What should we expect of cardiac rehabilitation in CHF patients ?

Ph Meurin

Les Grands Prés

Mr H… adressed for cardiac rehabilitation (outpatient)

- 62 years old
- COPD (Tobacco coming off in 2005)
- Chronic Heart Failure:

  - Discovered in 2007:
    - ✔ Sinusal rythm, absence of bundle branch block, LVEF = 30%
    - ✔ Coronary angiography: normal

  - Evolution:
    - ✔ hospitalisations for heart failure:
      - 2007: once
      - 2008: twice
      - 2009: february, april, july.
      - Treatment: nebivolol 5mg,perindopril,furosemide 80 mg

Initial Evaluation (October 2009)

- Physical:
  - 1.70m/90 kg; breathless NYHA 4 (wheezing), moderate inferior limbs oedemas

- Paraclinic investigations:
  - EKG : sinusal rythm, thin QRS
  - Echo: LVEF: 25%, DTD:66mm, no dys-synchrony, sPAP: 60mmhg, E/Ea: 18
  - Bio: BNP= 2500; Na, creat, Hb: normal

- Quality of life poor:
  - walking and gardening stopped since the last hospitalisation (3 months)
  - depression

Decision: hospitalisation for cardiac rehabilitation

- Day 1-3 : IV diuretics
  - NYHA class: 2-3 Weight loss: 4 kg
  - sPAP: 45 mmhg; E/Ea: 11

- Day 4: CPX
  - 60 watts; Peak VO2: 9.5ml/kg/min

- Day 5-20:
  - Exercise training: gymnastics,resistance,bicycle
  - Daily follow-up
  - education

Evaluation when living the Cardiac Rehabilitation Center

- NYHA 1-2; weight loss: 8 kg
- CPX:

  - 90 watts, Peak VO2: 13.2ml/kg/min (+ 38%)
- Polygraphy:

  - Sleep apnea: AHI = 40.2 per hour
- Echo and EKG: non modified
- Treatment:

  - nebivolol 5mg,perindopril,furosemide 250 mg, spironolactone 25 mg
- Will continue to exercise regularly (as an out patient and at home)
- Re-adressed to his Cardiologist ;

  - discussion about defibrillator, CPAP

Cardiac Rehabilitation Centers
can improve the management of these patients

By doing what cannot be done at hospital
or during consultations

Not because the doctors are better

But because the structure is precisely organized to achieve this objective

This cannot be done neither at hospital nor in consultation

- Daily and multidisciplinary interventions

  - Medical and paramedical follow up (weight, dyspnea, sPAP, BNP…)

  -Treatment modifications

  - Exercise:
    - ✔ Exercise capacity improvement
    - ✔ Evolution of the patient while exercising (Blood pressure, heart rate…)
  - Education :
    - ✔ Warning signs
    - ✔ Diet (salt)
    - ✔ Drugs (VKA…)
  - Smoking cessation
  - psychologist

