IV Congresso
Novas Fronteiras em Cardiologia

Diabetic Cardiomyopathy

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Hôpital Henri Mondor APHP FRANCE

7 a 9 de Fevereiro 2014
Hotel Vila Galé Ericeira

CLINICAL CASE

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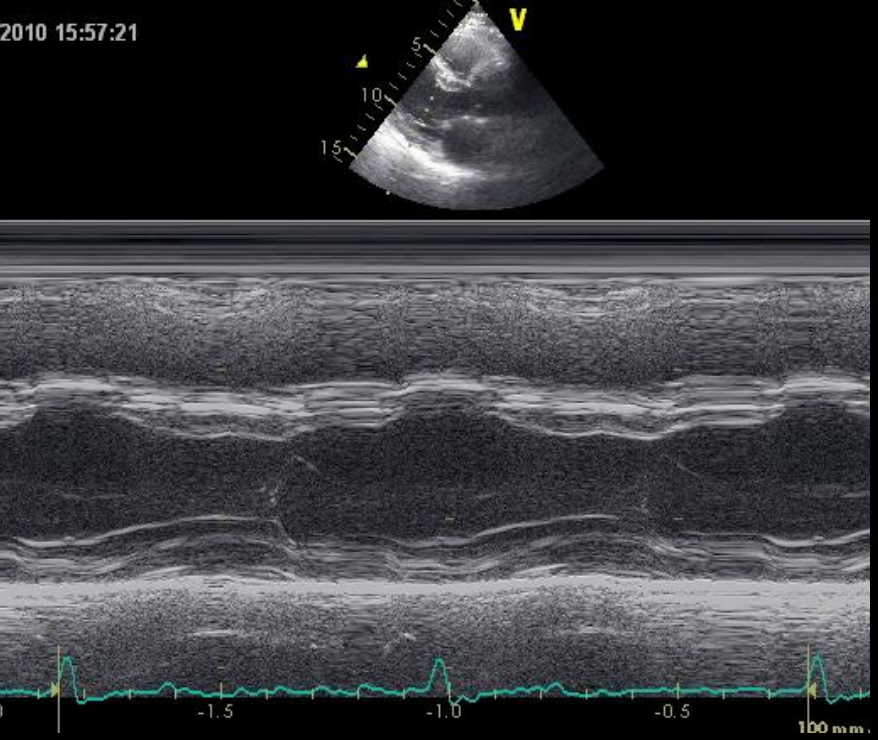
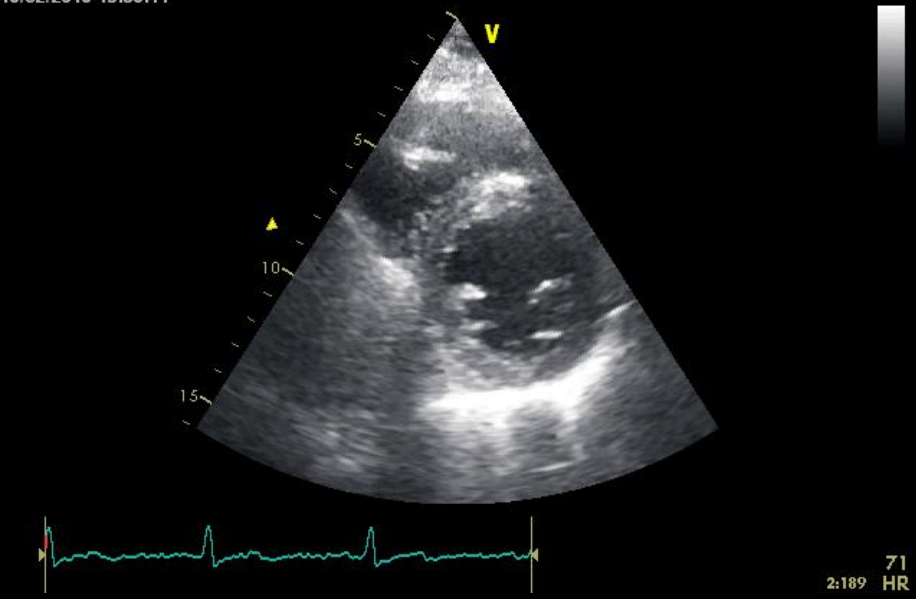
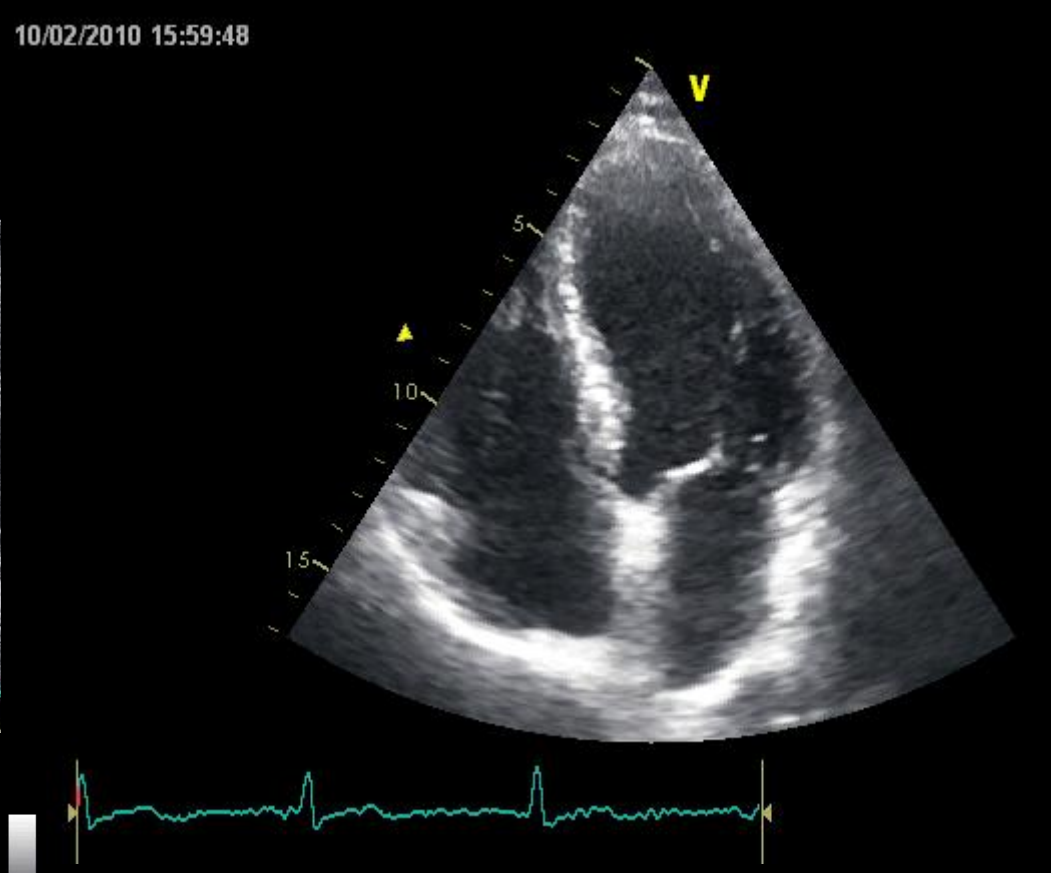
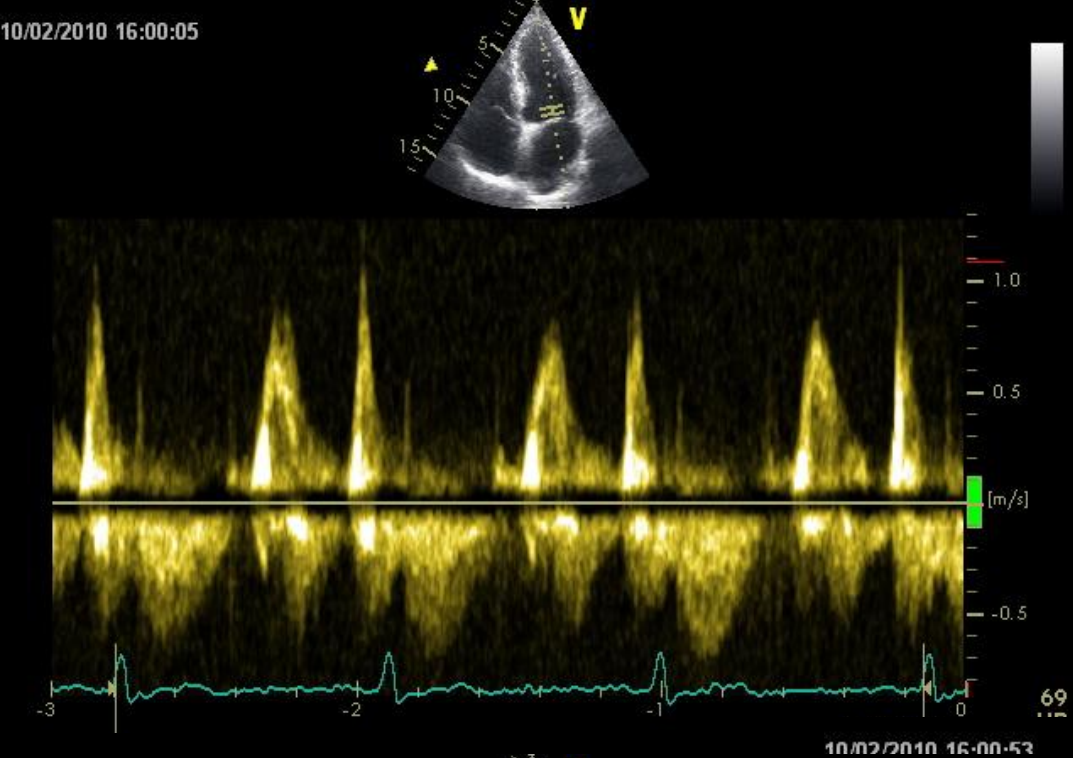
- Male, 58 years old
- Dyspnea (NYHA 2) but overweight (BMI: 27 kg/m^2)
- CV risk factors:
  - Diabetes mellitus for 6 years treated by metformine
    (Glycated hemoglobin 7.5%)
  - Smoking
- No sign of heart failure, coronary or other structural heart disease
- Blood pressure : 120/78 mmHg







LVEDD : 49 mm
LVESD : 29 mm
LVM index : 85 g/m²
LV FS : 40 %
LVEF : 65 %
LA area : 18 cm²



