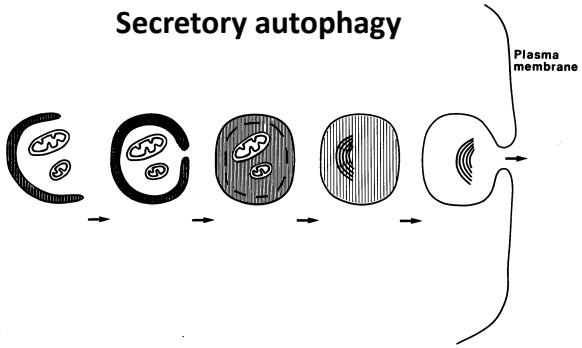


Fig. 77. Diagram summarizing the sequence of events during autophagocytosis in muscle fibres derived from the steps shown in Fig. 76. *Shaded area*, assumed localization of lysosomal enzymes

Handbook of Microscopic Anatomy
Volume II/6: Skeletal Muscle
Privatdozent Dr. H. Schmalbruch
1985

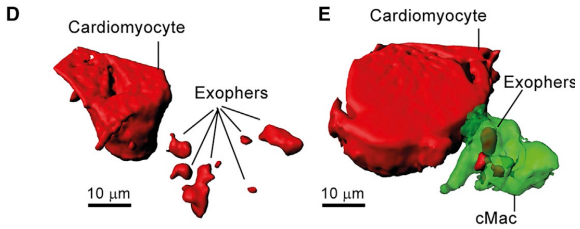
CellPress Cell

Article

A Network of Macrophages Supports Mitochondrial Homeostasis in the Heart

José A. Nicolás-Ávila,[1,25] Ana V. Lechuga-Vieco,[1,2,25] Lorena Esteban-Martínez,[1] María Sánchez-Díaz,[1] Elena Díaz-García,[1] Demetrio J. Santiago,[1] Andrea Rubio-Ponce,[1] Jackson LiangYao Li,[1,3] Akhila Balachander,[3] Juan A. Quintana,[1] Raquel Martínez-de-Mena,[1] Beatriz Castejón-Vega,[4] Andrés Pun-García,[1] Paqui G. Través,[5] Elena Bonzón-Kulichenko,[1,6] Fernando García-Marqués,[1] Lorena Cussó,[1,7,8,9] Noelia A-González,[1,10] Andrés González-Guerra,[1] Marta Roche-Molina,[1] Sandra Martín-Salamanca,[1]

(Author list continued on next page)



Can we develop a necrosis specific cardiac biomarker?

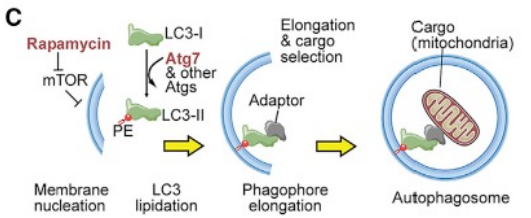
CellPress Cell

Article

A Network of Macrophages Supports Mitochondrial Homeostasis in the Heart

José A. Nicolás-Ávila,[1,25] Ana V. Lechuga-Vieco,[1,2,25] Lorena Esteban-Martínez,[1] María Sánchez-Díaz,[1] Elena Díaz-García,[1] Demetrio J. Santiago,[1] Andrea Rubio-Ponce,[1] Jackson LiangYao Li,[1,3] Akhila Balachander,[3] Juan A. Quintana,[1] Raquel Martínez-de-Mena,[1] Beatriz Castejón-Vega,[4] Andrés Pun-García,[1] Paqui G. Través,[5] Elena Bonzón-Kulichenko,[1,6] Fernando García-Marqués,[1] Lorena Cussó,[1,7,8,9] Noelia A-González,[1,10] Andrés González-Guerra,[1] Marta Roche-Molina,[1] Sandra Martín-Salamanca,[1]

(Author list continued on next page)



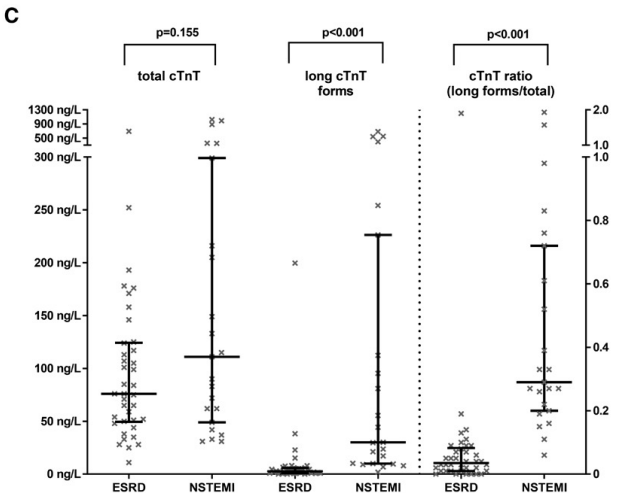
Circulation

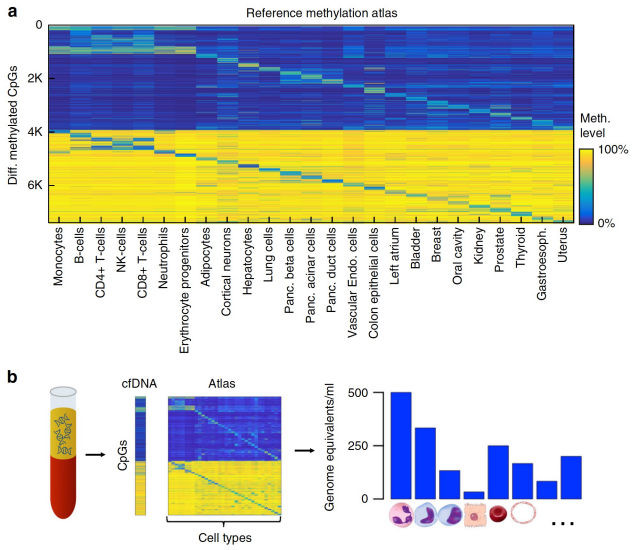
RESEARCH LETTER

Novel Troponin Fragmentation Assay to Discriminate Between Troponin Elevations in Acute Myocardial Infarction and End-Stage Renal Disease

K.E. Juhani Airaksinen, MD, PhD*; Rami Aalto, MSc*; Tapio Hellman, MD, PhD; Tuija Vasankari, MSc; Akseli Lahtinen, BSc; Saara Wittfooth, PhD

Circulation. 2022;146:1408–1410. DOI: 10.1161/CIRCULATIONAHA.122.060845





nature COMMUNICATIONS

ARTICLE

DOI: 10.1038/s41467-018-07466-6 OPEN

Comprehensive human cell-type methylation atlas reveals origins of circulating cell-free DNA in health and disease

Joshua Moss[1,2], Judith Magenheim[1], Daniel Neiman[1], Hai Zemmour[1], Netanel Loyfer[2], Amit Korach[3], Yaacov Samet[4], Myriam Maoz[5], Henrik Druid[6,7], Peter Arner[8], Keng-Yeh Fu[9], Endre Kiss[9], Kirsty L. Spalding[8,9], Giora Landesberg[10], Aviad Zick[5], Albert Grinshpun[5], A.M.James Shapiro[11], Markus Grompe[12], Avigail Dreazan Wittenberg[1], Benjamin Glaser[13], Ruth Shemer[1], Tommy Kaplan[2] & Yuval Dor[1]

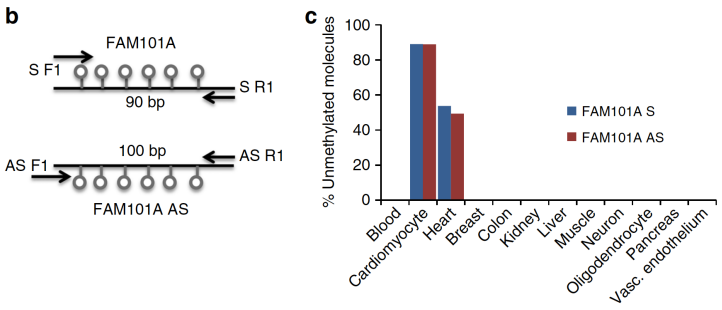
nature COMMUNICATIONS

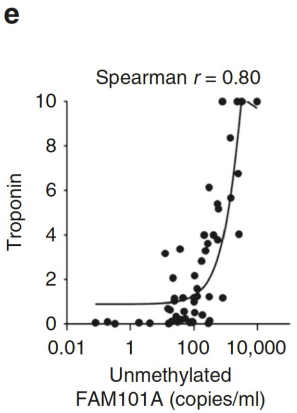
ARTICLE

DOI: 10.1038/s41467-018-03961-y OPEN

Non-invasive detection of human cardiomyocyte death using methylation patterns of circulating DNA

Hai Zemmour[1], David Planer[2], Judith Magenheim[1], Joshua Moss[1], Daniel Neiman[1], Dan Gilon[2], Amit Korach[3], Benjamin Glaser[4], Ruth Shemer[1], Giora Landesberg[5] & Yuval Dor[1]

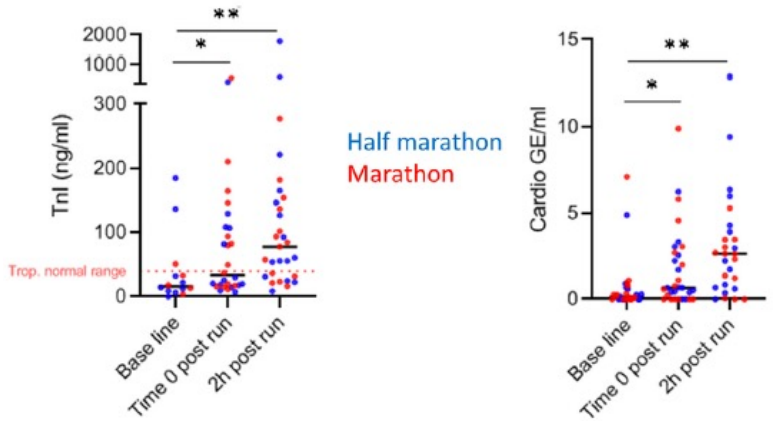




Cell Reports
Medicine

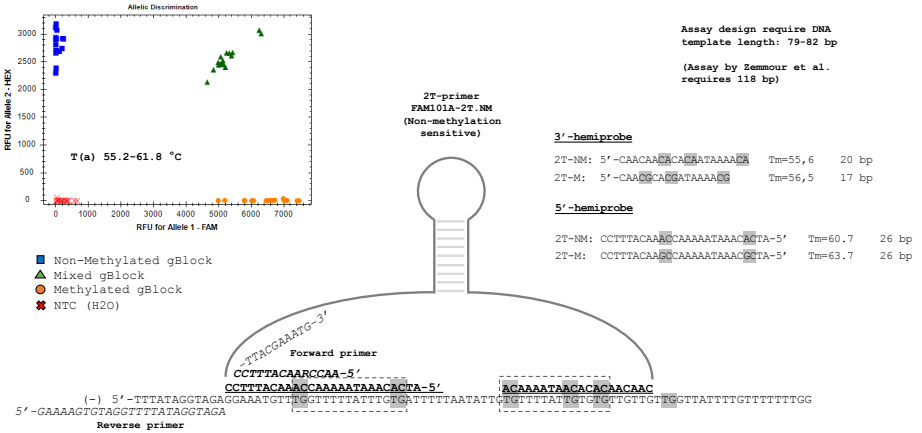
Article

Elevated cfDNA after exercise is derived primarily from mature polymorphonuclear neutrophils, with a minor contribution of cardiomyocytes

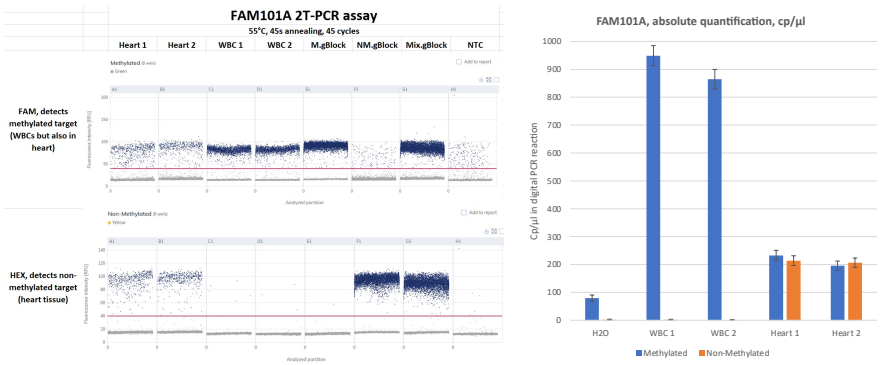


Cell Reports Medicine 4, 101074, June 20, 2023 [a] 2023

2T-PCR interrogating methylation status of FAM101A



Detection of tissue specific DNA in heart and white blood cells (WBCs) – digital 2T-PCR with FAM101A assay



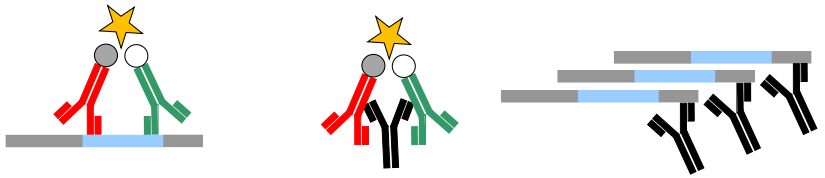
DE GRUYTER Clin Chem Lab Med 2016; 54(11): 1821–1829