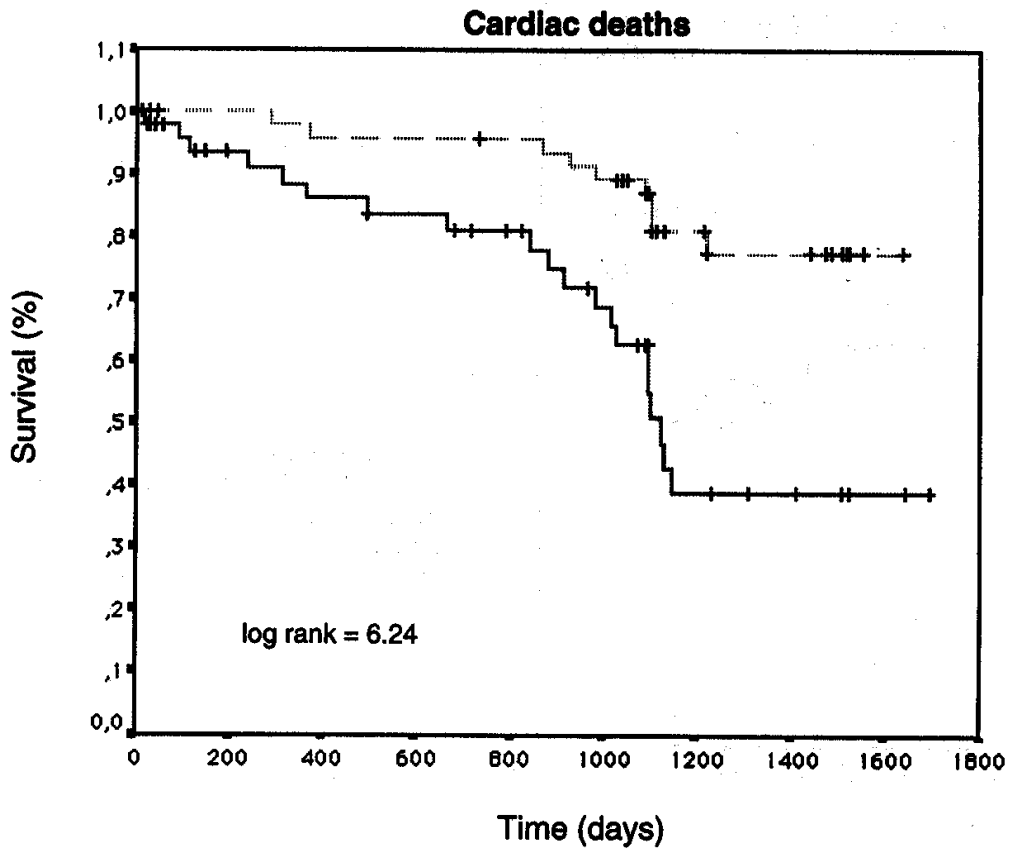
- Completeness of the evaluation (CPX, polygraphy…)

What can we expect of cardiac rehabilitation in CHF patients ?

- Exercise capacity and quality of life improvement
- Diminution of hospitalisations for acute heart failure:
  - Diet and drug adherence, warning signs…
  - Exercise training effect by itself
- Survival benefits
- prognostication