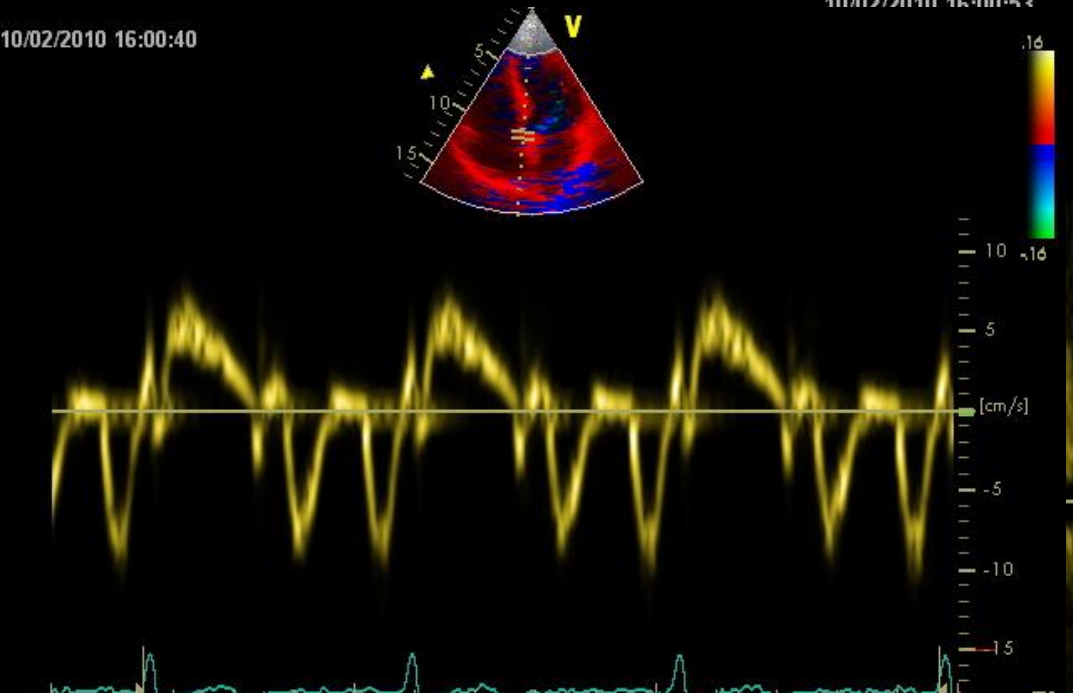
E/A : 0.9

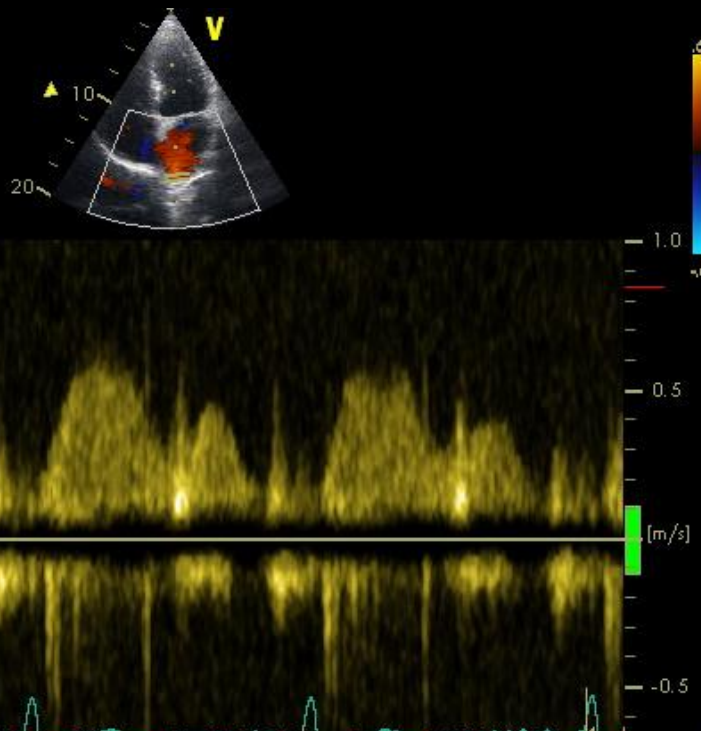
mDT : 190 ms

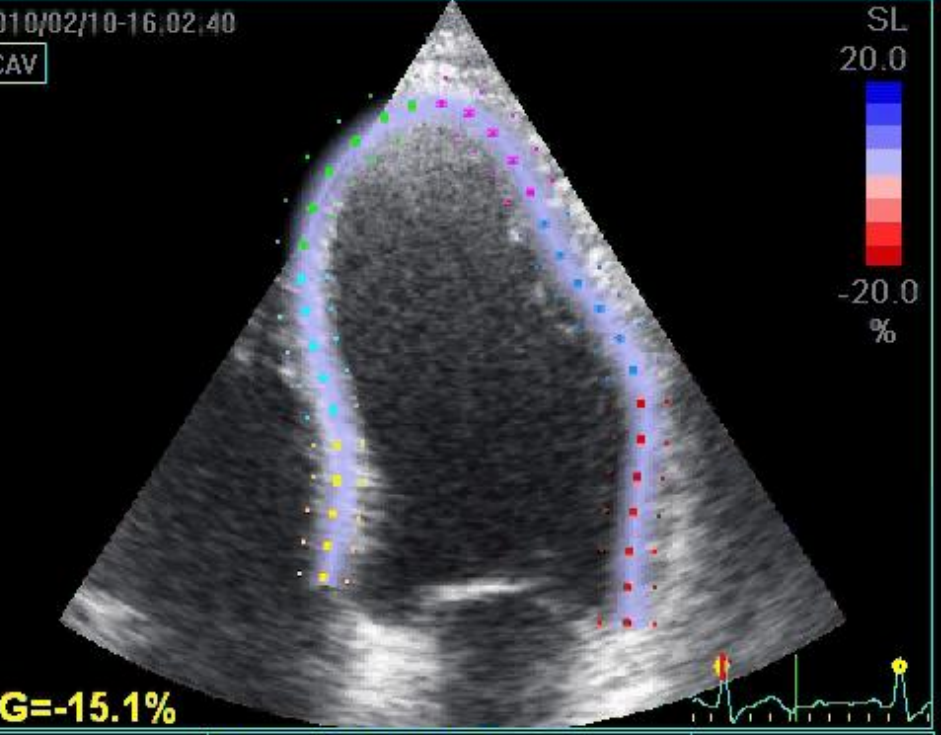
IVRT : 82 ms

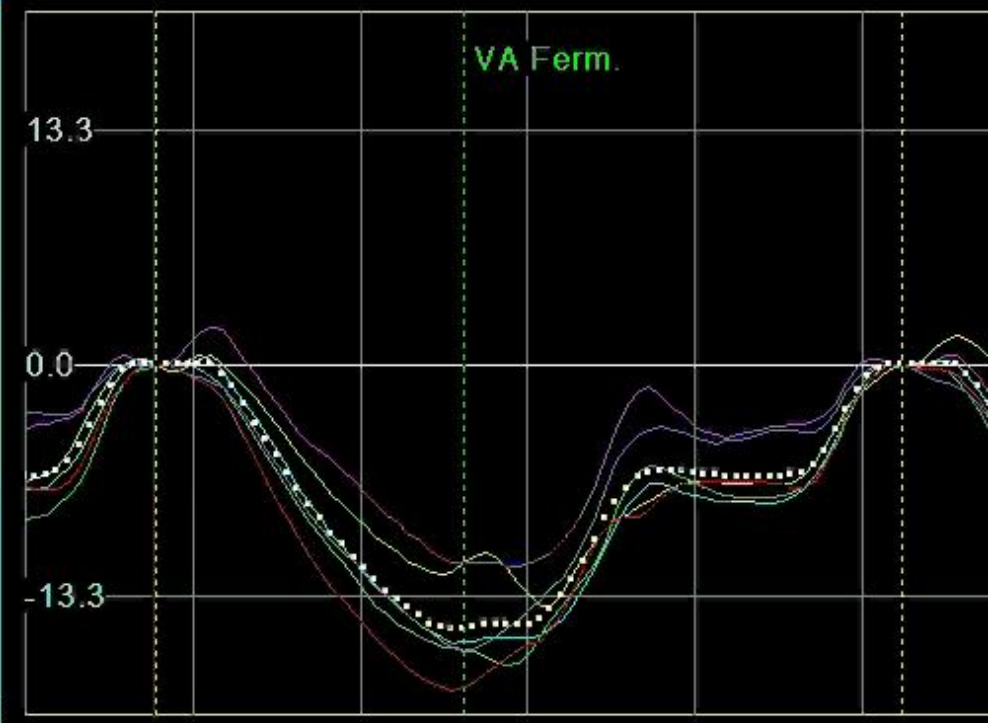
E/e´ : 10

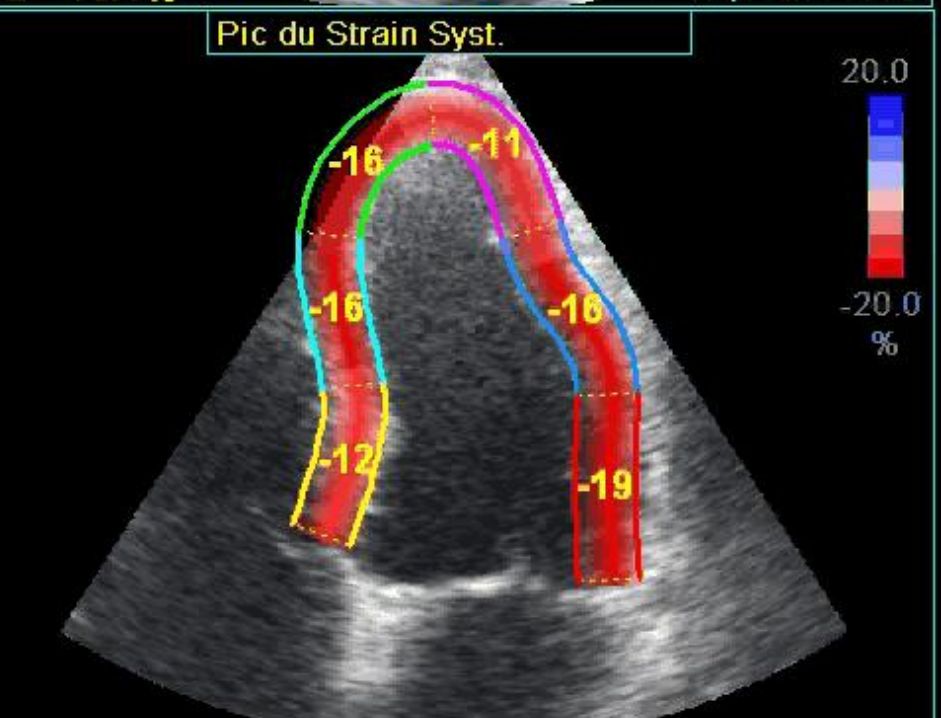
sPAP: 25 mmHg

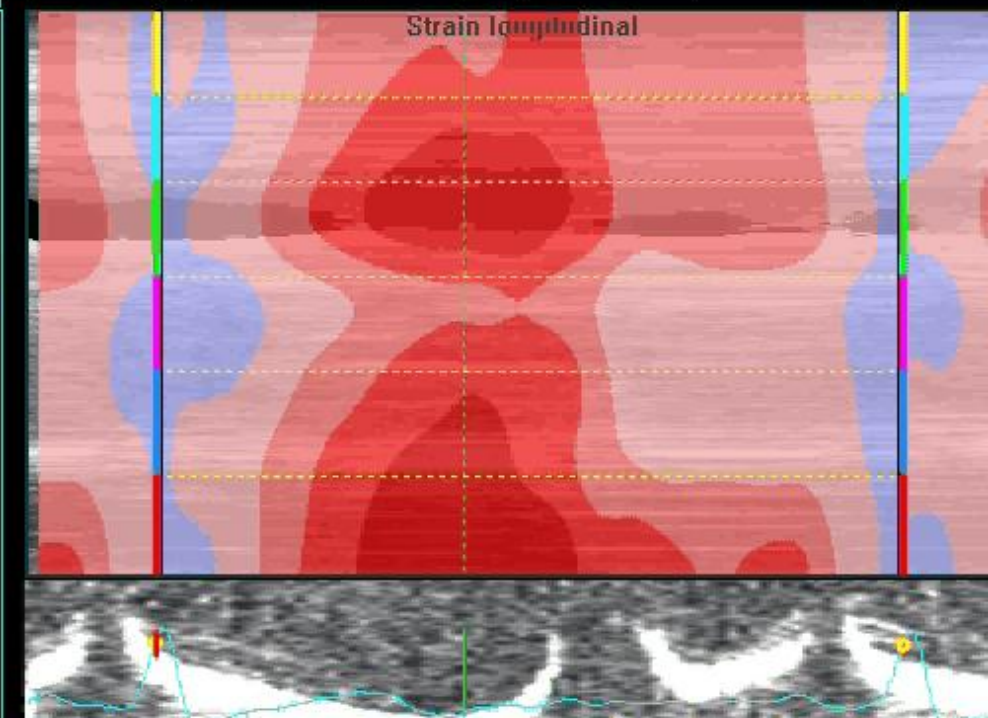


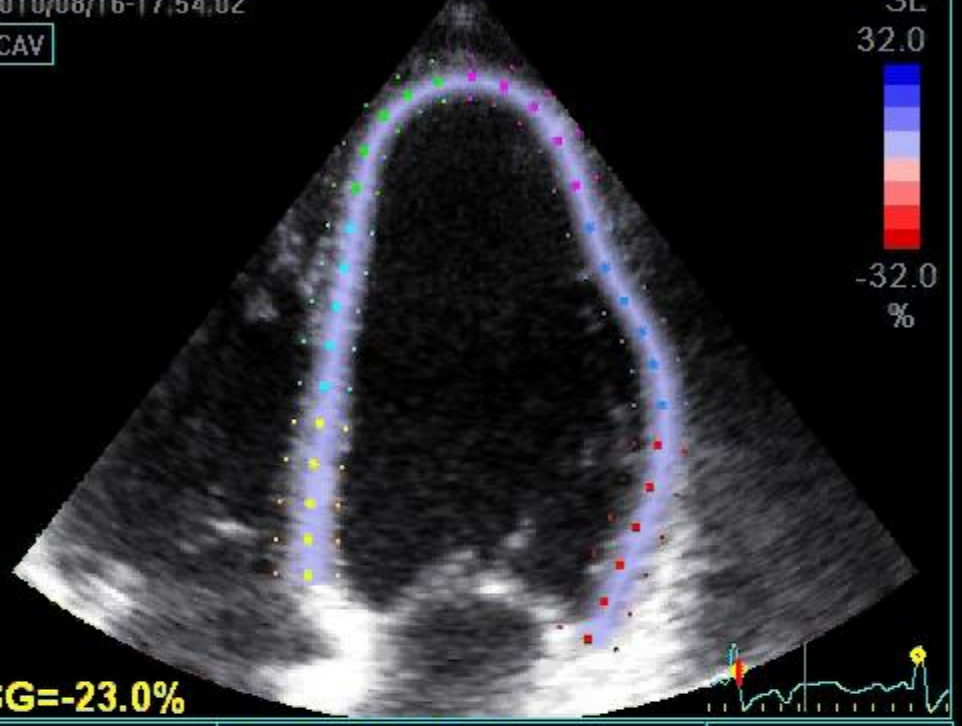


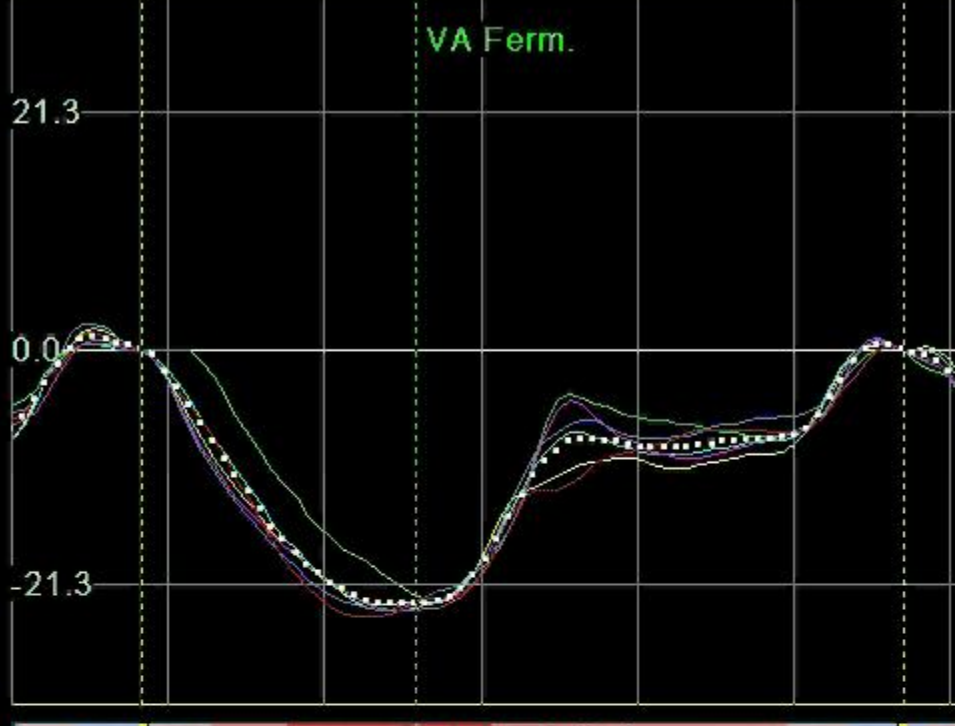

010/02/10-16:02:40
CAV
SL
20.0
-20.0
%
G=-15.1%

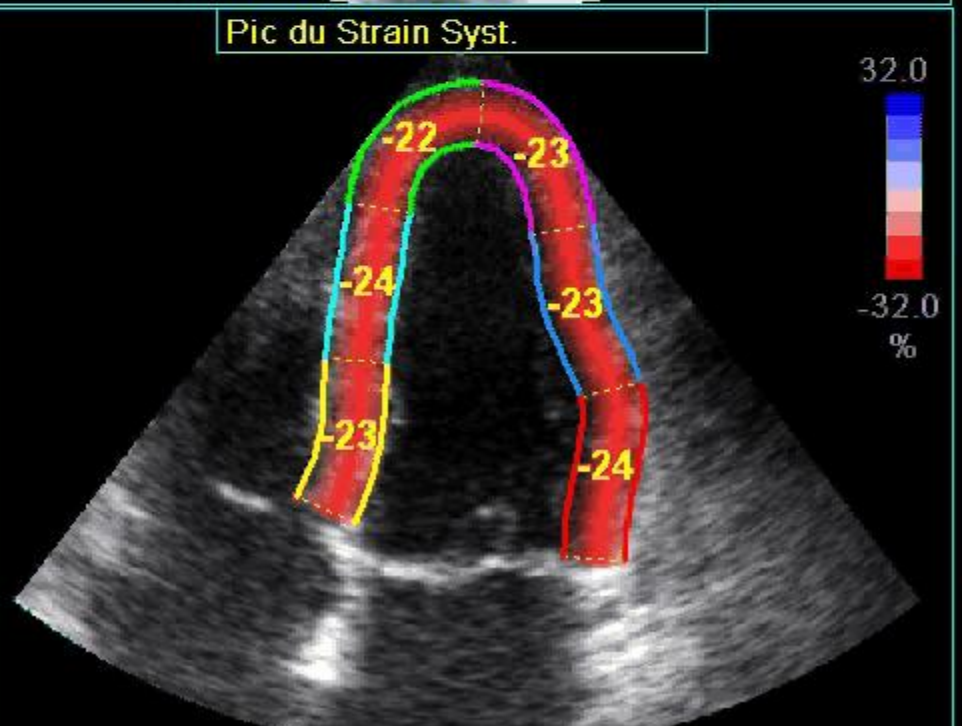

VA Ferm.
13.3
0.0
-13.3

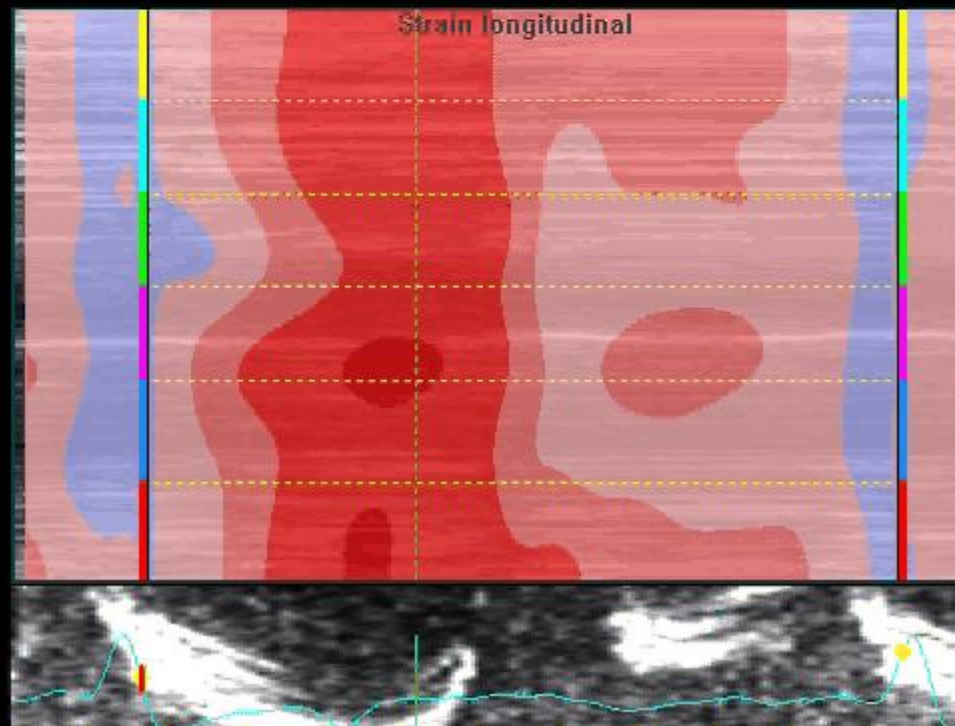

Pic du Strain Syst.
20.0
-20.0