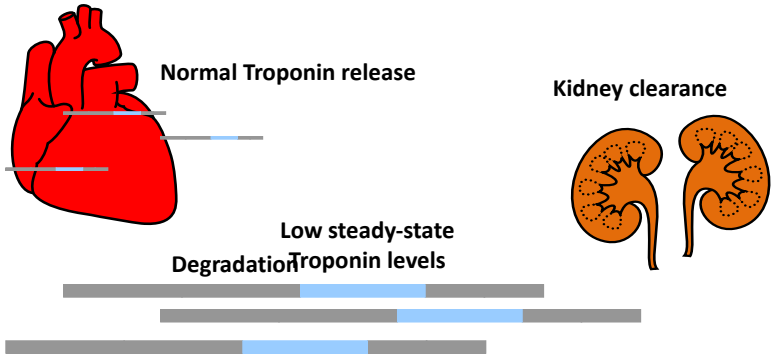
Janet V. Warner* and George A. Marshall

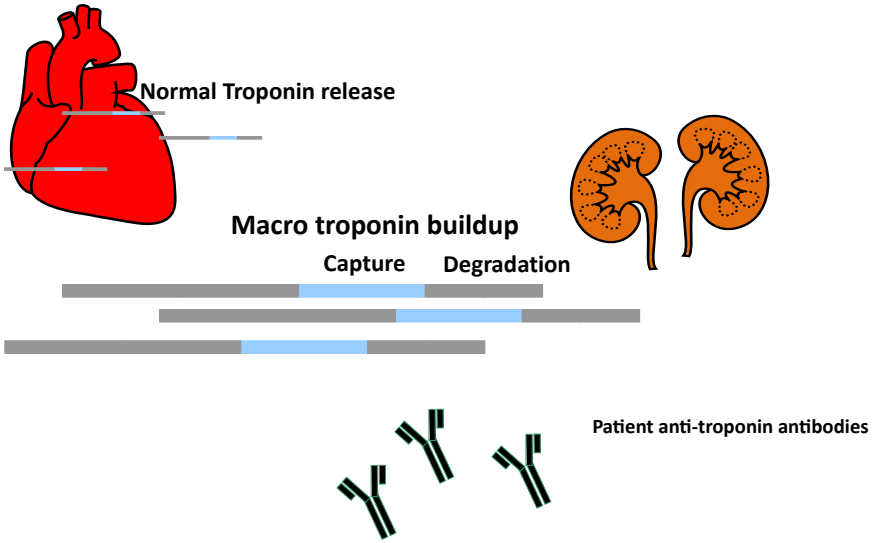
High incidence of macrotroponin I with a high-sensitivity troponin I assay

A few months after the introduction of the Architect high sensitive troponin-I (hsTnI) assay into our laboratory we noticed an increase in enquiries regarding possible false-positive troponin I results. Initial investigations revealed that the false-positive results were likely to be due to a high molecular weight complex in the patients' plasma.

cTn-assay **Heterophile antibodies** **Macrotroponin**







Typical findings if troponin interference

*Stable increased levels of troponin that do not match the clinic.

*Elevated levels persist long after a cardiac event, such as myocarditis

*Abnormal variation when reanalyzing the same sample or after dilution

*Abnormal difference between different troponin methods.

IFCC Guidelines 2023

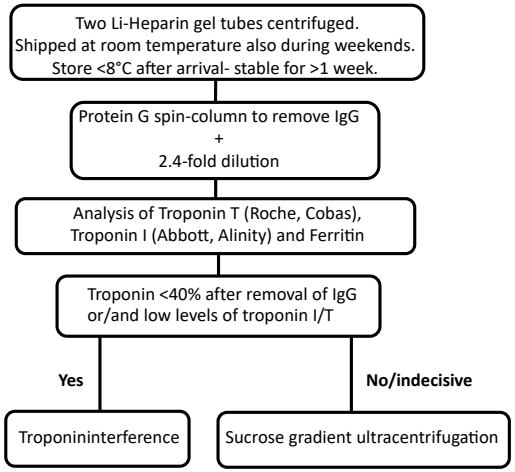
DE GRUYTER Clin Chem Lab Med 2023; aop

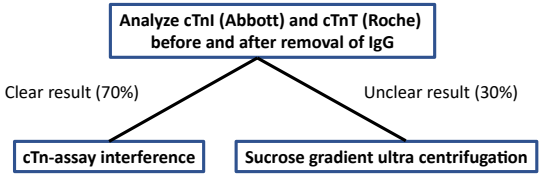
Guidelines and Recommendations

Ola Hammarsten*, Janet V. Warner, Leo Lam, Peter Kavsak, Bertil Lindahl, Kristin M. Aakre, Paul Collinson, Allan S. Jaffe, Amy K. Saenger, Richard Body, Nicholas L. Mills, Torbjørn Omland, Jordi Ordonez-Llanos and Fred S. Apple

Antibody-mediated interferences affecting cardiac troponin assays: recommendations from the IFCC Committee on Clinical Applications of Cardiac Biomarkers

The Sahlgrenska Troponin interference investigation protocol





Number of refferals	109
Median age	50 yrs (45-62)
Male sex	68%
Median cTnI if cTnI interference	72 ng/L (24-199)
Median cTnT if cTnT interference	36 ng/L (22-83)
Median recovery if cTn interference	8% (3%-26%)
cTnT or cTnT interference	97
cTnI interference	93
cTnT interference	22
cTnI and cTnT interference	18

Case 1: **Classical troponin I interference**
Male. 42yrs. STEMI two years ago. Six months ago stent thrombosis. Now presents at ER with infection and stable cTnI elevation around 100 ng/L. cMR show scarring from previous events. No clear sign of myocarditis. Lab workup normal.

Protein G affinity chromatography spinn column
cTnI 74 ng/L before IgG removal (URL <35 ng/L)
cTnI 1 ng/L after IgG removal
cTnT 6 ng/L before IgG removal (URL <14 ng/L)
cTnT 4 ng/L after IgG removal

Interpretation: Macro troponin I likely. Two necrotic events that immunized.

Case 2: **Unclear troponin assay interference**
Male. 40yrs. Previously healthy. ER due to chest pain. Elevated cTnI. Normal heart workup during a few weeks.

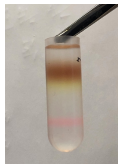
Protein G affinity chromatography spinn column
cTnI 34 ng/L before IgG removal (URL <35 ng/L)
cTnI 24 ng/L after IgG removal
cTnT 3.5 ng/L before IgG removal (URL <14 ng/L)
cTnT 3.5 ng/L after IgG removal

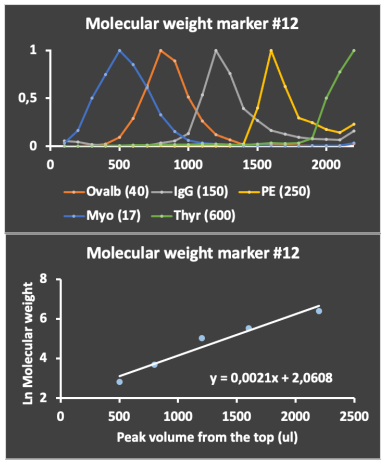
Interpretation: Cardiologist distrusts cTnI level. Discordant cTnT and cTnI levels. Likely troponin I assay interference.

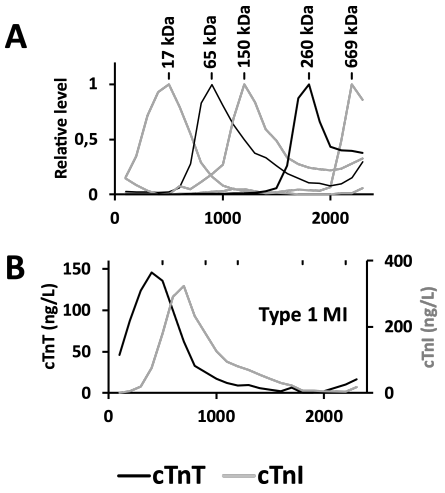
Case 2: Unclear troponin interference

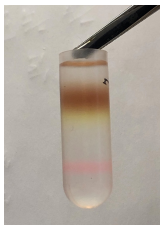
	cTnI
Before Ig removal	34 ng/L
After removal of IgA	15 ng/L
After removal of IgM	32 ng/L
After removal of IgG	24 ng/L

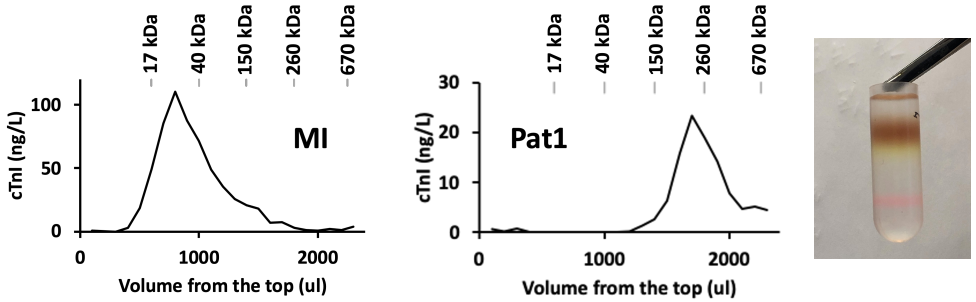
Sucrose gradient ultracentrifugation



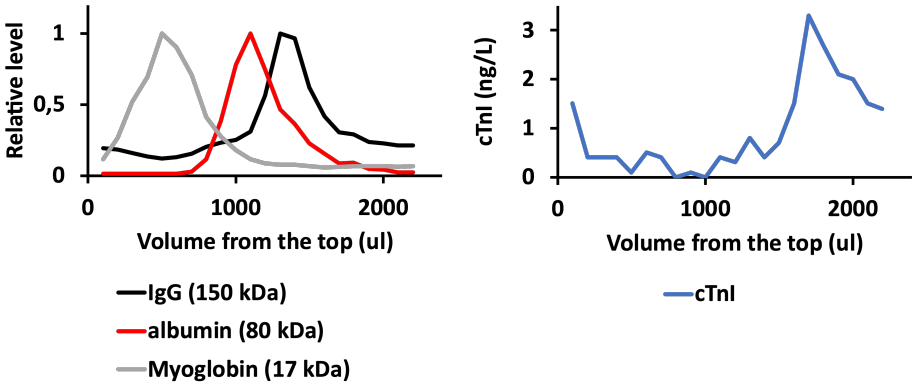








Case 2: Unclear troponin interference



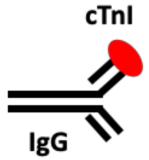
Sahlgrenska akademin
VID GÖTEBORGS UNIVERSITET

Läkare på Hjärtmottagningen NÄL
Norra Älvsborgs Länssjukhus
461 85 Trollhättan

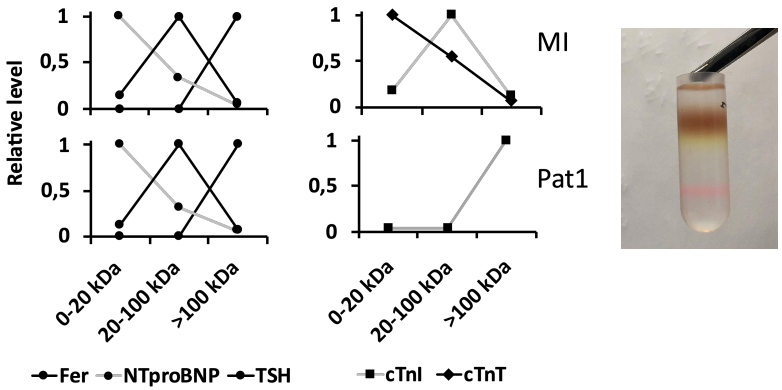
Tack för remissen på man född 1969
Din patient har makro Troponin I, det vill säga ett långlivat komplex mellan Troponin I och en antikropp av typen IgG. Det leder till stabila ökningar av Troponin I utan ökat läckage från hjärtat och anses vara ofarligt. Hos vissa patienter ebbar makro troponin bort, hos andra kvarstår antikropparna under lång tid i de få långtidsupföljningar som finns.

Din patient har en total nivå av Troponin I på: 218 ng/L
Din patient har en obunden Troponin I nivå på: 2 ng/L

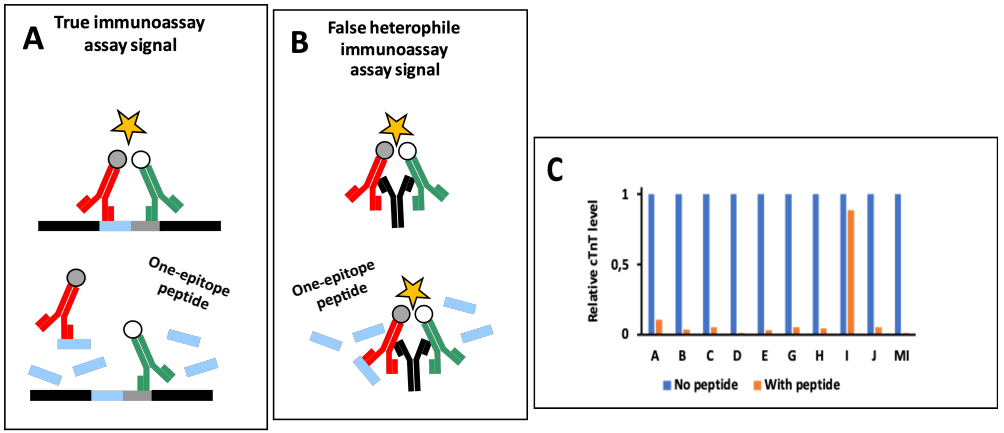
Din patient har normala nivåer troponin T på ca 10 ng/L som inte är bundet till IgG.