Survival benefits

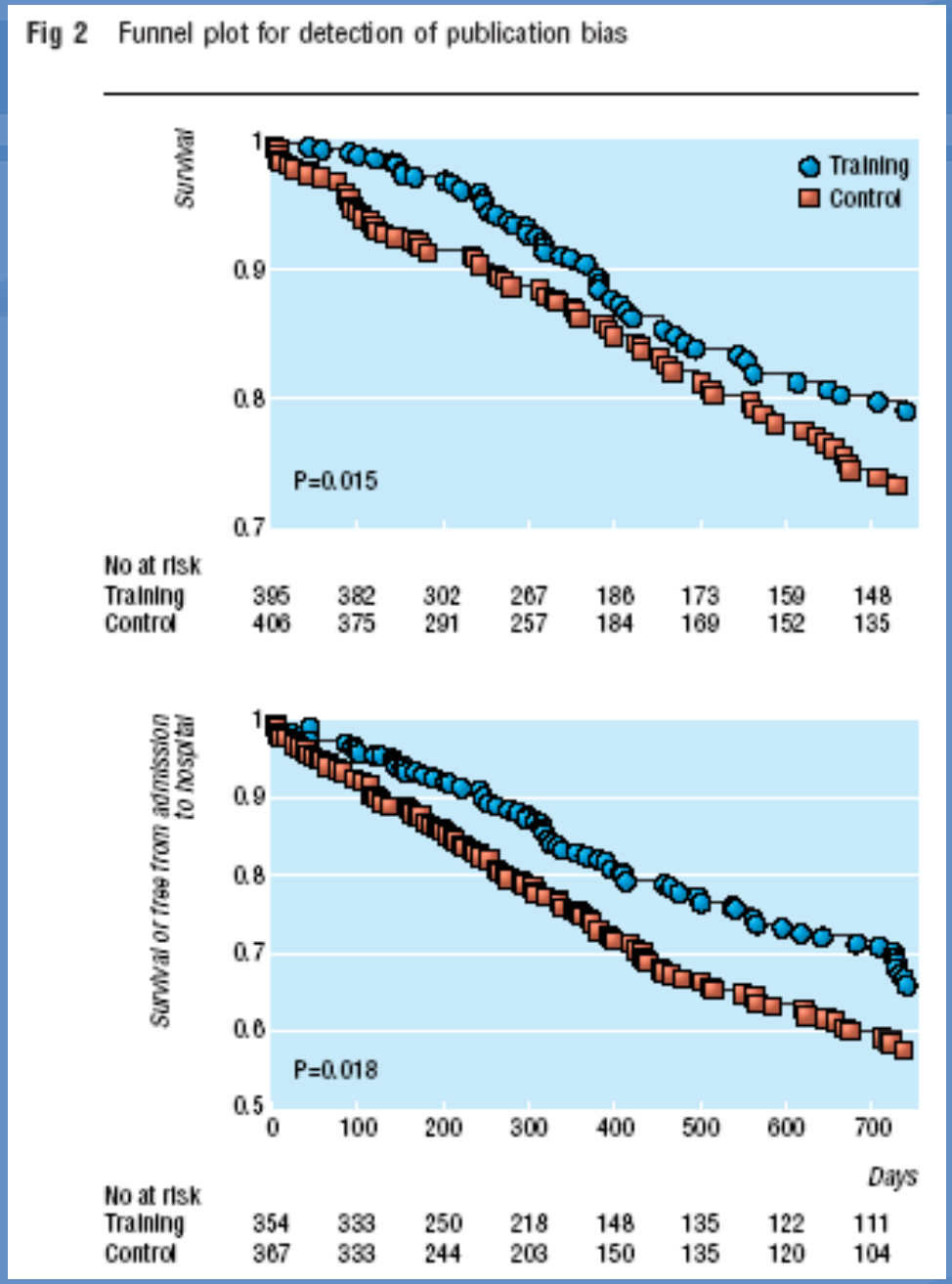
Many positive monocentric studies



No. OF PATIENTS AT RISK

Untrained	49	46	43	42	41	37	29	29	29	29
Trained	50	50	48	48	48	45	42	41	41	41

Belardinelli.R, Circulation 1999;99:1173-97



Méta-analysis : 801 patients

mortality reduction:

RR = 0.65 (p = 0.015)

ExTraMatch study; BMJ 2004;328:189-92

HF-ACTION study (2331 systolic CHF patients)

- Multicenter, randomized trial: exercise vs usual care
- Methodological problems :
  - Patients were not properly trained