%
-16
-11
-16
-16
-12
-19

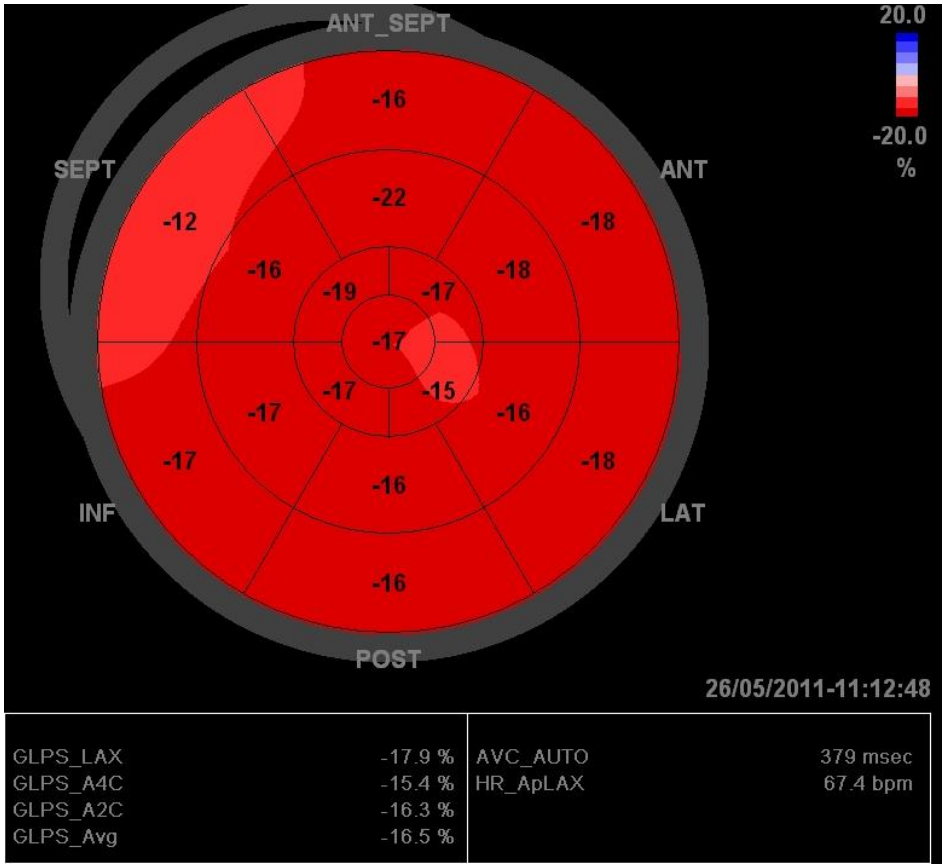

Strain longitudinal

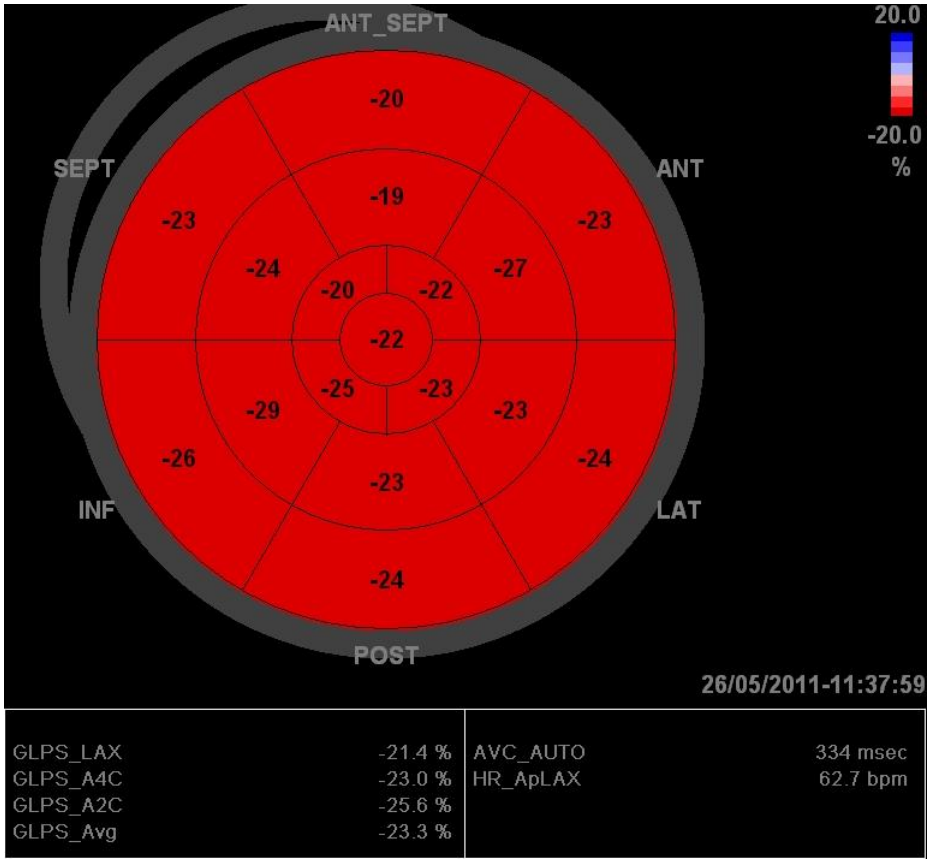

CAV
32.0
-32.0
%
G=-23.0%


VA Ferm.
21.3
0.0
-21.3


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

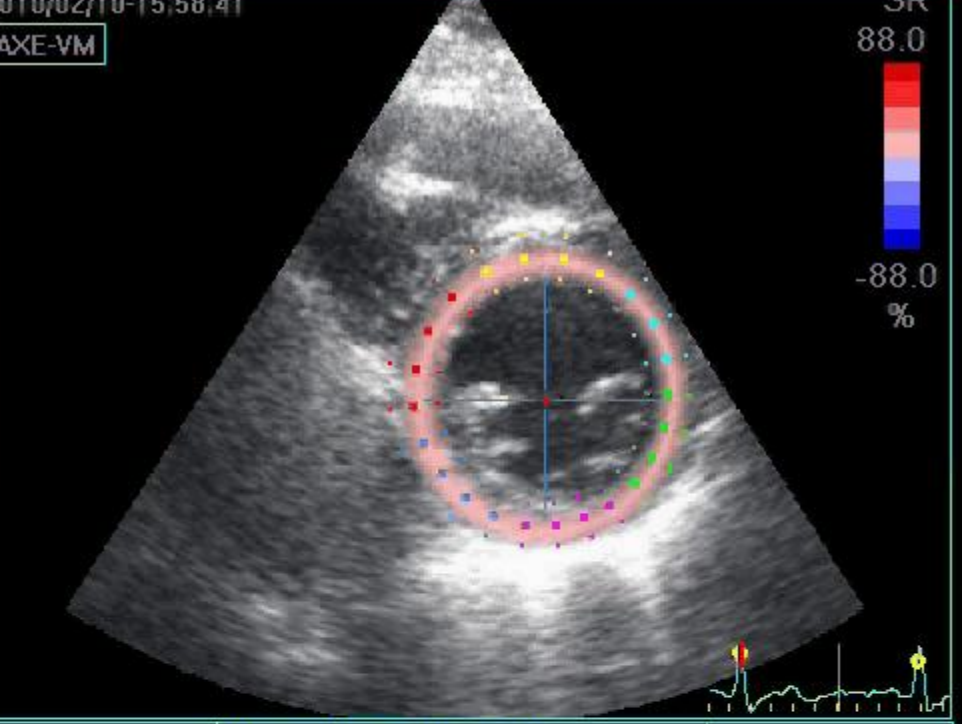

Strain longitudinal

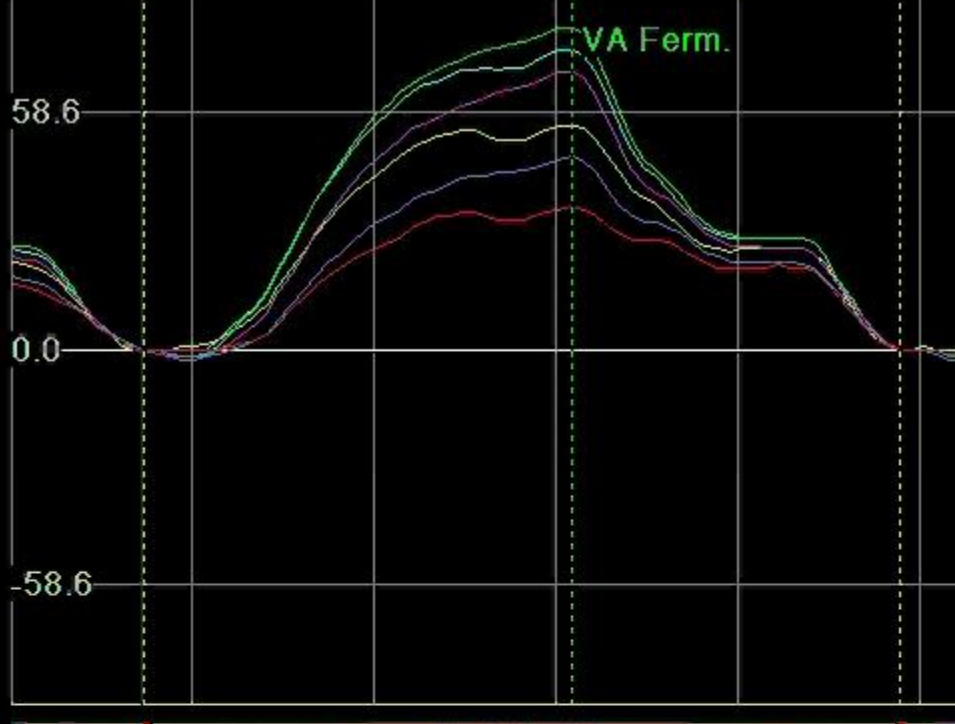


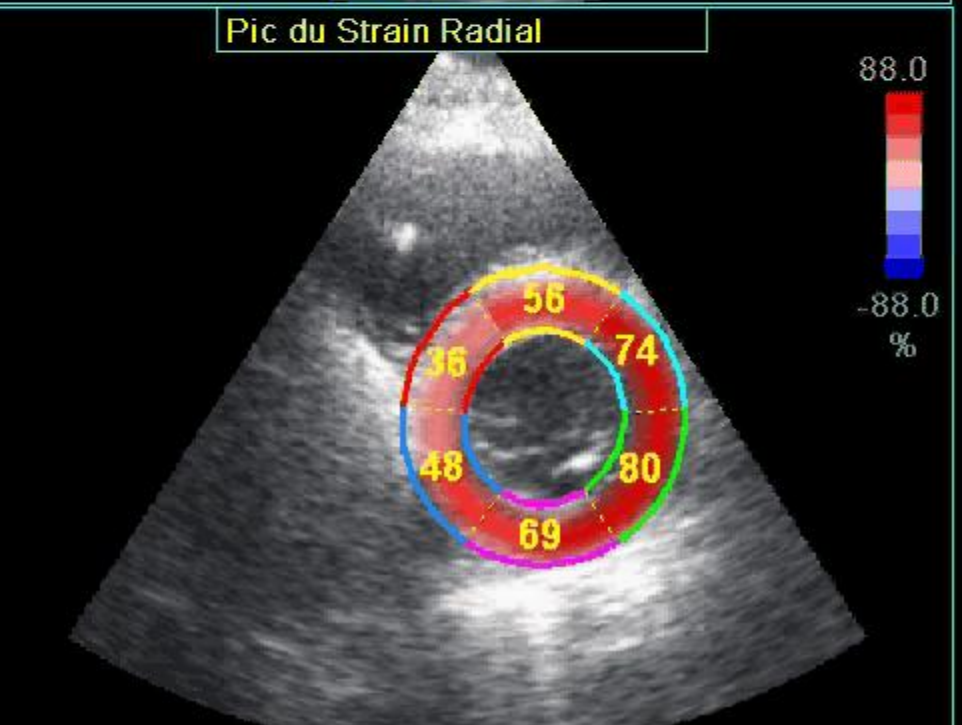


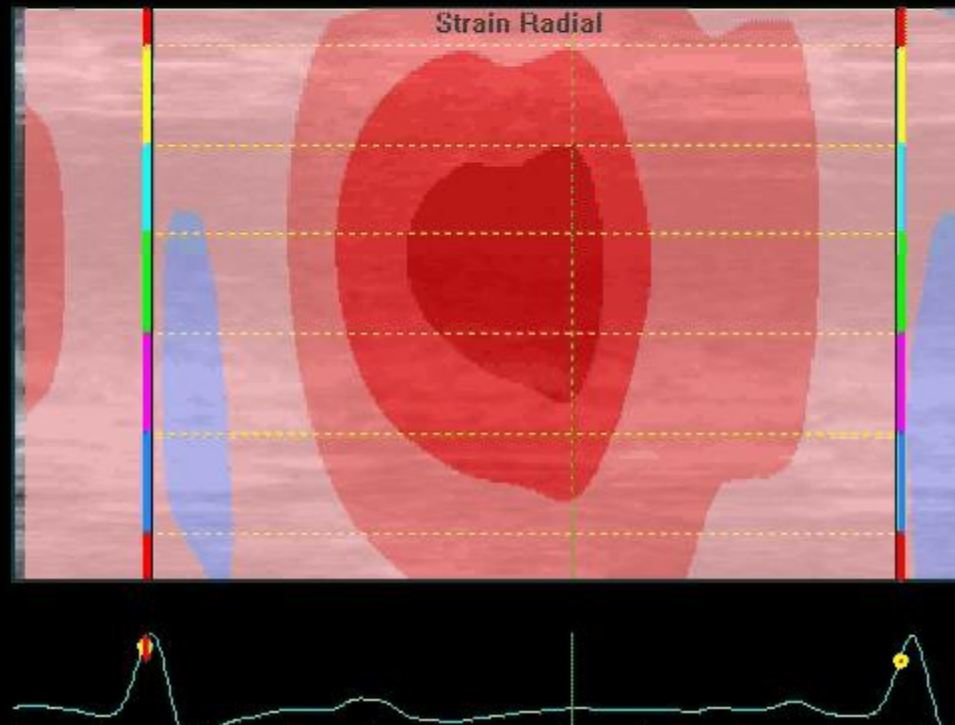
Jacques C
DM patient
LVEF : 65%
Global strain: 16.5%

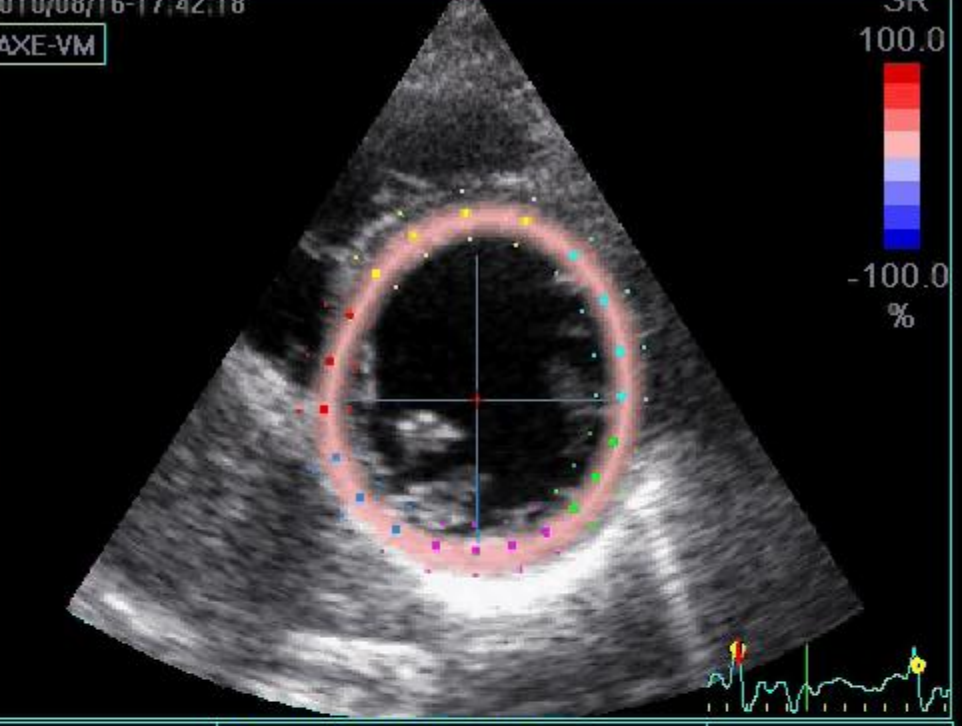
Paul D
Age-matched control
LVEF : 67%
Global strain: 23.3%


