Trening av pasienter med hjertesvikt

Asbjørn Støylen,
DR. med.
ISB,
NTNU

http://folk.ntnu.no/stoylen/lectures/#student

Trening ved hjertesvikt

- Er det ønskelig?
- Er det gunstig
  - Hva vinner man?
- Er det farlig?

- Hva slags trening?
  - Type,
  - Mengde,
  - Intensitet?

Hva vet vi?

- Kliniske studier
- Guidelines
- Eksperimentelle studier

Table 2 Summary of randomized exercise training studies in (LV) dysfunction and heart failure

Study	n pts	Clinical characteristics
Coats 1990[10]	11	Stable CHF, IHD, synus rhythm, NYHA II–III
Jetté 1991[55]	18	10 wk after the 1st anterior MI no previous history of
Koch 1992[76]	25	Stable CHF, IHD or IDCM, NYHA II–III
Meyer 1991	12	Stable CHF, sinus rhythm, NYHA II–III
Coats 1992[11]	17	Stable CHF, secondary to IHD sinus rhythm, NYHA
Davey 1992	22	Stable CHF, NYHA II–III
EAMI Study, Giannuzzi 1993[22]	31	5 wk after 1st anterior MI, NYHA II–III
Adamopoulos 1993[17]	12	Stable CHF, NYHA II, III
Belardinelli 1995[13]	27	Mild CHF, IHD or IDCM, NYHA II–III
Belardinelli 1995[13]	55	Stable CHF, IHD or IDCM, NYHA II–III
Hambrecht 1995[12]	22	Stable CHF, IHD or IDCM, NYHA II–III
Kiilavouri 1995[14]	20	Stable CHF, IHD or IDCM, NYHA II–III
Kiilavouri 1995[14]	27	Stable CHF, IHD or IDCM, NYHA II–III
Meyer 1996[19]	18	Stable CHF, IHD or IDCM, NYHA II–III
Meyer 1996[19]	16	Stable CHF, IHD or IDCM, NYHA II–II
Piepoli 1996[44]	12	Stable CHF, NYHA II–III
Magnusson 1996	11	Stable CHF, IHD or IDCM, NYHA II–IV (1 pt)
Hambrecht 1997[18]	18	Stable CHF, IHD, NYHA II–III
ELVD Study, Giannuzzi 1997[23]	77	3–4 wk after 1st MI, no history of HF
Willenheimer *et al.* 1998	49	Stable CHF, IHD or IDCM, 8 'Boston points;
Belardinelli 1999	99	Stable CHF, IHD or IDCM, NYHA II–III
CHANGE study, Wielenga *et al.* 1999	80	Stable CHF, IHD or IDCM, NYHA II–III
CHANGE study, Wielenga 1999[64]	80	Stable CHF, IHD or IDCM, NYHA II–III
ELVD CHF just completed, Giannuzzi 1999	86	Stable CHF, IHD or IDCM, NYHA II–III

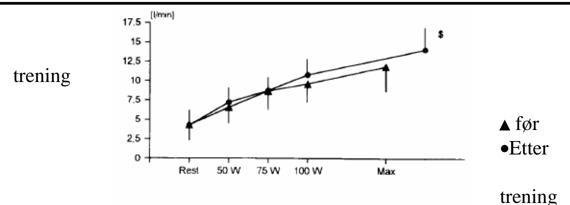
HF-ACTION

- 3000 pasienter.
- Pretesting av VO_{2max}
- Randomisering til trening vs usual care
- Initial supervisert trening 6-12 uker 60-70% av max HR
- Følges i 4 år (hjemmebasert maintenance program med regelmessige besøk)

