Cas clinique
Un patient diabétique coronarien

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Paris France

Cas Clinique

- Mme Z. âgée de 62 ans est suivie depuis 8 ans pour un diabète de type 2

- **Facteurs de risque cardiovasculaires :**
  - HTA traitée par Olmesartan and Hydrochlorothiazide.
  - Tabagisme actif (30 PA).
  - Diabète de type 2 (HbA1C 7.9%) traité par Metformine.

Signes fonctionnels

La patiente se plaint uniquement d'une dyspnée d'effort modérée sans précordialgies.

L'état général est bon sans arguments en faveur d'une rétinopathie diabétique(FO normal)

Examen clinique:

-Poids 70 kg Taille 165 cm

-Fréquence cardiaque: 74/mn

- Pression artérielle : 154/106 couché, 152/102 debout

-Bruits du coeur : normaux

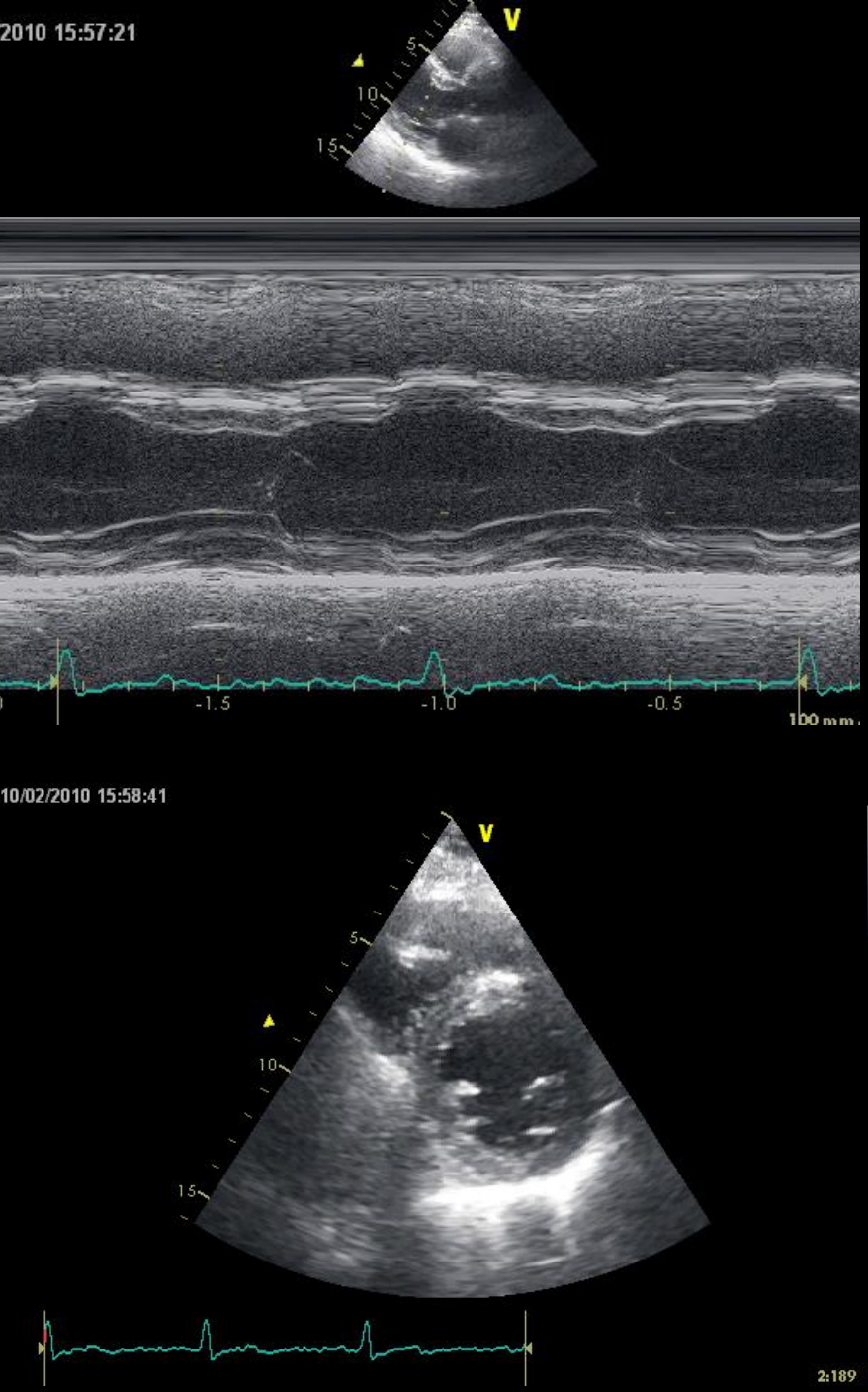
-ECG: Rythme sinusal, Index de Sokolow=31 mm, pas de trouble de repolarisation.

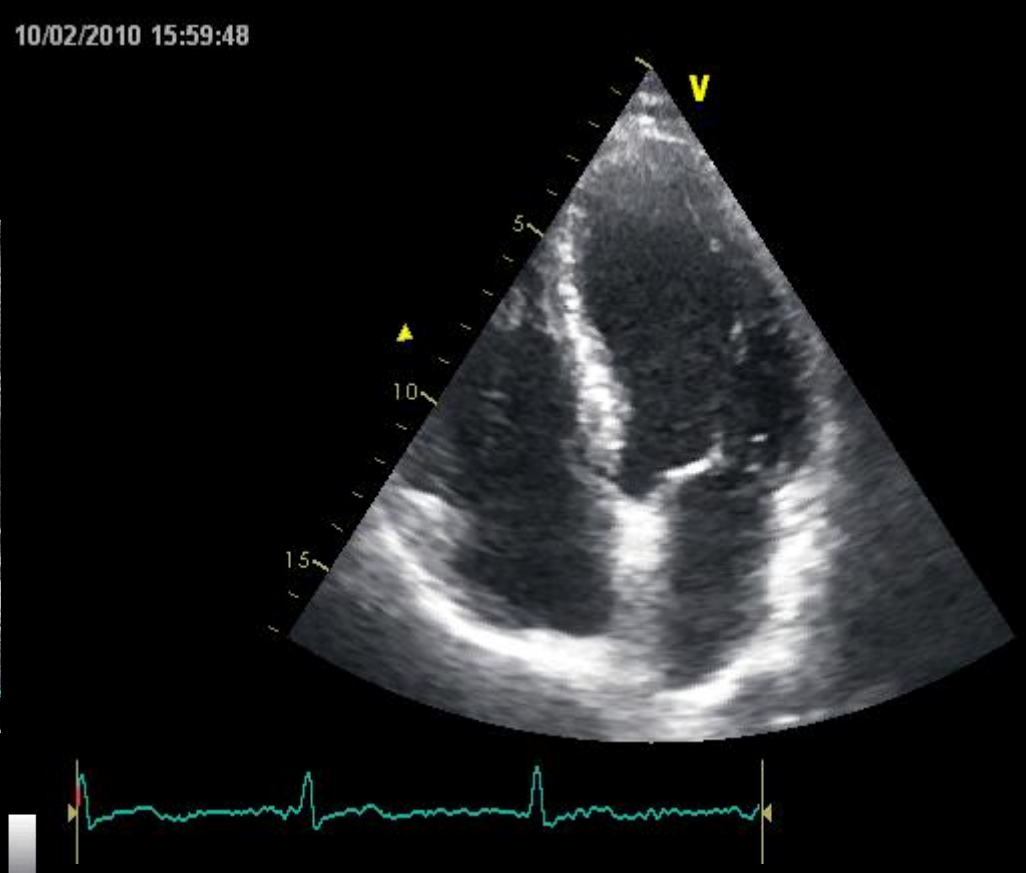
-Présence d’une microalbuminurie 85 mg/l

Questions

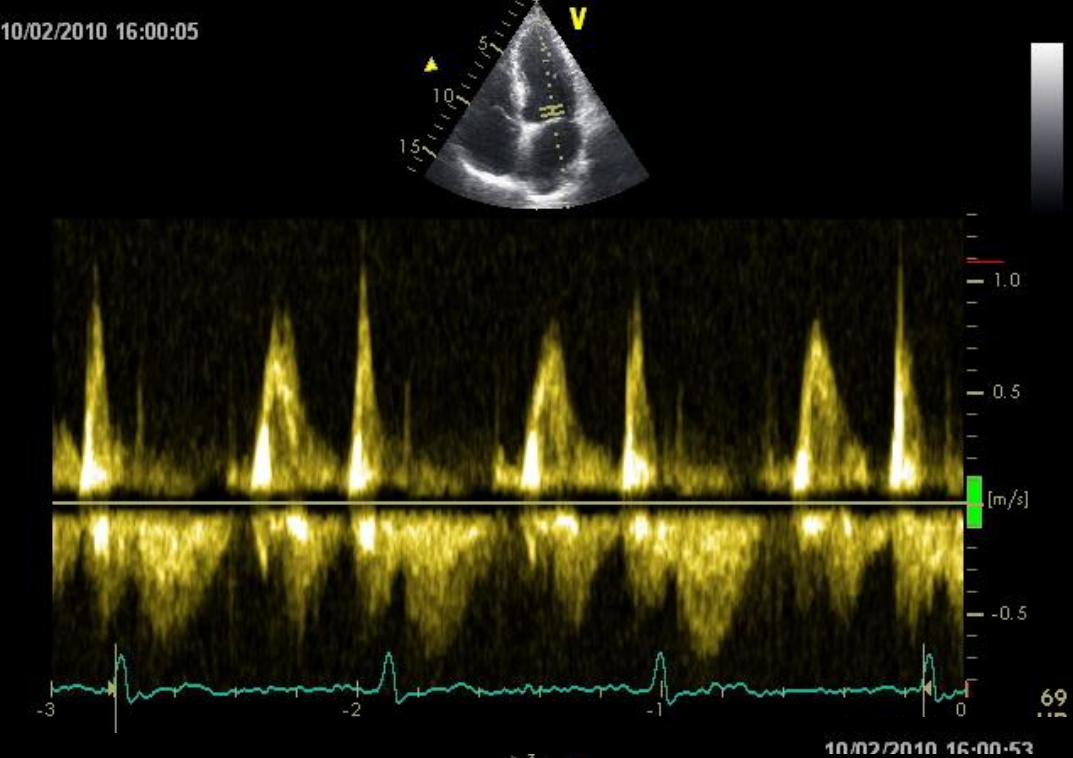
- Quels examens complémentaires jugez -vous utiles ?

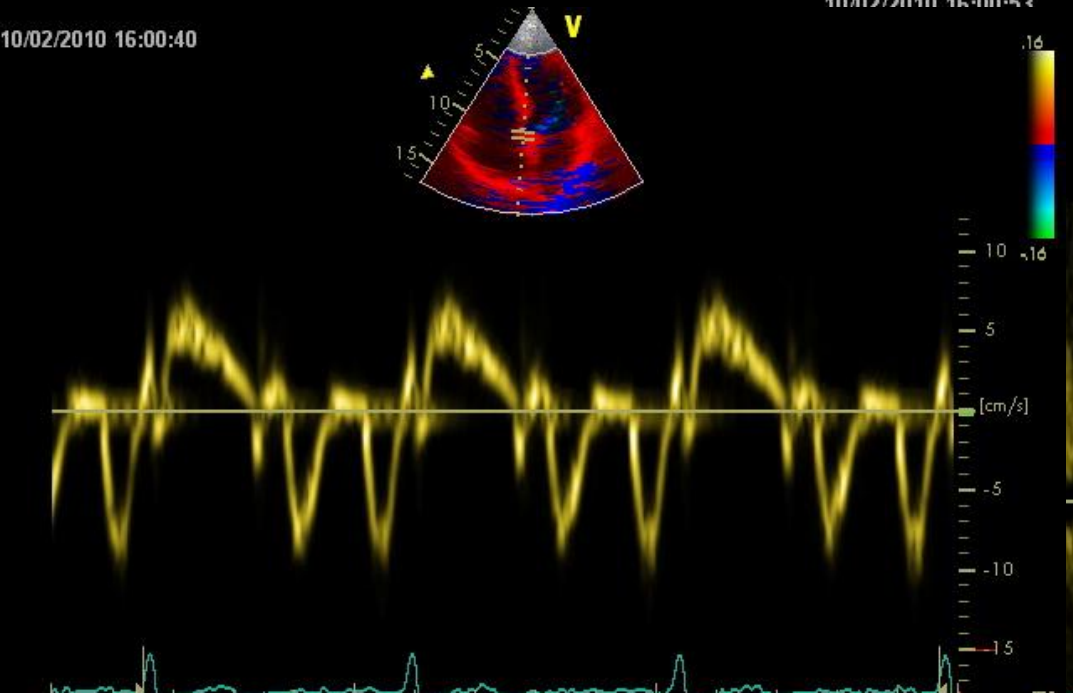
- Créatinine : 14mg/l
- NA +: 141 meq/l K+ 4.2 meq/l
- Doppler cervical : plaques non sténosantes des deux carotides
- Doppler MI: plaques non sténosantes des deux fémorales superficielles. Aorte abdominale: minimes calcifications