O' Connor C, Whellan D, Lee K et al. JAMA 2009; 301: 1439-50

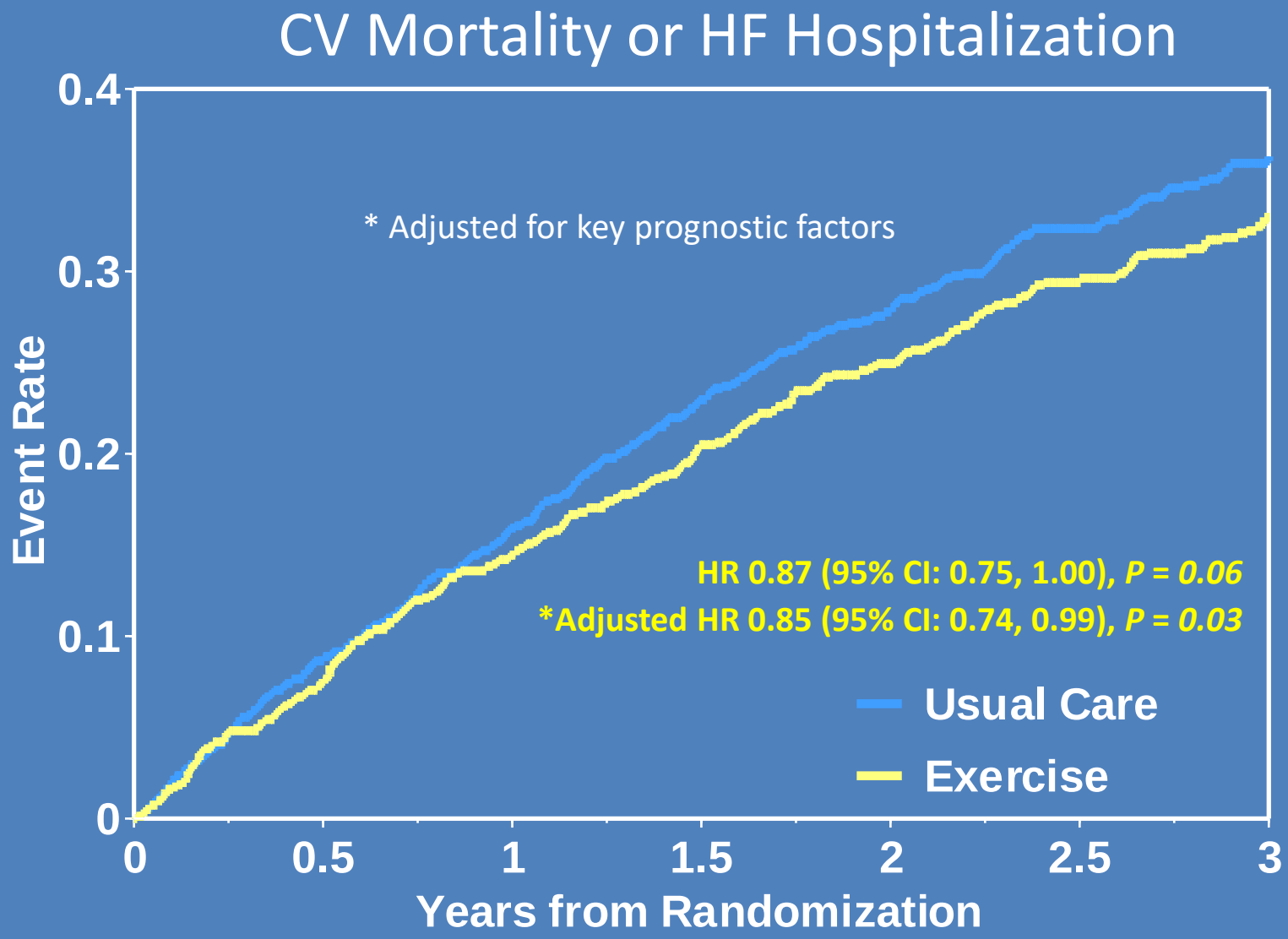
Median Change in 6-Minute Walk and Cardiopulmonary Exercise (CPX) Tests

Baseline to 3 months*	Usual Care	Exercise Training	*P*-value
6-minute walk distance (m)	5	20	<0.0001
CPX exercise duration (min.)	0.3	1.5	<0.0001
Peak VO_2 (mL/min/kg)	0.2	**0.6 (= 4%)**	<0.0001

Baseline to 12 months*	Usual Care	Exercise Training	*P*-value
6-minute walk distance (m)	12	13	0.26
CPX exercise duration (min.)	0.2	1.5	<0.0001
Peak VO_2 (mL/min/kg)	0.1	0.7	<0.0001