- Primært endepkt: All cause mortality and all cause hospitalisation

Whellan et al 2007

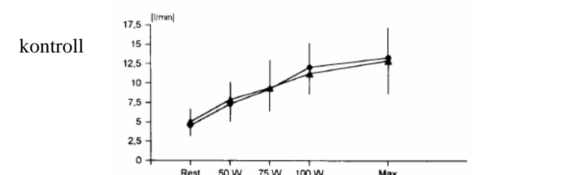
trening



▲ før
●Etter

trening

kontroll



Hambrecht 1995

CHANGE studien

- 80 pasienter, 41 randomisert til trening
- Trening 3g / uke
- Intensitet til 60% av differanse mellom resting og max på test.
- Økning i exercise time og anaerob terskel.
- Ingen økning i VO_{2max}
- Ingen adverse effects.
  - (Wielenga EHJ 1999)
- Leder: trening er nå mellom fase II og fase III i dokumentasjon
  - (Meyer EHJ 1999)

Livskvalitet:

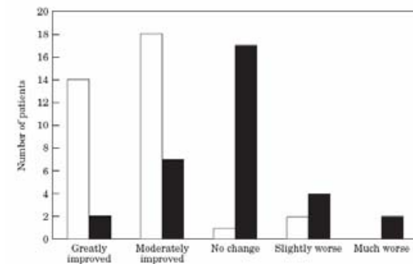


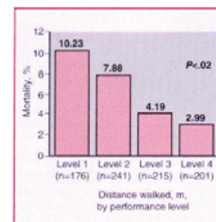
Figure 1 Overall assessment of general well-being. □=training; ■=control.

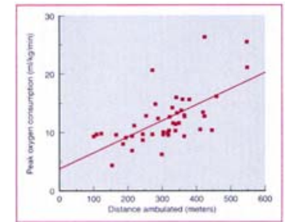
Wielenga 1999

Belardinelli 1999

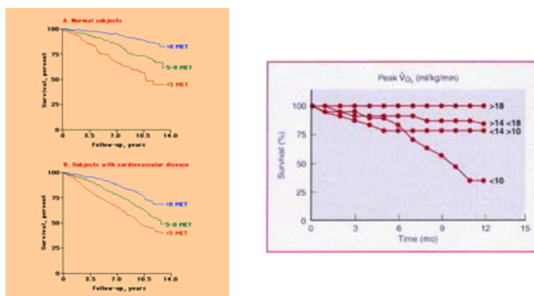
- 99 pas, 50 trening, 49 kontroll. EF 28%
- Trening på 60% av VO_{2max} 3x/uke i 8 uker, deretter 2x i et år!!!!
- Økning i VO_{2max} og QoL med trening i startfasen.
- Ingen endring i vedlikeholdsperioden
- Ingen endring i EF
- Signifikant lavere mortalitet (9/50 18%) vs 20/49 (41%) og non fatale endepunkter (8 vs. 17).
- MEN: svært høy mortalitet sammenlignet med andre materialer med tilsvarfende EF.
- Ingen pasienter på betablokker

Funksjonsnivå og overlevelse





VO_{2max} og overlevelse:



Myers 2002

Kussmaul 1991

Funksjonsnivå og overlevelse:

- Prognose avh. av funksjonsnivå
- Bedret funksjon → bedre prognose?
- Ingen holdbare endepunktsstudier
- Funksjonsnivå og VO_{2max} er <u>surrogatendepunkt</u> i forhold til overlevelse
- Jfr. CRT: MIRACLE og MUSTIC, < 400 pas.
  - Bedre funksjonsnivå
  - Bedre EF
  - Ikke sign bedre overlevelse

Surrogatendepunkter:

- Fysiologiske parametre:
  - Selv om fysiologiske parametre er assosiert med overlevelse, er det ikke gitt at den bedringen en ser med intervensjon vil føre til bedre overlevelse:
    - Cholesterolsenkning, BT behandling……
- Overlevelse
  - Må dokumenteres i endepunktsstudier, som må være av en viss størrelse:
  - Manglende dokumentasjon av økt overlevelse vil ikke si at det ikke er økt overlevelse, kan skyldes at studiene er for små
- Livskvalitet
  - Er et eget endepunkt – for symptomatisk behandling
    - Ortopedi, PCI/CABG ved stabil angina, øyekirurgi……

Safety:

TABLE 3. Studies on Exercise Training in Chronic HF Due to Systolic Dysfunction: Adverse Events

Authors (Year of Publication)	No. of Patients	EF, %	Exercise Program: Duration, wk	Exercise Program: Intensity (% Peak HR or $\dot{V}O_2$)	Adverse Events
(1) Conn et al (1982)	10	29	5 to 8	70% to 80% HR	None during training
(2) Sullivan et al (1988)	12	24	16 to 24	75% $\dot{V}O_2$	Worsened HF (n=1); exhaustion (n=1)
(3) Jette et al (1991)	7	24	4	70% to 80% HR	Worsened HF (n=3); ventricular tachycardia (n=1)
(4) Meyer et al (1991)	12	23	6	70% to 80% HR	Worsened congestive HF (n=1)
(5) Coats et al (1992)	17	19	8	70% to 80% HR	None during training
(6) Koch et al (1992)	12	26	12	Individualized protocol	None during training
(7) Belardinelli et al (1995)	16	31	8	40% $\dot{V}O_2$	None during training
(8) Belardinelli et al (1995)	36	28	8	60% $\dot{V}O_2$	Atrial fibrillation (n=1); hypotension (n=2)
(9) Hambrecht et al (1995)	12	26	24	70% $\dot{V}O_2$	Atrial arrhythmia (n=1)
(10) Keteyian et al (1996)	15	21	24	60% to 80% HR	None during training
(11) Kavanagh et al (1996)	15	22	52	50% to 60% $\dot{V}O_2$	None during training but worse HF (n=5) after training
(12) Kiilavuori et al (1996)	12	24	24	50% to 60% $\dot{V}O_2$	Not reported
(13) Wilson et al (1996)	32	23	12	60% to 70% HR	Extreme exhaustion (n=3)
(14) Demopoulos et al (1997)	16	21	12	50% to 80% $\dot{V}O_2$	None during training
(15) Dubach et al (1997)	12	32	8	70% to 80% $\dot{V}O_2$	None during training
(16) Meyer et al (1997)	18	21	3	50% $\dot{V}O_2$	None during training
(17) European Heart Failure Training Group (1998)	134	25	6 to 16	70% to 80% HR	None during training
(18) Hambrecht et al (1998)	10	24	24	70% $\dot{V}O_2$	None during training
(19) Belardinelli et al (1999)	50	28	52	60% $\dot{V}O_2$	None during training
(20) Hare et al (1999)	9	26	11	Resistance training	None during training

HR indicates heart rate (bpm).

Styrketrening

TABLE I Changes in Systolic and Diastolic Blood Pressure, Heart Rate, Rate-Pressure Product, and End-Diastolic and End-Systolic Volumes During Cycling and Leg Press Exercises

	Rest	Leg Press	Cycling
Systolic blood pressure (mm Hg)	157 ± 7	189 ± 8*	199 ± 13*
Diastolic blood pressure (mm Hg)	77 ± 2	98 ± 4*	86 ± 3*†
Heart rate (beats/min)	66 ± 4	86 ± 5*	107 ± 4*†
Rate-pressure product	103 ± 6	161 ± 7*	213 ± 17*†
End-diastolic volume (ml)	257 ± 26	269 ± 27	268 ± 24
End-systolic volume (ml)	179 ± 22	188 ± 22	180 ± 23

*p <0.05 compared with rest; †p <0.05 compared with leg press.
Values are expressed as mean ± SEM.

TABLE II Changes in Cardiac Output, Stroke Volume, Total Peripheral Resistance, Ejection Fraction, and Systolic Blood Pressure to End-Systolic Volume Ratio During Cycling and Leg Press Exercises

	Rest	Leg Press	Cycling
Cardiac output (L/min)	5.2 ± 0.5	6.9 ± 0.5*	9.3 ± 0.7*†
Stroke volume (ml)	77 ± 5	80 ± 4	87 ± 5*†
Total peripheral resistance (mm Hg•L^{-1}•min^{-1})	23 ± 2	20 ± 2	14 ± 1*†
Ejection fraction (%)	31 ± 2	32 ± 2	34 ± 2
Systolic BP/ESV ratio	0.9 ± 0.1	1.1 ± 0.1*	1.2 ± 0.2*†

*p <0.05 compared with rest; †p <0.05 compared with leg press.
Values are expressed as mean ± SEM.
BP = blood pressure; ESV = end-systolic volume.