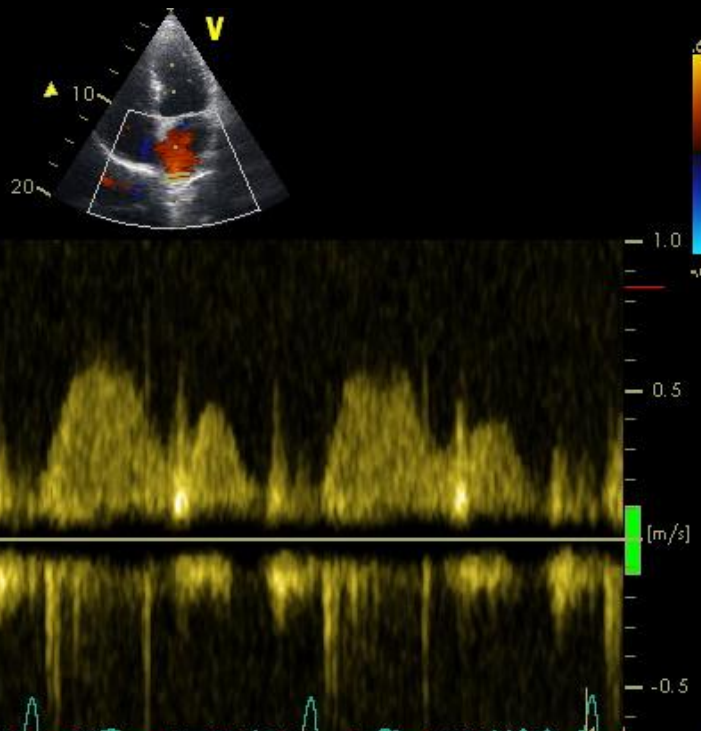




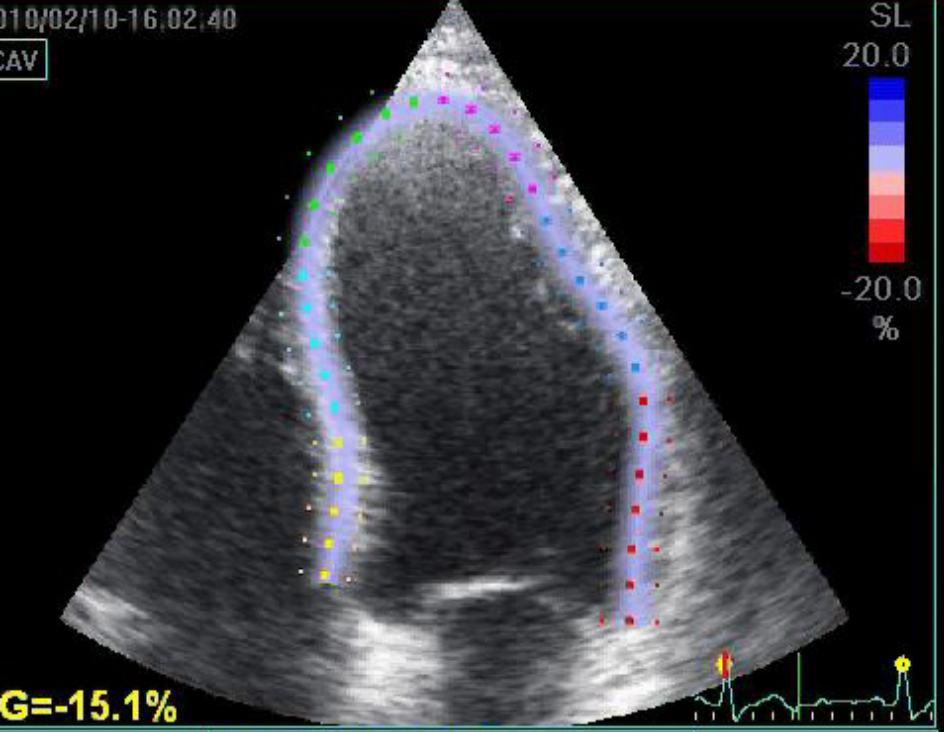
DTDVG : 49 mm
DTSVG : 29 mm
IMVG : 85 g/m²
FEVG: 65 %
Aire OG : 18 cm²

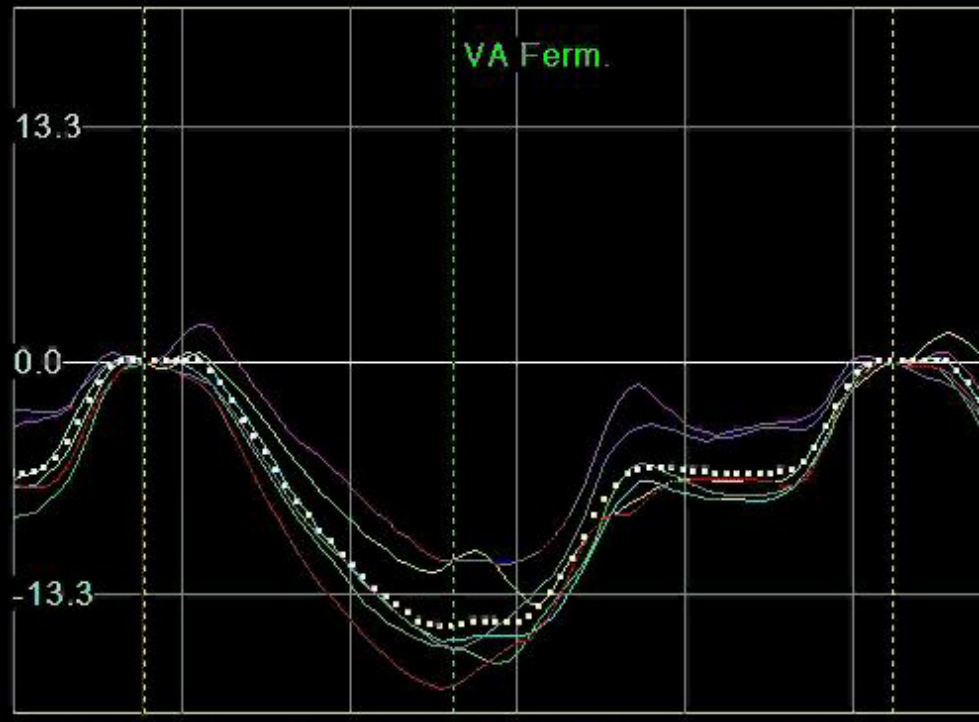


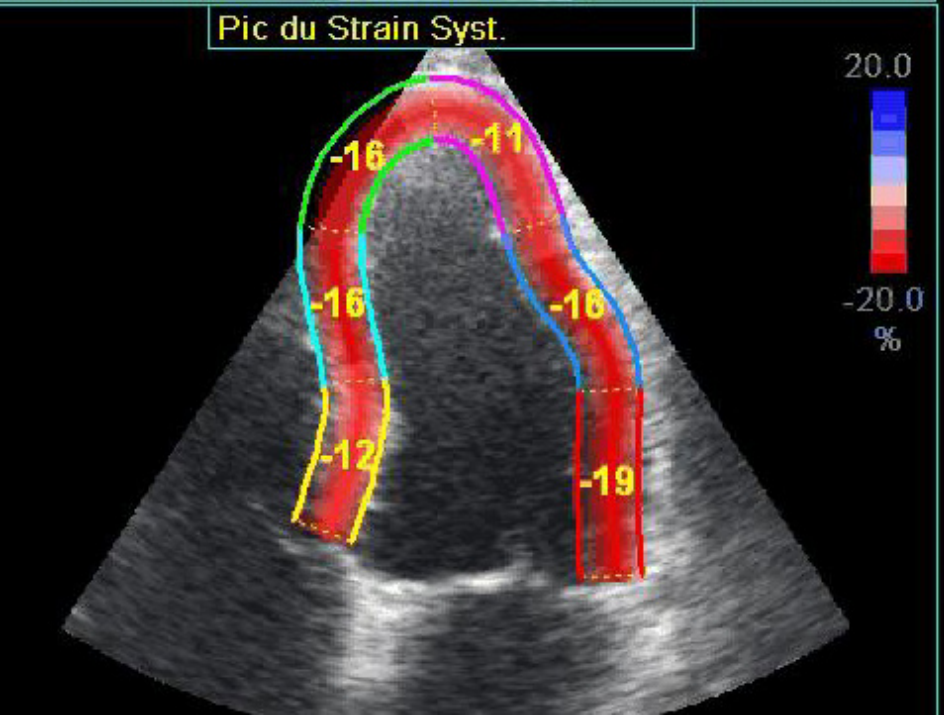


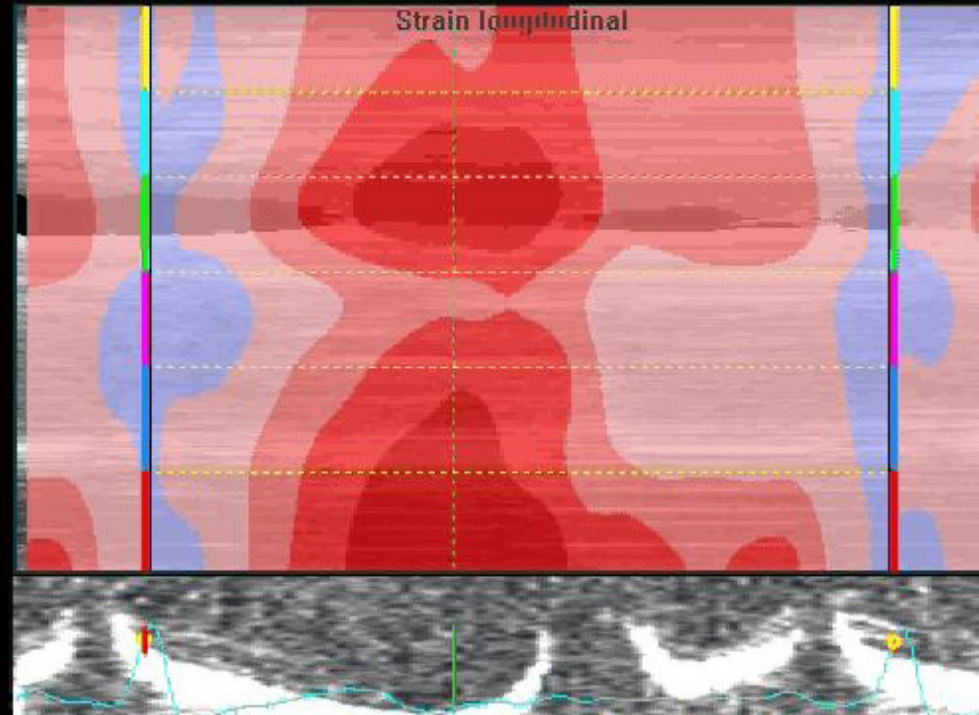


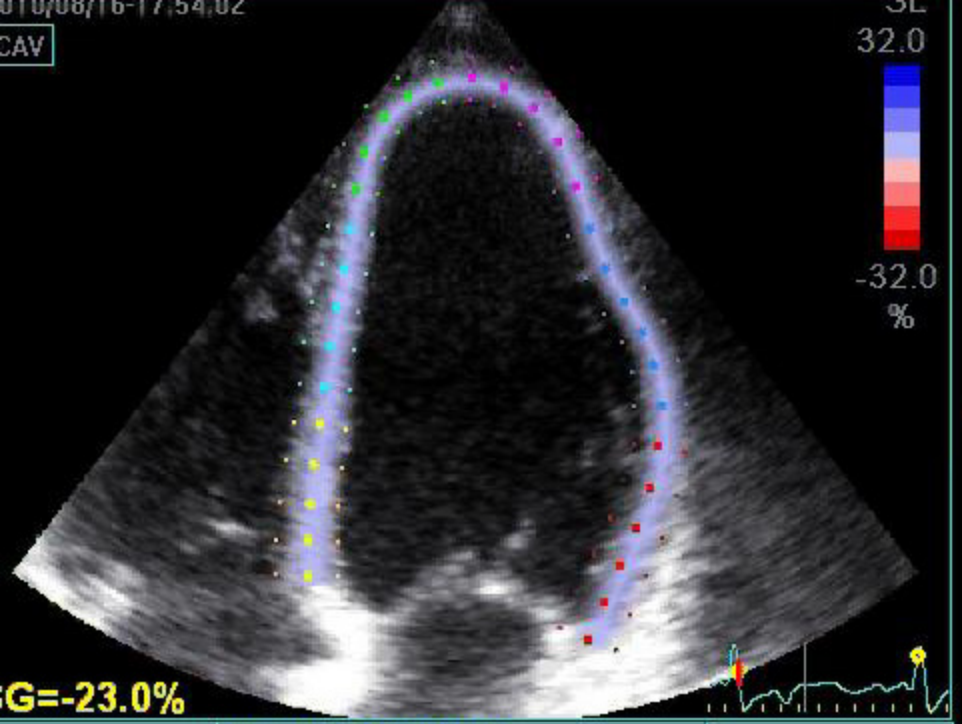
E/A : 0.9
mDT : 190 ms
IVRT : 82 ms
E/e´ : 10
PAPs: 25 mmHg