Further development of sucrose gradient ultracentrifugation



Ny metod att avslöja Heterofila antikroppar



CANCERFONDEN

ALF Avtal om läkarutbildning och forskning mellan Västra Götalandsregionen och Göteborgs universitet

Hjärt-Lungfonden

Thanks

Ärftliga arytmisjudomar – diagnos och handläggning

Kristina Haugaa

Fredag 26 januari 2024, 08.15-10.15

Framtidens kardiologer

Ärftliga arytmisjukdomar – diagnos och handläggning

Kristina Haugaa, MD, PhD
Prof MedH Karolinska institutet,
ÖL Karolinska universitetssjukhuset

Seksjonsledare Oslo universitetssjukhus
Professor Universitetet i Oslo

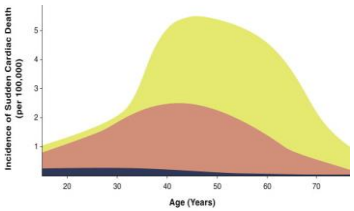
1

Cardiogenetics

- **Cardiomyopathies**
  - → Progressive disease
    - Rare during childhood
  - → Hypertrophic HCM
  - → Dilated DCM
  - → Arrhythmogenic ACM/ ARVC
  - → Left ventricular non-compcation
  - → Syndromic connective tissue disease
    - Marfan etc
- **Ion channelopathies**
  - → Non progressive disease
    - Risk from birth
    - Risk can change during life
  - → Long QT syndrome (LQTS)
  - → Brugada syndrome (BrS)
  - → Catecholaminergic polymorphic ventricular tachycaridia (CPVT)
  - → Early repolarization syndrome

2

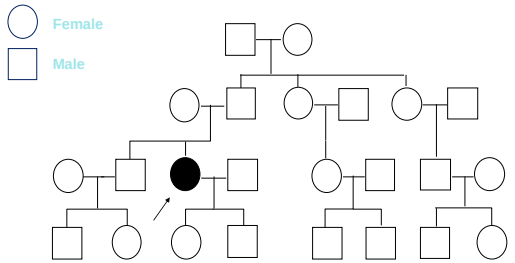
Sudden cardiac death



Genetic cardiac diseases
Exercise induced sudden cardiac death
Autosomal dominant inheritance

3

Autosomal dominant inheritance



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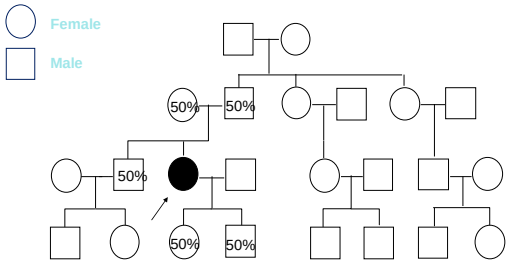
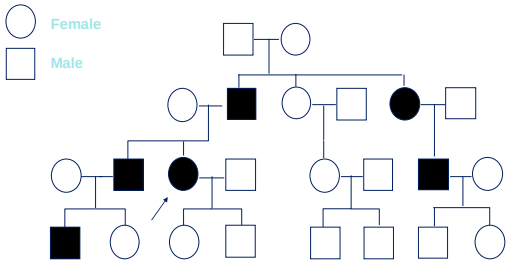
Autosomal dominant inheritance



5

One index patient - 5 genetic positive family members



6

Cardiogenetic disorders, management

- **Counselling**
- Inheritance
- Penetrance
  - → What is my risk of developing disease?
  - → What is the risk for my (future) children?
  - → When should children be genetically tested?
- Professions
  - → Athletic profession
  - → Driving licenses
- Insurances
- Pregnancy
  - → Preimplantation genetic testing

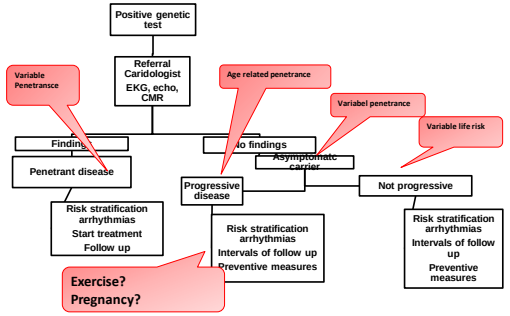
- **Clinical management**
- Ventricular arrhythmias
  - → SCD risk stratification
    - Anti arrhythmic drugs
    - Ablation
    - ICD
- Afib
  - → Anti coagulation
- Heart failure
  - → Medication, CRT-D
  - → Heart transplant
- Exercise advice
- Pregnancy

7

Why is it important to perform genetic testing?

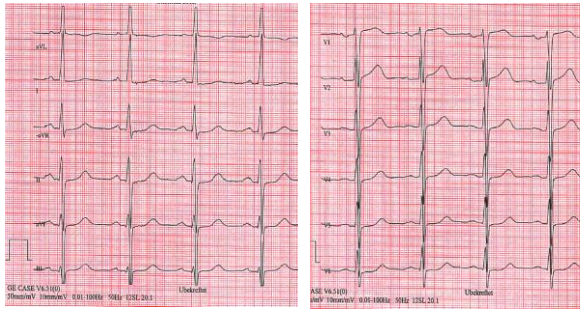
- A positive test result:
  - Helps diagnosis
  - Allows focused family examination
  - Prognostic information by genotype
- A negative test result
  - → Does not exclude inherited disease
  - → Different yield of genetic testing

- Therapeutic consequences
  - → Patients
  - → Family members



8

24 år kvinna, dyspne vid ansträngning



9

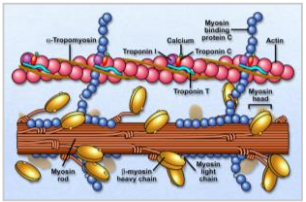
Utredning?

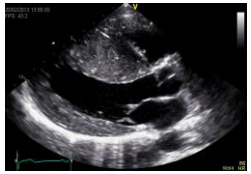
10

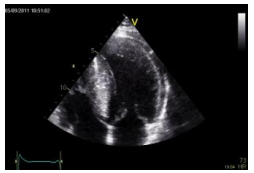
11

Hypertrofisk kardiomyopati

- Prevalens: 1:500
- Vänster ventrikulär hypertrofi > 15 mm utan någon annan förklarande orsak
- Genbärare: diagnos HCM vid 13 mm







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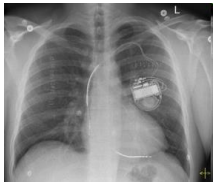
HCM behandling

Medikamentell behandling og livsstilsråd

- Symtom dyspn, hjärtsvikt, plötslig död, AF, angina
- Minska pulsen
- Betablock /Ca antagonist
- Antiarrytmisk
- Betablock / Amiodarone
- Antikoagulation på AF
- Antikoagulation oavsett CHADS VASC-score
- Holter var 6 mån vid förmaksdiameter > 45 mm
-

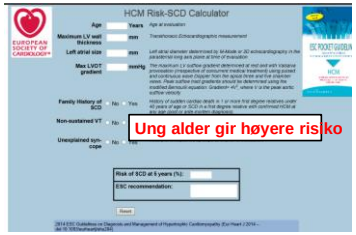


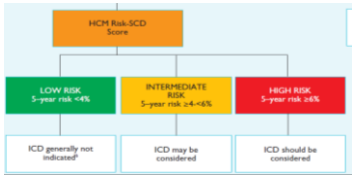
13

Arytmirisiko

- Ventrikulär arytmier
- ICD
- HCM-risk calculator
-

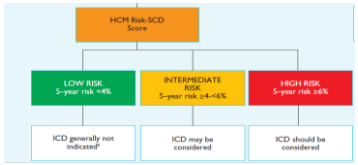
- **ICD forblir en klinisk vurdering**
- **bedömining**

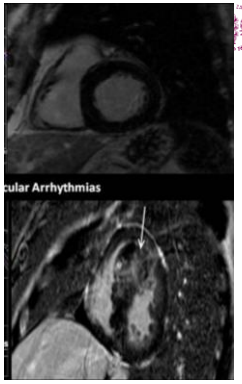




14

MR cor





KARDIOLOGISK

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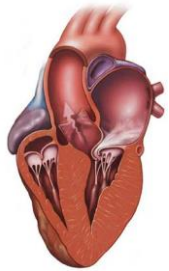
HCM
Vem ska utredas genetisk?

- Septum > 1.5cm utan någon annan förklarande orsak.
- Indikationen stärkt:
- HCM i familjen
- plötslig död i familjen

- Positivt gentest:
- Famlie undersökning
- koncentrera kliniska resurser till mutationspositiva individer
-
- Ktr var 1-5 år i friska mutationsbärare (EKG, eko)
- Barn
- Ungdom
- Vuxen
-
-
- Negativt gentest
- EKG utan hypertrofitecken – Avlagringssjukdom?
- Muskelsjukdomar?
-



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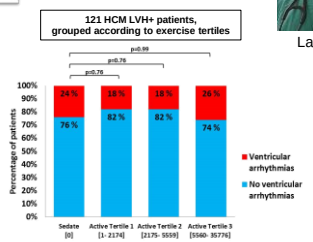
Kan HCM patienterna träna?

Inget samband mellan idrott över tid och incidens av ventrikulära arytmier

Större kaviteter hos dem som tränade och förbättrad diastolisk funktion

Neutral eller gynnsam effekt av träning hos HCM-patienter



Lars Dejgaard

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Exercise

- → Patients with HCM should avoid competitive sports activities, but should maintain a healthy lifestyle
- → Advice on recreational activities should be tailored to symptoms and the risk of disease-related complications including sudden cardiac death
- → Asymptomatic family members, no restrictions

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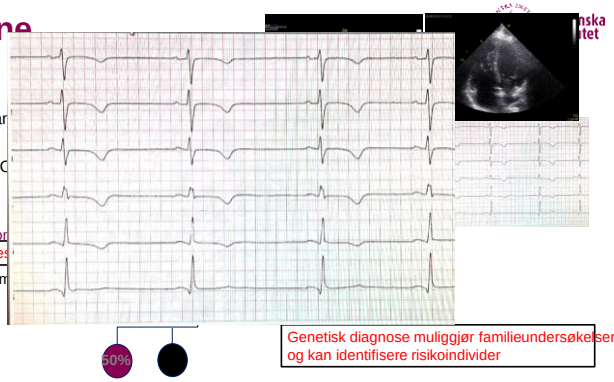
22 år kvinne

- Hjertestans ved har
- Ekko
  - → Lett dilatert RV
  - → EF normal
  - → PKP2 positiv
    - sikkert sykdo
    - Genetisk tes
    - Fam

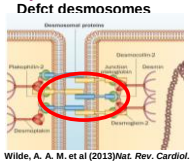


Genetisk diagnose muliggjør familieundersøkelser og kan identifisere risikoindivider

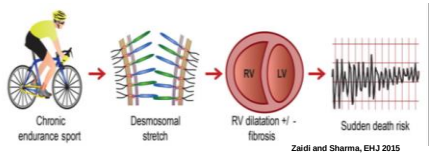
20

Arrhythmogenic right ventricular cardiomyopathy (ARVC)

Defect desmosomes



Wilde, A. A. M. et al (2013)*Nat. Rev. Cardiol.*



Zaidi and Sharma, EHJ 2015

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ARVC Symptomer

- Ventrikulär takykardi från höger kammare
- Monomorf VT
- vänster grenblock
- Plötslig hjärtdöd (50% debutsymptom!)
- Hjärtsvikt

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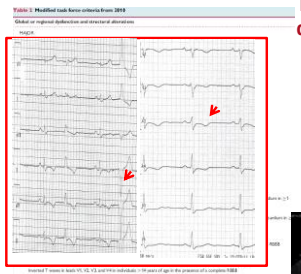
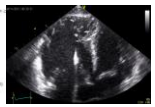
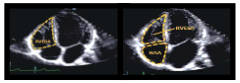
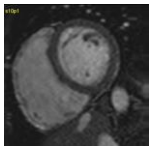
Task force criteria for ARVC diagnosis









- Imgaging
  - Echo
  - CMR
- Biopsy
- ECG
  - Repolarization
  - Depolarization
  - Signal average ECG
- Holter
  - Ventricular arrhythmias
  - Ventricular premtature complexes
- Genetic findings / Family history

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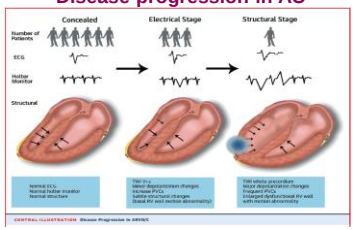
Arytmogen höger ventrikulär kardiomyopati
Förebyggande av plötslig död och behandling

- Diagnostisera
- screening?
- Genetisk testning
-
- Aktivitetsbegränsningar
- Icke-tävlings sporter
- Läkemedelsbehandling
- Betablockerare
- Sotalol
- Amiodaron
- Hjärtsviktsbehandling efter indikation
- Icd
-

Disease progression in AC



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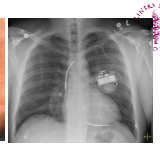
ICD behandling



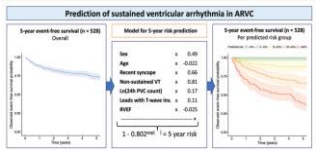
ICD sekundär prevention
- Överlevd hjärtstopp
- Syncope
- Dokumenterad VT

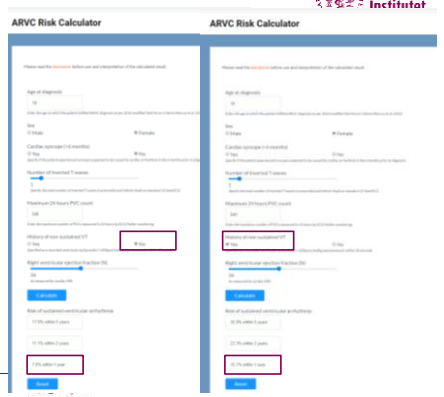
ICD primär prevention
I
CD komplikationer
- Tunnväggig höger kammare, unga patienter växer

AC risk calculator arvcrisk.com

A new prediction model for ventricular arrhythmias in arrhythmogenic right ventricular cardiomyopathy

EHJ 2019





Vigorous physical activity impairs myocardial function in patients with arrhythmogenic right ventricular cardiomyopathy and in mutation positive family members

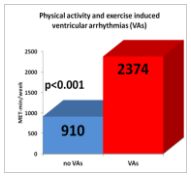
European J Heart failure 2014

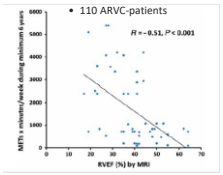
Jørg Saberniak[1,2], Nina E. Hasselberg[1,2], Rasmus Borgquist[3], Pyotr G Platonov[3], Sebastian I. Sarvari[1,2], Hans-Jørgen Smith[4], Margareth Ribe[1,2], Anders G. Holst[5], Thor Edvardsen[1,2], and Kristina H. Haugaa[1,2]*

Jørg Saberniak

Can ARVC patients exercise?