McKelvie 1995

Styrketrening

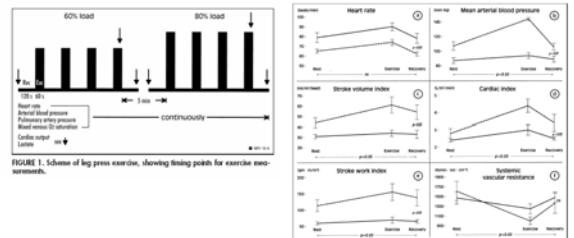


FIGURE 1. Scheme of leg press exercise, showing timing points for exercise measurements.

Meyer 1999

Styrketrening:

- Bedre perifert O_2 – opptak
- Bedre arbeidsøkonomi (subjektiv bedre form)
- Motvirke sviktbetinget myopati?

ESC Guidelines

Guidelines for the diagnosis and treatment of chronic heart failure: executive summary (update 2005)

The Task Force for the Diagnosis and Treatment of Chronic Heart Failure of the European Society of Cardiology

Authors/Task Force Members: Karl Swedberg, Chairperson,* Göteborg (Sweden) *Writing Committee:* John Cleland, Hull (UK), Henry Dargie, Glasgow (UK), Helmut Drexler, Hannover (Germany), Ferenc Follath, Zurich (Switzerland), Michel Komajda, Paris (France), Luigi Tavazzi, Pavia (Italy), Otto A. Smiseth, Oslo (Norway).

Exercise
Exercise improves skeletal muscle function and therefore overall functional capacity. Patients should be encouraged and advised on how to carry out daily physical and leisure time activities that do not induce symptoms. Exercise training programs are encouraged in stable patients in NYHA class II–III. Standardized recommendations for exercise training in heart failure patients by the European Society of Cardiology have been published.[42]

Working Group Report

Recommendations for exercise testing in chronic heart failure patients

Working Group on Cardiac Rehabilitation & Exercise Physiology and Working Group on Heart Failure of the European Society of Cardiology

EHJ 2001

Testing før trening

Table 2 Exercise testing in chronic heart failure: key points

1. Exercise testing in stable chronic heart failure only
2. Directly measured oxygen uptake is preferable to estimate of METs
3. Individualized protocol (ramp, Naughton)
4. Stage increments of 1 MET are recommended
5. Optimal test duration 8–12 min
6. Walking test for submaximal testing

EHJ 2001

Working Group Report

Recommendations for exercise training in chronic heart failure patients

Working Group on Cardiac Rehabilitation & Exercise Physiology and Working Group on Heart Failure of the European Society of Cardiology*

EHJ 2001

Relative and absolute contraindications to exercise training among patients with stable chronic heart failure

Absolute contraindications

1. Progressive worsening of exercise tolerance or dyspnoea at rest or on exertion over previous 3 to 5 days
2. Significant ischaemia at low rates (<2 METS, ≅50 W)
3. Uncontrolled diabetes
4. Acute systemic illness or fever
5. Recent embolism
6. Thrombophlebitis
7. Active pericarditis or myocarditis
8. Moderate to severe aortic stenosis
9. Regurgitant valvular heart disease requiring surgery
10. Myocardial infarction within previous 3 weeks
11. New onset atrial fibrillation

Relative and absolute contraindications to exercise training among patients with stable chronic heart failure

Relative contraindications

1. ≥1·8 kg increase in body mass over previous 1 to 3 days
2. Concurrent continuous or intermittent dobutamine therapy
3. Decrease in systolic blood pressure with exercise
4. New York Heart Association Functional Class IV
5. Complex ventricular arrhythmia at rest or appearing with exertion
6. Supine resting heart rate ≥100 beats . min^{-1}
7. Pre-existing comorbidities