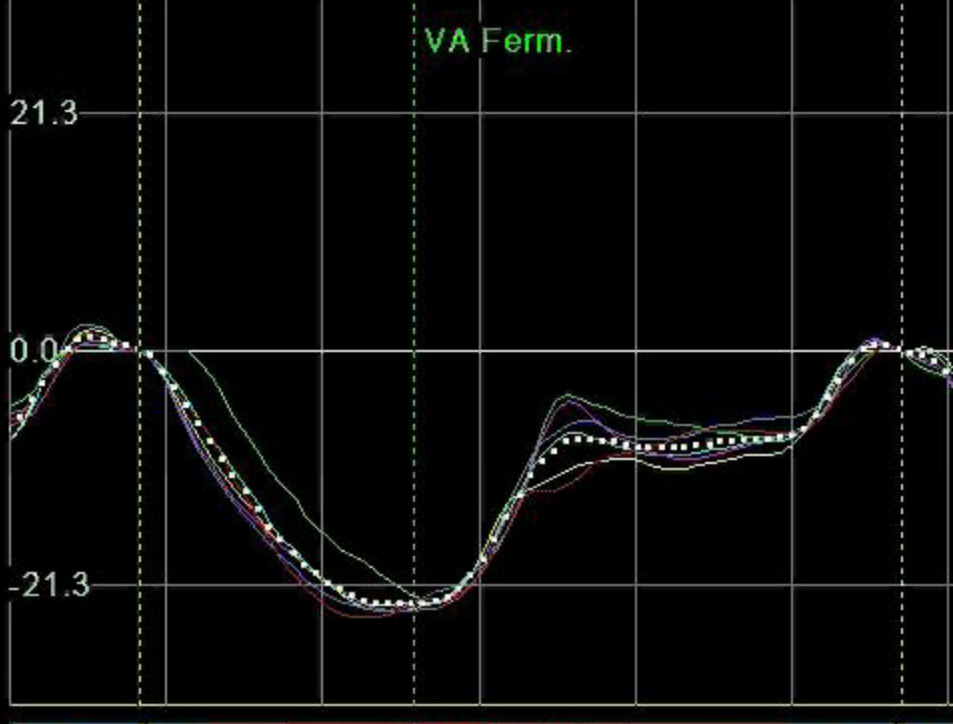

010/02/10-16:02:40
CAV
SL
20.0
-20.0
%
G=-15.1%

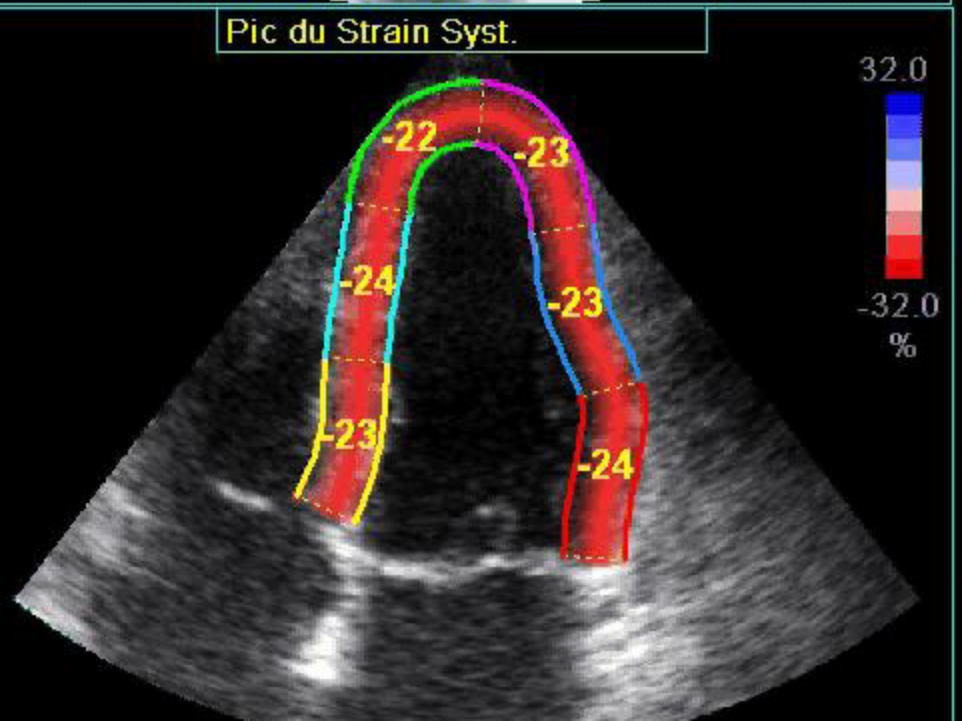

VA Ferm.
13.3
0.0
-13.3

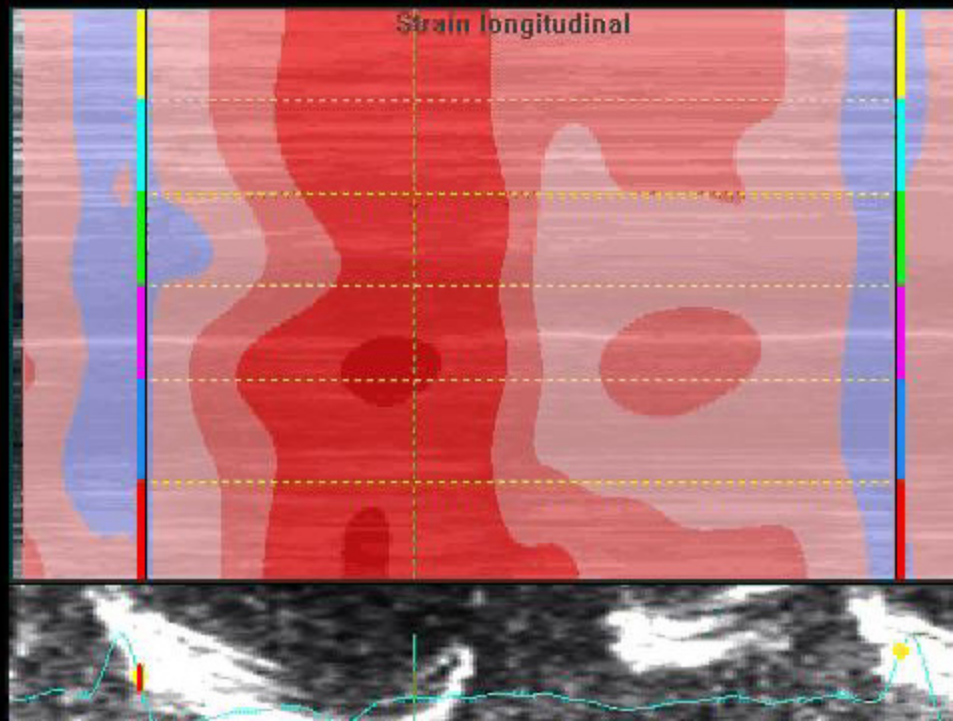

Pic du Strain Syst.
20.0
-20.0
%
-16
-11
-16
-16
-12
-19


Strain longitudinal


CAV
32.0
-32.0
%
G=-23.0%

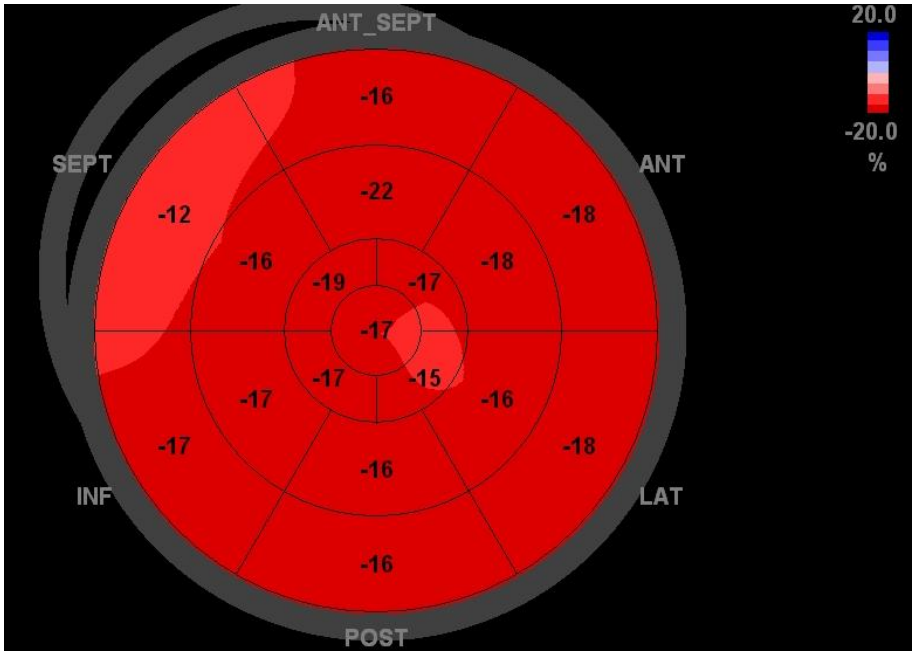

VA Ferm.
21.3
0.0
-21.3


Pic du Strain Syst.
32.0
-32.0
%
-22
-23
-24
-23
-23
-24

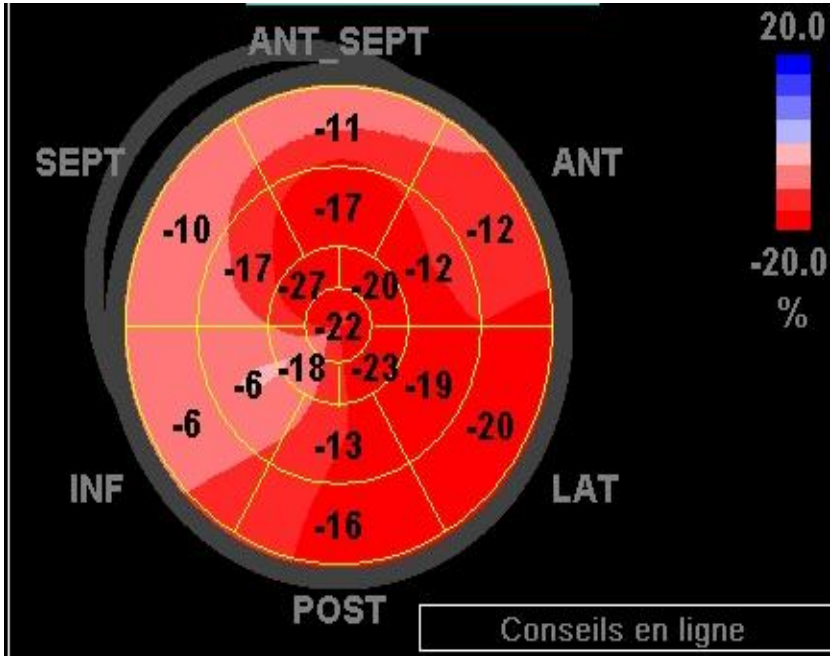

Strain longitudinal

Echocardiographie d'effort

- 80 watts
- Troubles de cinétique segmentaire

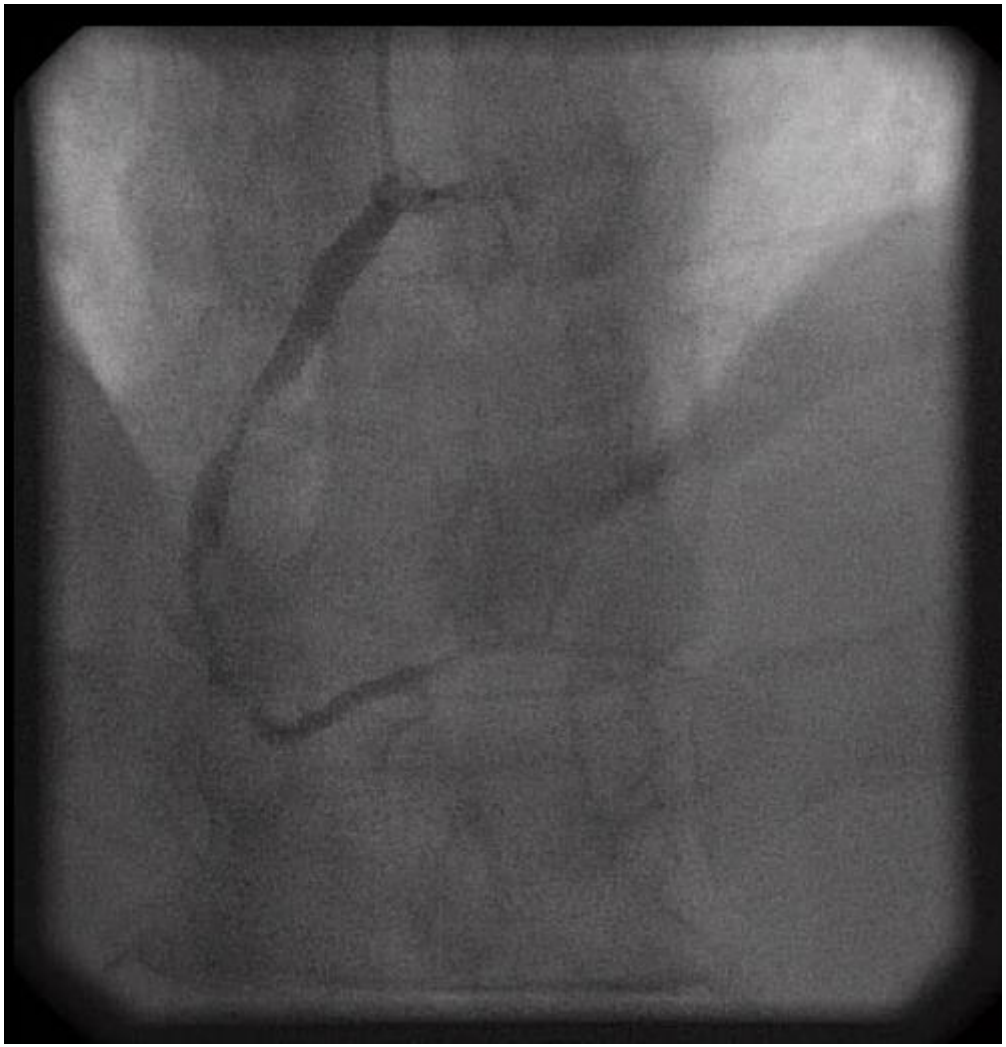


BASE

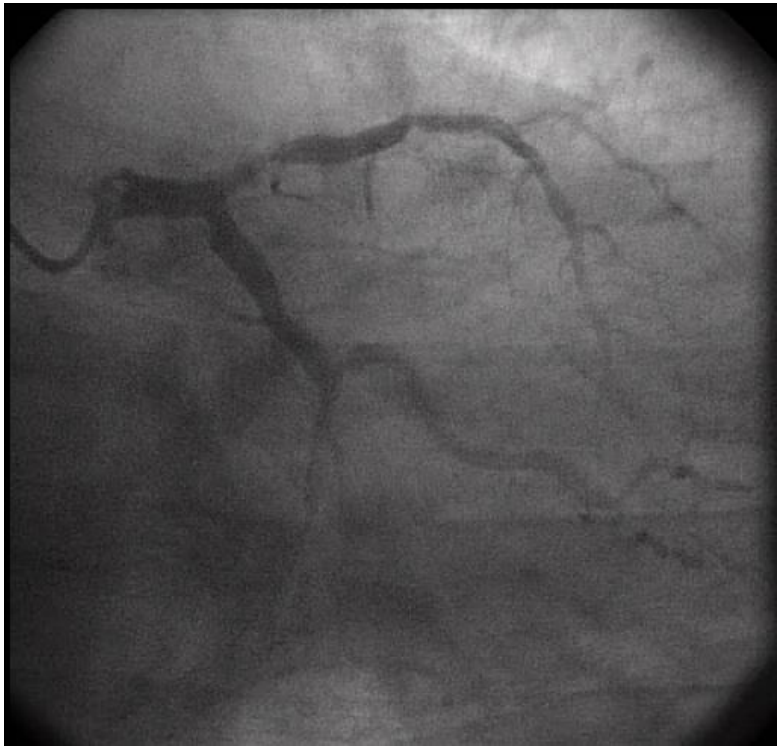


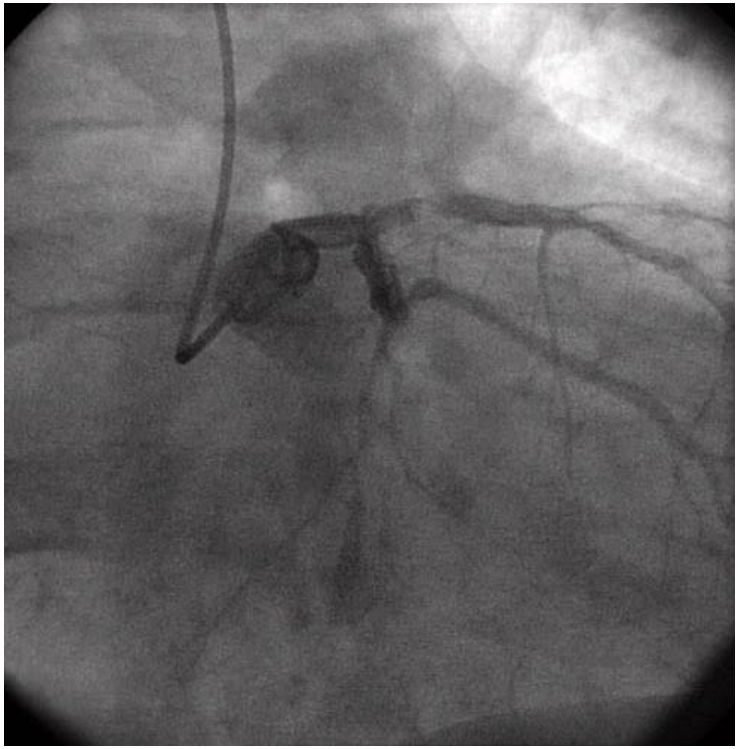
PIC

Coronarographie



Coronarographie





SYNTAX score 33.5
EUROSCORE à 7

Questions

- Quel traitement envisagez-vous?

ESC GUIDELINES ON DIABETES AND CARDIOVASCULAR DISEASES

Pr. Michel KOMAJDA

Institute of Cardiology - IHU ICAN

Pitie Salpetriere Hospital - University Pierre and Marie Curie, Paris (France)

DEFINITION

A metabolic disorder characterized by chronic hyper glycaemia resulting from defects in insulin secretion or action or both.

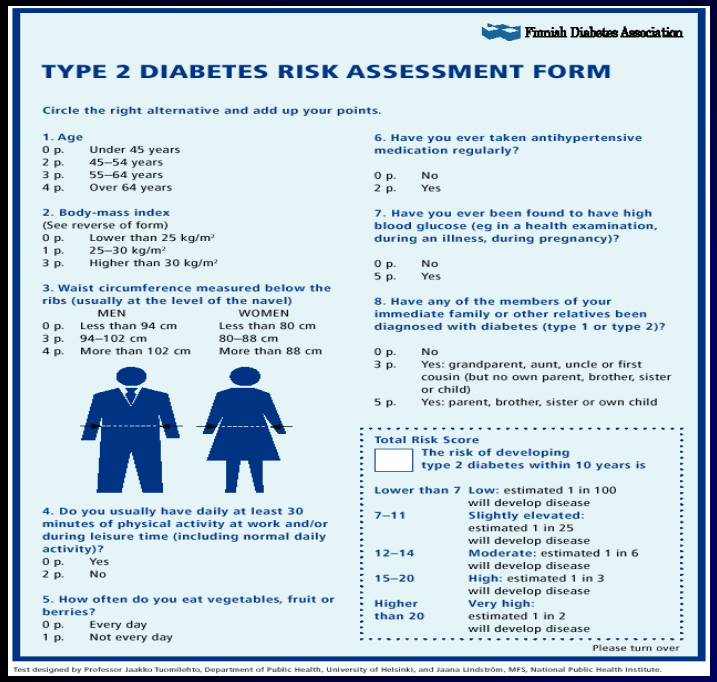
- Fasting plasma glucose ≥ 7 mmol/l

- HbA1C ≥ 6.5%

-On two consecutive measures

- 2 hour post load plasma glucose ≥ 11.1 mmol/l

Screening methods for disorders of glucose metabolism



Finnish Diabetes Association

TYPE 2 DIABETES RISK ASSESSMENT FORM

Circle the right alternative and add up your points.

1. Age
0 p. Under 45 years
2 p. 45–54 years
3 p. 55–64 years
4 p. Over 64 years

2. Body-mass index
(See reverse of form)
0 p. Lower than 25 kg/m²
1 p. 25–30 kg/m²
3 p. Higher than 30 kg/m²

3. Waist circumference measured below the ribs (usually at the level of the navel)

	MEN	WOMEN
0 p.	Less than 94 cm	Less than 80 cm
3 p.	94–102 cm	80–88 cm
4 p.	More than 102 cm	More than 88 cm

4. Do you usually have daily at least 30 minutes of physical activity at work and/or during leisure time (including normal daily activity)?
0 p. Yes
2 p. No

5. How often do you eat vegetables, fruit or berries?
0 p. Every day
1 p. Not every day

6. Have you ever taken antihypertensive medication regularly?
0 p. No
2 p. Yes

7. Have you ever been found to have high blood glucose (eg in a health examination, during an illness, during pregnancy)?
0 p. No
5 p. Yes

8. Have any of the members of your immediate family or other relatives been diagnosed with diabetes (type 1 or type 2)?
0 p. No
3 p. Yes: grandparent, aunt, uncle or first cousin (but no own parent, brother, sister or child)
5 p. Yes: parent, brother, sister or own child