AXE-VM
88.0
-88.0
%

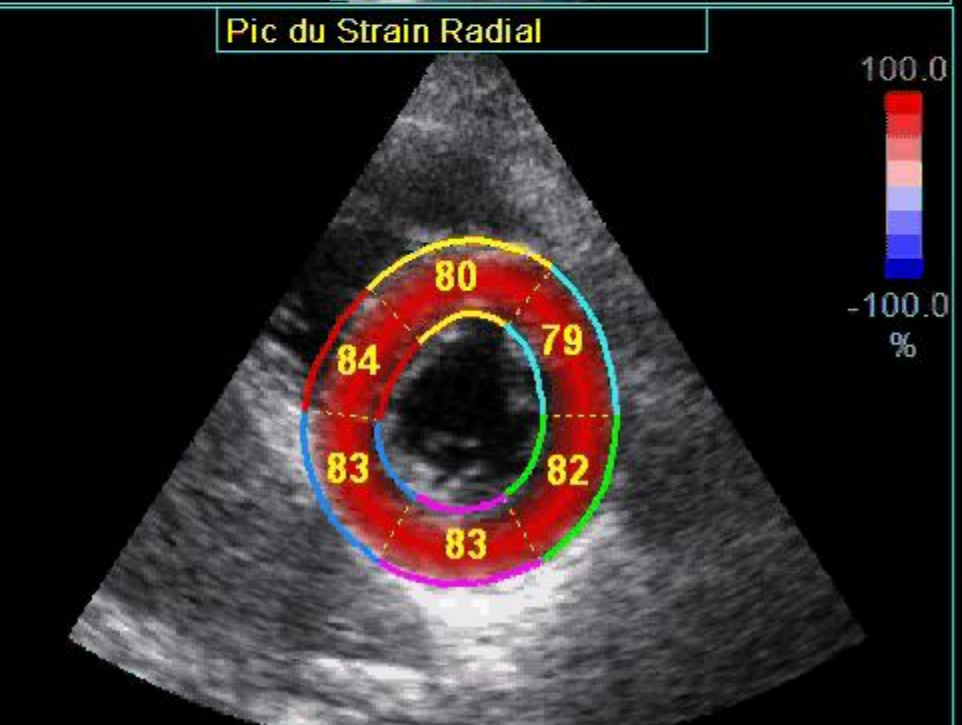

VA Ferm.
58.6
0.0
-58.6

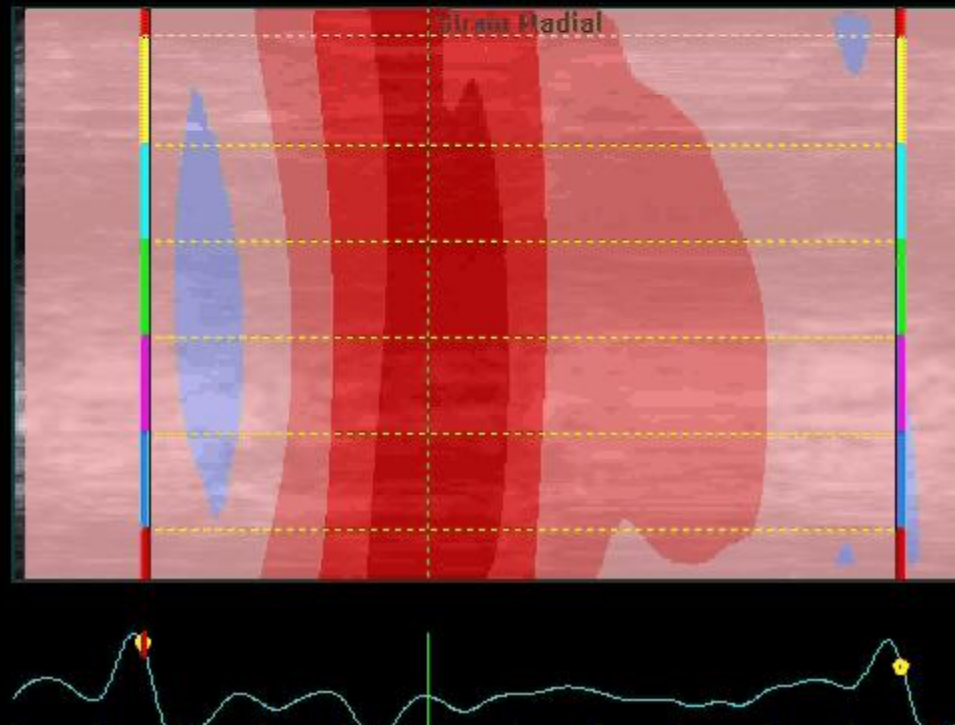

Pic du Strain Radial
88.0
-88.0
%
56
74
36
48
80
69


Strain Radial

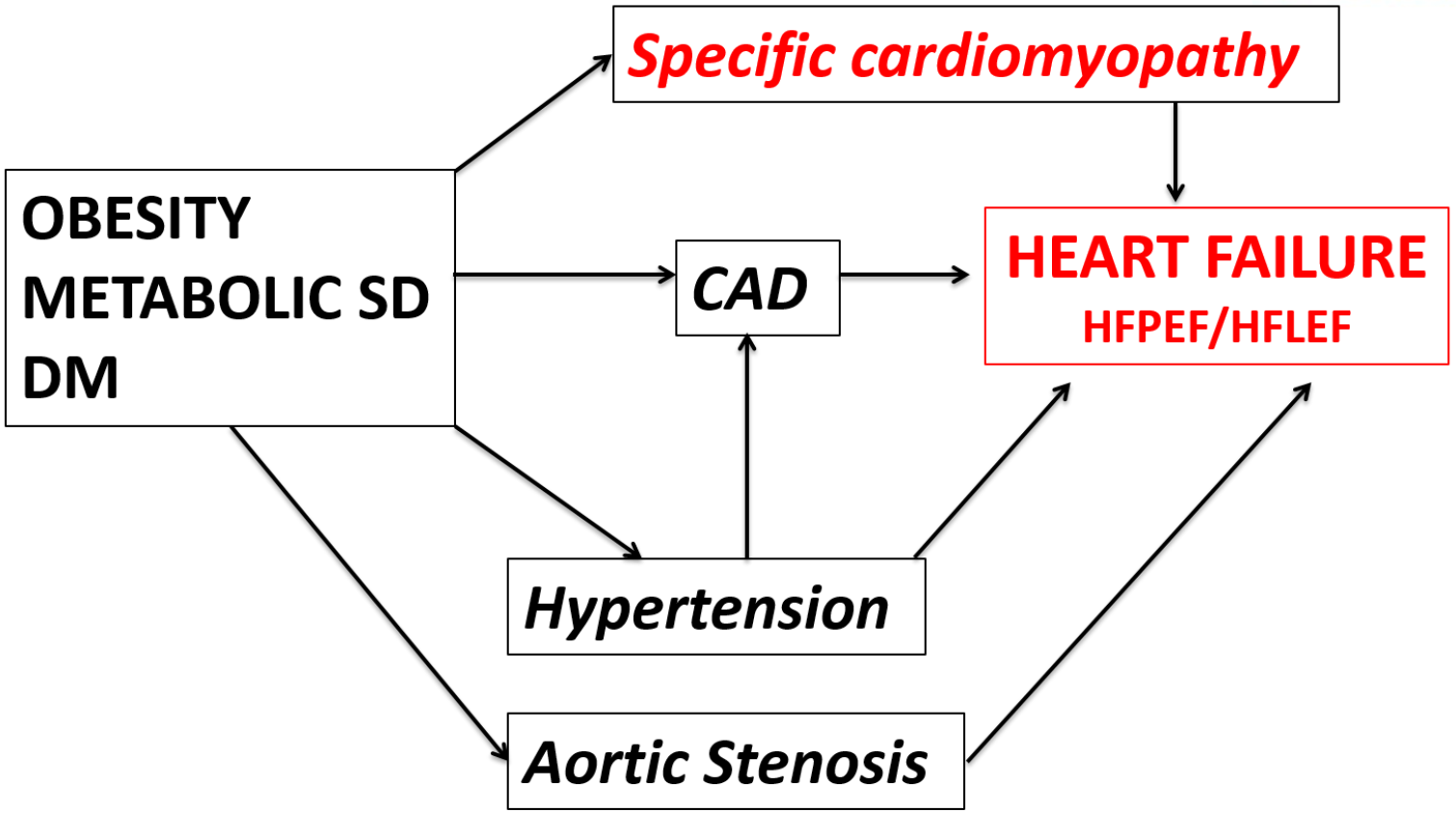

AXE-VM
100.0
-100.0
%


VA Ferm.
66.6
0.0
-66.6

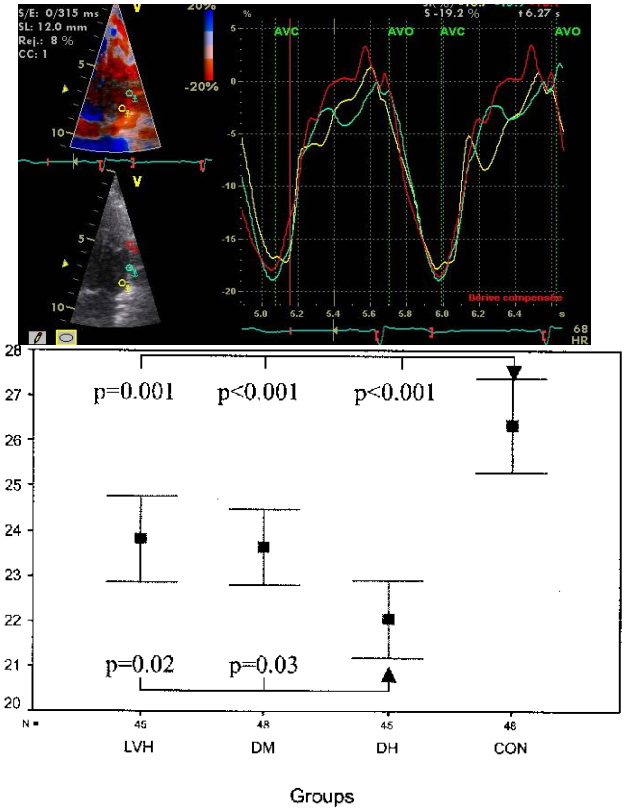

Pic du Strain Radial
100.0
-100.0
%
80
79
84
83
82
83


Strain Radial

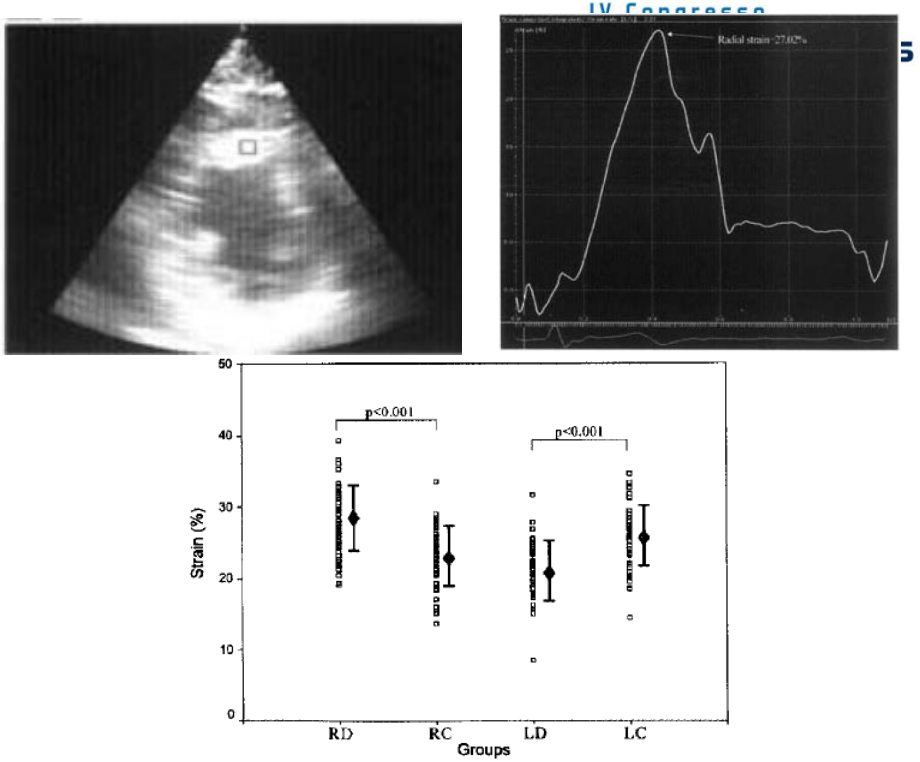
Metabolic and cardiovascular diseases



Diabetic cardiomyopathy:
Preclinical systolic dysfunction

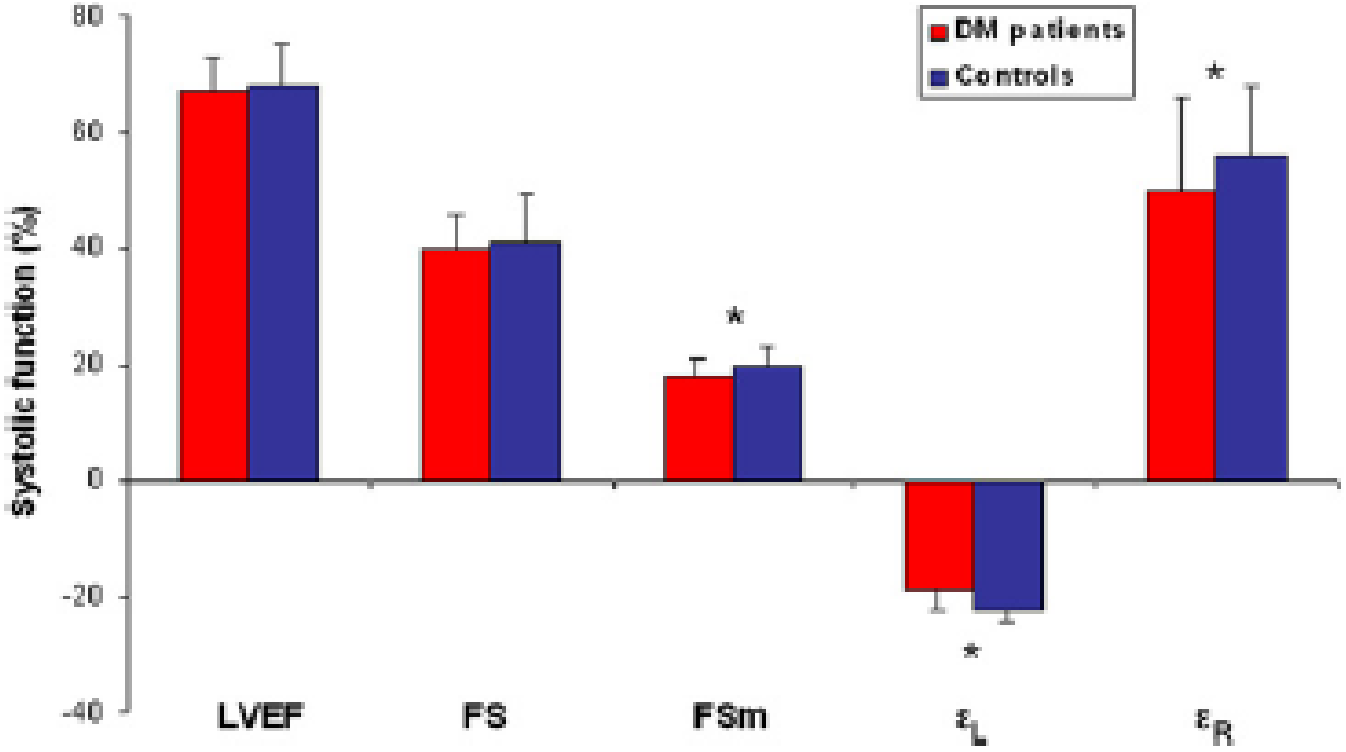


Fang ZY, JACC 2003



Fang ZY, Clin Sci 2003

Impaired Myocardial Radial Function in Asymptomatic Patients with Type 2 Diabetes Mellitus: A Speckle-Tracking Imaging Study



Ernande L et al; J Am Soc Echocardiogr 2010;23:1266-72

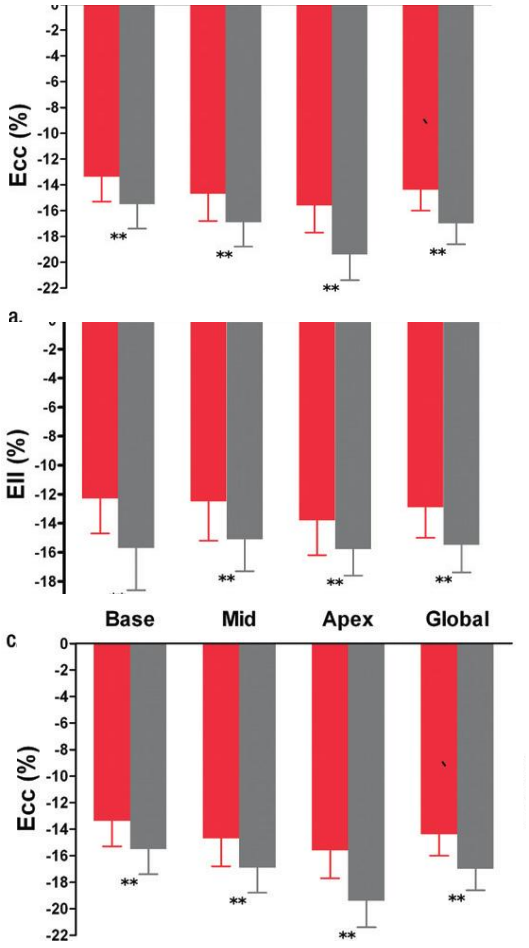
Impaired Myocardial Radial Function in Asymptomatic Patients with Type 2 Diabetes Mellitus: A Speckle-Tracking Imaging Study