Table 3 Relative criteria necessary for the initiation of an aerobic exercise training programme

- Compensated heart failure for at least 3 weeks
- Ability to speak without dyspnoea (with a respiratory rate of <30 breaths . min^{-1})
- Resting HR of <110 beats . min^{-1}
- Less than moderate fatigue
- Cardiac index of ≥2 l . min^{-1} . m^{-2} (for invasively monitored patients)
- Central venous pressure of <12 mmHg (for invasively monitored patients)

Table 4 Relative criteria indicating the need to modify or terminate the training programme

- Marked dyspnoea or fatigue (≥14 on Borg scale)
- Respiratory rate of >40 breaths . min^{-1} during exercise
- Development of an S_3 or pulmonary rales
- Increase in pulmonary rales
- Increase in the second component of the second sound (P_2)
- Poor pulse pressure (<10 mmHg difference between systolic and diastolic BP)
- Decrease in BP (of >10 mmHg) during progressive exercise
- Increased supraventricular or ventricular ectopy during exercise
- Diaphoresis, pallor or confusion

Anbefalinger ESC

- Gå, sykle
- Intervalltrening: 30 s drag – 50% av max arbeid 40 – 80% av VO_{2max}, 60 sek hvile (10W).
- Gradvis økning i intensitet 40 til 80% forhold til symptomer og klinisk status
- Styrketrening? "Promising"
- Safety: Trenger større studier

AHA position paper:

- **Recommendations:**
- The Committee on Exercise, Rehabilitation, and Prevention of the American Heart Association Council on Clinical Cardiology concludes that **exercise training in patients with HF seems to be safe and beneficial overall in improving exercise capacity, as measured by peak V˙ O2, peak workload, exercise duration, and parameters of submaximal exercise performance. In addition, QOL improves in parallel to the improvements in exercise capacity.** Furthermore, benefits have been reported in muscle structure and physiological responses to exercise, such as improvements in endothelial function, catecholamine spillover, and oxygen extraction in the periphery, among others. In summary, this position statement will serve as guide to health professionals to better understand the exercise limitations of the patient with HF and aid in directing their patients to engage in physical activity. Therefore, insurers and third-party payers should support exercise training programs in patients with chronic HF that follow recommendations and patient selection as discussed in this position statement.

Piña et al Circulation 2003

St. Elsewhere hospital
Avdeling for thoraxkirurgi

Fød.nr: 300240 98765
Navn: Bertil Bypass
Adr: Graftveien 3
3300 Venestad

Epikrise

Pasienten ble innlagt for å få utført aortokoronar bypass, etter påvist hovedstammestenose. Ukomplisert inngrep på hjerte-lungemaskin. Post-operativt forløp ukomplisert.

Han skrives ut med følgende medikamenter og råd:

Albyl-E: 75 til 500 mg daglig, etter eget ønske.
Selo-zok: 50 til 400 mg daglig, etter eget ønske
Pravachol: Doseres til LDL-kolesterol 1,5 – 4.
Trening: Minimum ½ time tre ganger i uka, intensitet 50 – 90 % av max hjertefrekvens.

Med vennlig hilsen

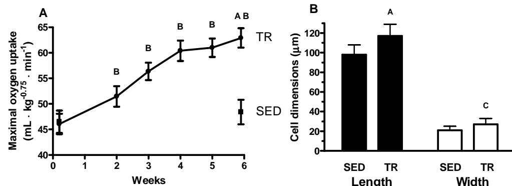
Guido Guidelines
Assistentlege

VO_2:

Ficks formel:

$$CO = VO_2 / AV\text{-}O_2\text{-diff}$$
$$VO_2 = CO \times AV\text{-}O_2\text{-diff}$$