Total Risk Score ☐ **The risk of developing type 2 diabetes within 10 years is**

Lower than 7	**Low:** estimated 1 in 100 will develop disease
7–11	**Slightly elevated:** estimated 1 in 25 will develop disease
12–14	**Moderate:** estimated 1 in 6 will develop disease
15–20	**High:** estimated 1 in 3 will develop disease
Higher than 20	**Very high:** estimated 1 in 2 will develop disease

Please turn over

Test designed by Professor Jaakko Tuomilehto, Department of Public Health, University of Helsinki, and Jaana Lindström, MFS, National Public Health Institute.

Questionnaire:
Diabetes Risk Score

- Random glucose
  + symptoms
- Fasting glucose
- HbA1c

Oral glucose tolerance test

75 g glucose in 200 ml H_2O
at 0 and after 120 minutes

Diagnostic criteria of diabetes and other disorders of glucose metabolism

Diagnostic Tool	Criteria according to WHO	Criteria according to ADA
Diabetes		
HbA_{1c}	**Can be used** If measured ≥6.5% (48 mmol/mol)	**Recommended** ≥6.5% (48 mmol/mol)
	Recommended	
FPG	≥7.0 mmol/L (≥126 mg/dl)	≥7.0 mmol/L (≥126 mg/dl)
	or	**or**
2hPG*	≥11.1 mmol/L (≥200 mg/dl)	≥11.1 mmol/L (≥200 mg/dl)
IGT		
FPG	<7.0 mmol/L (<126 mg/dl)	<7.0 mmol/L (<126 mg/dl)
		Not required
2hPG*	≥7.8 – <11.1 mmol/L (≥140 – <200 mg/dl)	If measured 7.8 – 11.0 mmol/L (140 – 198 mg/dl)
IFG		
FPG	6.1-6.9 mmol/L (110 – 125 mg/dl)	5.6 – 6.9 mmol/L (100 – 125 mg/dl)
2hPG*	**If measured** <7.8 mmol/L (<140 mg/dl)	--

Recommendations for diagnosis of disorders of glucose metabolism

Recommendations	Class[a]	Level[b]
It is recommended that the diagnosis of diabetes is based on HbA_{1C} and FPG combined or on an OGTT is still in doubt.	I	B
It is recommended that an OGTT is used for diagnosing IGT.	I	B
It is recommended that screening for potential T2DM in people with CVD is initiated with HbA_{1C} and FPG and that an OGTT is added in people if HbA_{1C} and FPG are inconclusive.	I	A
Special attention should be considered to the application of preventive measures in women with disorders of glucose metabolism.	IIa	C
It is recommended that people at high risk for T2DM receive appropriate lifestyle counselling to reduce their risk of developing DM.	I	A

Cardiovascular risk assessment

- DM = high cardiovascular risk

- DM + one other risk factor / organ damage = very high risk.

ESC Guidelines, CV Prevention, 2012

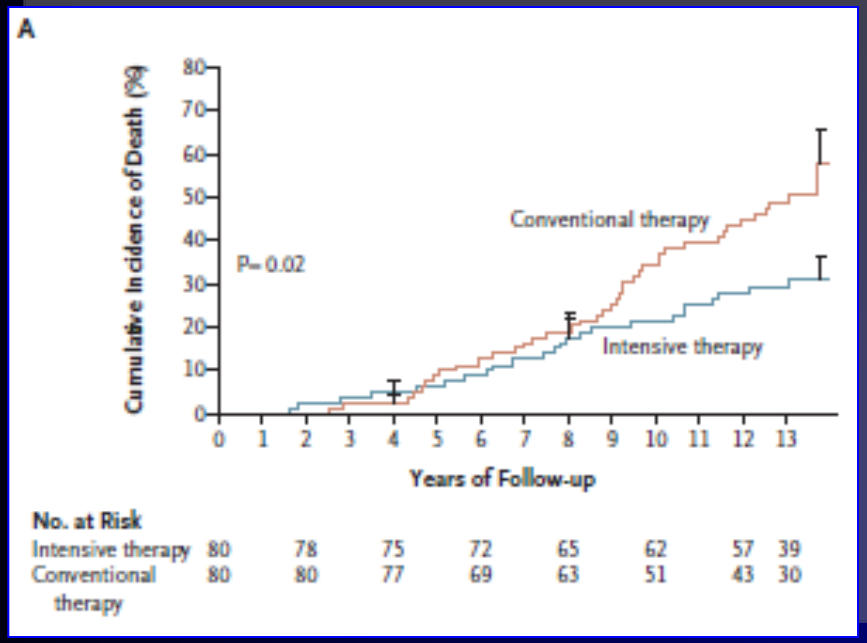
Risk Assessment

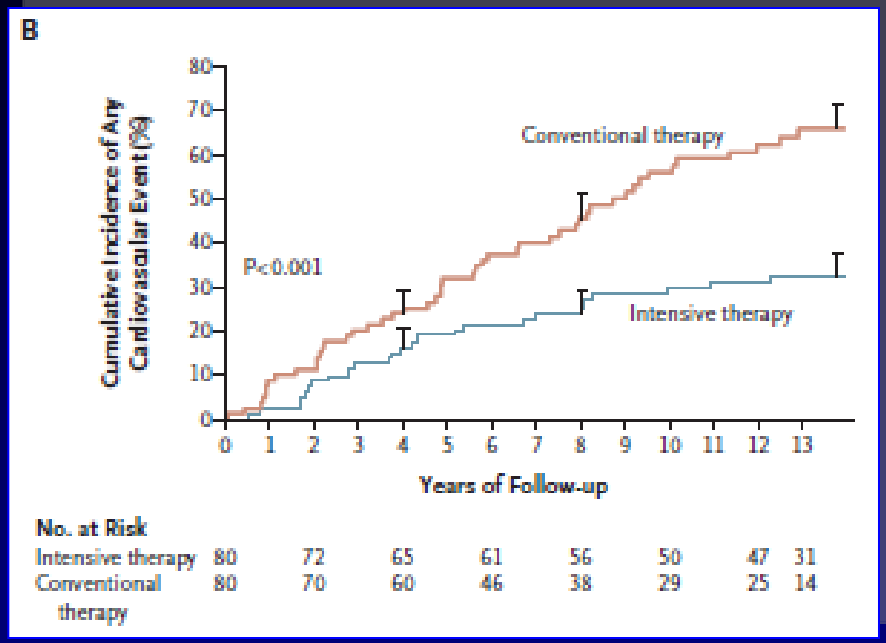
- Classical risk factors (smoking, BP, lipids, lifestyle, family history)
- Glycaemic status
- Macro vascular disease (coronary / cerebrovascular / HF / PAD)
- Micro vascular disease (retinopathy / nephropathy / neuropathy)
- Arrhythmias