	DM group (n = 114)	Controls (n = 88)	*P* value
Radial (ϵ_R, %)			
Anteroseptal	44 ± 16	52 ± 14	.001
Anterior	47 ± 17	54 ± 14	.004
Anterolateral	50 ± 18	57 ± 14	.009
Inferolateral	54 ± 18	59 ± 15	.069
Inferior	54 ± 17	59 ± 17	.64
Inferoseptal	49 ± 17	56 ± 16	.009
ϵ_R (%)	50 ± 16	56 ± 12	.003
Longitudinal (ϵ_L, %)			
Septal wall			
Base	-16 ± 4	-19 ± 3	<.001
Mid	-18 ± 4	-20 ± 3	<.001
Apex	-23 ± 5	-24 ± 4	.19
Lateral wall			
Base	-19 ± 5	-22 ± 4	<.001
Mid	-18 ± 4	-21 ± 3	<.001
Apex	-21 ± 6	-23 ± 4	<.001
ϵ_L (%)	-19 ± 3	-22 ± 2	<.001

Ernande L et al; J Am Soc Echocardiogr 2010;23:1266-72

Diabetic cardiomyopathy:

Preclinical systolic dysfunction



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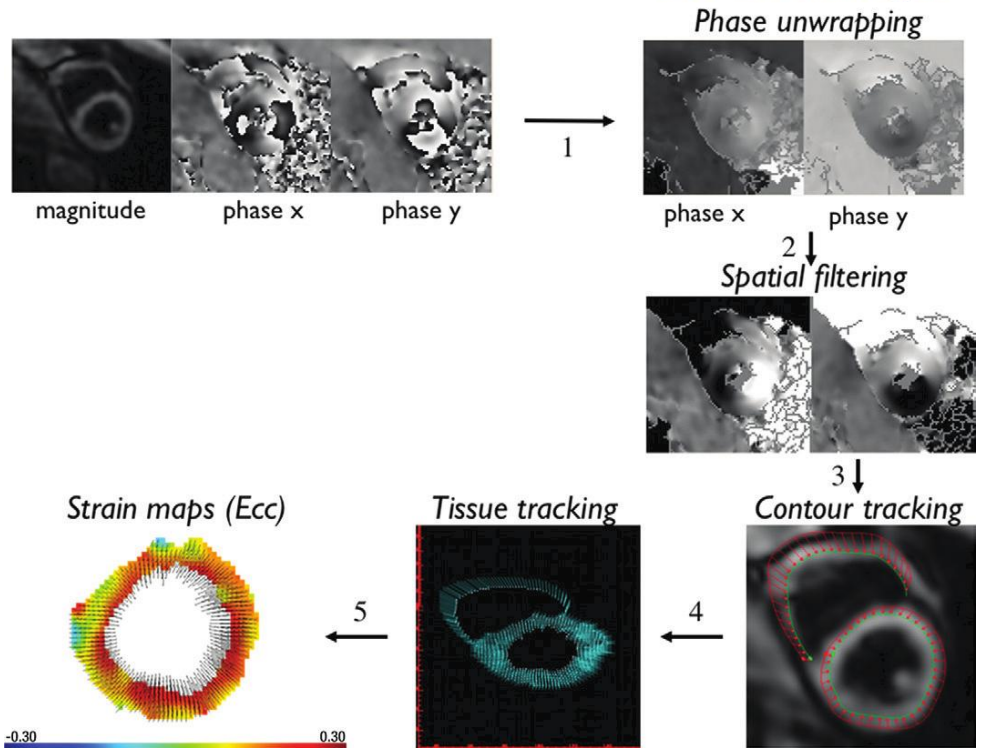


Ernande L, Radiology 2012

Preclinical diabetic cardiomyopathy and outcome

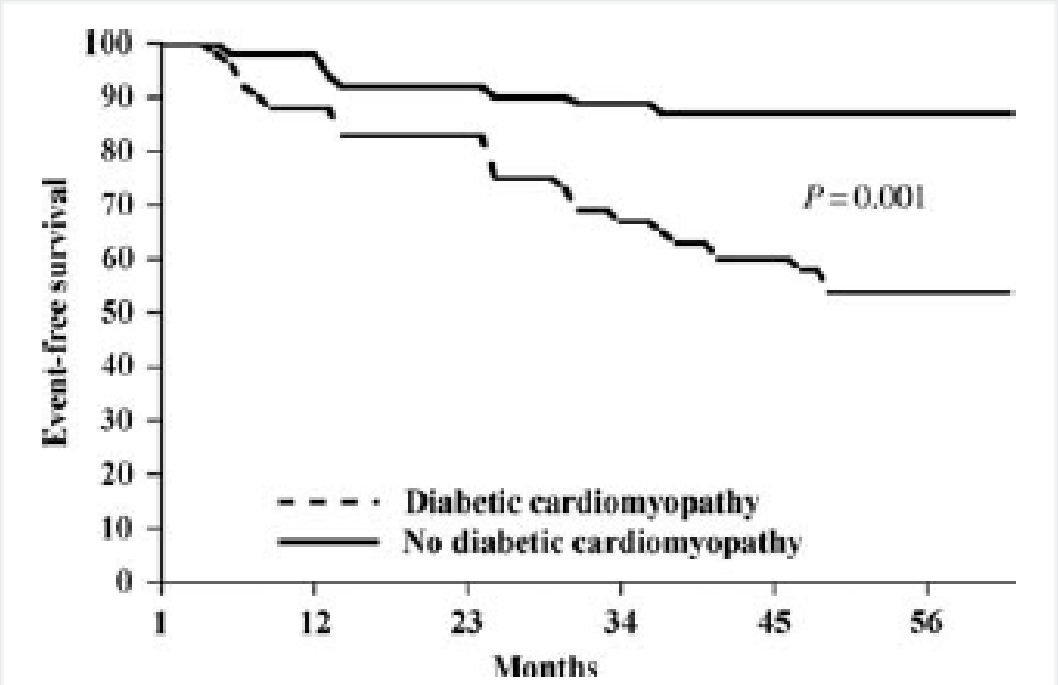
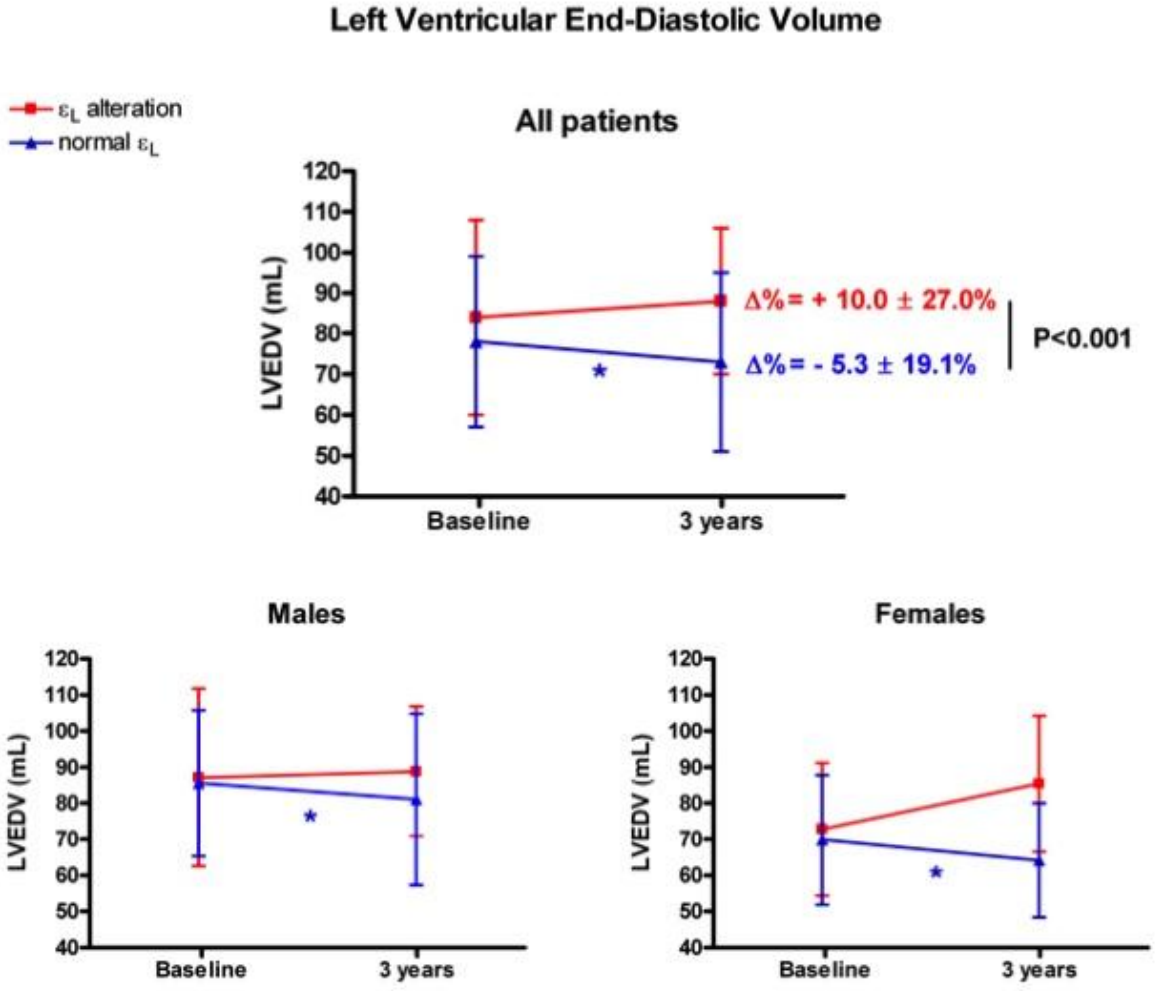