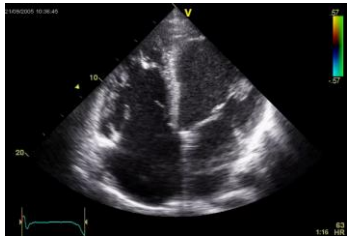
Exercise aggravates and accelerates ARVC disease

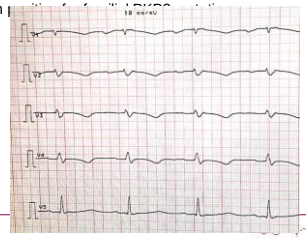




Biventricular ARVC

- 38 y o male, previous competitive swimmer, DCM
- EF 15%, repetetive VTs
- ECG: low voltage, T-wave inversion V1-V4
- Cardiac Tx at 41 y (2005)
- 2 years post Tx, cousine diagnosed with ARVC (2007)
- Mutation p





- Diagnosis of AC was missed in 2005
- Genetic diagnosis from 2007

Summary

- ARVC is a highly arrhythmogenic disease
- Risk stratification include
  - Male sex
  - nsVT
  - Structural changes
    - When structural changes are present – arrhythmic risk is high
- Clear association with exercise
  - High intensity is most harmful
- Close follow up in patients with no ICD
  - Holter monitoring

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Dilated cardiomyopathy

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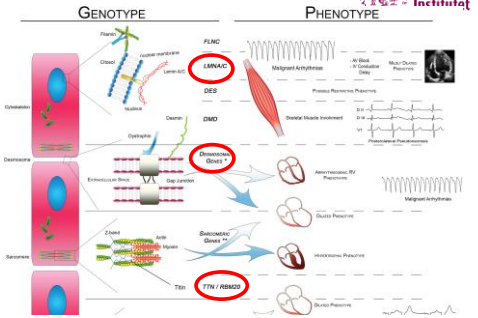
Dilated cardiomyopathy

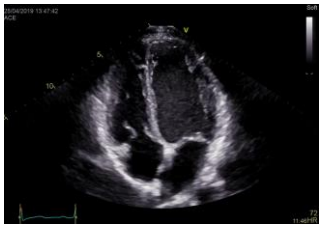
- Approx 50% of ”idiopathic” DCM has a genetic etiology
- Actionable prognostic genotype



Merlo et al. European Journal of Heart Failure, 20, 228-239, 2017

32

2 cases with dilated cardiomyopathy

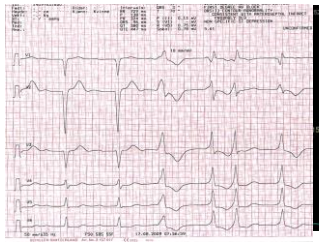


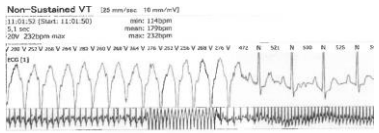
33

Lamin A/C

- 43 y o woman
- DCM
- ECG:
  - → AV block
  - → Afib
  - → VPC
- Holter; nsVT

- Genetic testing:





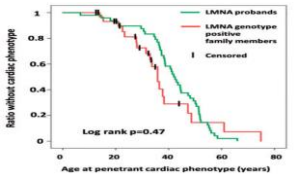
34

Lamin A/C cardiomyopathy: young onset, high penetrance, and frequent need for heart transplantation EHJ 2017

Nina Eide Hasselberg[1,2,3], Trine Fink Haland[1,2,3], Jørg Saberniak[1,2,3], Pål Haugar Brekke[1], Knut Erik Berge[4], Trond Paul Leren[4], Thor Edvardsen[1,2,3] and Kristina Hermann Haugaa[1,2,3]*

Nina Hasselberg

- High penetrance
- Early disease
- High need of transplantation



35

Lamin A/C

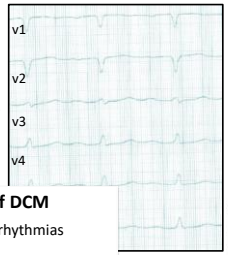
- **AV-block**
- **AF**
- **Frequent VPB / VT**
- **DCM**

- Actionable genotype
  - High penetrance
  - High incidence of malignant arrhythmias
    - When AV block requires pacemaker – ICD indication
  - Exercise restrictions

36

Titin

- 48 y o woman
- Dilated LV, reduced EF,
- ECG: low voltage, AV block 1st degree
- Holter: nsVT



- **Most common genetic cause of DCM**
  - Higher incidence of malignant arrhythmias
    - ICD awareness before EF<35%
  - Monitoring for Afib
  - High need of cardiac Tx
  - Good response to medical treatment
  - Involved in peripartum cardiomyopathy

37

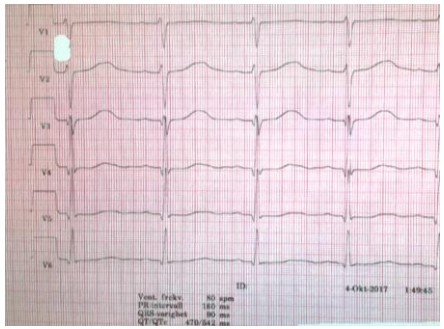
38

Woman 25 y

39

- 6 months post partum
- Seizures during sleep, suspected epilepsy,

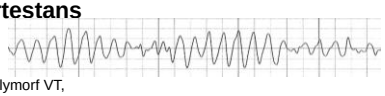
- Genetic testing:
- Heterozygous for mutation in KCNH2 =LQT2
- Postpartum risk x18
-



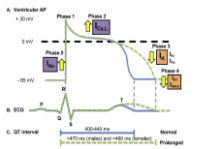
Lang QT tid syndrom

40

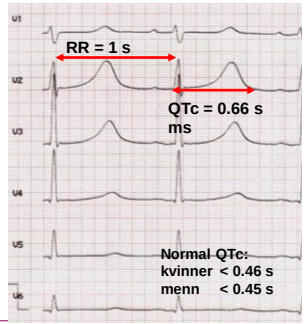
- **Forlenget QTc**
- **Synkope / hjertestans**



Polymorf VT,
Torsade des Pointes



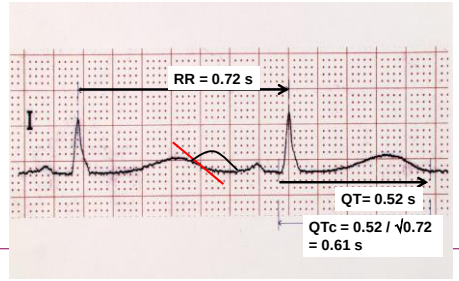
Giudicessi J, Ackerman MJ, Curr Probl Cardiol 2013



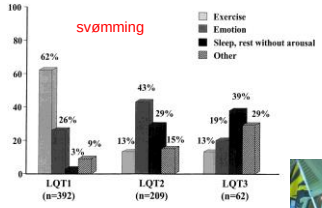
41

- QTc = QT /√RR
- U-bølge
- AF
- breddeøket QRS eller PM-rytme? QT-tid antatt forlenget hvis over 0,50s
- Normalverdier:
  - menn: ≤ 0,45 s
  - kvinner: ≤ 0,46 s

QTc > 500 ms
= høyrisikopasient



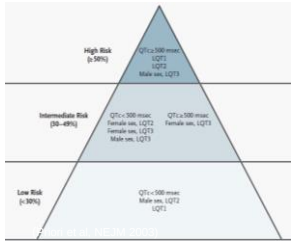
Trigger for arytmi



Schwartz et al Circulation 2001

With permission

Risikostratifiserin g for plutselig død



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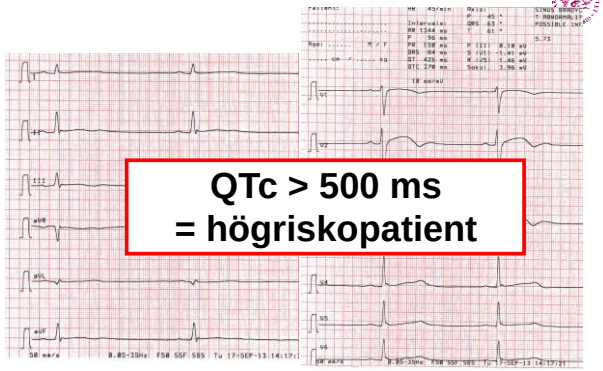
17 år gammel mann, hyppige synkoper



QTc > 500 ms
= högriskopatient

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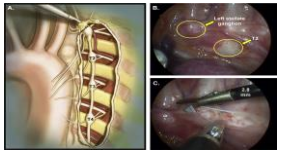
LQTS Treatment / life style advise

- LQT1, LQT2 and LQT3
- Beta-blocker, high doses
- Nadolol
- No competitive sports
- No QT prolonging medication (www.Crediblemeds.org)
- No swimming alone (LQT1)
- Pregnancy, childbirth, postpartum (LQT2)
- ICD
- (Sympatectomy)

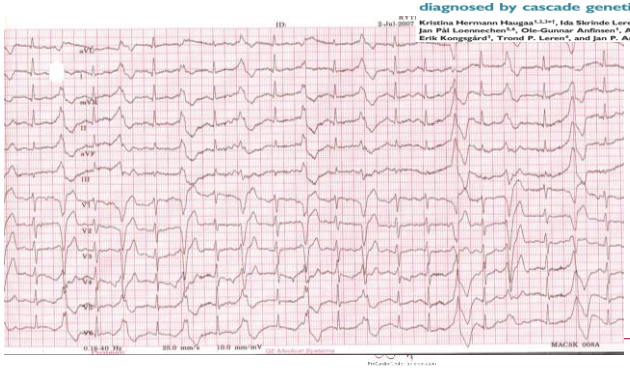
With permission



KARDIOLOGISK AVDELING

45

Arbets EKG
18 år man, rep synkope



CLINICAL RESEARCH

High prevalence of exercise-induced arrhythmias in catecholaminergic polymorphic ventricular tachycardia mutation-positive family members diagnosed by cascade genetic screening

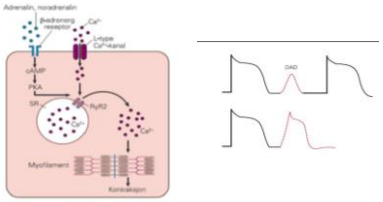
46

Katekolaminerg polymorf ventrikkeltakykardi

- Mutation i ryanodinreceptor 2 gen (RyR2), påverkar ca-homeostas
- Prevalens 1:10 000
-

— Debut oftast i barndomen, ungdomsår med adrenergisk utlösta synkopor, arytmier
— VES, polymorf VT, VF
— OBS Simning
—

Diagnostik
Familj Anamnes
Arbete EKG
Gentest RyR2



IS Leren, K Haugaa et al Tidsskriftet 2010

47

Katekolaminerg polymorf ventrikkeltakykardi

- Diagnostisera!
- Högdosera betablock
- Nadolol
- Flekainid
-
- ICD?
- Undvik högintensidrott
- Sympathectomy
- inte simma/bada ensam
-

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Cardiogenetic testing summary

- Genetic testing gives important actionable information
  → Cardiomyopathies and ionchannelopathies
- Genotype – phenotype specific features
  → Close follow up for ventricular arrhythmias
    - need of ICD
  → Penetrance
    - Family counselling
  → Exercise dependence
    - Exercise restrictions

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Kardio-onkologi – Vad varje kardiolog måste veta

Agneta Månsson Broberg

Fredag 26 januari 2024, 10.45-12.45

Specifika lagar och regler vid hjärtsjukdom

Sofia Kjellberg Lindgren

Fredag 26 januari 2024, 14.05-15.00

Hjärt- och kärlsjukdomar – regelverk och bedömning av medicinsk lämplighet för körkort

Kurs för ST-läkare i kardiologi
26 januari 2024

Sara Magnusson, utredare sektion Trafikantregler Transportstyrelsen
Sofia K Lindgren, överläkare sektion Prövning Trafikant Transportstyrelsen

TRANSPORT STYRELSEN

Innehåll i presentationen

- Bakgrund
- Genomgång av reglerna
- Fallbeskrivningar
- Frågor och svar

TRANSPORT STYRELSEN

Medicinska krav för körkortsinnehav

- EU:s körkortsdirektiv – innehåller ”minimikrav om psykisk och fysisk lämplighet att framföra motordrivna fordon”
- Kraven är implementerade i körkortslagen, körkortsförordningen och Transportstyrelsens föreskrifter
- Föreskrifterna handlar till exempel om vad som gäller för körkortsinnehav vid olika hjärt- och kärlsjukdomar, vid diabetes, syn, epilepsi, demens etc.

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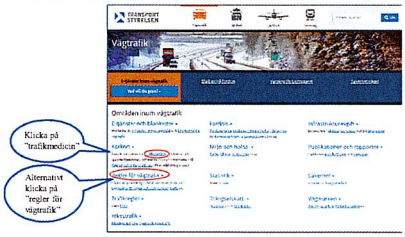
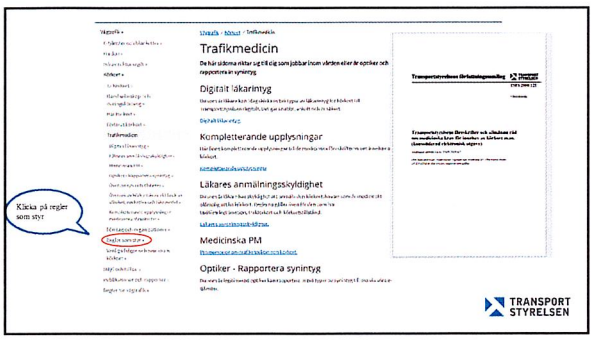
Var hittar du föreskrifterna?



TRANSPORT STYRELSEN



Definition körkortsbehörigheter

Lägre behörigheter

- Moped, bil, motorcykel eller traktorkort
- AM, A1, A2, A, B, BE eller traktorkort

Högre behörigheter

- Lastbil, buss eller taxiförarlegitimation
- C1, C1E, C, CE, D1, D1E, D, DE eller taxiförarlegitimation

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Reglerna för körkort vid hjärt- och kärlsjukdomar

5 kap. Hjärt- och kärlsjukdomar

- reglerar förutsättningar för körkortsinnehav vid förekomst av sjukdomstillstånd kopplade till hjärta/kärl

17 kap. Läkarintyg mm.