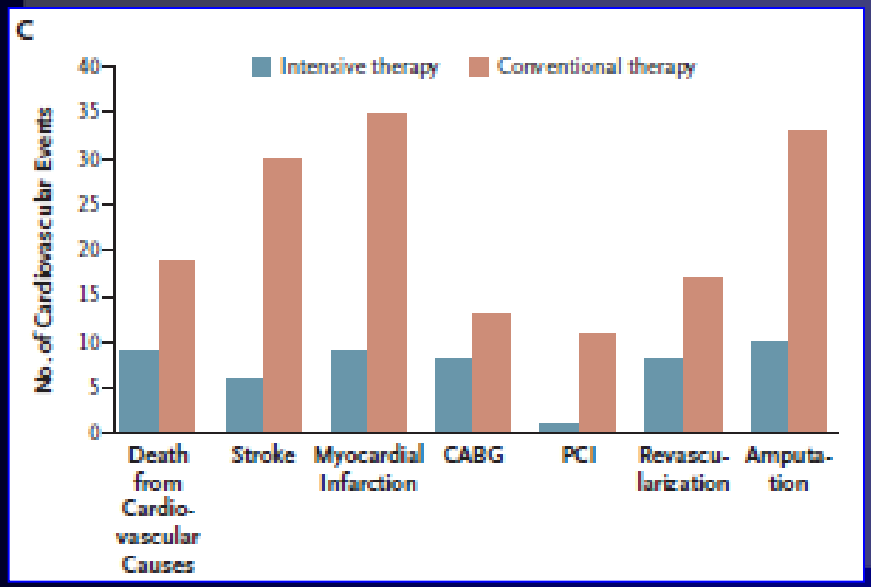
Multifactorial management of CV risk

- Patient education and empowerment
- Life style advice
- Smoking cessation
- Personalised treatment of blood pressure, lipids, glycemic control and thrombotic risk.

Steno-2







Gaede P et al., N Engl J Med, 2008;358:580-91

Life style intervention

- Daily consumption of vegetable and fruits
- Increased dietary fibre intake
- Moderate intake of simple carbohydrates
- Reduced total dietary fat intake
- Replacement of saturated fat by mono-unsaturated / poly-unsaturated
- Physical activity $\geq$ 30 mn / day, 150 mn / week
- Weight reduction $\geq$ 5% if BMI $\geq$ 25 kg/m^2

Glucose Control : glycaemic control in diabetes

Recommendations	Class[a]	Level[b]
It is recommended that glucose lowering is instituted in an **individualized manner**, taking duration of DM, co-morbidities and age into account.	I	C
It is recommended to apply right glucose control, targeting a near-normal HbA_{1C} (<7.0% or <53 mmol/mol) to decrease microvascular complications in TIDM and T2DM.	I	A
A HbA_{1C} target of ≤7.0% (≤53 mmol/mol) should be considered for the prevention of CVD in T1 and T2DM.	IIa	C
Basal bolus insulin regimen, combined with frequent glucose monitoring, is recommended for optimizing glucose control in TIDM.	I	A
Metformin should be considered as first-line therapy in subjects with T2DM following evaluation of renal function.	IIa	B

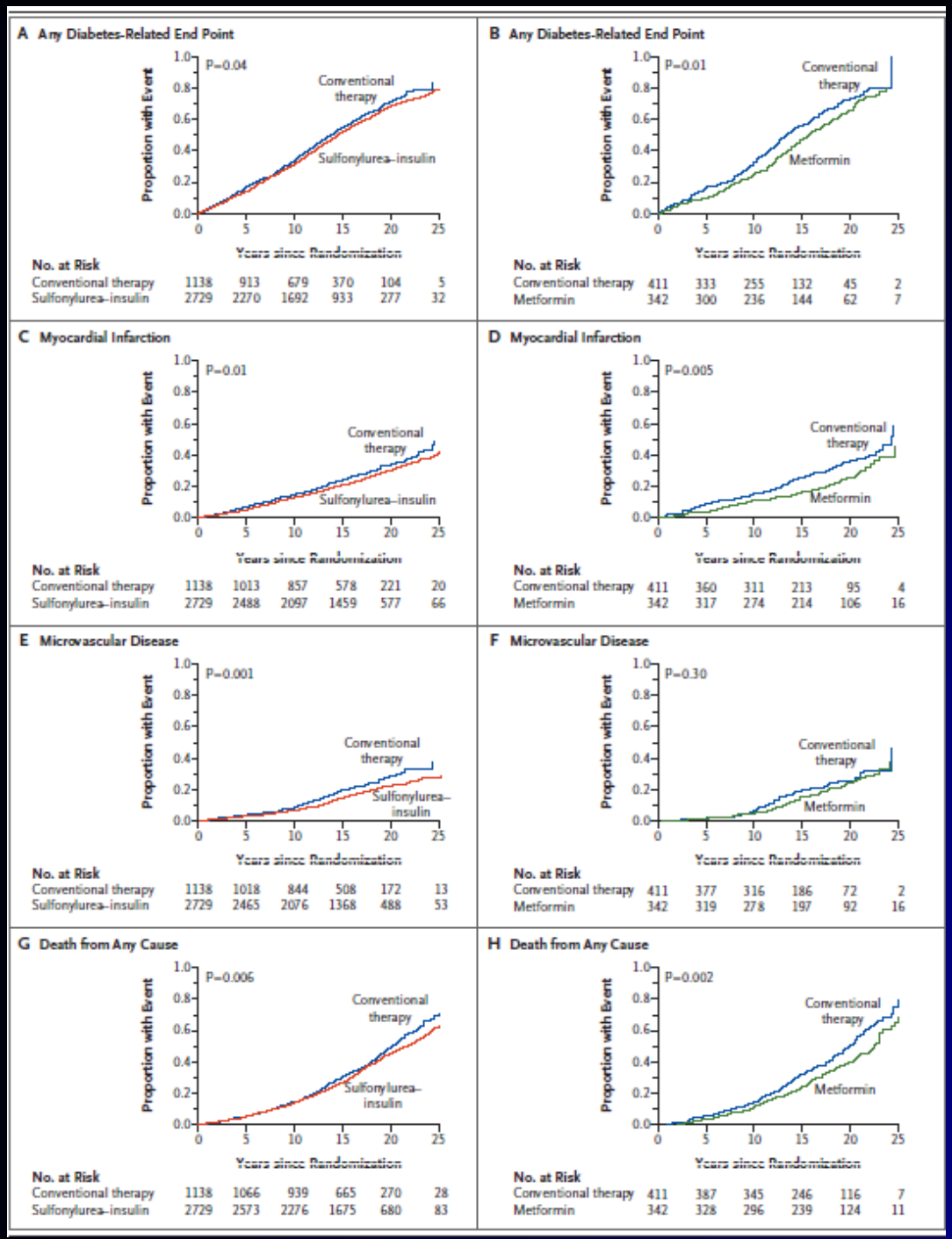
Pharmacological treatment options for T2DM

Drug class	Effect	Weight change	Hypoglycaemia (monotherapy)	Comments
Metformin	Insulin sensitizer	Neutral/loss	No	Gastrointestinal side-effects, lactic acidosis, B_{12} deficiency. Contraindications, low eGFR, hypoxia, dehydration
Sulphonylurea	Insulin provider	Increase	Yes	Allergy. Risk for hypoglycaemia and weight gain.
Meglitinides	Insulin provider	Increase	Yes	Frequent dosing. Risk for hypoglycaemia.
Alfa-glucosidase inhibitor	Glucose absorption inhibitor	Neutral	No	Gastrointestinal side-effects. Frequent dosing
Pioglitazone	Insulin sensitiser	Increase	No	Heart failure, oedema, fractures, urinary bladder, cancer (?)
GLP-I agonist	Insulin provider	Decrease	No	Gastrointestinal side-effects. Pancreatitis. Injectable
DPP-4 inhibitor	Insulin provider	Neutral	No	Pancreatitis
Insulin	Insulin provider	Increase	Yes	Injectable. Risk for hypoglycaemia and weight gain.
SGLT2 inhibitors	Blocks renal glucose absorption in the proximal tubuli.	Decrease	No	Urinary tract infections.

eGFR = estimated glomerular filtration rate ; GLP-I = glucagon-like peptide I; DDP = Diabetes Prevention Program ; SGLT2 = sodium glucose co-transporter 2.

Cardiovascular safety of glucose lowering agents

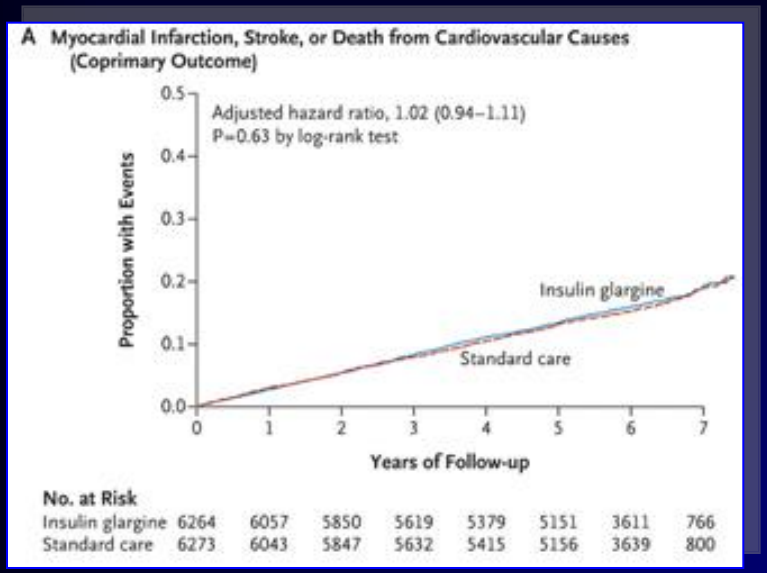
METFORMIN	? +
SULPHONYLUREA	?
INSULIN	? + (ORIGIN)
PIOGLITAZONE	+ (PRO ACTIVE) - HF
GLINIDES	=
GLP1 AGONISTS	?
DPP4 Inhibitors	+ (SAVOR – EXAMINE HF ?
Na – Glucose Co Transporter 2 (SGLT-2) inhibitors	?