High Intensity Exercise Increases VO_{2max} and Cardiomyocyte Size in Mice

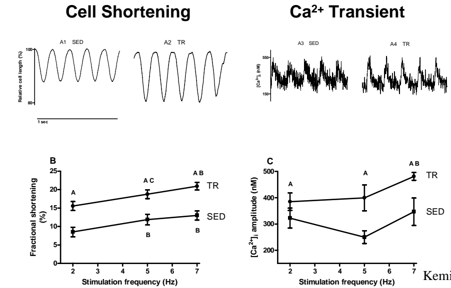


Kemi -04

High Intensity Exercise Enhances Cardiomyocyte Contractility and Ca^{2+} Handling in Mice

Cell Shortening

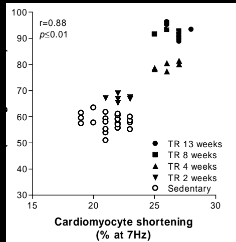
Ca^{2+} Transient



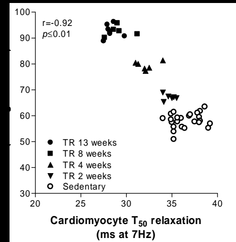
Kemi -04

Aerobic Capacity **(VO_{2max})** and Contractility

Systolic Contraction



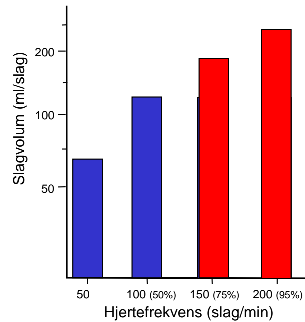
Diastolic Relaxation



Kemi OJ et al 2004. Circulation 109: 2897-2904
Wisloff U et al 2001. Cardiovasc Res 50: 495-508

Ved hvilken intensitet når vi maksimalt slagvolum?

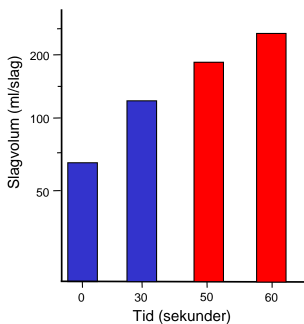
Et avgjørende spørsmål for valg av treningsintensitet!



Maksimalt slagvolum nås ved 90-95% av maksimal hjertefrekvens

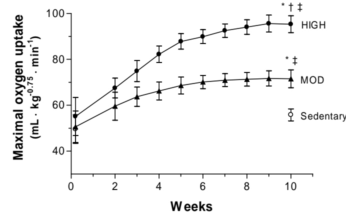
Hvor raskt når vi maksimalt slagvolum?

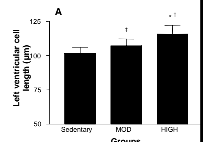
Et avgjørende spørsmål for varighet på treningen!



Maksimalt slagvolum nås etter 1-2 minutter eller så raskt du når optimal intensitet (90-95% av maksimal hjertefrekvens)

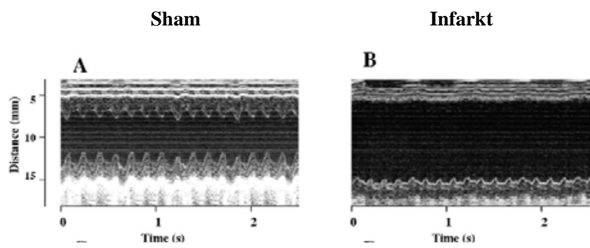
Hvor hardt?



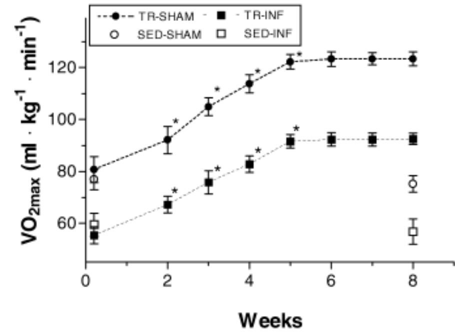


Kemi 2004

Eksperimentell hjertesviktmodell (rotte med infarkt)



Wisløff et al 2002 (Ekko: Loennechen)