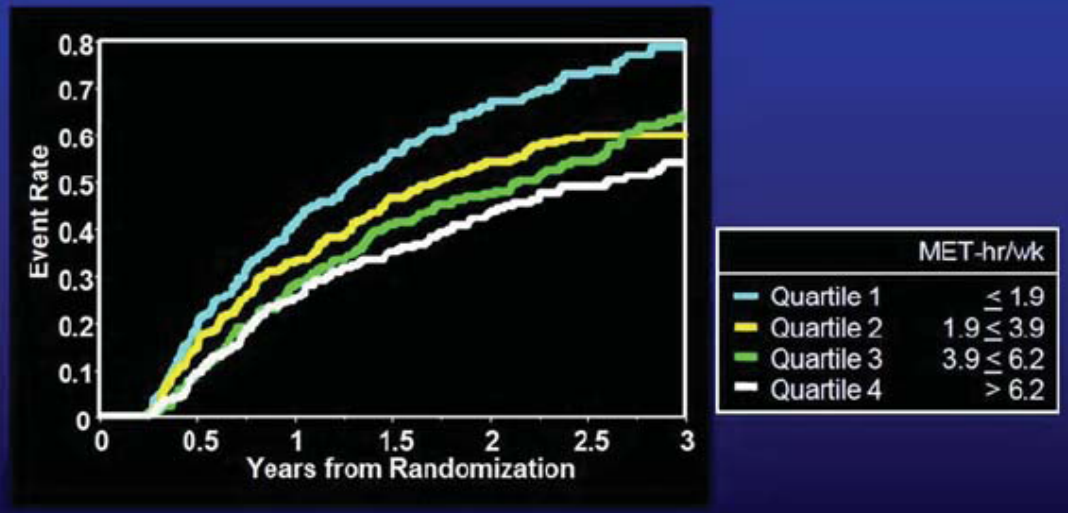
* Complete case analysis

Exercise training is a very potent treatment as it works, even with these major flaws



A dose response analysis of patients enrolled in HF-ACTION

SJ Keteyian et al.



1 MET-hr increase in the volume of exercise performed per Week is associated with **5% lower risk** for all-cause death or all cause hospitalization

Risk reduction per 1 MET/Wk

	HR (CI)*	χ^2	P-value
All-Cause Death or Hosp.	0.95	8.8	0.003
CV Death or Hosp.	0.95	6.8	0.009
CV Death or HF Hosp.	0.89	16.7	< 0.0001

Quality of Life and Exercise Capacity Improvement

Exercise Capacity Improvement

Authors (Year of Publication)	No. of Patients	Exercise Program: Duration, wk	Exercise Program: Activity, Intensity, and Frequency	$\dot{V}o_2$ Increase, % (Outcome vs Controls)
Jette et al (1991)[56]	18	4	Mon–Fri. AM: Jog at 70% to 80% max HR for 5 min 3×/wk; calisthenics 30 min; cycle 15 min at 70% to 80% max HR. PM: Walk 30 to 60 min.	22 in group with EF <30%
Belardinelli et al (1992)[63]	20	8	Cycle at 40% peak $\dot{V}o_2$ 3×/wk.	20
Coats et al (1992)[57]	17	8	Cycle 20 min at 60% to 80% max HR 3×/wk.	18
Belardinelli et al (1995)[58]	55	8	Cycle 40 min at 60% $\dot{V}o_2$max 3×/wk.	12
Hambrecht et al (1995)[59]	22	3	Walk 10 min 6×/d at 70% $\dot{V}o_2$max 2×/wk.	31
Keteyian et al (1996)[60]	29	24	Rating of perceived exertion, 12–14. Treadmill, cycle, rowing, and arm ergometer at 60% exercise capacity for 33 min 3×/wk.	16.3
Radaelli et al (1996)[64]	6	5	Cycle 20 min 5 d/wk.	15
Dubach et al (1997)[67]	25	4	Walk 60 min 2×/d; cycle 40 min 4×/wk at 80% $\dot{V}o_2$max.	26
Tyni-Lenne et al (1997)[65]	16	8	Knee extensor: 60 repeats/min for 15 min for 8 wk (at 65% peak work rate for 4 wk and then 75% peak work rate for 4 wk).	14
Callaerts-Vegh et al (1998)[66]	17	8	Walk 1 h, 2×/d; cycle 45 min at 70% to 80% HR reserve 4×/wk.	30.9
Reinhart et al (1998)[67]	25	8	Cycle 40 min at 70% to 80% max capacity 4×/wk; walk 1 hour 2×/d.	29
Belardinelli et al (1999)[62]	99	8 (plus maintenance)	Cycle at 60% peak $\dot{V}o_2$ 3×/wk for 8 wk. Maintenance: 2×/wk for 12 mo.	18 at 2 mo; 23 at 14 mo
Taylor (1999)[68]	8	8	Train 30 min at 45% to 70% peak $\dot{V}o_2$ 3×/wk.	17.6
Sturm et al (1999)[69]	26	12 (plus maintenance)	Step aerobics and cycle at 50% capacity for 12 wk; then step aerobics 100 min/wk and cycle 50 min/wk.	23.3
Keteyian et al (1999)[70]	43	24	Treadmill, cycle, and arm ergometer at 60% to 80% max HR for 33 min 3×/wk.	14.3

HR indicates heart rate (bpm); max, maximum.