- innehåller bland annat krav på vilken specialistkompetens som krävs vid utfärdande av vissa intyg

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Disposition av 5 kap. 2-21§

- Medfödd hjärtsjukdom
- Arytmier och synkope
- Pacemaker och ICD
- Ischemisk hjärtsjukdom och stroke
- Hjärtsvikt och hjärttransplantation
- Hjärtklaffssjukdom
- Hypertoni
- Kardiomyopatier
- Perifera kärlsjukdomar

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Hjärt-kärl sjukdom är ofta hinder...MEN

- I många fall kan innehav medges under förutsättning att ”tillståndet är **väl behandlat** och i övrigt inte bedöms innebära en **trafiksäkerhetsrisk**” även om själva diagnosen utgör hinder
- Ofta **olika krav** för lägre och högre behörigheter
  - strängare kriterier för högre behörigheter

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Anmälan om olämplighet

- Ange gärna kapitel och paragraf enligt Transportstyrelsens föreskrifter
- Alla läkare kan anmäla, men specialistläkare behöver kontrasignera (för att TS ska kunna återkalla körkortet)
- Informera patienten innan anmälan

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Så kallat muntligt körförbud?

- Tillsägelse kan användas om ett medicinskt tillstånd är ett hinder, men förväntas blir bättre tex efter insatt behandling eller operation
- Läkaren tar på sig ett stort ansvar- att patienten följer tillsägelsen
- Inget förbud i juridisk mening
- Tillsägelsen bör inte vara längre än 6 månader
- I allmänna råd: exempel på lämplig observationstid

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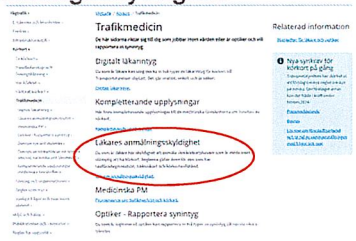
Information om läkares anmälningsskyldighet



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Portalparagrafen i 5 kap.

- 1 § Hjärt- och kärlsjukdomar, som innebär en **påtaglig risk** för att hjärnans funktioner akut försämras eller som i övrigt innebär en trafiksäkerhetsrisk, utgör hinder för innehav av alla behörigheter
- Högre behörigheter innebär ökad trafiksäkerhetsrisk - ska beaktas

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Vad betyder ”påtaglig risk för att hjärnans funktioner akut försämras”?

Symptom som kan tyda på att hjärnans funktion kan försämras:

- akut bröstsmärta
- kraftig andfåddhet
- uttalad trötthet
- akut yrsel
- konfusion eller medvetslöshet

Påtaglig risk = er kliniska bedömning.
Värdera orsak, klinisk form, behandlingsresultat och utveckling

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Vad betyder att ”tillståndet är väl behandlat och i övrigt inte bedöms innebära en trafiksäkerhetsrisk”?

- Det medicinska tillståndet ska vara **effektivt behandlat**
- **Trafiksäkerhetsrisken -** ska bedömas låg för att medge innehav.
  - Innebär graden av sjukdomen, trots behandling, att det finns oförmåga eller risk för plötslig oförmåga att framföra ett fordon är det inte förenligt med innehav av körkort

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Dessa tillstånd är alltid hinder- gäller vid högre behörighet

- ICD (8 §)
- Mekanisk hjärtpump (11 §)
- Aortaaneurysm som överstiger 5,5 cm i diameter (20 §)

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Fallbeskrivning 1
Mentometerfrågor

TRANSPORT STYRELSEN

Medfödd hjärtsjukdom, hjärttransplantation och grav hypertoni 2,12,16§§

Hinder för **alla** behörigheter MEN inget hinder om det är välbehandlat och i övrigt inte innebär en trafiksäkerhetsrisk

- *Efter hjärttransplantation:* ***Lägre:*** *individuell bedömning.* ***Högre:*** *observationstid* ***minst 12 månader.***
- *Vid hjärt-lungmaskin: bedöm kognitiva funktioner enligt kap. 10.*

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Arytmier och synkope 3-6 §§

Hinder för **alla** behörigheter MEN kan medges om tillståndet är väl behandlat och inte bedöms innebära en trafiksäkerhetsrisk.

- Arytmi (oavsett typ) samt synkope
- Takyarytmi, vid strukturella hjärtsjukdomar och VT
- Vasovagal synkope (ingen arytmi och ingen hjärtsjukdom)

Observationstid minst 3 månader, upprepad synkope 6 månader.

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Arytmier 3-6 §§

Hinder för **högre** behörigheter MEN innehav kan medges om tillståndet är väl behandlat och inte bedöms innebära en trafiksäkerhetsrisk.

- bradyarytmier med AV-block II (Mobitz typ 2), AV-block III eller alternerande skänkelblock
- takyarytmier med förekomst av polymorf kortvarig VT, ihållande VT eller med indikation för implanterbar defibrillator (ICD)

Observationstid minst 3 månader.

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Pacemaker och ICD 7-8 §§

Behandling med **pacemaker**

- **inte** hinder för **lägre** behörigheter
- högre behörighet kan medges om tillståndet är *väl behandlat* och *inte* bedöms innebära en *trafiksäkerhetsrisk*

Behandling med **ICD**

- **alltid** hinder för **högre** behörigheter
- lägre behörigheter kan medges om tillståndet är *väl behandlat och* inte bedöms innebära en *trafiksäkerhetsrisk*

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Fallbeskrivning 2
Mentometerfrågor

TRANSPORT STYRELSEN

Ischemisk hjärtsjukdom 9 §

Hinder för innehav av **alla** behörigheter, MEN kan medges vid välbehandlat tillstånd utan trafiksäkerhetsrisk

- *observationstid **minst 4 veckor lägre** behörighet*
- *observationstid **minst 6 veckor högre** behörighet*

Ok vid **stabil angina pectoris** förutsatt att symptom inte uppträder vid lindrig ansträngning

TRANSPORT STYRELSEN

Hjärtsvikt 11 §

- Hinder för innehav av **alla** behörigheter…
  - … men **lägre** behörigheter kan innehav medges vid **NYHA I-III** vid välbehandlat tillstånd och som inte innebär trafiksäkerhetsrisk
  - … men **högre** behörigheter kan innehav medges vid **NYHA I-II** vid **EF** är **minst 35 %** vid välbehandlat tillstånd och som inte innebär trafiksäkerhetsrisk

Mekanisk hjärtpump är hinder vid högre behörighet oavsett funktionsklass

TRANSPORT STYRELSEN

Hjärtklaffssjukdom 13-15 §§

- Större paragrafer - kolla gärna föreskriften!
- Hinder för innehav av **alla** behörigheter vid förekomst av
  - aortastenos, aortainsufficiens, mitralisstenos, mitralisinsufficiens med episoder av **synkope** eller om funktionsförmågan bedöms till **NYHA IV**
- Hinder för innehav av **högre** behörigheter vid:
  - funktionsförmåga **NYHA III eller IV**
  - ejektionsfraktion **under 35 %**
  - mitralisstenos med uttalad pulmonell hypertension
  - uttalad aortastenos vid ekokardiografi
  - aortastenos med synkope

TRANSPORT STYRELSEN

Hjärtklaffssjukdom 13-15 §§

- Efter klaffkirurgi: innehav medges av **alla** behörigheter om tillståndet är väl behandlat och inte innebär en trafiksäkerhetsrisk

  Observationstid:
  ***Lägre - individuell** bedömning i det enskilda fallet*
  Högre - minst 4 veckor
- Vid hjärt-lungmaskin: bedöm kognitiva funktioner enligt kap. 10.

TRANSPORT STYRELSEN

Kardiomyopatier 17-19 §§

- Mer reglerat i föreskriften
- Hinder för innehav av **alla** behörigheter, men massa OM och MEN utifrån sjukdomstillståndet….

Har du en patient med kardiomyopati hänvisar vi till att läsa mer detaljerat i föreskriften.

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Perifera kärlsjukdomar 20-21 §§

- Thorakalt eller abdominellt aortaanerysm: om aortadiametern kan medföra **avsevärd risk för plötslig bristning** och därmed **plötsligt nedsatt funktionsnivå.**
  - Hinder **alla** behörigheter
- Aortadiametern överstiger **5,5 cm** 
  - Hinder **högre** behörigheter
- Karotisstenos
  - Kan vara ett hinder vid **högre** behörighet. Kardiologisk utredning bör göras. Risk för stroke? Risk för hjärtinfarkt?

TRANSPORT STYRELSEN

Kap. 1 Inledande bestämmelser

- 4 § anger att förhållanden som innebär en trafiksäkerhetsrisk utgör hinder för körkort
- 5 § anger att ledning ska hämtas från andra kapitel om det medicinska förhållandet har nära anknytning till krav som finns där.
  - "Vid en sammantagen bedömning av olika medicinska förhållanden kan hinder för innehav föreligga även om förhållandena var för sig inte utgör hinder enligt 2–15 kap."

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Take-home message: Kolla föreskrifterna och läs allmänna råd.

Frågor?

TRANSPORT STYRELSEN

Framtidens kardiologer
25-26 januari, 2024
Clarion Hotel Sign, Stockholm

Kardioonkologi-Onkokardiologi

Kardiovaskulär toxicitet vid cancerbehandling.

Agneta Månsson Broberg överläkare, docent
ME Kardiologi Karolinska Universitetssjukhuset
agneta.mansson.broberg@ki.se

Karolinska Institutet | KAROLINSKA UNIVERSITETSSJUKHUSET

1

Disclosures

Talarersättning: Pfizer, Orion/ Abbott Heart Failure and Cardio Oncology, BMS, Ipsen

Forskningsstöd: Amgen 2023

2

2

Dagens program

- Introduktion
- Riskvärdering och hantering av hjärt- och kärlsjukdom i relation till cancerbehandling
- Exempel på kardiotoxiska behandlingar (antracykliner, antimetaboliter, antiHer2, tyrosinekinasehämmare, immuncheckpointhämmare)

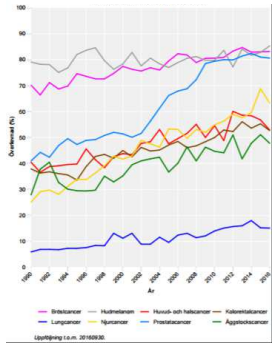
- Kardioonkologisk approach och kardioprotektion
- Hjärtkärlsjukdom under cancerbehandling
- Uppföljning

3

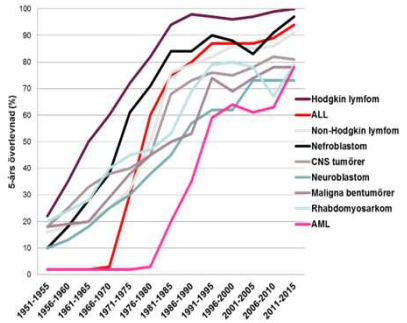
3

Ökande andel långtidsöverlevande

5-årsöverlevnad vuxna



5-årsöverlevnad barn



www.rcc.se

Källa – Registerdata från Svenska Cancerregistret och Svenska barncancerregistret, G Gustafsson, P Lähteenmäki och T Óskarsson

4

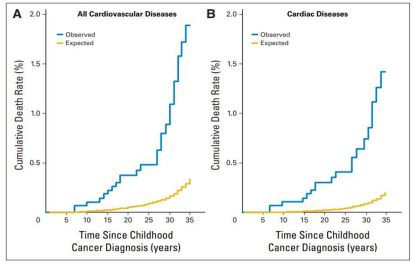
4

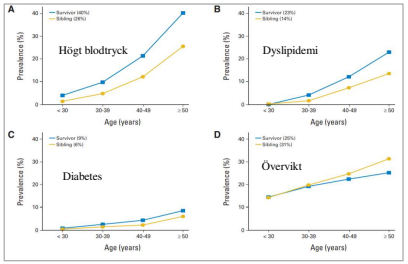
Kardiovaskulär toxicitet vid cancerbehandling.

- ❖Är det viktigt- patienterna är ju botade från cancern?
  (Är det ens relevant? Hur ser långtidsprognosen ut för patienterna?)
- ❖Vad vet vi mer om risken?
  (Vilken behandling är värst? Är vissa mer känsliga än andra? Har riskvärdering betydelse i förväg?)
- ❖Finns det skyddande behandling?
  (Strategier för multihit, neurohormonell protektion, specifik protektion)

5

Ju längre man lever efter cancerbehandling desto större risk att få hjärt och kärlsjukdom





Tukenova M et al. J Clin Oncol (2010) 28:1308-1315

Armstrong GT et al. J Clin Oncology 2013.

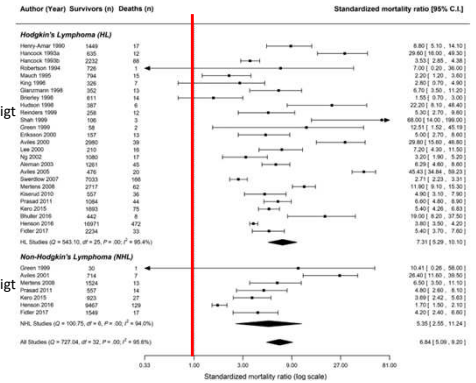
6

Ökad risk för kardiovaskulär död

(median ålder 25 år vid behandling, median followup 13.8 år)

7x högre risk
för att dö för tidigt

5x högre risk
för att dö för tidigt



Long-term risk of cardiovascular mortality in lymphoma survivors: A systematic review and meta-analysis, Volume: 7, Issue: 9: 4801-4813, 15 August 2018, DOI: (10.1002/cam4.1572)

7

Sämre prognos vid hjärtsvikt pga cancerterapi (Cancer Therapy Induced Heart Failure, CTRHF)

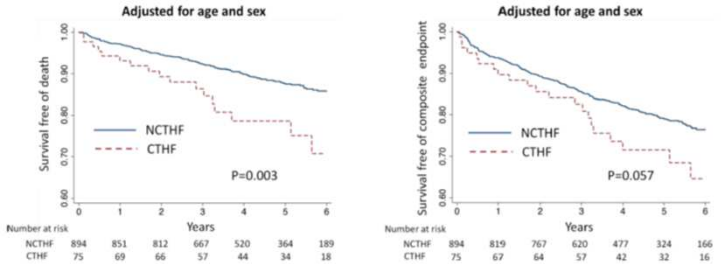


Figure 1 Kaplan-Meier curves for death and composite endpoint. The composite endpoint was defined as the composite outcome of left ventricular assistant device implantation, heart transplantation or all-cause mortality. CTHF, cancer therapy-induced heart failure; NCTHF, non-cancer therapy-induced heart failure.