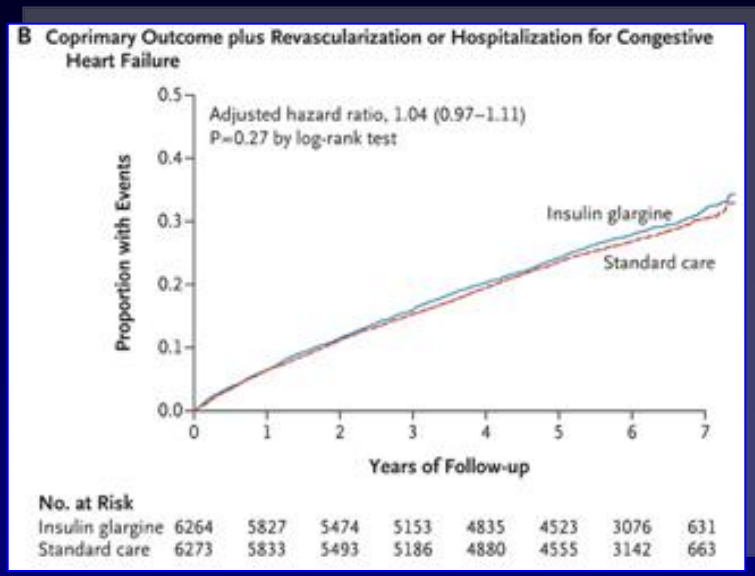


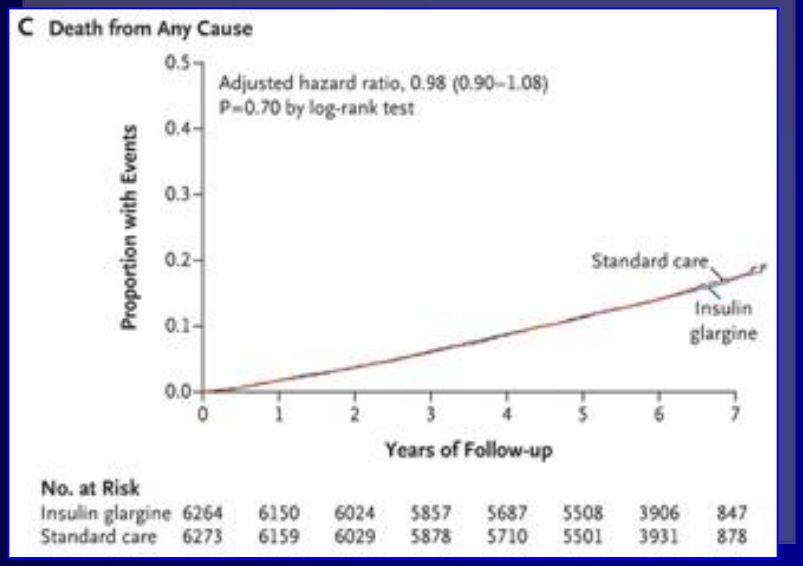
UKPDS

Holman RR et al, N Engl J Med 2008;359:1577-1589

ORIGIN







N Engl J Med, 2012 Jul 26;367(4):319-28

Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus (SAVOR) – TIMI 53

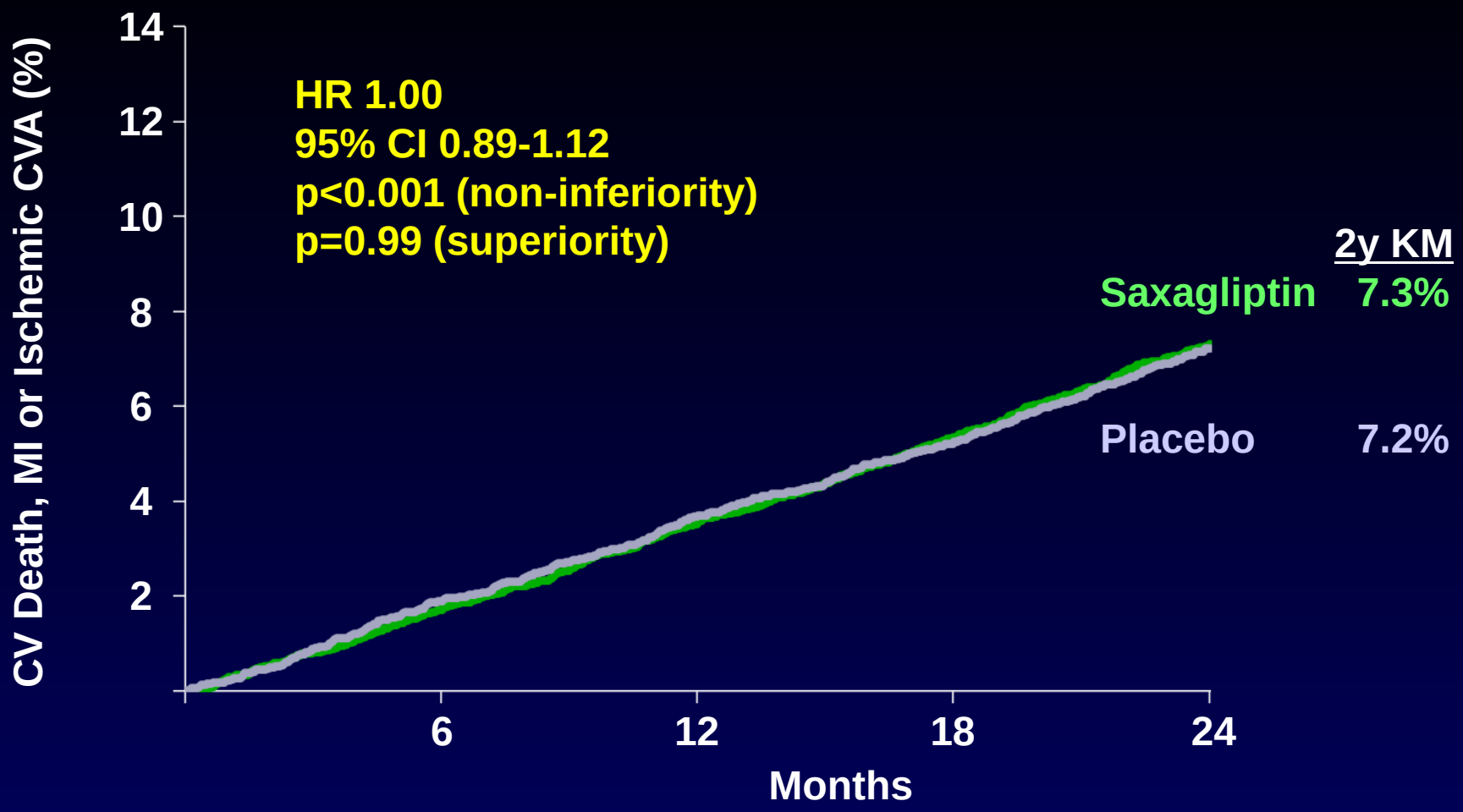
Deepak L. Bhatt, MD, MPH
On behalf of the SAVOR-TIMI 53 Steering Committee and Investigators

European Society of Cardiology

Amsterdam - September 2, 2013

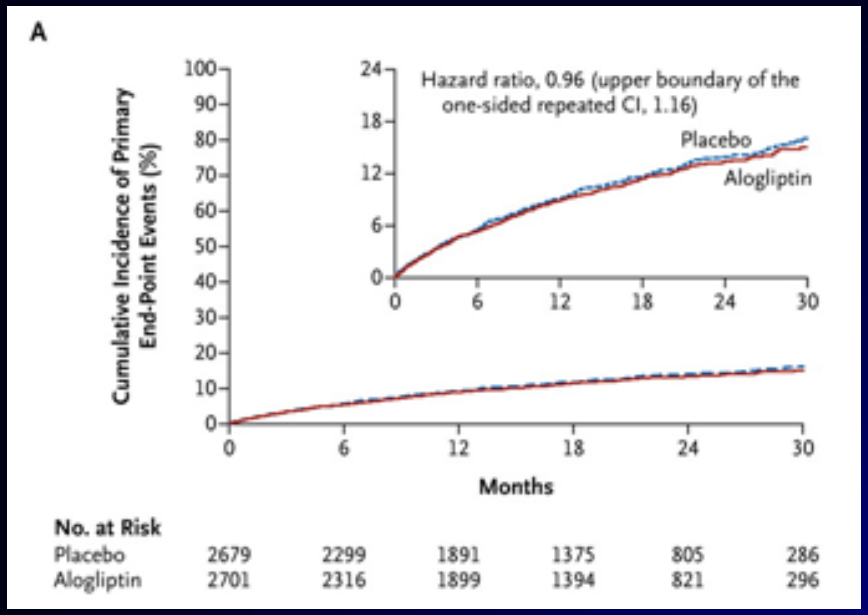
NCT01107886; Funded by AstraZeneca and Bristol-Myers Squibb

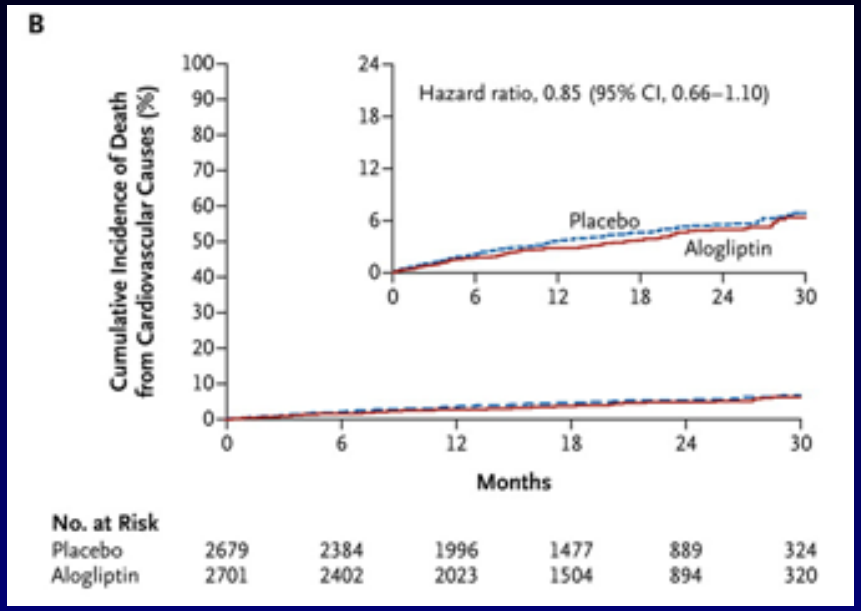
Primary Endpoint

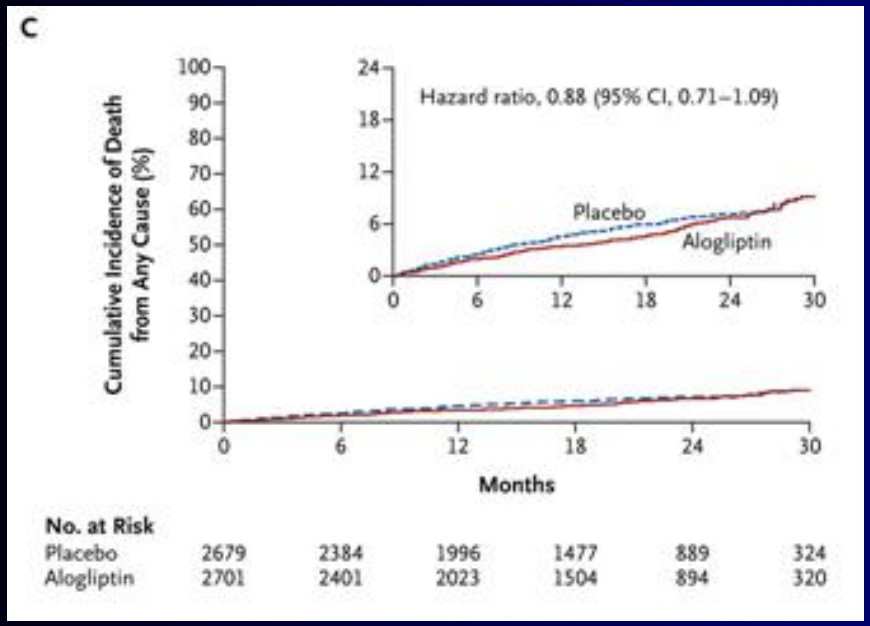


Placebo	8212	7983	7761	7267	4855
Saxagliptin	8280	8071	7836	7313	4920

EXAMINE

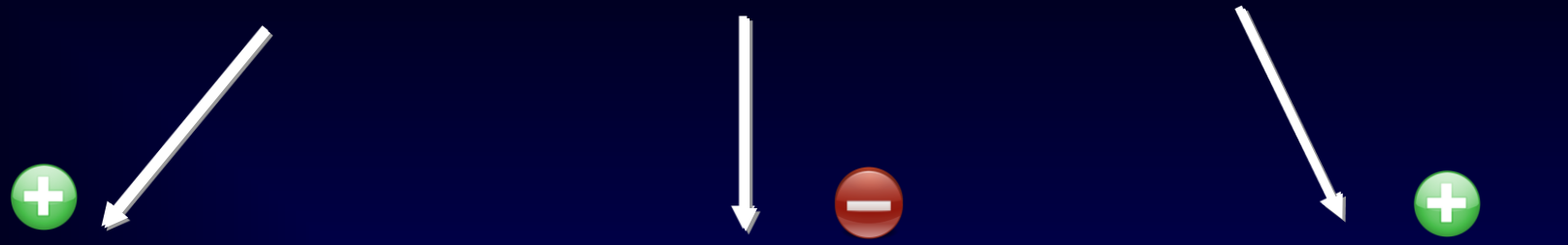






White WB, N Engl J Med, September 2, 2013
DOI: 10.1056/NEJMOA1305889

Intensive Glucose Control



Microvascular disease

(DCCT – UKPDS)

Macrovascular Medium Term

(ACCORD, ADVANCE, VADT, ORIGIN) except recent DM w/o CVD

Macrovascular Long Term

(DCCT – UKPDS)

Individualized Care

Glycaemic control individualised care

- HbA1c <53 mmol/mol (7.0%)
- HbA1c 42–48 mmol/mol (6.0–6.5%)
  in selected patients with
  - short disease duration
  - long life expectancy
  - no significant cardiovascular disease
- HbA1c <58–64 mmol/ ol (7.5-8.0%)
  in elderly patients with
  - long-standing and/or complicated disease
- All targets to be achieved without
  - hypoglycaemia or other adverse effects

Special Considerations

- Chronic kidney disease
  - AVOID METFORMIN / ACARBOSE / SUs in advanced CKD
  - DPP4 inhibitors / Pioglitazone
- Elderly subjects : target $HbA_1C < 7.5 – 8\%$

Heart Failure

- T2 DM is a major risk factor for HF
- Combination of T2 DM and HF increases substantially the risk of mortality.
- Pharmacological management similar to non DM.
- Some antidiabetic drugs contra indicated (glitazones)

Individual Endpoints

ITT Population	2-year KM rate (%) Placebo (N=8,212)	Saxagliptin (N=8,280)	HR	*p value for superiority*
CV Death	2.9	3.2	1.03 (0.87-1.22)	0.72
MI	3.4	3.2	0.95 (0.80-1.12)	0.52
Ischemic Stroke	1.7	1.9	1.11 (0.88-1.39)	0.38
Hosp for Cor. Revasc	5.6	5.2	0.91 (0.80-1.04)	0.18
Hosp for UA	1.0	1.2	1.19 (0.89-1.60)	0.24
Hosp for Heart Failure	2.8	3.5	1.27 (1.07-1.51)	0.007
All-Cause Mortality	4.2	4.9	1.11 (0.96-1.27)	0.15