↑ PVO2 de 12 à 31%

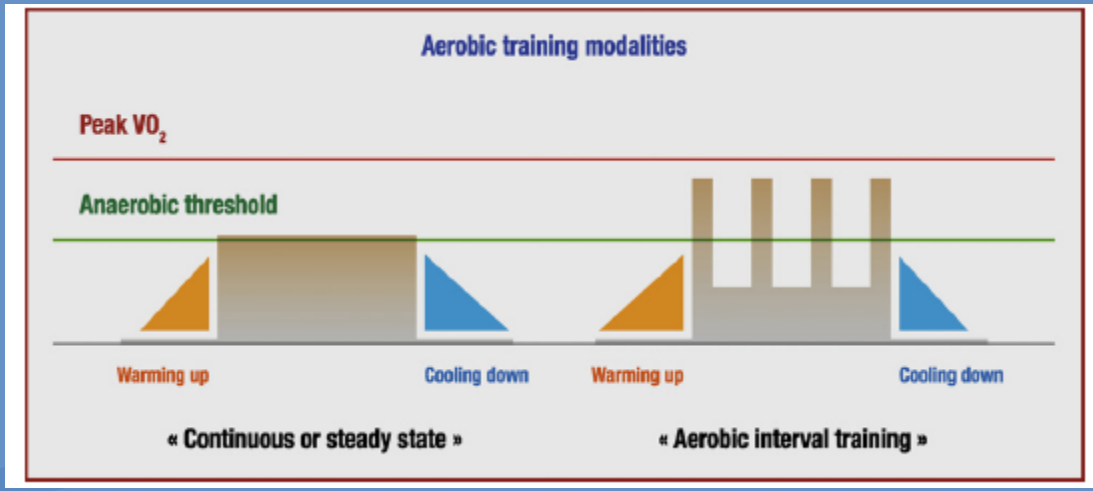
1- Pina et al, circulation 2003.
2- Wisloff et al. Circulation 2007;115:3086-3094

Exercise capacity improvement seems do depend on

- Adherence
- Exercise session type
  - Intensity
  - Frequency
  - Aerobic and/or resistance
  - Continuous or Interval Training:
    - ✔ Wisloff study :Peak Vo2 improvement: (?)
      - ◈ CT: +14%
      - ◈ IT: +46%

Treatment ?

- ◈ betablockers ?



Wisloff et al. Circulation 2007;115:3086-3094

Prognostication

Main prognostic factors

- LVEF, E/A
- BNP,Haemoglobinemia,creatininemia,natremia
- Ergometric Parameters:

  - Peak VO2, VE/VCO2 slope, T1/2VO2, circulatory Power, chronotropic recovery
- Rythm (sinusal or not), larges QRS…

The absence of exercise capacity improvement after an exercise training program: a strong prognostic factor in CHF Patients

Tabet JY, Meurin P, Beauvais F, Weber H, Renaud N, Thabut G, Cohen-Solal A, Logeart D, Ben Driss A.Circ Heart Fail. 2008 Nov;1(4):220-6.

Methods

- Inclusion criteriae
  - CHF patients with LVEF<45%
  - Able to undergo an ETP in a cardiac rehabilitation center
- Exercise training program
  - 3 to 5 training sessions per week for 4 to 8 weeks
    - ✔ 30 mn at HR = HR observed at the VT
    - ✔ Gym
- Follow-up : 2 years
- End Point : MACE = Death, TX and hospitalization for acute heart failure

Results

Results (1) : Population and Training Results

- 155 patients, 53±12 years old
- NYHA 2.4±0.6, LVEF = 29.5±7.1%, PVO_2 = 16.2 ± 4.1 ml/kg/min
- male 81%, SR 91%
- Treatment
  - ACE or ARB: 91%
  - Diuretics: 98%
  - B-blockers: 91%
- After ETP completion
  - PVO2 Improvement :2.2 ml/kg/min (median value 2 ml/kg/min): + 15%.