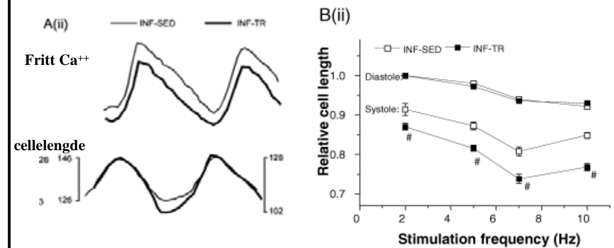
Wisløff et al 2002

	SED-SHAM	TR-SHAM
Right ventricular mass (mg)	318.8±29.2	405.1±45.3**
Left ventricular mass (mg)	876.4±74.1	1097.6±84.5**
Left ventricular cell length (μm)	119.3±1.8	134.3±1.8**
Left ventricular cell width (μm)	25.50±1.0	25.43±1.1
Left ventricular infarction (%)	–	–

	SED-INF	TR-INF
Right ventricular mass (mg)	717.3±76.6	555.2±68.6**
Left ventricular mass (mg)	1575.1±67.0	1339.0±90.1**
Left ventricular cell length (μm)	156.0±1.5	138.7±1.2**
Left ventricular cell width (μm)	35.96±1.1	28.63±1.6**
Left ventricular infarction (%)	43.8±2.2	44.9±2.7

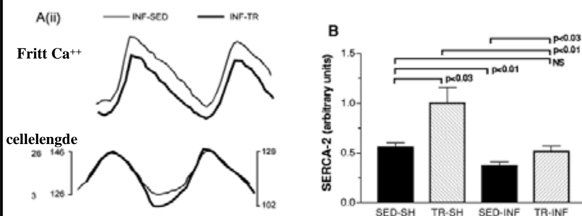
Wisløff et al 2002

Trening og hjertesvikt



Wisløff et al 2002

Trening og hjertesvikt



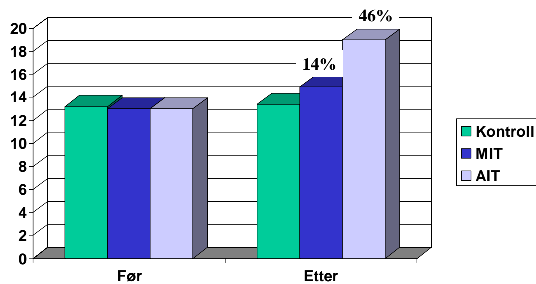
Wisløff et al 2002

Egne resultater:

- 27 pasienter (20 menn, 7 kvinner), mean alder 75,5
- Alle på β-blokker og ACE-hemmer
- LVEF < 40%, NYHA "2,5"
- Randomisert til høy intensitet, moderat intensitet og kontroll.
- Trening 2 g/uke pluss en gang hjemme med tilsvarende intensitet i 12 uker.
  - AIT: Intervall 5 min oppvarming 60% av HRmax, 4 min drag på 90%, 3 min pauser på 70% og 3 min etter siste drag.
  - MIT: 70% av HR max justert for treningsmengde
  - Pulsstyrt med økende intensitet ettersom formen ble bedre