Figure 1 Event-free survival (death, acute coronary syndrome, hospitalization for cardiac reasons, new diagnosis of heart failure, and ≥1 increase in NYHA functional class) in patients with and without diabetic cardiomyopathy.

Kiencke S et al; European Journal of Heart Failure (2010) 12, 951–957

Preclinical diabetic cardiomyopathy and outcome

Systolic strain alterations and LV remodelling



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Ernande L, JASE 2014

Preclinical diabetic cardiomyopathy:
Diastolic Dysfunction

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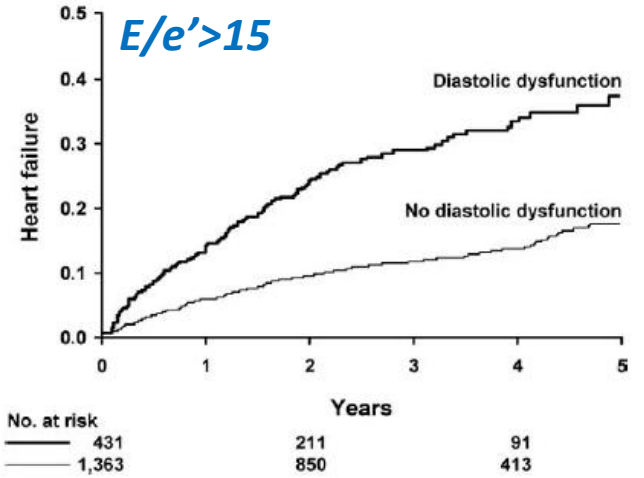

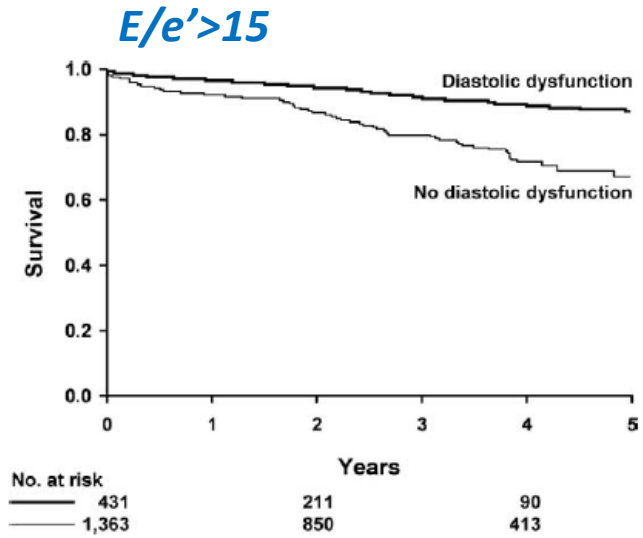

- High prevalence of DD in diabetic patients: 21-75% but
  - High heterogeneity of the studies
  - Few control groups
- Classically considered as the first marker of diabetic cardiomyopathy
- Prognosis value of E/e'

Poirier P, Diabetes care 2010

Preclinical diabetic cardiomyopathy:

Diastolic Dysfunction : An early marker ?

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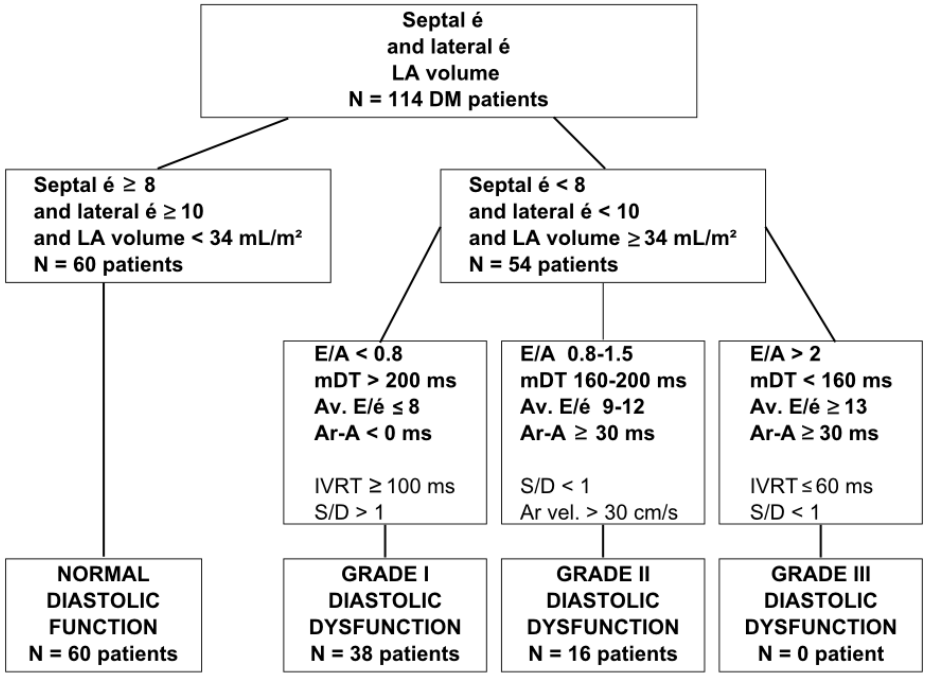
Variable	Controls (n = 88)	Patients with DM (n = 114)	P
LV systolic function			
LVEF (%)	68 ± 7	67 ± 6	.12
Longitudinal systolic strain (%)	−22 ± 2	−19 ± 3	<.001
Radial systolic strain (%)	56 ± 12	50 ± 16	.003
Diastolic function			
LA volume index (mL/m^2)	22 ± 6	24 ± 6	.16
LA area (cm^2)	14 ± 3	17 ± 3	<.0001
E/A ratio	1.2 ± 0.2	1.1 ± 0.2	<.001
mDT (msec)	180 ± 27	225 ± 52	<.0001
IVRT (msec)	74 ± 10.5	83 ± 11.0	<.0001
e′ (cm/sec)	10.3 ± 2.3	8.3 ± 2.4	<.0001
E/e′ ratio	7.7 ± 1.7	10.9 ± 3.6	<.0001
E/e′ ratio/SV	0.102 ± 0.03	0.143 ± 0.056	<.0001
$T_{E-e'}$ (msec)	15.1 ± 12.7	15.9 ± 17.0	.07
IVRT/$T_{E-e'}$	8.0 ± 7.0	10.2 ± 1.2	.11
SR_E (s^{-1})	−1.5 ± 0.2	−1.5 ± 0.3	.07
SR_A (s^{-1})	−0.9 ± 0.2	−1.2 ± 0.3	<.0001
E/SR_E ratio	524 ± 97	602 ± 170	.002



Systolic strain alteration (<18%): 63%

-28% DM patients with normal diastolic function

Prevalence DD (ASE/EAE): 47%

Ernande L, JASE 2010

Preclinical diabetic cardiomyopathy:

Diastolic Dysfunction : An early marker ?

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- Diastolic dysfunction is frequent in diabetic patients but is not specific of diabetes
- Mostly associated with age, BMI, and hypertension

Table 3 Independent factors associated with diastolic functional parameters

	E/A ratio		E/e′ ratio		e′		mDT		IVRT		E/SR_E ratio		E/e′ ratio/SV	
Diastolic parameter	β	P	β	P	β	P	β	P	β	P	β	P	β	P
Age	−0.01	.02			−0.15	<.001							0.16	.008
RPP	−0.00005	<.0001	0.001	<.0001	−0.0004	.009							0.00009	<.0001
Diabetes (yes vs no)			1.8	.001			39	<.0001	0.36	<.001			0.02	.03
Smokers (yes vs no)			−1.8	.001										
Hypertension (yes vs no)			1.8	.001							8.5	.004	0.03	.003
BMI					−0.13	.003					0.59	.03		
LDL cholesterol							−12	.001						

Ernande L, JASE 2010

Preclinical diabetic cardiomyopathy:
Myocardial steatosis

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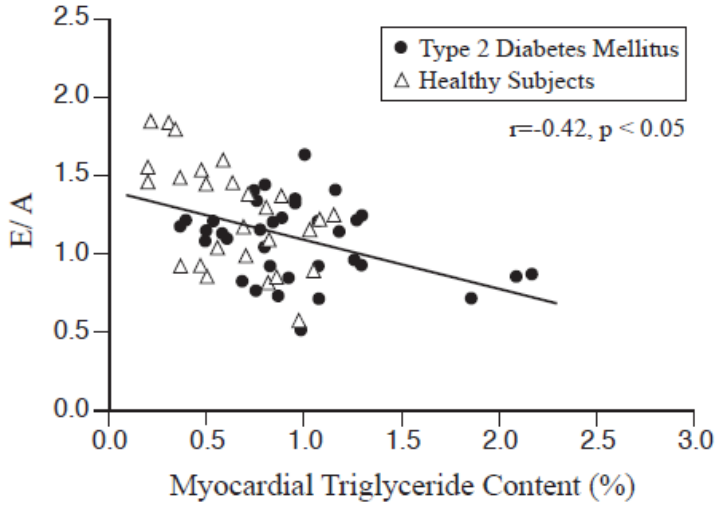
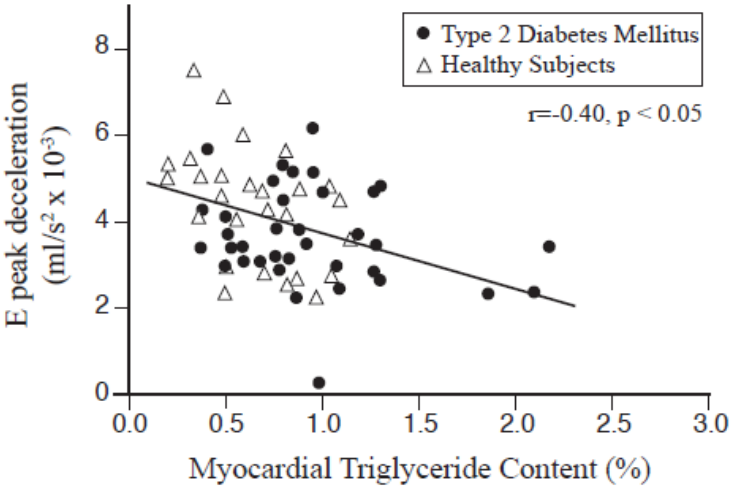
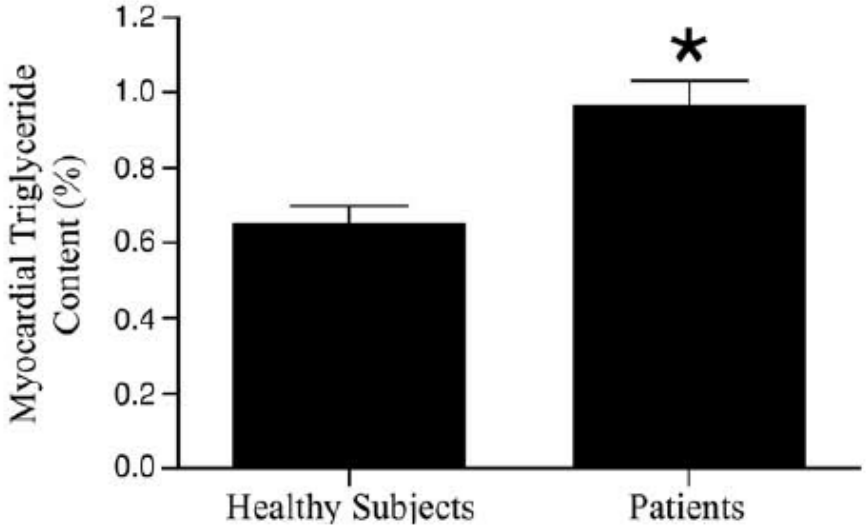