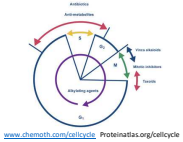
Kombinerad endpoint död, LVAD eller hjärt-trx

Nadruz W et al. Heart 2019 105(1):34-41

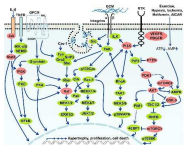
8

Vilka cancerbehandlingar gäller det?

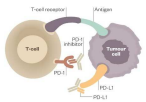
Cell phase where chemo agents work



www.chemoth.com/cellcycle Proteinatlas.org/cellcycle



Lal H et al. JACC 2013



Konventionell cytostatika

Riktad cancerbehandling

Immunbehandling

Strålbehandling

	Arrhythmia	Cardiomyopathy	Arterial vascular disease	Venous thrombo/embolism	Pulmonary hypertension	Systemic hypertension	Pericardial disease	Valvular heart disease
Conventional chemotherapies								
Anthracyclines (doxorubicin, epirubicin)		✓						
Alkylating agents (cyclophosphamide, melphalan)	✓	✓	✓					
Antimetabolites (5-fluorouracil, capecitabine, cytarabine)		✓	✓				✓Cytarabine	
Microtubule-binding agents (paclitaxel)	✓		✓					
Platinum-based therapy (cisplatin)			✓	✓		✓		
Antibiotic (bleomycin)			✓		✓			
Immunomodulatory drugs (thalidomide)	✓			✓				
Targeted agents								
Proteasome inhibitors (bortezomib, carfilzomib)		✓	✓			✓		
HDAC inhibitors (vorinostat)	✓							
CDK4/CDK6 inhibitors (ribociclib)	✓							
mTOR inhibitors (everolimus)	✓	✓	✓	✓		✓		
HER2 inhibitors (pertuzumab, trastuzumab)		✓						
VEGF inhibitors (bevacizumab, sunitinib)		✓	✓	✓		✓		
BCR-ABL1 inhibitors (dasatinib, nilotinib, ponatinib)	✓		✓	✓	✓Dasatinib			
BTK inhibitors (ibrutinib)	✓							
ALK inhibitors (alectinib, ceritinib, crizotinib)	✓				✓			
BRAF inhibitors (dabrafenib)	✓	✓						
MEK inhibitors (binimetinib, cobimetinib, trametinib)	✓	✓			✓			
Immunotherapies								
Immune checkpoint inhibitors	✓	✓	✓	✓	✓		✓	
CAR T cell therapy	✓	✓	✓	✓	✓		✓	
Other therapies								
Radiation therapy	✓	✓	✓		✓		✓	✓

Guha et al 2014. Pharmaceutical journal.

Joerg Herrmann. Adverse cardiac effects of cancer therapies: cardiotoxicity and arrhythmia. Nature review Cardiology 2020

9

CANCERTERAPIER DÄR BASELINE RISKVÄRDERING REKOMMENDERAS

Cancer treatment class	Cancer indication	Treatment-related CV toxicity
Anthracycline chemotherapy (doxorubicin, epirubicin, daunorubicin, idarubicin)	Breast cancer, lymphoma, acute leukaemia, sarcoma	Heart failure Asymptomatic LVSD Atrial and ventricular arrhythmias
HER2-targeted therapies (trastuzumab, pertuzumab, trastuzumab emtansine (T-DM1), lapatinib, neratinib, tucatinib)	HER2+ breast cancer HER2+ gastric cancer	Heart failure Asymptomatic LVSD Hypertension
VEGF inhibitors TKIs (sunitinib, pazopanib, sorafenib, axitinib, vinzasnib, cabozantinib, regorafenib, lenvatinib, vandetanib) and antibodies (bevacizumab, ramucirumab)	VEGF TKIs: renal cancer, hepatocellular cancer, thyroid cancer, colon cancer, sarcoma, GIST Antibodies: breast cancer, ovarian cancer, gastric cancer, gastro-oesophageal cancer, colon cancer	Hypertension Heart failure Asymptomatic LVSD Myocardial ischaemia and infarction QTc prolongation
Multi-targeted kinase inhibitors: second and third generation BCR-ABL TKIs (ponatinib, nilotinib, dasatinib, bosutinib)	Chronic myeloid leukaemia	Arterial thrombosis (myocardial infarction, stroke and PAOD[a]) Venous thromboembolism Hypertension Heart failure and asymptomatic LVSD Atherosclerosis[a] QTc prolongation[b] Pulmonary hypertension[a]
Proteasome inhibitors (carfilzomib, bortezomib, ixazomib) **Immunomodulatory drugs** (lenalidomide, pomalidomide)	Multiple myeloma	Heart failure[a] Asymptomatic LVSD[a] Myocardial ischaemia and infarction Atrial and ventricular arrhythmias Venous thromboembolism Arterial thrombosis Hypertension
Combination RAF and MEK inhibitors (dabrafenib + trametinib, vemurafenib + cobimetinib, encorafenib + binimetinib)	Raf mutant melanoma	Heart failure and asymptomatic LVSD Hypertension QTc prolongation[a]
Androgen deprivation therapies **GnRH agonists** (goserelin, leuprorelin) **Antiandrogens** (abiraterone)	Prostate cancer ER+ breast cancer[c]	Atherosclerosis Myocardial ischaemia and infarction Diabetes mellitus Hypertension
Immune checkpoint inhibitors: anti-programmed cell death 1 inhibitors (nivolumab, pembrolizumab) **anti-cytotoxic T-lymphocyte-associated protein 4 inhibitor** (ipilimumab) **anti-programmed death-ligand 1 inhibitors** (avelumab, atezolizumab, durvalumab)	Melanoma (metastatic and adjuvant) Metastatic renal cancer, non-small cell lung cancer, small cell lung cancer, refractory Hodgkin's lymphoma, metastatic triple negative breast cancer, metastatic urothelial cancer, liver cancer, MMR-deficient cancer	Myocarditis including fulminant myocarditis Pericarditis Non-inflammatory heart failure Ventricular arrhythmias AV block Acute coronary syndromes including atherosclerotic plaque rupture and vasculitis

- **Antracykliner**
- **Anti Her 2 terapier**
- **VEGF inhibitorer**
- BCR-Abl TKI
- Proteasominhibitorer
- MEK/RAF
- Antiandrogenterapier
- **ICI**

Lyon et al EHJ 2020

10

Guidelines!

Karolinska Institutet | KAROLINSKA UNIVERSITETSSJUKHUSET

ESC European Society of Cardiology — European Heart Journal (2022) **00**, 1–133 — ESC GUIDELINES

2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS)

Developed by the task force on cardio-oncology of the European Society of Cardiology (ESC)

Authors/Task Force Members: Alexander R. Lyon*† (Chairperson) (United

ESMO — ANNALS OF ONCOLOGY

SPECIAL ARTICLE

Management of toxicities from immunotherapy: ESMO Clinical Practice

POSITION PAPER

Baseline cardiovascular risk assessment in cancer patients sche

cardiotoxic cancer t

statement and new

the Cardio-Oncolog

Heart Failure Assoc

Society of Cardiolog

International Cardic

POSITION PAPER

Expert consensus for multimodality imaging evaluation of adult patients during and after cancer therapy: a report from the American Society of Echocardiography and the European Association of Cardiovascular Imaging

ESMO

SPECIAL ARTICLE

Management of cardiac disease in cancer patients throughout oncological treatment: ESMO consensus recommendations

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ESC European Society of Cardiology — European Heart Journal (2022) **00**, 1–133 https://doi.org/10.1093/eurheartj/ehac244 — ESC GUIDELINES

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Authors/Task Force Members: Alexander R. Lyon*† (Chairperson) (United

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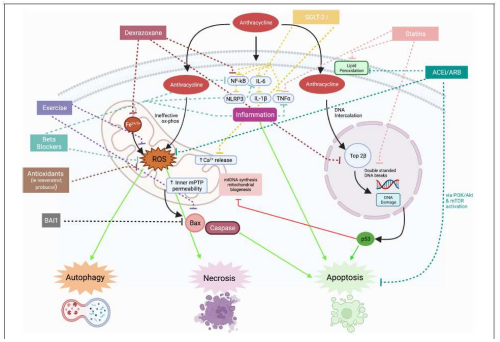
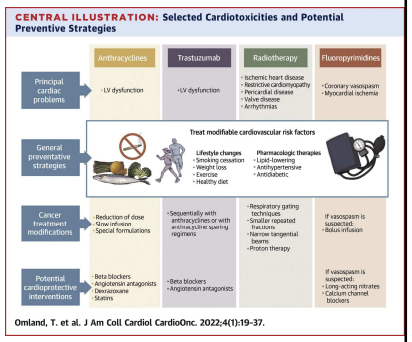
Strategier för kardioprotektion





Vuong T et al. Frontiers in Cardiovascular Medicine 2022

Omland et al. JACC Cardioonc 2022

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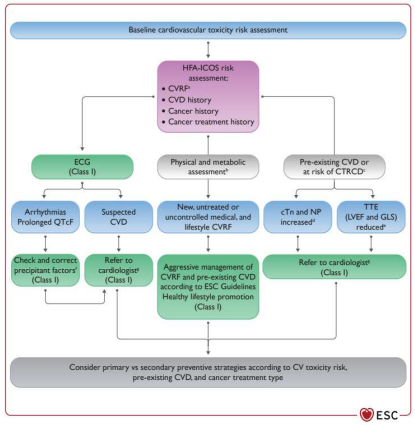
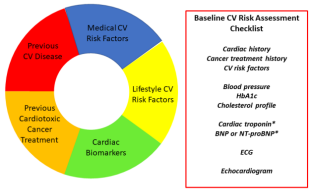
RISKVÄRDERING UTGÖR GRUNDEN





Lyon et al EHJ 2022

Modif från Visseren et al EHJ 2021

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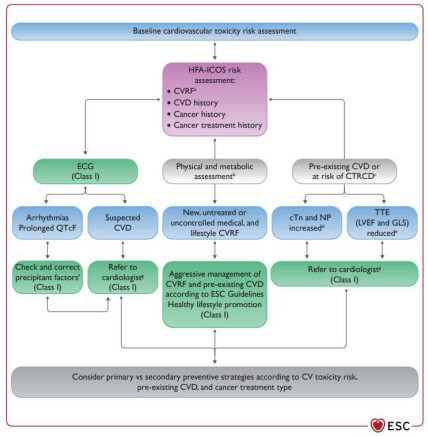
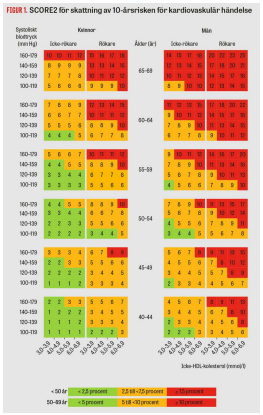
RISKVÄRDERING UTGÖR GRUNDEN





Lyon et al EHJ 2022

Modif från Visseren et al EHJ 2021

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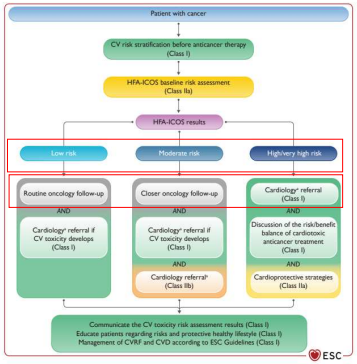
STRATEGI



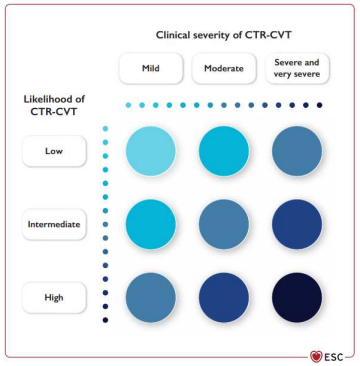


Figure 6 General cardio-oncology approach after Heart Failure Association–International Cardio-Oncology Society cardiovascular toxicity risk assessment. CV, cardiovascular; CVD, CV disease; CVRF, CV risk factors; ESC, European Society of Cardiology; HFA, Heart Failure Association; ICOS, International Cardio-Oncology Society. *Cardio-oncology referral is recommended when available; alternatively, patients should be referred to a specialized cardiologist with expertise in managing CVD in patients with cancer.

Lyon et al EHJ 2022

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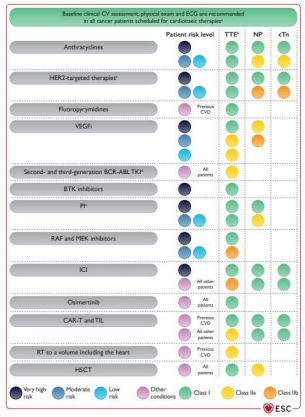
BASELINEUTVÄRDERING VIKTIGT



Recommendation Table 2 — Recommendations for electrocardiogram baseline assessment

Recommendations	Class[a]	Level[b]
An ECG is recommended in all patients starting cancer therapy as part of their baseline CV risk assessment.	I	C
In patients with an abnormal baseline ECG,[c] referral to a cardiologist[d] is recommended.	I	C

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Recommendation Table 3 — Recommendation for cardiac biomarker assessment prior to potentially cardiotoxic therapies

Recommendation	Class[a]	Level[b]
Baseline measurement of NP[c] and/or cTn[d] is recommended in all patients with cancer at risk of CTRCD if these biomarkers are going to be measured during treatment to detect CTRCD.[4,53,55]	I	C

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cTn, cardiac troponin; CTRCD, cancer therapy-related cardiac dysfunction; NP, natriuretic peptides.