Results(2) : events

- End point : 27 cardiac events
  - death n=12, TX n=5, acute HF n=10

- Which parameters could predict the outcome?
  - Baseline parameters
  - Exercice capacity improvement after the ETP

Univariate Analysis

	Chi2	P level
Age	1.2	0.27
NYHA class (I-II vs. III-IV)	**7**	**0.001**
Ischemic etiology	3.6	0.06
Diabetes	0.4	0.5
Atrial Fibrillation	**8.1**	**0.003**
LVEF	**11**	**0.01**
E/A ratio	**8.1**	**0.004**
E/Ea ratio	**5**	**0.02**
Systolic PAP	**8.3**	**0.02**
Plasma BNP	**15**	**<0.0001**
Creatininemia level	3.0	0.08
Haemoglobin level	**4.0**	**0.04**
Ventilatory threshold	3.3	0.06
PVO_2	**7.8**	**0.005**
Chronotropic reserve	**8.0**	**0.04**
VE/VCO_2 slope	**5.4**	**0.04**
ΔPVO_2	**15.8**	**0.0007**

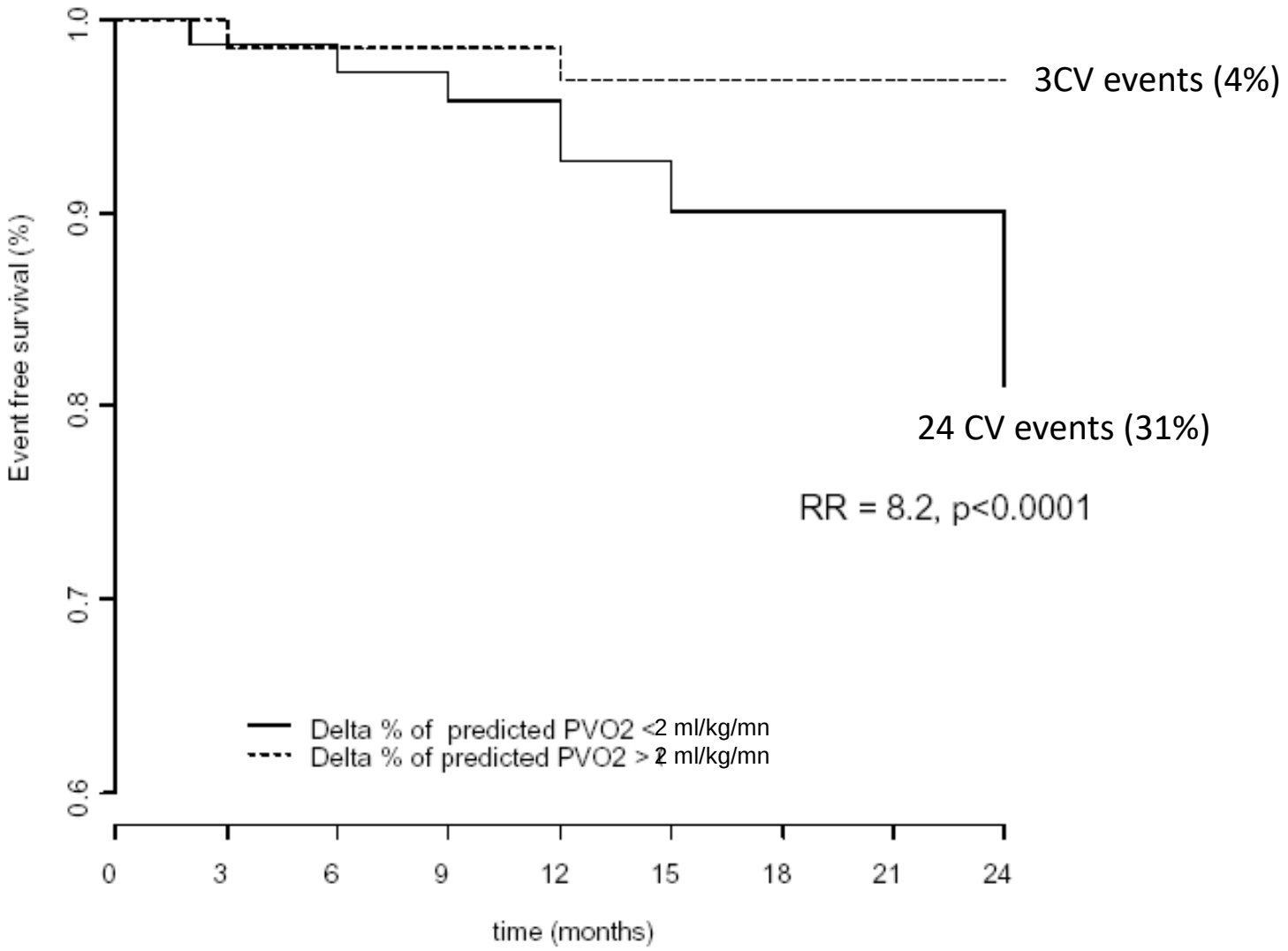
Multivariate Analysis

	Chi2	P	RR (95% CI)
Δ PVO_2	**5.6**	**0.01**	**0.87 (0.77-0.99)**
BNP level	**7.5**	**0.01**	**1.002 (1.001-1.004)**
LVEF	1	0.2	0.92 (0.81-1.05)
NYHA (III-IV vs. I-II)	1.3	0.24	0.42 (0.07-2.43)
Atrial Fibrillation	0.9	0.3	2.6 (0.3-18)

Do unresponsive patients have a worse prognosis than responsive ones ?

-Responsive patients PVO2 Improvement >2ml/kg/min (median value)

-Unresponsive patients PVO2 I <2 ml/kg/min


Event free survival (%)
1.0
0.9
0.8
0.7
0.6
0
3
6
9
12
15
18
21
24
time (months)
3CV events (4%)
24 CV events (31%)
RR = 8.2, p<0.0001
Delta % of predicted PVO2 <2 ml/kg/mn
Delta % of predicted PVO2 >2 ml/kg/mn

Conclusion 1

Cardiac rehabilitation :

- Stabilisation (drugs…) and close follow up
- Repeated clinical,echographic,ergometric,biological (…) assessments
- Education
- Exercise training…

Conclusion 2