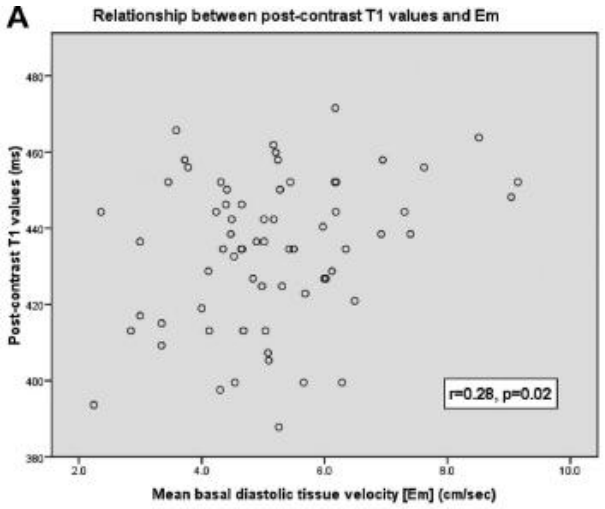


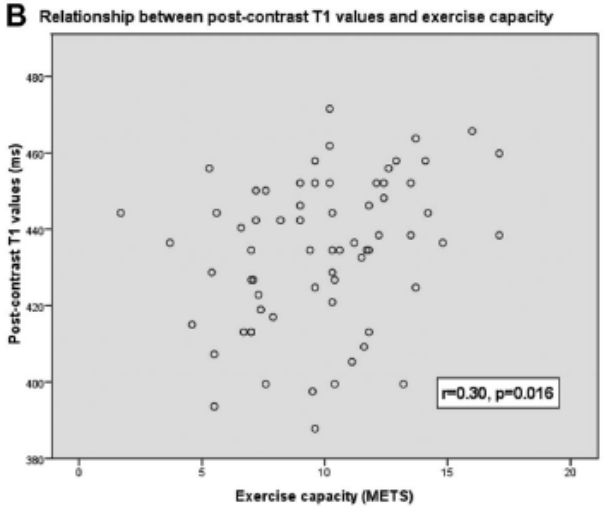


Rijzewijk LJ, JACC 2008

Preclinical diabetic cardiomyopathy:

Myocardial interstitial fibrosis, T1 mapping





Characteristics	Diabetic Patients (n=50)	Controls (n=19)	*P* Value*
Magnetic resonance imaging			
LV mass index, g/m^2	49.0±7.6	50.9±8.7	0.24
LVEDVI, mL/m^2	79.1±14.4	79.8±17.1	0.60
LVESVI, mL/m^2	33.3±7.6	34.7±7.5	0.23
LVEF, %	58.1±4.6	56.2±3.8	0.10
Cardiac output, L/min	6.5±1.3	6.2±2.2	0.44
Global contrast-enhanced myocardial T_1 time, ms	425±72	504±34	<0.001
Echocardiography			
Heart rate, beats/min	74±12	67±12	0.10
Transmitral E/A ratio	1.13±0.34	1.19±0.52	0.97
Deceleration time, ms	194±44	266±68	<0.001
Pulmonary S/D ratio	1.31±0.28	1.22±0.22	0.20
Global longitudinal strain, %	−16.1±1.4	−20.2±1.0	<0.001
Septal E′, cm/s	7.3±1.1	8.7±1.8	0.005
Septal E/e′ ratio	10.0±3.3	8.4±2.0	0.03

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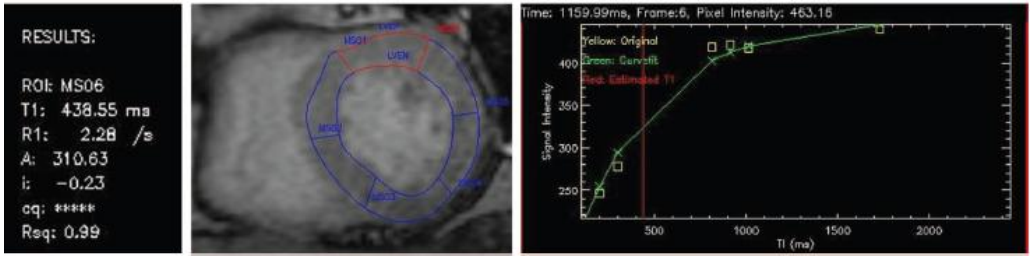
Ng ACT, Circ CVI 2012
Jellis C, Circ CVI 2012



Preclinical diabetic cardiomyopathy:

Pathophysiology

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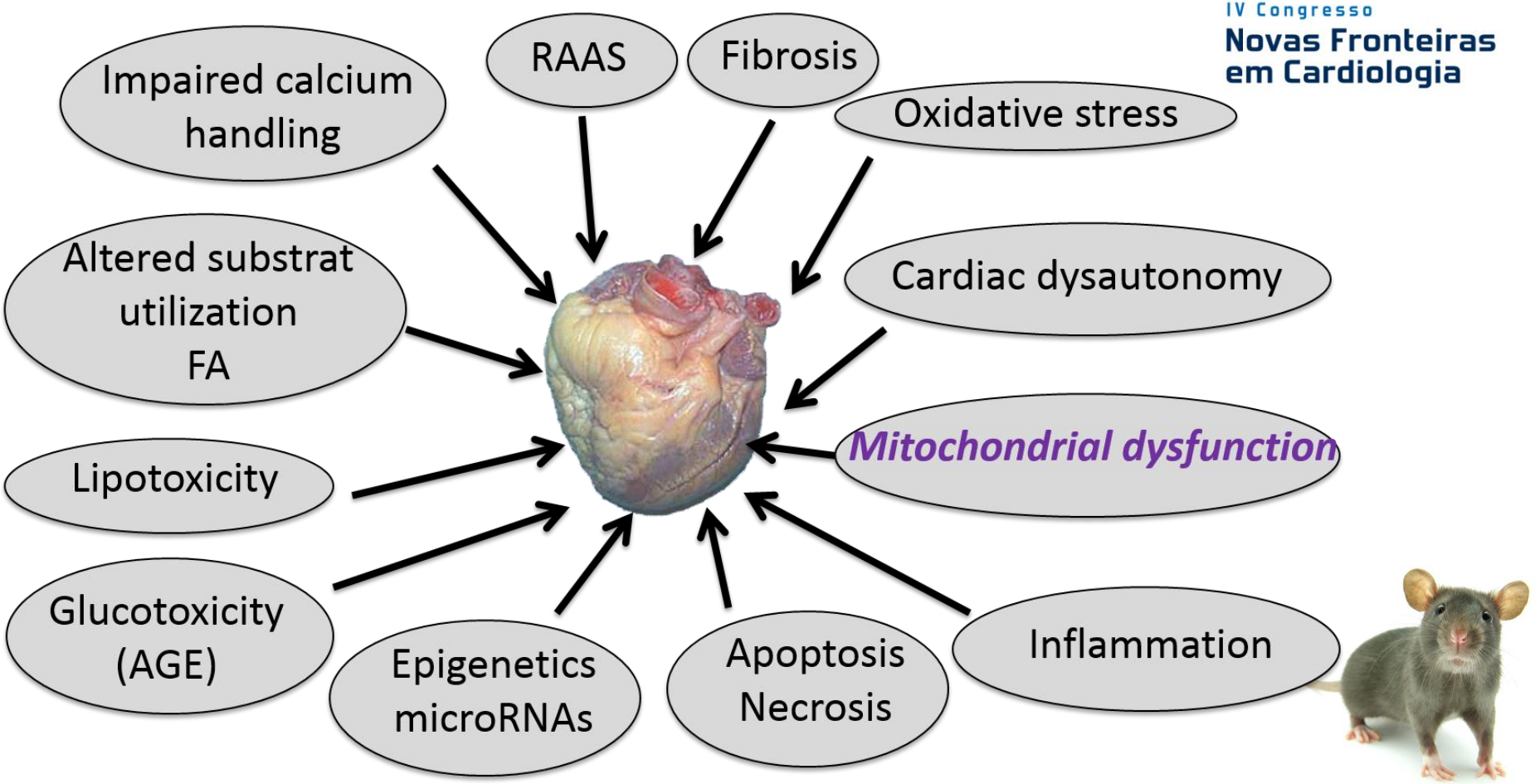
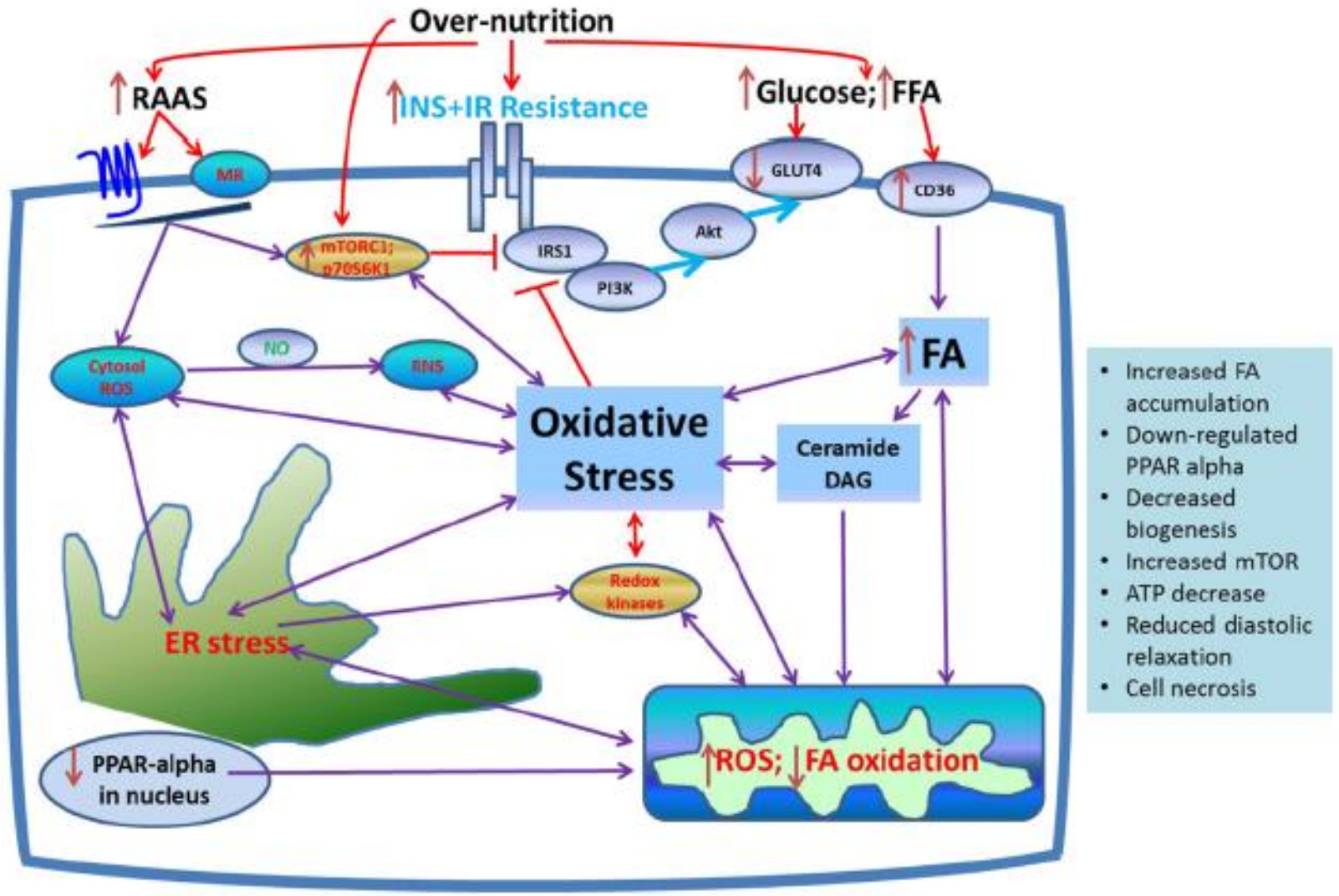
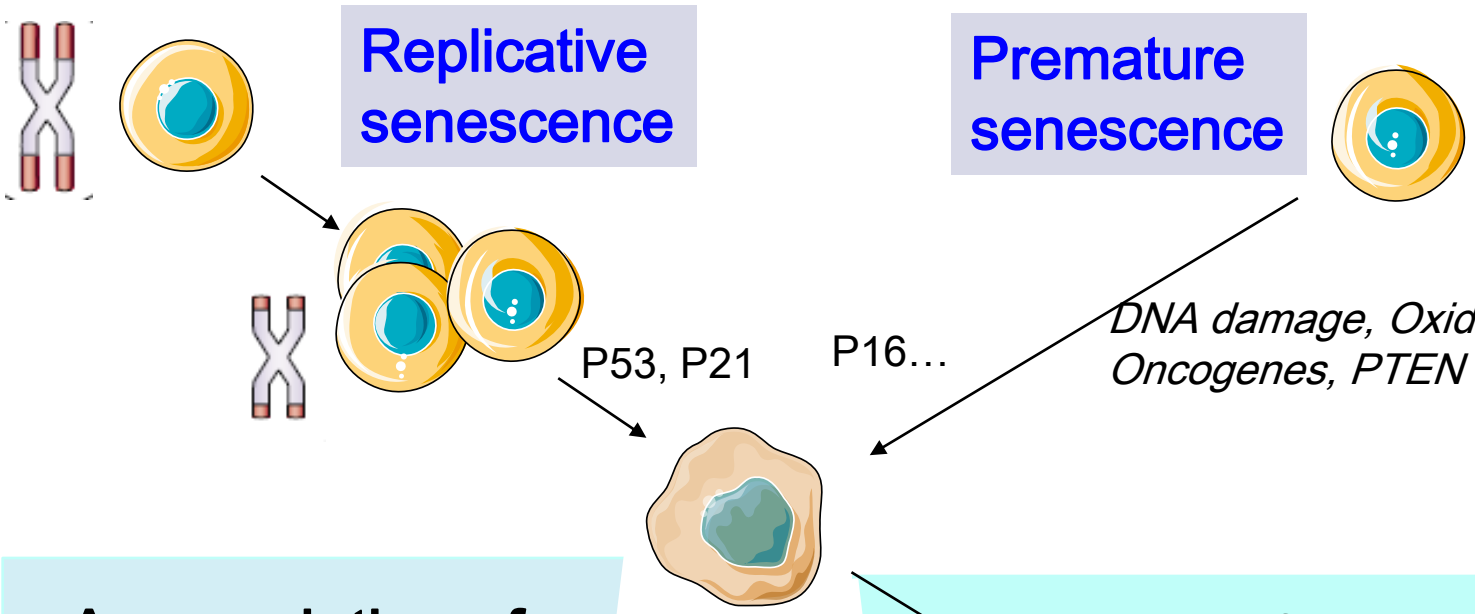


Impact of over-nutrition mediated by insulin resistance on development of cellular oxidative stress and subsequent metabolic cardiomyopathy in the heart.



Diabetic cardiomyopathy:a premature aging process?