Recommendation Table 4 — Recommendations for cardiac imaging modalities in patients with cancer

General	Class[a]	Level[b]
Echocardiography is recommended as the first-line modality for the assessment of cardiac function in patients with cancer.[4,12,54,94]	I	C
3D echocardiography is recommended as the preferred echocardiographic modality to measure LVEF.[77–79,89]	I	B
GLS is recommended in all patients with cancer having echocardiography, if available.[75,80,81,89,90,93,95,100,102,103]	I	C
CMR should be considered for the assessment of cardiac function when echocardiography is unavailable or non-diagnostic.[83,104,105]	IIa	C
MUGA may be considered when TTE is not diagnostic and CMR is not available.[106–108]	IIb	C
Baseline cardiac imaging prior to potentially cardiotoxic therapies[c]		
Baseline comprehensive TTE is recommended in all patients with cancer at high risk and very high risk of CV toxicity before starting anticancer therapy.[4,54]	I	C

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3D, three-dimensional; CMR, cardiac magnetic resonance; CTR-CVT, cancer therapy-related CV toxicity; CV, cardiovascular; GLS, global longitudinal strain; LVEF, left ventricular ejection fraction; MUGA, multigated acquisition nuclear imaging; TTE, transthoracic echocardiography.

[a]Class of recommendation.

[b]Level of evidence.

[c]Specific recommendations for baseline CV imaging in patients with cancer at low or moderate risk of CTR-CVT are included in Section 5.

[d]Except asymptomatic patients referred to breakpoint cluster region-Abelson oncogene locus therapy (BCR-ABL) where baseline TTE should be considered (see Figure 7 and Section 5.3.3).

Lyon et al. ESC Cardionocology guidelines. EHJ 2022.

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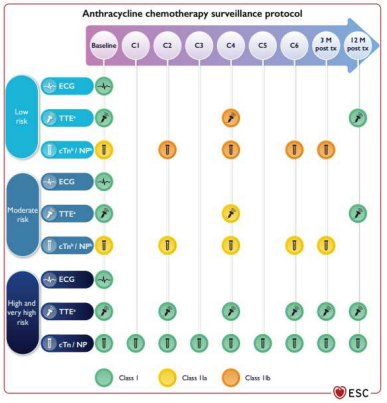
ANTRACYKLINBEHANDLING



Recommendation Table 7 — Recommendations for baseline risk assessment and monitoring during anthracycline chemotherapy and in the first 12 months after therapy

Recommendations	Class[a]	Level[b]
TTE		
Baseline echocardiography[c] is recommended in all patients with cancer before anthracycline chemotherapy.[7,9,24,208–210]	I	B
In all adults receiving anthracycline chemotherapy, an echocardiogram is recommended within 12 months after completing treatment.[208]	I	B
In high- and very high-risk patients, echocardiography is recommended every two cycles and within 3 months after completing treatment.[24,208–210]	I	C
In moderate-risk patients, additional echocardiography should be considered after a cumulative dose of ≥250 mg/m² of doxorubicin or equivalent.[7]	IIa	C
In low-risk patients, additional echocardiography may be considered after a cumulative dose of ≥250 mg/m² of doxorubicin or equivalent.[7]	IIb	C
Cardiac serum biomarkers		
Baseline measurement of NP and cTn is recommended in high- and very high-risk patients prior to anthracycline chemotherapy.[55,65,211]	I	B
Baseline measurement of NP and cTn should be considered in low- and moderate-risk patients prior to anthracycline chemotherapy.[211]	IIa	C
cTn and NP monitoring before every cycle during anthracycline chemotherapy and 3 and 12 months after therapy completion is recommended in high- and very high-risk patients.[55,175,211]	I	B
cTn and NP monitoring every two cycles during anthracycline chemotherapy and within 3 months after therapy completion should be considered in moderate-risk patients and in low-risk patients receiving a cumulative dose of ≥250 mg/m² of doxorubicin or equivalent.[55,59,212,213]	IIa	C
cTn and NP monitoring every two cycles during anthracycline chemotherapy and within 3 months after therapy completion may be considered in low-risk patients.[55,59,212,213]	IIb	C

Continued

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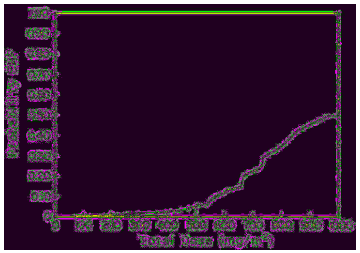
ANTRACYKLINBEHANDLING

Klassiska dos-relaterad riskbehandling

kumulativ dos av doxorubicin	incidens av hjärtsvikt
300 mg/m²	1.7 %
400 mg/m²	4.7 %
500 mg/m²	15.7 %
650 mg/m²	48.0 %

kumulativ dos av doxorubicin	andel pat med kardiellt event
150 mg/m²	7%
250 mg/m²	9%
350 mg/m²	18%
450 mg/m²	38%
550 mg/m²	65%



Swain et al. Cancer 2002

19

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ANTRACYKLINTOXICITET_mekanismer

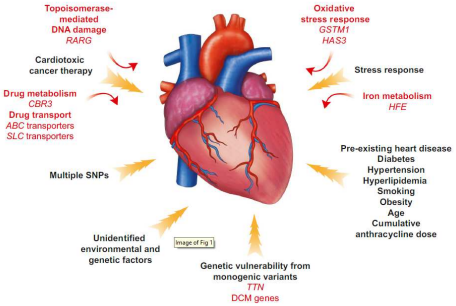

Fig 1. Contributors to cancer therapy-induced cardiovascular toxicity. A combination of clinical and genetic risk factors leads to increased risk of developing toxicity upon cancer therapy treatment. Elucidation of genetic contributors of cancer therapy-induced cardiovascular toxicity facilitates understanding of its molecular mechanism and development of its therapeutic strategies.

Kim et al_2022_ Frontiers in Cardiovascular medicine

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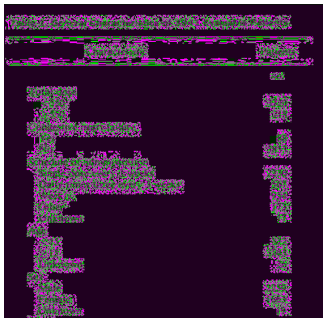
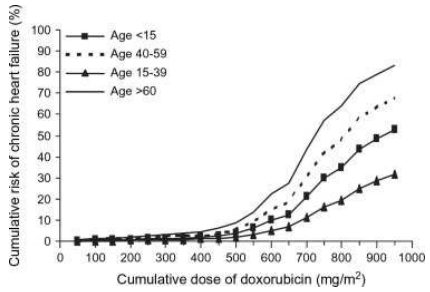
Väldigt unga och gamla har en ökad risk





Von Hoff et al D. Risk factors for Doxorubicin Induced congestive heart failure. Annals of internal medicine 1979

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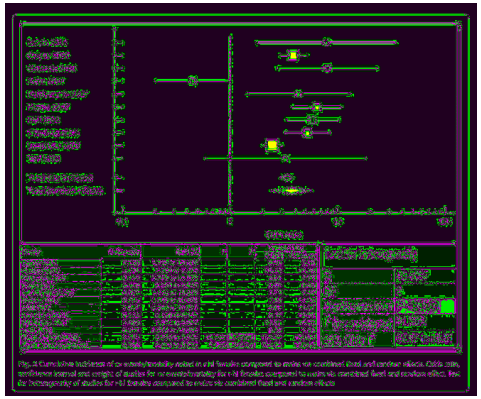
Kvinnligt kön = större känslighet?



Khalid et al. Gender disparity. Cardio-Oncology_2020

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Strategier för prevention och protektion

Recommendation Table 5 — Recommendations for primary prevention of cancer therapy-related cardiovascular toxicity

Recommendations	Class[a]	Level[b]
Management of CVRF according to the 2021 ESC Guidelines on CVD prevention in clinical practice is recommended before,[c] during, and after cancer therapy.[19]	I	C
Dexrazoxane should be considered in adult patients with cancer at high and very high CV toxicity risk when anthracycline chemotherapy is indicated.[d,158]	IIa	B
Liposomal anthracyclines should be considered in adult patients with cancer at high and very high CV toxicity risk when anthracycline chemotherapy is	IIa	B
ACE-I or ARB and beta-blockers recommended for HF[f] should be considered for primary prevention in high- and very high-risk patients receiving anthracyclines and/or anti-HER2 therapies.[145,150,155–157,159,160,175]	IIa	B
ACE-I or ARB and beta-blockers recommended for HF[f] should be considered for primary prevention in high- and very high-risk patients receiving targeted cancer therapies that may cause HF.[g]	IIa	C
Statins should be considered for primary prevention in adult patients with cancer at high and very high CV toxicity risk.[h,149:176–185]	IIa	B

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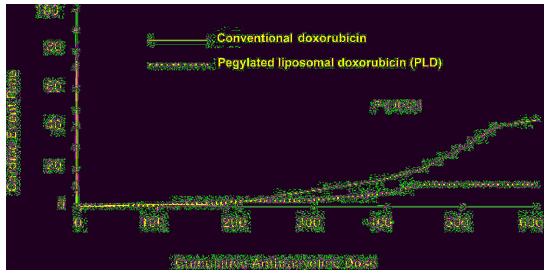

Cardiac eventfree survival for PLD vs cnventional doxorubicin. Metastatic breast cancer. N= 509.

Rahman A. et al. International Journal of nanomedicine 2007

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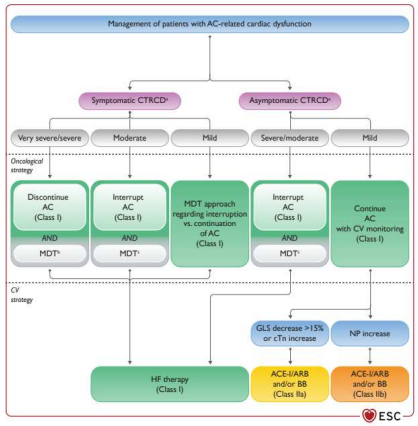

Lyon et al, EHJ, 2022

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Strålning

TABLE 2 Risk Factors and Long-Term Manifestations of Chest and Mediastinal Radiotherapy

Risk factors for developing RACD and RAPD

- Younger age at the time of XRT (<50 yrs)
- Presence of cardiovascular risk factors or established cardiopulmonary disease
- Lack of shielding or cobalt as a source of radiation
- High cumulative dose(>30 Gy) or high dose of radiation fractions (>2 Gy/day)
- Tumor in or next to the heart
- Anterior or left chest radiation
- Concomitant chemotherapy (e.g., anthracyclines)

Potential manifestations of chest and mediastinal XRT

Pericardium
- Constrictive pericarditis due to extensive fibrous thickening, adhesions, chronic constriction and can be associated with chronic pericardial effusion. Associated with significantly higher surgical mortality

Cardiac muscle
- Diffuse subclinical myocardial fibrosis with associated progressive systolic and diastolic dysfunction
- Nonischemic cardiomyopathy can occur as an advanced stage of the disease due to extensive fibrosis with severe diastolic dysfunction and signs and symptoms of heart failure (heart failure with preserved ejection fraction more common than reduced ejection fraction)
- Ischemic cardiomyopathy can occur due to advanced CAD

Valves
- Valve apparatus and leaflet thickening, fibrosis, shortening, and calcification predominant on left-sided valves
- Thickening and calcification of aortomitral curtain very commonly seen
- Valve regurgitation more common than stenosis
- Aortic valve stenosis most common stenotic lesion

Coronary artery disease
- Accelerated CAD often seen at a much younger age
- Concomitant atherosclerotic risk factors further enhance development of CAD
- Can occur ≤5 yrs after exposure
- Coronary ostia and proximal segments are typically involved
- CAD significantly increases the risk of myocardial infarction and death

Carotid artery disease
- Radiotherapy induced lesions are more extensive, involving longer segments and atypical areas of carotid segments

Other vascular disease
- Calcification of the ascending aorta and aortic arch (porcelain aorta)
- Lesions of any other vascular segments present within the radiation field

Conduction system disease
- Ectopy, tachyarrhythmia, baseline sinus tachycardia and autonomic dysfunction commonly seen
- Increased risk of pacemaker implantation due to conduction system disease

Lungs
- Progressive pulmonary fibrosis
- Recurrent pleural effusions

CAD = coronary artery disease; RACD = radiation-associated cardiac disease; RAPD = radiation-associated pulmonary disease; XRT = radiotherapy.

- Kranskärlssjukdom
- Klaffsjukdom
- Hjärtsvikt
- - HFpEF
- - restriktiv hjärtsvikt
- Konstriktiv perikardit
- Sinus takykardi
- Fortledningssjukdomar

Desai et al. Radiation associated cardiac disease JACC

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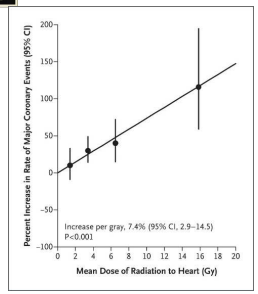
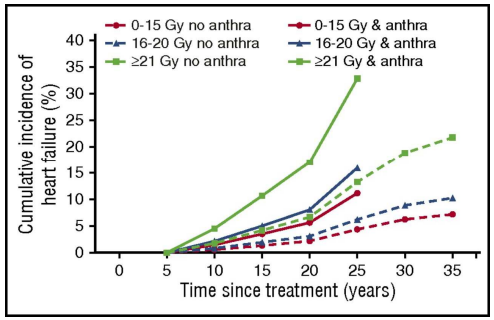
Strålbehandling-dosrelaterad toxicitet





Ungefär 2,5 faldig ökning vid 20Gy; 7,5% ökad risk per GY
Inget tröskelvärde, linjärt
Genomsnittslig debut 19 år efter beh

Darby et al. NEJM 2013

Van Nimwegen F et al, J Clin Oncol 2016:34

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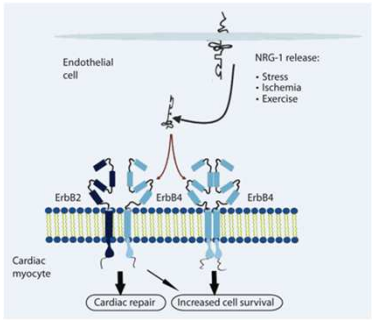
Anti Her2 behandling



- Her 2 tumörmarkör på vissa bröstcancerceller
- uttrycks också på hjärtmuskelcellen
- antiHer2behandling ökar risken för vänsterkammar-dysfunktion
  - dos-oberoende
- Reversibel (?) men oklart i kombination med antracyklineffekt

Suter TM et al. J Clin Oncol. 2007;25:3859-3865.