- Absence of improvement in exercise capacity after an ETP has a strong prognostic value for cardiac events independently of LVEF, NYHA status and BNP level.

Conclusion 3

All CHF patients should undergo an Exercise training program, which:

- Improves exercice capacity and quality of life
- Probably improves prognosis
- Helps to stratify CHF prognosis

Cost-effectiveness

- Economical evaluation of a treatment:
  - Cost of a life-year saved
  - Theoretically< 20 000 $ ……

- Some costs:
  - Tobacco cessation in a coronary artery disease patient: 1000$
  - cardiac rehabilitation[1] for a CHF patient: 1773$
  - CABG in a left main stenosis patient[2]: 3800$
  - Simvastatin in secondary prevention[2]: 5800$
  - Carvedilol in CHF[2]: 13000$

1- Georgiou D et al.Am J Cardiol 2001;87:984-88.
2- Mark DB, Hlatky MA. Circulation 2002;106:626-30

	Responsive patients n=77	Unresponsive patients n=78
Male (%)	80	81
Age, n (y)	52±12	55±13
Ischemic etiology (%)	48	60
Diabetes, n (%)	32 (20)	18 (23)
Sinus rhythm, n (%)	75 (97) *	69 (89)
LVEF (%)	31±6	28±7*
NYHA class	2.4±0.6	2.4±0.7
E /A ratio	1.4±0.8	1.4±0.8
Systolic PAP (mmHg)	34±6	37±11
BNP (pg/ml)	496±354	447±486
Creatininemial(mmol/l)	103±28	109±31
Haemoglobin (g/dl)	13.2±1.5	12.7±1.6
Ventilatory threshold (ml O_2/kg/min)	12.1±3.2	12.1±3.2
Chronotropic reserve (bpm)	47±20	43±21
PVO_2 (ml O_2/kg/min)	16.2±4.4	16.3±4.0
VE/VCO_2 slope	33±8	37±7
Number of ET sessions	19±11	23±12
Bisoprolol n, (dose (mg)) Carvedilol n, (dose(mg))	66, (3.5±2.6) 12, (26±39)	57, (3.7±2.9) 8, (21±12)

Lifestyle Interventions

Isn't there a pill that will accomplish the same thing?