Blood pressure control in diabetes

Recommendations	Class[a]	Level[b]
Blood pressure control is recommended in patients with DM and hypertension to lower the risk of cardiovascular events.	I	A
It is recommended that a patient with hypertension and DM is treated in an individualized manner, targeting a blood pressure of < 140/85 mmHg.	I	A
It is recommended that a combination of blood pressure lowering agents is used to archiveve blood pressure control.	I	A
A RAAS blocker (ACE-I or ARB) is recommended in the treatment of hypertension in DM, particularly in the presence of proteinuria or microalbuminuria.	I	A
Simultaneous administration of two RAAS blockers should be avoided in patients with DM.	III	B

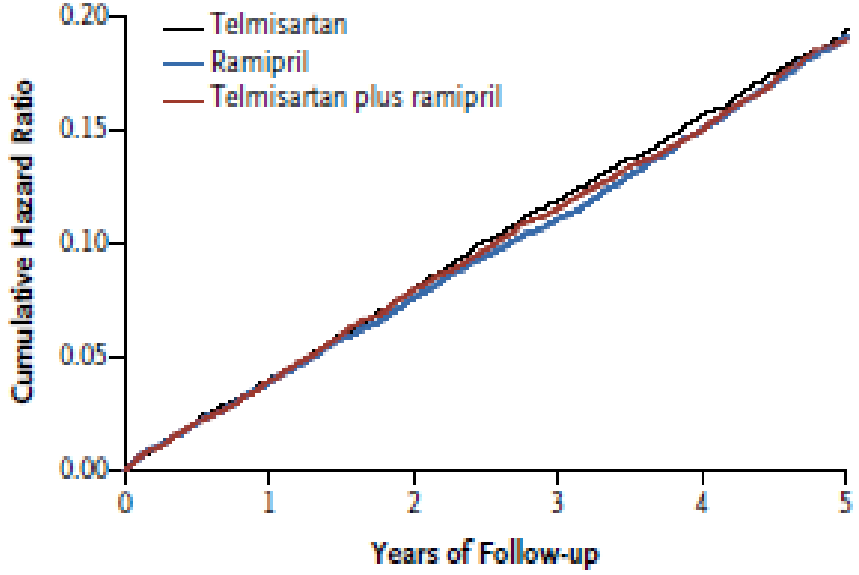
Blood Pressure
Meta-analysis 13 RCTs

	Intensive **BP** $\leq$ 135	**Standard** **BP** $\leq$ 140
All cause mortality	**HR = 0.90**	
Stroke	**HR = 0.83**	
Serious adverse events	**HR = 1.40**	

Bangalore, Circulation, 2011;123, 2795

Blood pressure control
treatment targets - individualised care

- Lowering systolic blood pressure ≤140/≤85 mm Hg has favourable cardiovascular effects
- A systolic blood pressure target <130 mm Hg may be considered in the presence of nephropathy with overt proteinuria
- A blood pressure <130/80 mm Hg may increase the risk for adverse events in elderly patients and those with a long diabetes duration
- The risk/benefit balance of intensive blood pressure management needs to be carefully considered and individualised

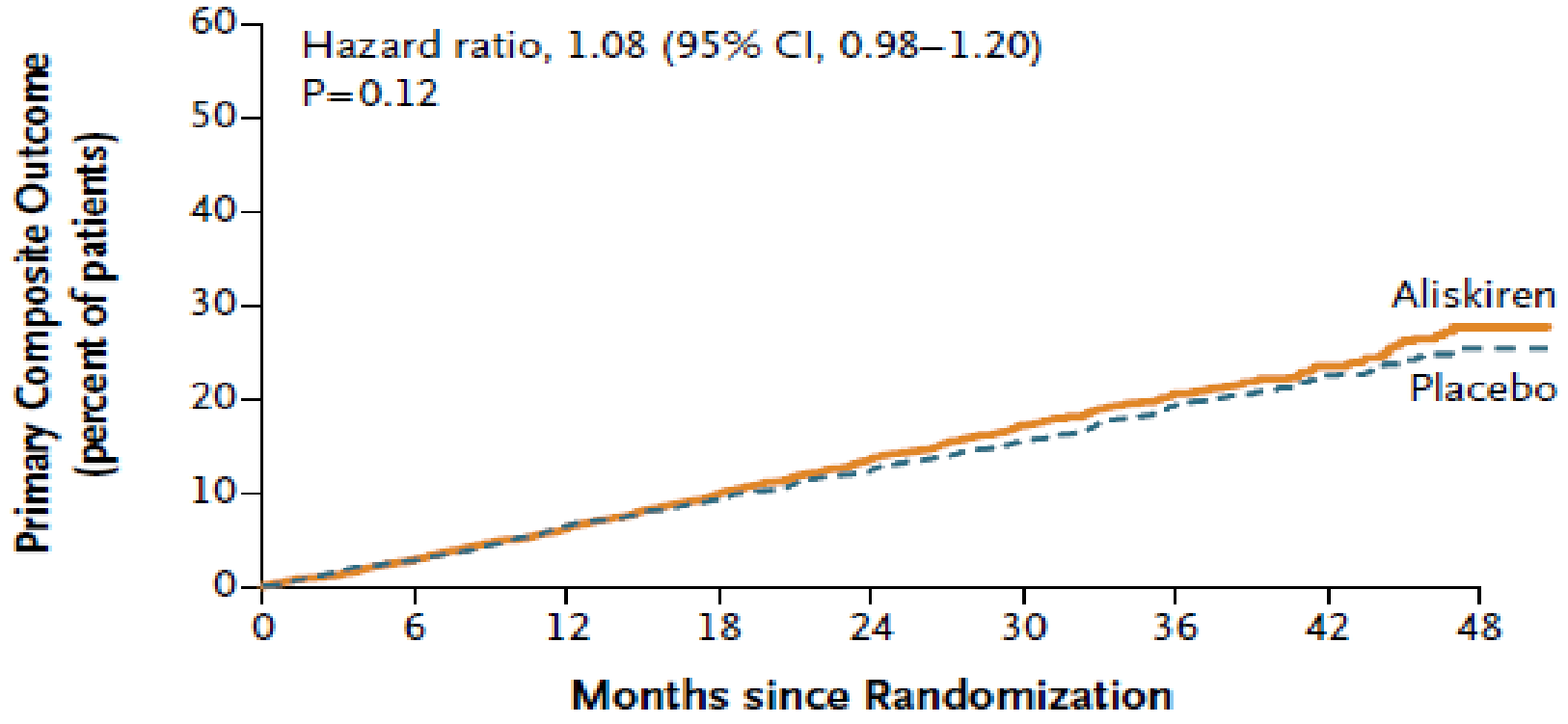


No. at Risk						
Telmisartan	8542	8177	7778	7420	7051	1687
Ramipril	8576	8214	7832	7472	7093	1703
Telmisartan plus ramipril	8502	8133	7738	7375	7022	1718

ON TARGET

N Engl J Med, 2008, 358(15):1547-1559

ALTITUDE



No. at Risk									
Aliskiren	4274	4088	3914	3661	2926	2233	1302	642	82
Placebo	4287	4111	3908	3686	2995	2292	1349	646	82

Recommendations for lipid control in patients with diabetes

Recommendations	Class	Level
Statin therapy is recommended in patients with T1DM and T2DM at very high risk (i.e. if combined with documented CVD, severe CKD or with one or more CV risk factors and/or target organ damage) with an LDL-C target of <1.8 mmol/L (<70 mg/dL) or at least a ≥50% LDL-C reduction if this target goal cannot be reached.	I	A
Statin therapy is recommended in patients with T2DM at high risk (without any other CV risk factor and free of target organ damage) with an LDL-C target of <2.5 mmol/L (<100 mg/dL).	I	A
Statins may be considered in T1DM patients at high risk for cardiovascular events irrespective of the basal LDL-C concentration.	IIb	C
It may be considered to have a secondary goal of non–HDL-C <2.6 mmol/L (<100 mg/dL) in patients with DM at very high risk and of <3.3 mmol/L (<130 mg/dL) in patients at high risk.	IIb	C
Intensification of statin therapy should be considered before the introduction of combination therapy with the addition of ezetimibe.	IIa	C
The use of drugs that increase HDL-C to prevent CVD in T2DM is not recommended.	III	A

Revascularisation in people with diabetes

Recommendations	Class	Level
Optimal medical treatment should be considered as preferred treatment in patients with stable CAD and DM unless there are large areas of ischaemia or significant left main or proximal LAD lesion.	IIa	B
CABG is recommended in patients with DM and multivessel or complex (SYNTAX Score >22) CAD to improve survival free from major cardiovascular events.	I	A
PCI for symptom control may be considered as an alternative to CABG in patients with DM and less complex multivessel CAD (SYNTAX score ≤22) in need of revascularization.	IIb	B
Primary PCI is recommended over fibrinolysis in DM patients presenting with STEMI if performed within recommended time limits.	I	B
In DM patients subjected to PCI, DES rather than BMS are recommended to reduce risk of target vessel revascularization.	I	A
Renal function should be carefully monitored after coronary angiography/PCI in all patients on metformin.	I	C
If renal function deteriorates in patients on metformin undergoing coronary angiography/PCI it is recommended to withhold treatment for 48 h or until renal function has returned to its initial level.	I	C

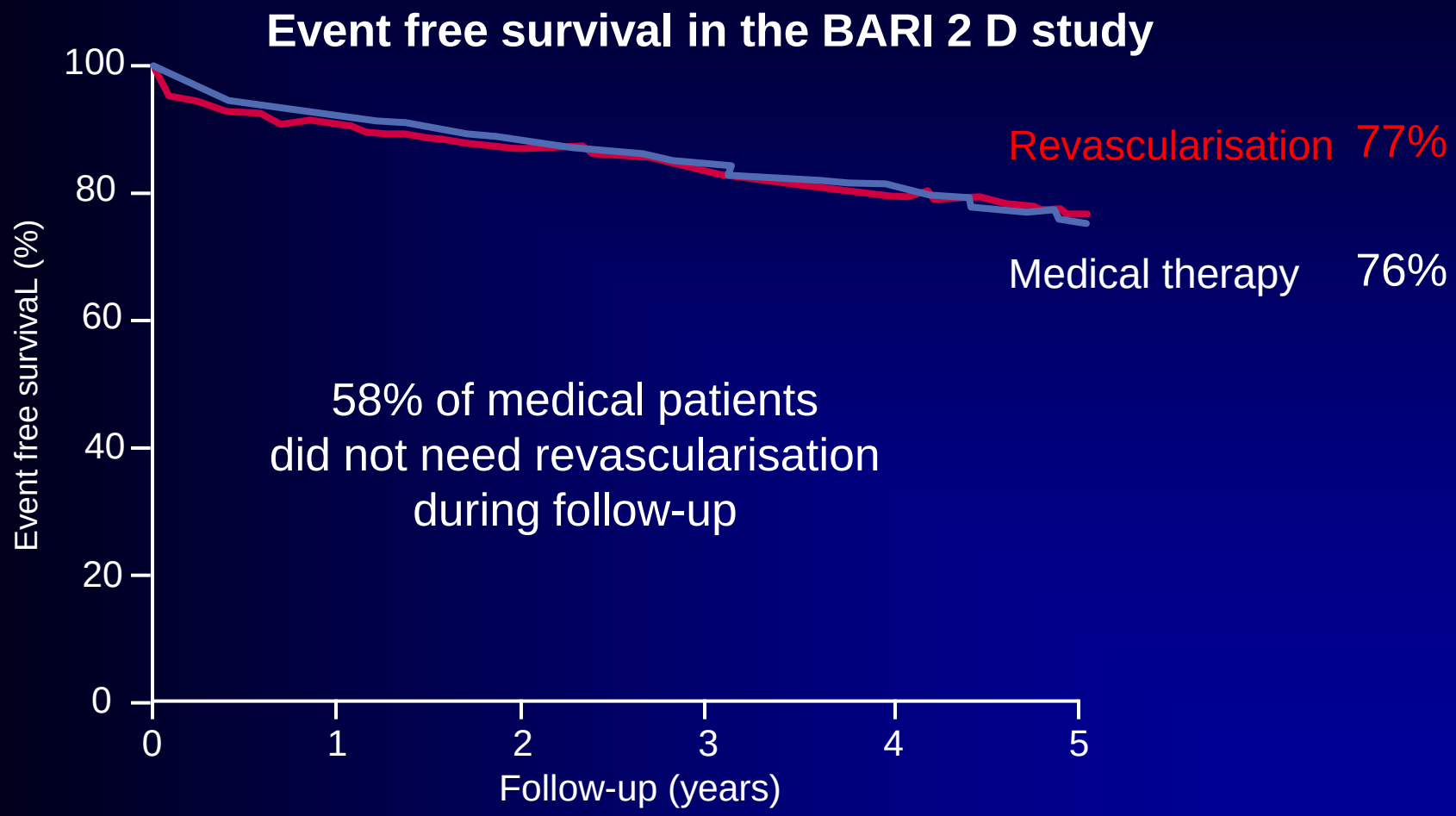
Options for Revascularisation

1. Acute coronary syndromes:

   Early revascularization (as in non DM)