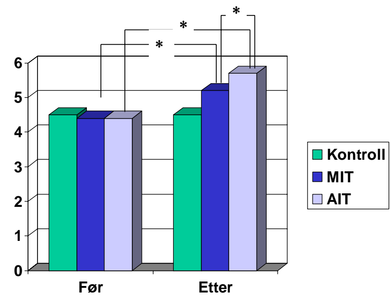
Wisløff 2007

VO_{2max}



Tilsvarende for arbeidsøkonomi, aerob terskel og intensitet Wisløff 2007

Livskvalitet



Wisløff 2007

	Kontroll		MIT		AIT	
	Pre	Post	Pre	Post	Pre	Post
LVDD	67.2 ± 8.1	67.8 ±12.5	69.1 ± 8.6	68.2 ± 6.5	66.7 ± 6.8	59.0 ± 6.8
LVDV	250.5 ± 64.4	242.1 ± 62.3	245.5 ± 53.1	230.3 ± 41.0	248.1 ± 79.6	202.9 ± 72.0
EF	26.2 ± 8.0	26.6 ± 9.7	32.8 ± 4.8	33.5 ± 5.7	28.0 ± 7.3	38.0 ± 9.8
SV	53.4 ± 15.3	55.0 ± 13.7	63.5 ± 12.7	63.1 ± 15.7	57.1 ± 14.3	67.0 ± 19.9
HR	60 ± 11	59 ± 11	55 ± 10	54 ± 12	65 ± 14	61 ± 13
TVIs	4.73 ± 1.23	4.79 ± 1.34	4.80 ± 1.10	5.16 ± 0.96	4.79 ± 1.32	5.86 ± 1.53
E	0.6 ± 0.1	0.5 ± 0.2	0.7 ± 0.3	0.6 ± 0.1	0.7 ± 0.1	0.8 ± 0.2
Ea	4.0 ± 1.4	3.9 ± 1.9	4.6 ± 0.8	4.7 ± 1.6	4.5 ± 1.3	6.7 ± 1.6
E/Ea	15.1 ± 4.3	15.1 ± 6.4	15.1 ± 5.4	12.9 ± 3.8*	16.0 ± 3.5	11.8 ± 1.9
IVRT	110.2 ± 68.7	109.5 ± 64.8	112.4 ± 23.4	105.7 ± 25.6	100.7 ± 18.9	122.8 ± 41.4

Wisløff 2007

Konklusjon:

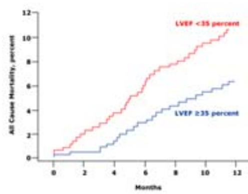
- Høy intensitet ser ut til å gi vesentlig bedre effekt på hjertefunksjon. Signifikant:
  - Revers remodellering med red. volum
  - Økt EF, slagvolum og cardiac output
  - Bedret kontraktilitet og diastolisk relaksasjon
  - Redusert fylningstrykk
- Høyere hvile slagvolum tyder på delvis dekompensering før trening
- Effekten av 12 ukers intervensjon ser ut til å holde seg i et par år (upubl.)

Høy intensitets aerob trening

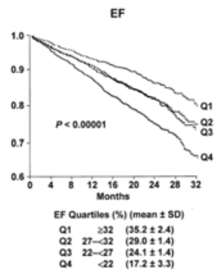
- Er bare prøvd ut på postinfarktsvikt
- Gir bedre effekt på livskvalitet
- Gir bedre effekt på fysiologiske parametre som er assosiert med økt overlevelse
- Mangler dokumentasjon av sikkerhet
  - Derfor: utprøvende behandling
- Har ingen dokumentasjon av overlevelsesgevinst.

Mulig effekt av høy aerob intensitet trening:

- 10% absolutt bedring i EF
  - Kunne forventes å gi 4% absolutt reduksjon i årlig mortalitet (fra 10% til 6%)
- MEN:
  - Ingen safetystudie av AIT
  - Ingen endepunktsstudie
- Endepunktsstudie vil trenge ca 1500 pasienter fulgt i to år
- Ca 30 sentra?
- Pris: > 2 mill EUR



SOLVD 2000



Val-HeFT 2004

JFR CRT: CARE HF 800 pas.

- Biventrikulær pacing ved grenblokk og hjertesvikt (EF<30% - mean 25%)
- Bedring 6,9% vs. 3,7%(regr. to the mean)
- Red. i årlig mortalitet til 8% vs. 12%

Konklusjoner:

- Er det ønskelig?
- Er det gunstig?
  - Hva vinner man?
- Er det farlig?
- Hva slags trening?
  - Type?
  - Mengde?
  - Intensitet?

- Sviktpasienter bør trene
- Det gir bedret:
  - fysisk kapasitet
  - QoL
- Ingen dokumentasjon av økt overlevelse
- Moderat aerob intensitets trening er sikkert
  - ?
  - ?
  - ?