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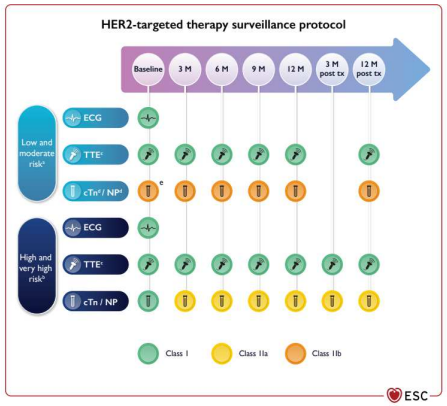

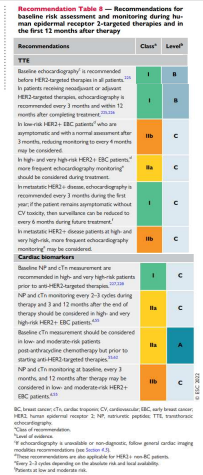

Recommendation Table 8 — Recommendations for baseline risk assessment and monitoring during human epidermal receptor 2-targeted therapies and in the first 12 months after therapy

Recommendations	Class	Level
TTE		
Baseline echocardiography is recommended before HER2-targeted therapies in all patients.	I	B
In patients receiving neoadjuvant or adjuvant HER2-targeted therapies, echocardiography is recommended every 3 months and within 12 months after completing treatment.	I	B
In low-risk HER2+ EBC patients who are asymptomatic and with a normal assessment after 3 months, reducing monitoring to every 4 months may be considered.	IIb	C
In high- and very high-risk HER2+ EBC patients, more frequent echocardiography monitoring should be considered during treatment.	IIa	C
In metastatic HER2+ disease, echocardiography is recommended every 3 months during the first year. If the patient remains asymptomatic without CV toxicity, then surveillance can be reduced to every 6 months during future treatment.	I	C
In metastatic HER2+ disease patients at high- and very high-risk, more frequent echocardiography monitoring may be considered.	IIb	C
Cardiac biomarkers		
Baseline NP and cTn measurement are recommended in high- and very high-risk patients prior to anti-HER2-targeted therapies.	I	C
NP and cTn monitoring every 2–3 cycles during therapy and 3 and 12 months after the end of therapy should be considered in high- and very high-risk HER2+ EBC patients.	IIa	C
Baseline cTn measurement should be considered in low- and moderate-risk patients post-anthracycline chemotherapy but prior to starting anti-HER2-targeted therapies.	IIa	A
NP and cTn monitoring at baseline, every 3 months, and 12 months after therapy may be considered in low- and moderate-risk HER2+ EBC patients.	IIb	C

BC, breast cancer; cTn, cardiac troponin; CV, cardiovascular; EBC, early breast cancer; HER2, human epidermal receptor 2; NP, natriuretic peptide; TTE, transthoracic echocardiography.
[a]Class of recommendation.
[b]Level of evidence.
[c]If echocardiography is unavailable or non-diagnostic, follow general cardiac imaging modalities recommendations (see Section 4.2).
[d]These recommendations are also applicable for HER2+ non-BC patients.
[e]Every 2–3 cycles depending on the absolute risk and local availability.
[f]Patients at low and moderate risk.

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Lyon et al, EHJ, 2022

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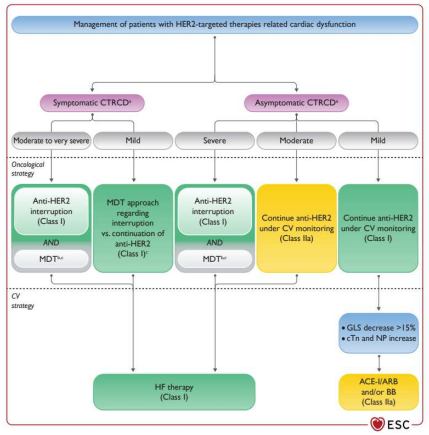

Lyon et al, EHJ, 2022

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Recommendation Table 9 — Recommendations for baseline risk assessment and monitoring during fluoropyrimidine therapy

Recommendations	Class[a]	Level[b]
Baseline CV risk assessment and evaluation including BP measurement, ECG, lipid profile, HbA1c measurement, and SCORE2/SCORE2-OP[c] or equivalent is recommended[19] before starting fluoropyrimidines.	I	C
A baseline echocardiogram is recommended in patients with a history of symptomatic CVD before starting fluoropyrimidines.	I	C
Screening for CAD[d] may be considered in patients at high and very high risk of CAD[c] before fluoropyrimidines.	IIb	C

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BP, blood pressure; CAD, coronary artery disease; CV, cardiovascular; CVD, cardiovascular disease; ECG, electrocardiogram; HbA1c, glycated haemoglobin; SCORE2, Systematic Coronary Risk Estimation 2; SCORE2-OP, Systematic Coronary Risk Estimation 2—Older Persons.
[a]Class of recommendation.
[b]Level of evidence.
[c]SCORE2 (<70 years) or SCORE2-OP (≥70 years) CV risk stratification: <50 years: low risk <2.5%, moderate risk 2.5% to <7.5%, high risk ≥7.5%; 50–69 years: low risk <5%; moderate risk 5% to <10%; high risk ≥10%; ≥70 years: low risk <7.5%, moderate risk 7.5% to <15%, high risk ≥15%.
[d]According to pre-existing CVD and local protocols.[23,24]

Lyon et al, EHJ, 2022

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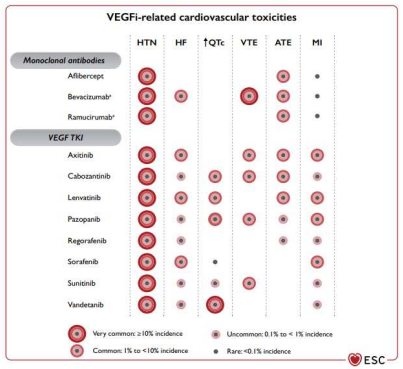
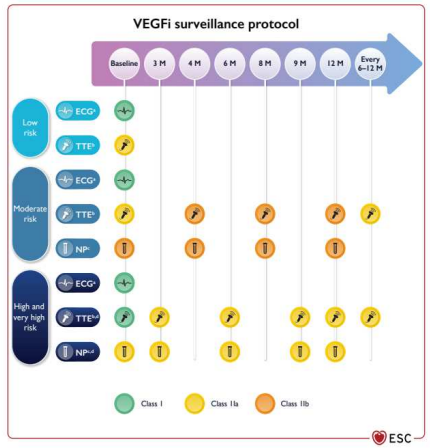
VEGF HÄMMARE





Lyon et al, EHJ, 2022

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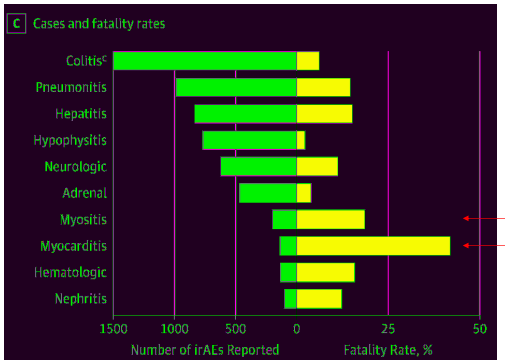
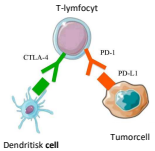
ICI-myocarditer är ovanliga 0,5-2% men inte sällan fatala





Overlap syndrome
- ICI myocarditis
- myosit
- myastenia gravis

Ref: Lipe et al,: Am J Emergency Med 2021

Wang et al. Fatal toxic effects associated with immune checkpoint inhibitors. JAMA Oncology 2018. Dec 1; 4(12):1721-1728

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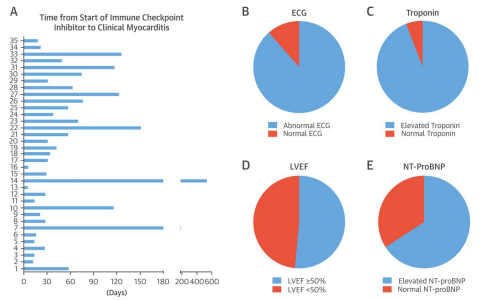
Heterogen klinisk presentation



Riskfaktorer oklart:
Tidigare autoimmunsjd? DM?
Tidigare hjärtsjukdom?
Kombination med andra ICI dubblerar risken
Samtidig myosit är vanligt

.

Biomarkörer
Troponin
NT proBNP

Alla symptom och fynd: Dyspné, takykardi, ödem, palpitationer, myalgi, syncope, yrsel, Trötthet, bröstsmärta, arytmier (VT, FFI, retledningshinder), Troponin, NT proBNP

Mahmood et al. Myocarditis in Patients Treated With Immune Checkpoint Inhibitors (J Am Coll Cardiol 2018;71:1755–64)

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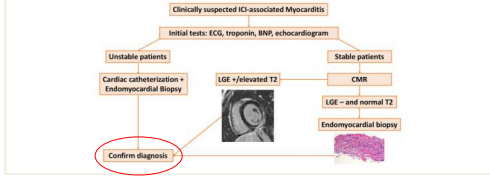
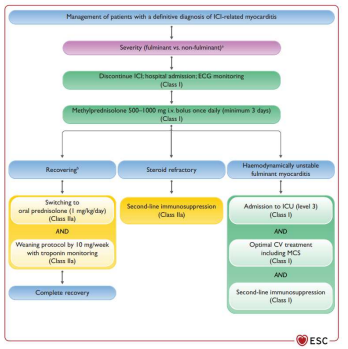


- Bekräfta diagnos!
- Tidig MR
- PET-CT?
- **Biopsi om neg**



- Höga doser cortison
- Vid påverkad hjärtfunktioneller behandlingsrefraktär patient
- Andra linjes immunsuppression, TNF α blockad; IL6
- Abatacept/ ruxolitinib
- Mykofenolatmofetil
- plasmaferes

Zhang L et al. Cardiovascular magnetic resonance in immune checkpointinhibitor- associated myocarditis. EHJ (2020), 41, 1733-1743
Zhang L et al. Cardiotoxicity of Immune Checkpoint Inhibitors Curr Treatment options Cardio Med (2019) 21-32

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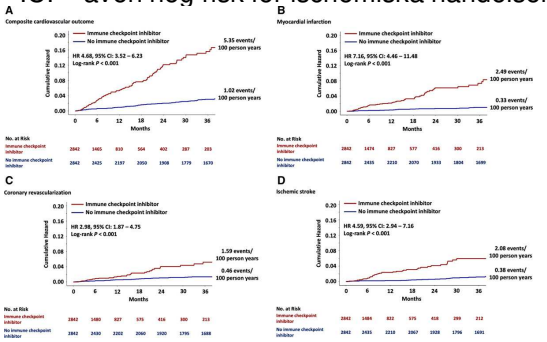
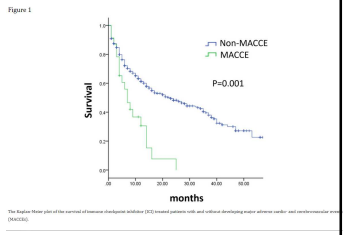
ICI – även hög risk för ischemiska händelser





580 patients
MACCE incidence 3.9 %
3 y follow up

Drobni et al. Circulation 2020
3000 + 3000

Wu et al. Acta Cardiol Sin. 2022

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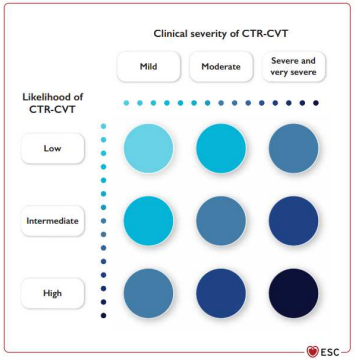
Take home message

- Adekvat cancerbehandling förlänger livet.
- Många cancerbehandlingar kan påverka den kardiovaskulära hälsan under eller efterbehandlingen, vilket i allvarliga fall kan leda till att behandlingen behöver avbrytas.
- En kardiovaskulär riskvärdering där både patient- och behandlingsrelaterade faktorer ingår bör göras före varje cancerbehandling.
- Patienter med hög risk för kardiotoxicitet bör bedömas och optimeras avseende hjärt- och kärlsjukdom för att minska risken för kardiotoxicitet och för att förbättra utfall både för cancern och hjärtsjukdomen = längre liv.



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PROGRAM - Torsdag 25 januari 2024 Clarion hotel Sign	
08.30-09.15	Registrering + fika (ingår)
09.15-09.30	Styrelsen hälsar välkommen
09.30-11.30	**PAH – vadå? En föreläsning från grunden** Göran Rådegran och Anna Werther Evaldsson (Skånes universitetes-sjukhus, Lund)
11.30-12.30	Lunch (ingår)
12.30-12.35	AZ
12.35-14.30	**DT-kranskärl** Kari Feldt (Karolinska universitetssjukhuset, Stockholm)
14.30-15.00	Fika (ingår)
15.00-17.00	**Biokemi för kardiologer** Ola Hammarsten (Sahlgrenska universitetssjukhuset, Göteborg)
17.00-17.05	**Årets handledare**
17.05-17.20	**Quiz**
18.00-	Kursmiddag (ingår)

PROGRAM - Fredag 26 januari, 2024 Clarion hotel Sign	
08.15-10.15	**Ärftliga arytmisjudomar – diagnos och handläggning** Kristina Haugaa (Karolinska universitetssjukhuset, Stockholm)
10.15-10.45	Fika (ingår)
10.45-12.45	**Kardio-onkologi – Vad varje kardiolog måste veta** Agneta Månsson Broberg (Karolinska universitetssjukhuset, Stock-holm)
12.45-13.45	Lunch (ingår)
14.00-14.05	Pfizer
14.05-15.05	**Specifika lagar och regler vid hjärtsjukdom** Sofia Kjellberg Lindgren, Transportstyrelsen
15.05-15.30	**Quiz, utvärdering och avslut**