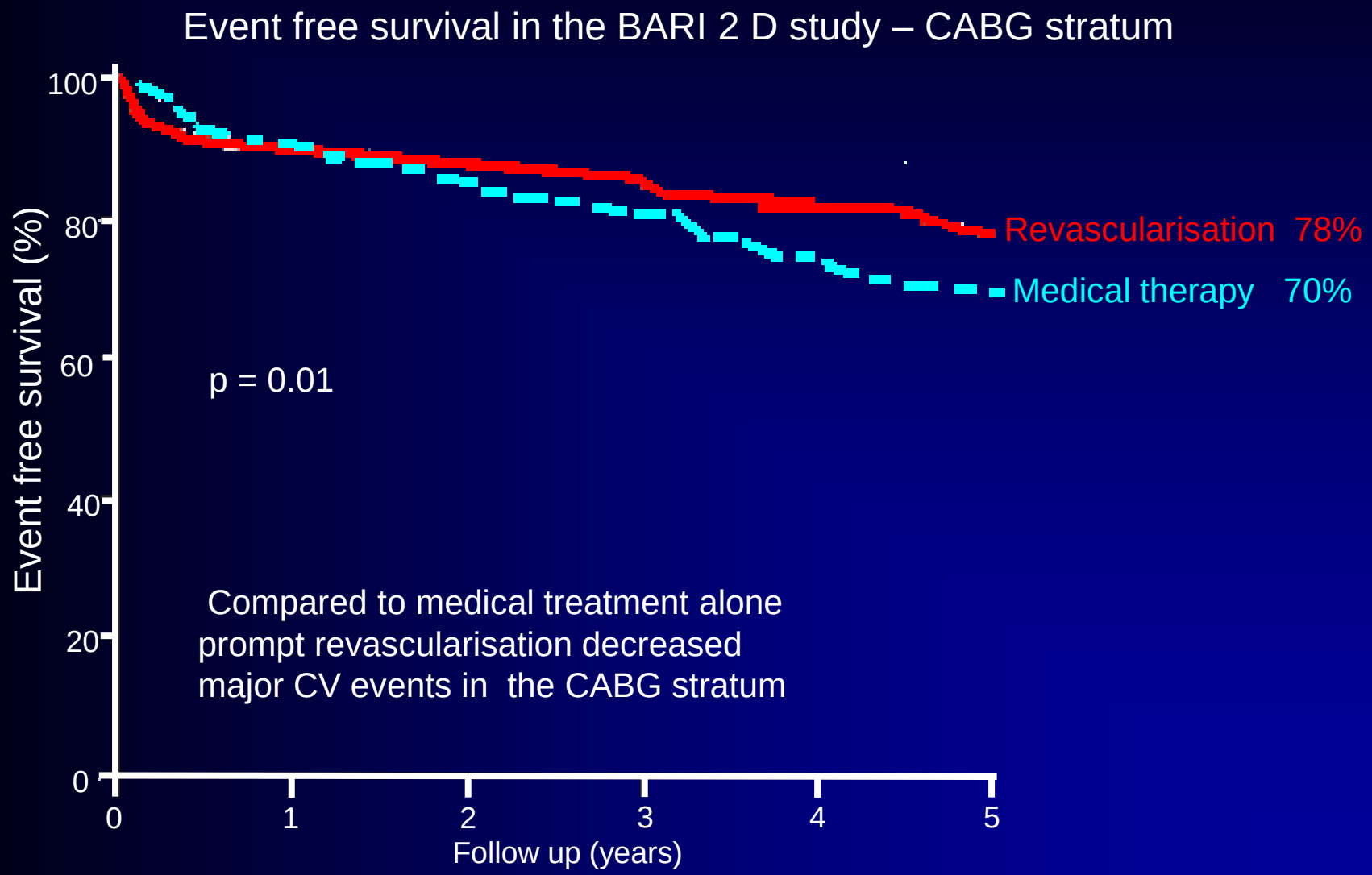
2. Stable coronary artery disease :
   - CABG preferred option if myocardial area at risk is large .
   - PCI with DES may be performed for symptom control in single and two-vessel disease

Myocardial revascularisation vs. medical therapy in people with diabetes



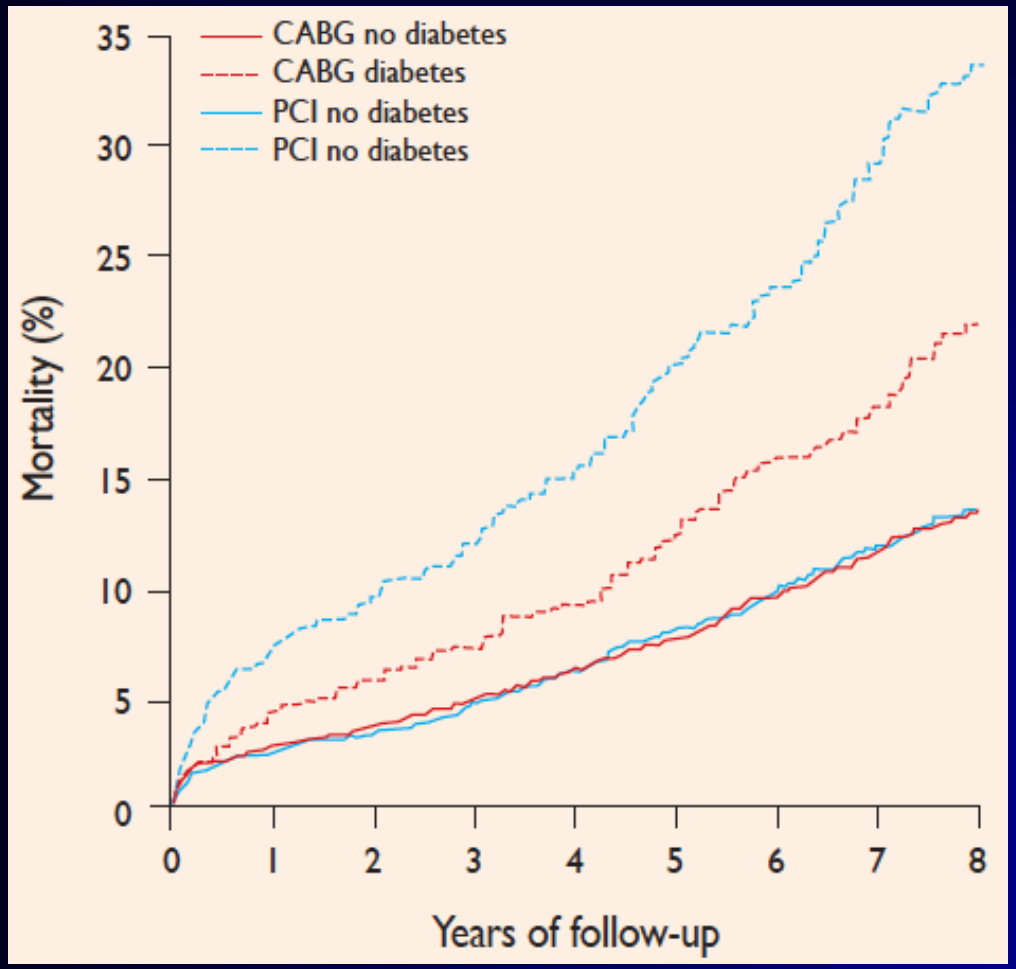
BARI 2D Study group New Engl J Med 2009; 360: 2503

Myocardial revascularisation vs. medical therapy in people with diabetes



BARI 2D Study group New Engl J Med 2009; 360: 2503

CABG *vs* PCI – Clinical Evidence
Meta-analysis



PCI diabetes (bare metal stents)

CABG diabetes

CABG no diabetes
PCI no diabetes (BMS)

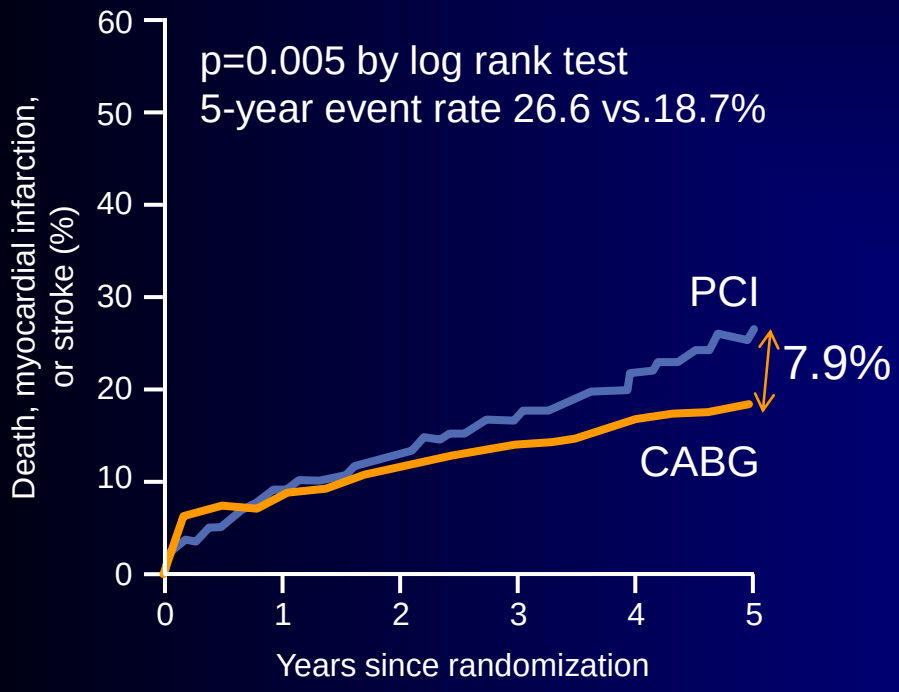
1233 patients with Diabetes

Hlatky et al Lancet 2009: 1190

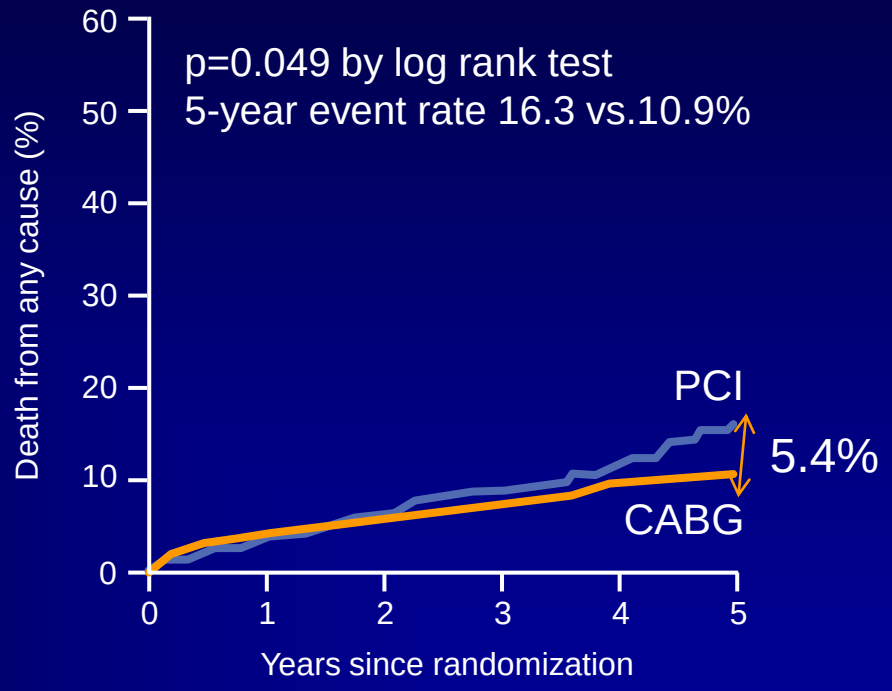
CABG vs. PCI in people with diabetes

The FREEDOM trial

Primary Outcome



Death



Farkouh et al New Engl J Med 2012; 367: 2375

Recommendation for antiplatelet therapy in people with diabetes

Recommendations	Class	Level
Antiplatelet therapy with aspirin in DM-patients at low CVD risk is not recommended.	III	A
Antiplatelet therapy for primary prevention may be considered in high risk patients with DM on an individual basis.	IIb	C
Aspirin at a dose of 75-160 mg/day is recommended as secondary prevention in DM.	I	A
A $P2Y_{12}$ receptor blocker is recommended in patients with DM and ACS for 1 year and in those subjected to PCI (duration depending on stent type). In patients with PCI for ACS preferably prasugrel or ticagrelor should be given.	I	A
Clopidogrel is recommended as an alternative antiplatelet therapy in case of aspirin intolerance.	I	B

Recommendations for the management of patients with stable and unstable CAD

Recommendations	Class	Level
Aspirin is indicated in patients with DM and CAD to reduce the risk for cardiovascular events.	I	A
Platelet $P2Y_{12}$ receptor inhibition is recommended in patients with DM and ACS in addition to aspirin.	I	A
Insulin-based glycaemic control should be considered in ACS patients with significant hyperglycaemia (>10 mmol/L or >180 mg/dL) with the target adapted to possible co-morbidities.	IIa	C
Glycaemic control, that may be accomplished by different glucose-lowering agents, should be considered in patients with DM and ACS.	IIa	B

GAPS OF EVIDENCE

- Long term CVD outcomes
- Metabolic effects of diuretics and beta-blockers
- Impact of glucose lowering drugs (Metformin, GLP_1 analogues, DPP_4 inhibitors) on the prevention of heart failure.
- Hypoglycaemia and sudden cardiac death

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