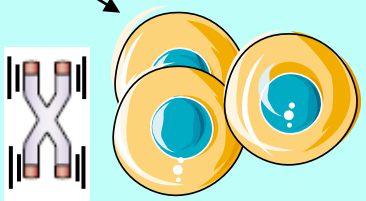


Accumulation of senescent cells

Loss of cell regeneration
Loss of tissue renewal

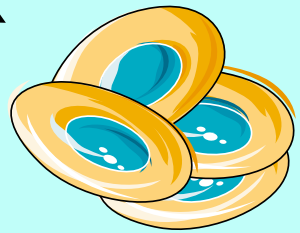
Senescent associated secretory phenotype (SASP
Cytokines, GF,
ECM components…

Inactivation of P53



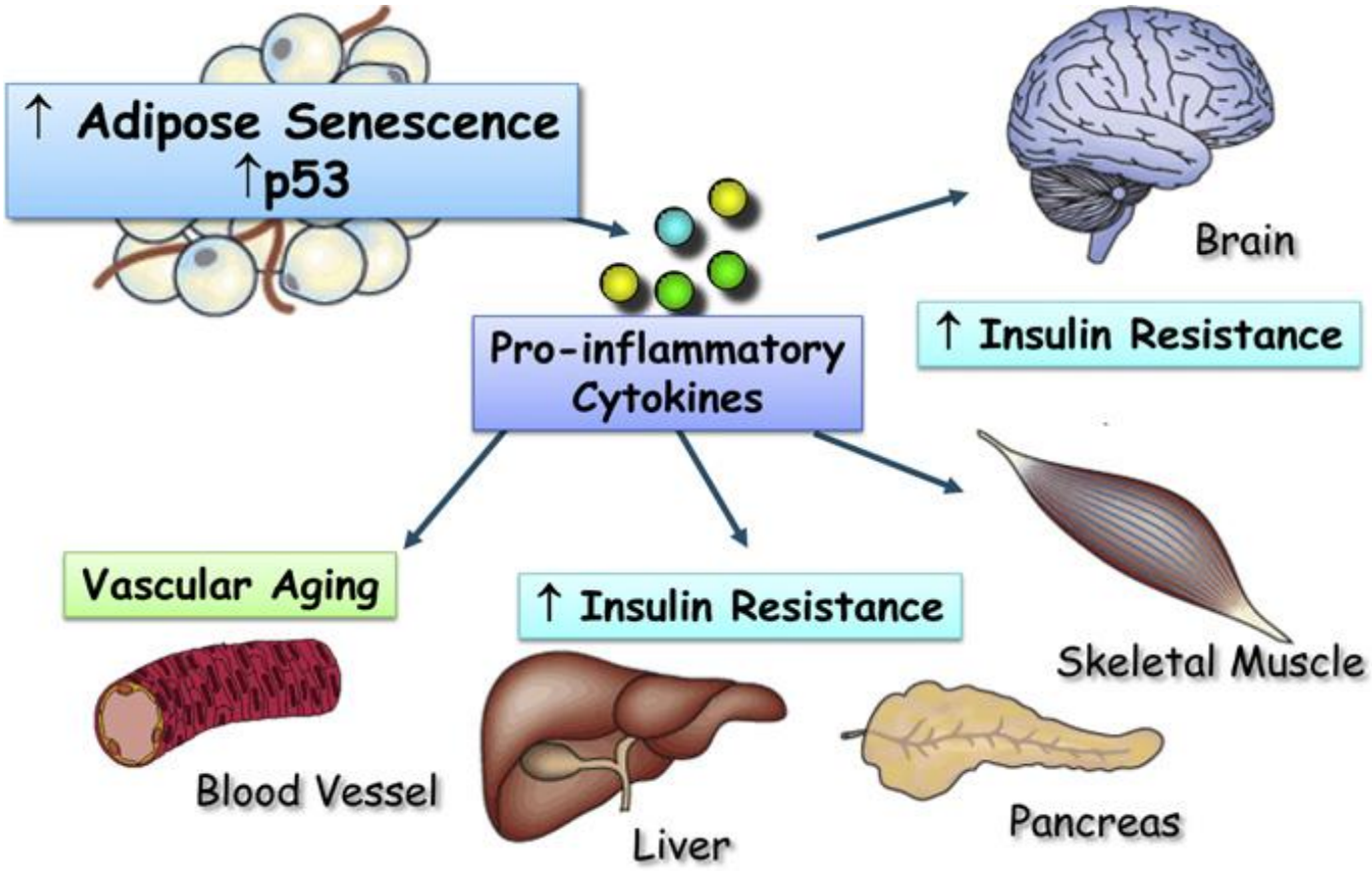
Cell crisis
Reexpression of telomerase

activation of proto-oncogenes (Ras, myc…)



Cell transformation

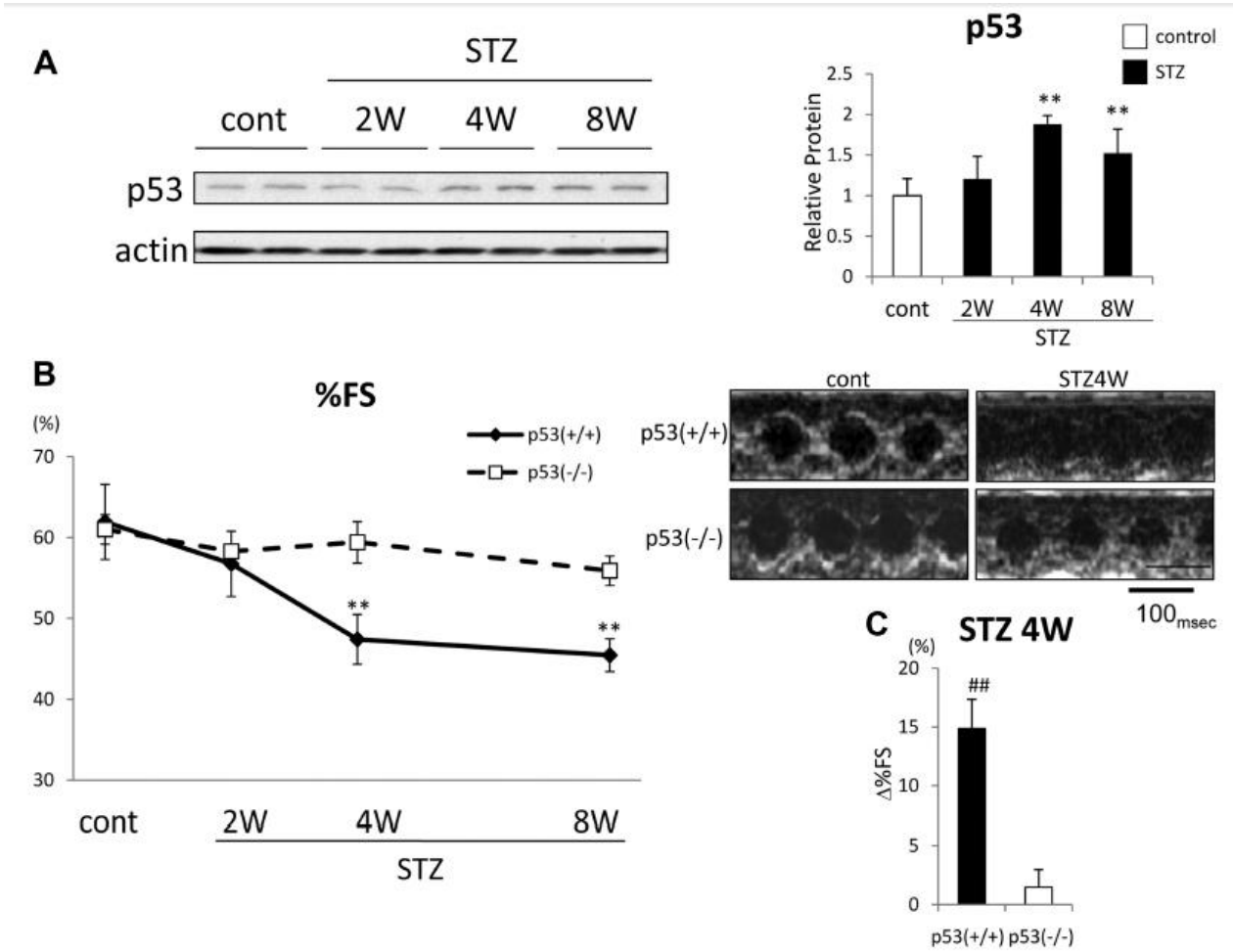
Diabetic cardiomyopathy: a premature aging process ?



Circulation
Heart Failure

American Heart Association®

p53 Promotes Cardiac Dysfunction in Diabetic Mellitus Caused by Excessive Mitochondrial Respiration-Mediated Reactive Oxygen Species Generation and Lipid Accumulation



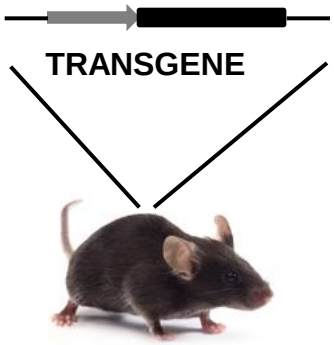
Project:
Interaction of metabolic disorders and ageing to

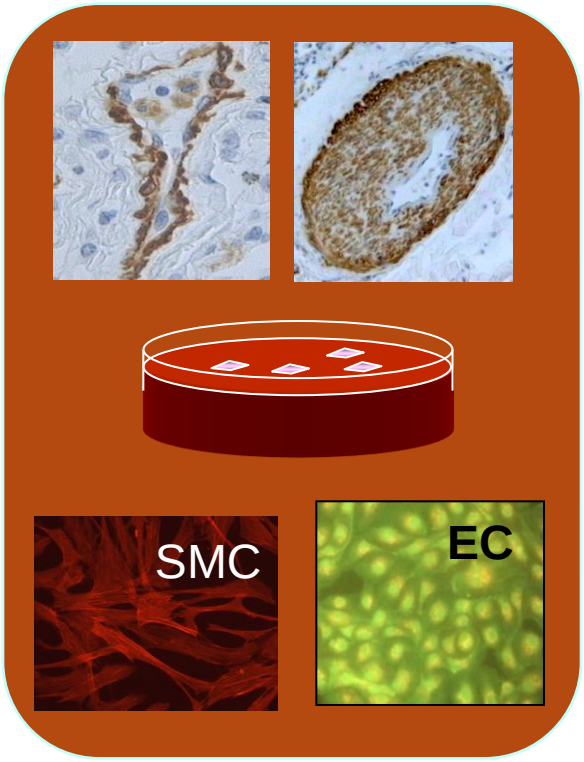
Animal models

Human adipose and myocardial tissue

Clinical studies

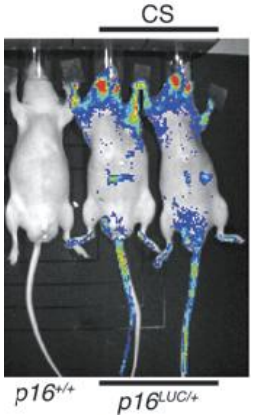
A-TVB





Cohorts

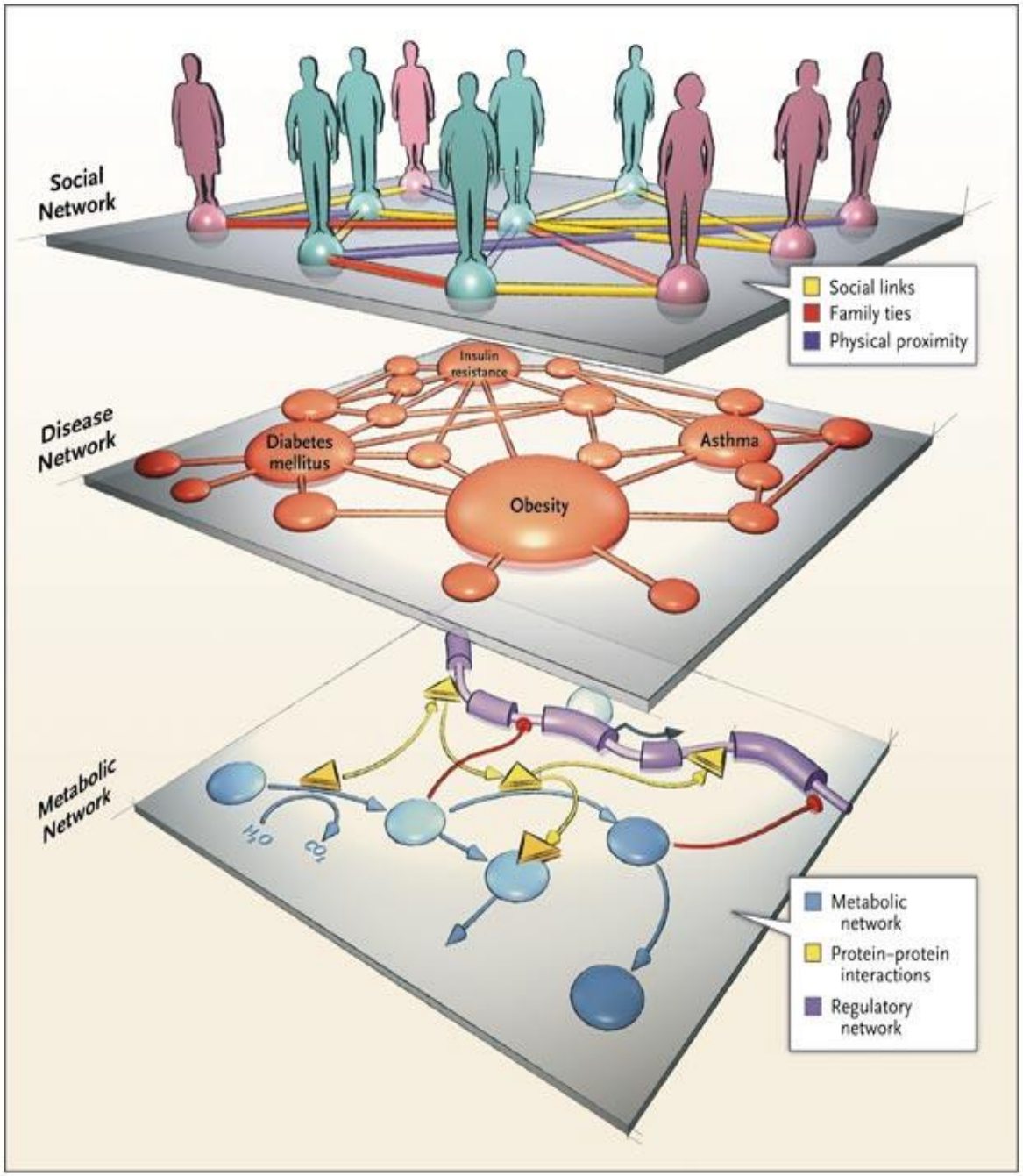
High fat
STZ
Ob/ob
Db/db
P53-/-
MdM2



p16$^{LUC/+}$ mice

(coll N Sharpless)
Chapell Hill (NC, USA)

Surgical Departments
Paris- Pitié salpétrière
Créteil- Henri Mondor


Social Network
Social links
Family ties
Physical proximity
Disease Network
Insulin resistance
Diabetes mellitus
Asthma
Obesity
Metabolic Network
H_2O
CO_2
Metabolic network
Protein–protein interactions
Regulatory network

I have been your « dévouée secrétaire »

THANK YOU !!!

GROUPE HOSPITALIER
HENRI MONDOR

Inserm

UPEC
Connaissance - Action
UNIVERSITÉ
PARIS-EST CRÉTEIL
VAL DE MARNE